



✉ P.O Box 3451  
SALT LAKE CITY, UT 84110  
☎ 385-401-4301  
🌐 uarc.io  
🐦 @uarc

December 2, 2020

Rebekkah Shaw  
SRC Executive Secretary  
346 S. Rio Grande  
Salt Lake City, UT 84101-1106

**Sent via Email: [SRCSecretary@utah.gov](mailto:SRCSecretary@utah.gov)**

Dear Rebekkah Shaw:

Pursuant to the Government Records and Management Act (GRAMA), Utah Code § 63G-2-403, I write on behalf of Utah Animal Rights Coalition (UARC), a 501(c)(3) non-profit organization, to appeal a denial of access to records regarding COVID-19 outbreaks on Utah mink farms. Because public health experts have widely recognized that mink on fur farms act as potential reservoirs for the virus that causes COVID-19, and that these animals have acted as sources for mutation for the virus, this crisis threatens the state's efforts to mitigate the impact of the ongoing COVID-19 pandemic as well as the state's imminent vaccination efforts. In light of this substantial public interest where *time is of the essence*, UARC respectfully requests that the State Records Committee (SRC) grant an expedited hearing for UARC's appeal, pursuant to Utah Code § 63G-2-403(4)(a)(1). UARC is also re-asserting its request for a fee waiver pursuant to Utah Code § 63G-2-203(4)(a), should the SRC order additional records released.

### **Timeline of Events**

- **October 14, 2020:** UARC submits its GRAMA request with the Utah Department of Agriculture and Food (the Department).<sup>1</sup> UARC's request was for various records related to outbreaks of COVID-19 on several Utah mink farms, which were already the subject of widespread media reports.
- **October 19, 2020:** The Department denies UARC's request.<sup>2</sup>
- **November 12, 2020:** UARC submits an administrative appeal to Kelly Pehrson, Chief Administrative Officer for the Department.<sup>3</sup>
- **November 24, 2020:** Kelly Pehrson denies UARC's administrative appeal.<sup>4</sup>

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<sup>1</sup> UARC's October 14, 2020 GRAMA request is attached as Exhibit A.

<sup>2</sup> The Department's October 19, 2020 denial is attached as Exhibit B.

<sup>3</sup> UARC's November 12, 2020 administrative appeal is attached as Exhibit C (minus exhibits).

<sup>4</sup> Mr. Pehrson's denial was noncompliant with GRAMA as it failed to provide the name and business address of the State Records Committee. *See* Utah Code § 63G-2-401(7)(b)(iii). Mr. Pehrson incorrectly cited a section of Utah Code governing the substance and form of SRC decisions and orders. Kelly Pehrson's November 24, 2020 administrative appeal denial is attached as Exhibit D.

## **COVID-19 is a matter of significant public concern**

On March 11, 2020, the World Health Organization (WHO) officially declared the rapidly spreading Coronavirus Disease 2019 (“COVID-19”) outbreak a pandemic. The causative pathogen was identified as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The COVID-19 pandemic has upended life around the globe, including in Utah. As of December 2, 2020, Utah has had more than 200,000 cases of COVID-19, with 907 deaths. Although promising vaccines and other pharmaceutical interventions are beginning to emerge, in the immediate future, the COVID-19 epidemic is almost surely to worsen, and may lead to further interventions by the state government to encourage or require social distancing, mask-wearing, or other non-pharmaceutical interventions aimed at curbing disease transmission. Unlike most European nations, the United States does not appear to have taken any discernable interventions to curb the risk emanating from its mink farms. Utah and Wisconsin are the two largest mink-producing states in the U.S.

In March 2020, Governor Gary Herbert issued what would be the first of many state public health emergency orders in an attempt to control the spread and impact of COVID-19.<sup>5</sup> These measures have had enormous reach, heavily restricting commerce, social activity, as well as the professional and personal lives of nearly all Utahns. Understanding the patterns of transmission of COVID-19, as well as the rationale and judgment behind our public officials’ ongoing efforts to combat the pandemic, is a matter of paramount public concern affecting the lives of all Utahns.

## **Zoonoses, “the spillover effect,” and viral mutation**

Like many infectious diseases, SARS-CoV-2, the virus that causes COVID-19, is a zoonotic pathogen, meaning it originated as an endemic disease in nonhuman animals before jumping the species barrier and infecting humans, a process known as the “spillover effect.”<sup>6</sup> While most pathogens that spillover to humans fail to result in widespread secondary transmission, occasionally such pathogens can result in serious pandemics, because humans represent a large social population of hosts who have not previously encountered the novel virus and are thus immunologically naïve. SARS-CoV-2 is one such case.<sup>7</sup>

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<sup>5</sup> Governor Gary Herbert. Executive Order 2020-1. Dated March 6, 2020. Available at <https://rules.utah.gov/wp-content/uploads/Utah-Executive-Order-No.-2020-1.pdf>. Attached as Exhibit E.

<sup>6</sup> Plowright RK, Parrish CR, McCallum H, et al. Pathways to zoonotic spillover. *Nat Rev Microbiol.* 2017;15(8):502-510. doi:10.1038/nrmicro.2017.45. Available at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5791534/>. Attached as Exhibit F.

<sup>7</sup> Munir K, Ashraf S, Munir I, et al. Zoonotic and reverse zoonotic events of SARS-CoV-2 and their impact on global health. *Emerg Microbes Infect.* 2020;9(1):2222-2235. doi:10.1080/22221751.2020.1827984. Available at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7594747/>. Attached as Exhibit G.

A growing body of research also reveals that humans infected with SARS-CoV-2 can, in some cases, transmit the virus to nonhuman populations, a process sometimes called the “spillback effect,” or “reverse zoonoses.” Domesticated animals who are intensively confined in laboratories or on agricultural operations are particularly susceptible to reverse zoonotic outbreaks, and these environments often have various biosecurity measures to prevent such incidents. SARS-CoV-2 infections have been identified in a handful of nonhuman species, but mink appear to be particularly susceptible to contracting the virus. To date, mink are the only species known to readily transmit the virus both to and from humans, a process known as bidirectional zoonoses.<sup>8</sup>

Bidirectional zoonotic viral transmission is particularly dangerous. Each time a virus enters a host and uses its cellular machinery to replicate copies of itself, there is a potential for viral mutation, or changing of the genetic code of the virus. The vast majority of viral mutations are harmless or self-limiting. However, on occasion, a virus can mutate in such a way that the virus becomes more transmissible or impactful to the host organism. It can also mutate to become more evasive of a host’s immune system, a biological process known as “antigenic drift.” The influenza virus is a classic example of a familiar virus that routinely mutates in ways that result in antigenic drift, which explains why new forms of the flu vaccine must be developed and distributed each flu season. Antigenic drift is a serious obstacle to vaccine development and efficacy. When a virus finds a new species to infect, this novel organism’s different immune system also acts upon the virus in unique ways, further increasing the chances of virus developing “antibody escape mutants.” This is why bidirectional viral transmission is a particularly dangerous phenomenon for viral mutation.<sup>9,10</sup>

With a larger reservoir of hosts contracting and replicating the virus, there is greater risk for mutation, including mutations that result in increased transmissibility, lethality, or antigenic drift. On an operation with intensive animal confinement, a viral mutation that causes the disease to spread more readily would also find fertile ground for quick and widespread transmission to thousands of hosts. This is one reason why infectious disease experts and veterinarians, such as those with the U.S. Department of Agriculture’s Animal and Plant Health

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<sup>8</sup> Gorman, James. Mink and the coronavirus: what we know. *The New York Times*. November 11, 2020. Available at <https://www.nytimes.com/article/mink-coronavirus-mutation.html>. Attached as Exhibit H.

<sup>9</sup> He, Shanshan and Han, Jie, A Dreadful Loop: Can Reverse Zoonosis of COVID-19 Seed Unrestrained Spread and Mutations in Wild Species and Transmission of Novel Strains to Humans?. *SSRN*. Published 2020 Oct 27. Available at <https://ssrn.com/abstract=3721791>. Attached as Exhibit I.

<sup>10</sup> Olival KJ, Cryan PM, Amman BR, et al. Possibility for reverse zoonotic transmission of SARS-CoV-2 to free-ranging wildlife: A case study of bats. *PLoS Pathog*. 2020;16(9):e1008758. Published 2020 Sep 3. doi:10.1371/journal.ppat.1008758. Available at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7470399/>. Attached as Exhibit J.

Inspection Service (USDA-APHIS), conduct regular surveillance of some domesticated animal populations (although, notably, not mink), and maintain voluntary reporting systems. It is critically important to quickly identify and respond to emerging threats.

### **SARS-CoV-2 first identified on Dutch mink fur farms**

Following unusual widespread mortality events on two different mink farms in the Netherlands, SARS-CoV-2 infections were first identified in mink by researchers in April 2020.<sup>11</sup> It is believed that in both cases, infected workers on these operations first gave the virus to the mink, who then spread it to one another. The researchers also found evidence that seven feral cats who lived near these two mink farms had also been recently infected. Mink appear to transmit SARS-CoV-2 much the same way humans do, via respiratory droplets, and when one mink is infected, it can quickly and easily spread throughout the whole farm. Mink on fur farms are typically confined in tiny shoebox-sized wire cages, in close quarters with one another, with one shed containing hundreds, if not thousands, of mink. There is no social distancing for these cruelly confined animals.<sup>12</sup>

By August, more than one-third of all Dutch mink farms had active COVID-19 outbreaks. Dutch public health officials soon concluded that “[i]t is undesirable that the virus continues to circulate on mink farms as there is a risk that, in the long term, this will lead to infections – via employees – of people outside the mink farm.”<sup>13</sup> The Dutch government ordered the industry be shuttered at the end of the next pelting season, which begins in November 2020 but can run as late as March 2021. Prior to this order, the Netherlands had been the world’s fourth largest mink producing country, with 130 active farms and annual exports valued at \$101 million.<sup>14</sup>

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<sup>11</sup> Oreshkova N, Molenaar RJ, Vreman S, *et al.* SARS-CoV-2 infection in farmed minks, the Netherlands, April and May 2020. *Euro Surveill.* 2020;25(23):2001005. doi:10.2807/1560-7917.ES.2020.25.23.2001005. Available at <https://pubmed.ncbi.nlm.nih.gov/32553059/>. Attached as Exhibit K.

<sup>12</sup> Representative photographs from mink farms are attached as Exhibit L.

<sup>13</sup> U.S. Department of Agriculture Foreign Agriculture Service. Dutch mink industry to close in 2021 due to coronavirus. Report Number NL2020-0042 dated Sep. 2, 2020. Available at <https://apps.fas.usda.gov/newgainapi/api/Report/DownloadReportByFileName?fileName=Dutch%20Mink%20Industry%20to%20Close%20in%202021%20Due%20to%20Coronavirus%20The%20Hague%20Netherlands%2008-28-2020>. Attached as Exhibit M.

<sup>14</sup> Reuters. Netherlands to close mink farms after coronavirus outbreaks. Aug. 27, 2020. Available at <https://www.reuters.com/article/us-health-coronavirus-netherlands/netherlands-to-close-mink-farms-after-coronavirus-outbreaks-idUSKBN25N2W2>. Attached as Exhibit N.

## **Danish fur farm outbreaks and identified viral mutation**

Prior to the COVID-19 pandemic, the Danish fur industry was the largest producer of mink pelts in the world, with an estimated 40% of the world's market share.<sup>15</sup> But similar to the experience in the Netherlands, the fur industry has been ravaged by COVID-19, with at least 216 out of 1,139 farms now coping with outbreaks. Most troublingly, using genomic sequencing, researchers have now identified several mutant strains of SARS-CoV-2 that arose on Danish mink farms, including one that has now resulted in an outbreak in the general human population, with more than 200 identified cases of human infection of this mutated virus.<sup>16</sup> More than a quarter million Danes in the region of Denmark where this mutant strain arose have now gone into lockdowns as a result of this new mutated virus, and the UK has banned all travel with Denmark.

This disease cluster has been called “cluster 5,” and is the result of a “mink variant strain” of the virus. The mutation has led to changes in the virus’s “spike protein,” a kind of “identification marker” on the surface of the virus that plays a crucial role in our body’s immune response.<sup>17</sup> This means that antibodies generated in humans by prior COVID-19 infections will likely “miss” this new variant strain. Additionally, the viral spike protein is the target of most COVID-19 vaccines currently in development, including the Pfizer and Moderna vaccines that may be nearing FDA market approval. If new mink variant strains continue to evolve and spread in the community, this will undermine the billions of dollars and months of intensive research and development for a COVID-19 vaccine, and will likely lead to additional lockdowns and social distancing requirements.

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<sup>15</sup> Olsen, Jan M. North Denmark in lockdown over mutated virus in mink farms. *Associated Press*. Nov. 6, 2020. Available at <https://apnews.com/article/mutated-virus-mink-farm-denmark-lockdown-98ede7f921eb6ef3b312e53743fc3edb>. Attached as Exhibit O.

<sup>16</sup> Murphy, Simon and Beaumont, Peter. Travel to UK from Denmark banned amid worries over COVID in mink. *The Guardian*. Nov. 7, 2020. Available at <https://www.theguardian.com/world/2020/nov/06/coronavirus-mutation-danish-mink-spreads-to-214-people>. Attached as Exhibit P.

<sup>17</sup> Baylis, Matthew. The COVID-carrying Danish mink are a warning sign – but is anyone heeding it? *The Guardian*. Nov. 10, 2020. Available at <https://www.theguardian.com/commentisfree/2020/nov/10/the-covid-carrying-danish-mink-are-a-warning-sign-but-is-anyone-heeding-it>. Attached as Exhibit Q.

Public health researchers and authorities across the globe are profoundly alarmed by this development. The WHO stated on November 6, 2020:

Minks were infected following exposure from infected humans. Minks can act as a reservoir of SARS-CoV-2, passing the virus between them, and pose a risk for virus spill-over from mink to humans. People can then transmit this virus within the human population. Additionally, spill-back (human to mink transmission) can occur. It remains a concern when any animal virus spills in to the human population, or when an animal population could contribute to amplifying and spreading a virus affecting humans. As viruses move between human and animal populations, genetic modifications in the virus can occur. These changes can be identified through whole genome sequencing, and when found, experiments can study the possible implications of these changes on the disease in humans.<sup>18</sup>

Danish authorities immediately recognized the gravity of the threat, with the state epidemiologist stating there is a potential that we will have “a pandemic that will start all over again, starting from Denmark.” Authorities have already issued an order to cull all of the mink and shut down their large mink farming industry. Danish Prime Minister Mette Frederiksen gave an emergency press conference about the situation, where he stated:

We have a great responsibility towards our own population, but with the mutation that has now been found we have an even greater responsibility for the rest of the world. The mutated virus in minks could pose a risk that future vaccines won't work as they should. It risks being spread from Denmark to other countries. The eyes of the world are on us.<sup>19</sup>

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<sup>18</sup> World Health Organization. SARS-CoV-2 mink-associated variant strain – Denmark. Nov. 6, 2020. Available at <https://www.who.int/csr/don/06-november-2020-mink-associated-sars-cov2-denmark/en/>. Attached as Exhibit R.

<sup>19</sup> Dyer O. Covid-19: Denmark to kill 17 million minks over mutation that could undermine vaccine effort. *BMJ*. 2020;371:m4338. Published 2020 Nov 9. doi:10.1136/bmj.m4338. Attached as Exhibit S

The fur farming industry has itself admitted the severity of the crisis. At the September 28, 2020 annual convention of Fur Commission USA, Dr. John Easley, DVM, Director of Research, stated:

[Researchers are] extremely confident that they've been able to demonstrate that [COVID-19] was brought on to farms by humans, the virus changed in the mink, and that changed virus was then transmitted back to people, and the people that got infected, transmitted that virus to other people. This is new information that is out now, so that is extremely important to the industry. It shows that mink can potentially be a reservoir for the virus, for the human population.<sup>20</sup>

The European Centre for Disease Prevention and Control (ECDC) has issued a Rapid Risk Assessment, aimed at offering information and guidance to EU member states about how to detect and control SARS-CoV-2 variants related to mink.<sup>21</sup> This report notes that mink variants of the virus “are able to circulate rapidly in mink farms and the human communities close to the farms.” And yet, the Department continues to refuse to even identify the *counties* where these outbreaks have occurred, threatening the health of these communities. Among other steps, the ECDC urges member states to implement “a systematic approach to testing and sequencing, particularly in mink farm workers and nearby communities.” It remains unclear whether the state of Utah has implemented *any* systematic disease surveillance or testing related to the COVID-19 outbreaks on Utah’s many fur farms. The Department appears determined to shroud the state’s response in secrecy.

If the existing mutated mink variant strain spreads further, or if we develop our own mutant strain on Utah mink farms, it very well may extinguish the promising hopes of a successful COVID-19 vaccine rollout in 2021. It may also lead to further lockdowns, disease, and death.

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<sup>20</sup> Video of this statement is available at <https://www.youtube.com/watch?v=o9dvnHcP2n0>.

<sup>21</sup> European Centre for Disease Prevention and Control (ECDC). Detection of new SARS-CoV-2 variants related to mink. Nov. 12, 2020. Available at <https://www.ecdc.europa.eu/sites/default/files/documents/RRA-SARS-CoV-2-in-mink-12-nov-2020.pdf>. Attached as Exhibit T.

## **COVID-19 & Utah's Mink Farming Industry**

For many years, Wisconsin and Utah have led the nation as the #1 and #2 leading producers of mink pelts. Even prior to COVID-19, the domestic mink farming industry, has been in a state of precipitous decline. According to USDA figures, for the period of 2014 – 2019, we have seen the following evidence of decline:<sup>22</sup>

- The market price of a mink pelt has decreased by 62%.
- The number of mink killed for their fur has decreased by 28% nationwide. In Utah, the number of mink killed has decreased 42%.
- Overall industry profits have decreased by 73%.

In August, Clayton Beckstead, mink farmer and spokesperson with the Utah Farm Bureau, told *The Washington Post* that half of all mink farms in Utah have closed in the past year, with only 38 farms remaining.<sup>23</sup> A variety of causes explain the mink industry's decline, but significant factors include states passing laws that prohibit the sale of fur products and a growing sentiment among consumers that fur products represent unnecessary cruelty to animals.

Utah was the first location of known COVID-19 cases on United States mink farms, with at least two farms having identified outbreaks in August 2020. Almost immediately, UARC recognized the serious risk of this situation, and wrote a letter of concern to the Governor's Office, which is coordinating the state's response, and urged him to implement a moratorium on additional breeding on these mink farms. We also launched a public call to action. More than 250 of our members and supporters in Utah subsequently wrote letters of concern to Governor Gary Herbert.

In October, media reports indicated that the problem had worsened, with 10,000 mink dead due to COVID-19 outbreaks and quarantines at nine separate fur farms.<sup>24</sup> Just as in Denmark and the Netherlands, these mink likely contracted the virus from workers before spreading the virus amongst themselves.

The state of Utah's response to this crisis on our mink farms has, at best, been appallingly inept. At worst, the state, and in particular the Department, appears to have been disseminating misleading information to allay legitimate worries about

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<sup>22</sup> USDA Economics, Statistics and Market Information System. *Mink*. Data derived from reports dated July 2015 & July 2019. Available at <https://usda.library.cornell.edu/concern/publications/2227mp65f>. Attached as Exhibit U.

<sup>23</sup> Brulliard, Karin. First U.S. cases of coronavirus in minks found at Utah fur farms. *The Washington Post*. Aug. 17, 2020. Available at <https://www.washingtonpost.com/science/2020/08/17/coronavirus-mink-first-us-cases/>. Attached as Exhibit V.

<sup>24</sup> Bekiempis, Victoria. Nearly 10,000 mink dead from COVID-19 outbreak at Utah fur farms. *The Guardian*. Oct. 11, 2020. Available at <https://www.theguardian.com/world/2020/oct/11/utah-10000-minks-dead-from-coronavirus>. Attached as Exhibit W.

the COVID-19 crisis on mink farms. As recently as October, Dr. Dean Taylor, state veterinarian with the Department, told the *Associated Press* that “[the Department] genuinely [doesn’t] feel like there is much of a risk going from the mink to people”<sup>25</sup> and other media organizations that the virus only follows a “unidirectional path” [from humans to mink].<sup>26</sup> Dr. Taylor’s public statements are simply at odds with the overwhelming evidence from news media, government reports, and peer-reviewed literature, which, even at that time, had demonstrated that bidirectional zoonotic transmission was and is occurring. For example:

- On May 20, 2020, the U.S. Department of Agriculture’s Global Agricultural Information Network circulated a public report stating that the Dutch government had conducted genomic sequencing research of its mink farm outbreaks and found that at least one employee was likely infected by a mink.<sup>27</sup>
- As early as June 11, 2020, research in the publicly accessible disease surveillance publication *Eurosurveillance* demonstrated evidence, via genomic sequencing, that SARS-CoV-2 viral particles were present on inhalable dust on Dutch mink farms, and that the disease had been transmitted from mink to humans on these farms.<sup>28</sup>
- In a September 1, 2020 manuscript partially titled “Jumping back and forth,” European public health researchers investigated COVID-19 outbreaks on 16 mink farms, and found that 68% of the tested mink farm residents, employees, or contacts had evidence of SARS-CoV-2 infection. Using whole genome sequencing, they concluded that there was “widespread circulation” of the virus among the mink, and that there had been “animal to human transmissions of SARS-CoV-2 in mink farms.”<sup>29</sup> These researchers’ findings

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<sup>25</sup> Aleccia, JoNel. Thousands of mink dead in COVID outbreak on Utah farms. *Associated Press*. Oct. 5, 2020. Available at <https://apnews.com/article/virus-outbreak-utah-animals-archive-2863345161adeebb318a3276e35e9501>. Attached as Exhibit X.

<sup>26</sup> Mossburg, C. At least 8,000 mink dead in Utah after contracting COVID-19. CNN. 8 Oct 2020. Available at [https://www.cnn.com/world/live-news/coronavirus-pandemic-10-08-20-intl/h\\_b1b17737445ac5cb60f54df4b0467c5d](https://www.cnn.com/world/live-news/coronavirus-pandemic-10-08-20-intl/h_b1b17737445ac5cb60f54df4b0467c5d). Attached as Exhibit Y.

<sup>27</sup> U.S. Department of Agriculture Foreign Agriculture Service. Additional control measures for Dutch mink industry in response to COVID-19. Report Number NL2020-0019 dated May 20, 2020. Available at [https://apps.fas.usda.gov/newgainapi/api/Report/DownloadReportByFileName?fileName=Additional%20Control%20Measures%20for%20Dutch%20Mink%20Industry%20In%20Response%20to%20COVID-19\\_The%20Hague\\_Netherlands\\_05-19-2020](https://apps.fas.usda.gov/newgainapi/api/Report/DownloadReportByFileName?fileName=Additional%20Control%20Measures%20for%20Dutch%20Mink%20Industry%20In%20Response%20to%20COVID-19_The%20Hague_Netherlands_05-19-2020). Attached as Exhibit Z.

<sup>28</sup> Oreshkova N, Molenaar RJ, Vreman S, *et al.* SARS-CoV-2 infection in farmed minks, the Netherlands, April and May 2020. *Euro Surveill.* 2020;25(23):2001005. doi:10.2807/1560-7917.ES.2020.25.23.2001005. Available at <https://pubmed.ncbi.nlm.nih.gov/32553059/>. Attached as Exhibit AA.

<sup>29</sup> Oude Munnink BB *et al.* Jumping back and forth: anthropozoonotic and zoonotic transmission of SARS-CoV-2 on mink farms [Internet]. Cold Spring Harbor Laboratory; 1 Sep 2020. Available from: <http://dx.doi.org/10.1101/2020.09.01.277152>. Attached as Exhibit BB.

were later published in *Science*,<sup>30</sup> often considered the most prestigious peer-reviewed scientific publication in the United States.

- The University of Minnesota’s Center for Infectious Disease Research and Policy (CIDRAP) published a news article titled “COVID-19 likely spreading from people to animals – and vice versa” on September 18, 2020, that largely concerned the spread of the disease from mink to humans.<sup>31</sup> CIDRAP is widely considered a global leader in addressing public health preparedness and emerging infectious disease response. CIDRAP also wrote on November 6, 2020 that when SARS-CoV-2 “is introduced to mink farms from humans, it can spread quickly, and possibly due to biological differences between minks and people, can accumulate mutations, which result in variants with the potential to jump back into humans.”<sup>32</sup>

Despite the available evidence, on October 14, 2020, in an email to *The Salt Lake Tribune* obtained by UARC via a GRAMA request, Dr. Taylor re-asserted the claim that SARS-CoV-2 does not transmit from mink to humans, claiming that “ALL studies so far indicated that the spread was from humans to mink and none indicate the reverse.”<sup>33</sup> There is no charitable way to interpret Dr. Taylor’s October 14, 2020 statement. He was simply either uninformed or being deceptive. UARC submitted a GRAMA request for information related to local studies or evaluations of SARS-CoV-2 on Utah mink farms, but the Department’s response appears to indicate that the state is not currently conducting or reviewing any such studies or surveillance.<sup>34</sup> It doesn’t appear that there are, in fact, any “studies” upon which the Department ostensibly based its public statements downplaying the possibility of mink-to-human transmission. In a November 10, 2020 article appearing in *Reuters*, Dr. Taylor appeared to again repeat his statement that “everything is still suggesting a one-way travel from people to the minks.”<sup>35</sup> It is incredibly troubling

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<sup>30</sup> Oude Munnink BB, Sikkema RS, Nieuwenhuijse DF, et al. Transmission of SARS-CoV-2 on mink farms between humans and mink and back to humans [published online ahead of print, 2020 Nov 10]. *Science*. 2020;eabe5901. doi:10.1126/science.abe5901. Available at

<https://science.sciencemag.org/content/early/2020/11/09/science.abe5901>. Attached as Exhibit CC.

<sup>31</sup> Van Beusekom, Mary. COVID-19 likely spreading from people to animals – and vice versa. *CIDRAP News*. Sep. 18, 2020. Available at <https://www.cidrap.umn.edu/news-perspective/2020/09/covid-19-likely-spreading-people-animals-and-vice-versa>. Attached as Exhibit DD.

<sup>32</sup> Schnirring, Lisa. Global COVID-19 total clears 49 million, experts weigh in on mink variant. *CIDRAP News*. Nov. 6, 2020. Available at <https://www.cidrap.umn.edu/news-perspective/2020/11/global-covid-19-total-clears-49-million-experts-weigh-mink-variant?fbclid=IwAR3ibB400Pjplwh6MCiLKjK-ehbtW243JBv6ZbwRF9Ihii8XfDfqw78bek>. Attached as Exhibit EE.

<sup>33</sup> Taylor, Dean. Email communication with *The Salt Lake Tribune*. Oct. 14, 2020. Obtained via GRAMA. Attached as Exhibit FF.

<sup>34</sup> Price, Amanda. Reply to GRAMA Request for the Utah Animal Rights Coalition. Oct. 19, 2020. Attached as Exhibit GG.

<sup>35</sup> Polansek, Tom. Coronavirus kills 15,000 U.S. mink, as Denmark prepares for nationwide cull. Nov. 10, 2020. Available at <https://www.reuters.com/article/health-coronavirus-usa-minks/coronavirus-kills-15000-u-s-mink-as-denmark-prepares-for-nationwide-cull-idINL1N2HW1WS>. Attached as Exhibit HH.

that our state's official response to this crisis appears to be to mislead the public and downplay what public health authorities around the globe recognize as a significant concern.

It must be pointed out that the Department's Mission Statement is to "promote the healthy growth of Utah agriculture," and the bulk of the Department's activities are geared towards protecting the financial interests of the agriculture industry in Utah.<sup>36</sup> The Department's failure to handle this crisis and publicly convey an accurate assessment of the public health risk posed by Utah mink farms may be fundamentally at odds with the Department's mission and ethos. Greater transparency may help provide insight as to why the Department's response has been so deficient.

In the Department's November 24, 2020 denial, Mr. Pehrson again re-asserted the public statements of Dr. Taylor that "current evidence does not support the existence of animal to human transmission within mink populations in the State of Utah." This is a controversial statement that is inconsistent with what public health authorities from across the globe have found via genomic sequencing in their own disease surveillance programs on mink farms. It is precisely because this statement is at odds with peer-reviewed published research in this field that UARC urgently seeks access to the records in dispute in this appeal. The public must assess these records in order to determine how the Department reached this unorthodox conclusion, and whether the state's public pronouncements and response have been oriented towards protecting the health of all Utahns or, instead, protecting the profitability of this one small but politically well-connected industry.

For reasons explained below, each denial by the Department was based on an incorrect reading or misapplication of state statute. Accordingly, UARC's request should be granted in full and a fee waiver granted.

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<sup>36</sup> Utah Department of Agriculture and Food. UDAF Mission, Values, and Priorities. Jun. 18, 2019. Available at <https://ag.utah.gov/about/>. Attached as Exhibit II.

Utah Code § 63G-2-204(2)(a) & 63G-2-206

In the Department's November 24, 2020 denial, Mr. Pehrson introduces a novel basis for denial, citing a provision of GRAMA that regulates the sharing of nonpublic records between governmental entities. UARC notes that this basis for denial and reference to this section of Utah Code was not mentioned in the Department's original October 19, 2020 denial. Mr. Pehrson, acting in his role as an appeals officer, is introducing a new argument during the appeals process on behalf of the Department in a manner that may be incompatible with the standards of *de novo* appeal proscribed by Utah courts. Mr. Pehrson's introduction of this argument during the appeals stage necessitates that UARC introduce a new response.

It is true that Utah Code § 63G-2-204(2)(a) allows a governmental entity to deny the release of records that the agency "has received under Section 63G-2-206." However, Section 63G-2-206 governs *only* the interagency sharing of records that have been properly classified as "private, controlled, or protected," and follow a specific procedure during the sharing of information outlined in Utah Code § 63G-2-206(4). It is UARC's assertion that none of the records in question can appropriately be classified as private, controlled, or protected, and the Department has failed to clearly state that it received this information in question in the manner outlined in Utah Code § 63G-2-206(4). It is UARC's position that these are public records that must be released, and this is precisely the dispute before the SRC in this appeal. Therefore, Mr. Pehrson's new reference to this provision of Utah Code is an empty exercise in question-begging that fails to address the controversy at hand.

In his appeal denial, Mr. Pehrson makes a remarkable new assertion that the records UARC seeks "have been classified as private, controlled, or protected" by another governmental entity. If the Department wishes to use this as a basis for denial, it must inform UARC "of the identity of the governmental entity from which the shared record was received," *See* Utah Code § 63G-2-204(2)(b)(ii). The Department's original October 19, 2020 did not contain this assertion, and neither did Mr. Pehrson's appeal to denial. The Department's failure to do so undermines UARC's procedural rights under GRAMA to promptly identify the governmental entity responsible for denying access to information that should rightfully be public.

To date, the Department has failed to identify which agency it claims has classified these records as nonpublic. The mere existence of correspondence with outside governmental entities does not, in and of itself, trigger the protections of Utah Code § 63G-2-206. The Department has also failed to specifically itemize which records in question have received such a classification. Indeed, it is hard to conceive how some of the requested records, such as correspondence between UDAF and private

entities like the Farm Bureau or representatives of the fur industry, could possibly fall under the scope of Utah Code § 63G-2-206.

Utah Code § 63G-2-206 governs the sharing of protected records *from* a state agency to another entity. The Department's interpretation of this statute that it encompasses federal agencies, which are not bound by the provisions of GRAMA, is creative. It is highly doubtful that representatives from federal agencies would ever vet their communications or record retention policies pursuant to our state's records management laws. It is widely understood that such a burden falls on state agencies. And in any case, UARC already has a pending federal Freedom of Information Act (FOIA) request with the U.S. Department of Agriculture (USDA) for its records related to COVID-19 outbreaks on U.S. mink farms. UARC and representatives of the USDA have had a number of telephonic meetings and have already come to an agreeable timeline to the release of information. The USDA has never indicated to UARC that it intends to deny access to the records it controls, although the records at dispute in this GRAMA appeal are mostly distinct from those which are retained by the USDA.

If the Department is alleging that the USDA, the CDC, or another entity is prohibiting the Department from releasing the information because that agency claims the records are classified under *GRAMA* "as private, controlled, or protected," then the Department needed to specifically state so in its original October denial and identify which governmental entity made that determination for which records. *See* Utah Code § 63G-2-204(2)(b)(ii). The Department failed to do so, depriving UARC of its procedural rights under GRAMA.

#### Utah Code § 63G-2-305(10)

Next, the Department denied access to "documents related to the identity of the mink farms or the ongoing investigation," which, presumably, also includes "protocols or documents reflecting precautions being taken or recommended be taken for Utah mink farms to reduce transmission of SARS-CoV-2" as well as "records revealing the 'stringent biosecurity measures' implemented on fur farms in response to the latest COVID-19 outbreaks." These records were requested by UARC, but not explicitly addressed in the Department's response.

The Department first cited 63G-2-305(10), reproducing all subsections (a) through (e) in its October 19, 2020 denial. Broadly, this subsection exempts "records created or maintained for civil, criminal, or administrative enforcement purposes or audit purposes, or for discipline, licensing, certification, or registration purposes," before listing five separate conditions, one of which *must* be met to satisfy this broad exemption. The Department did not initially make clear which subsection(s),

specifically, the Department is relying upon to deny access to the records sought by UARC, which hindered our ability to directly respond to their basis for denial in this appeal. However, in the Department's November 24, 2020 denial, Mr. Pehrson clarified that although all five subsections "could" apply, subsections (a), (b), and (c) are "most relevant" to this request.

Generally speaking, all five subsections cited by the Department clearly pertain to disclosures which could reasonably be expected to jeopardize the integrity of pending or future governmental proceedings, for example, identifying confidential human sources or requiring the government to reveal information that would "tip off" the subject of an ongoing investigation or audit, allowing them to take preparatory steps to thwart such investigation. It must be stressed, this exemption was clearly not intended to be a catch-all provision to exempt all records related to any enforcement purpose, as such an exemption would swallow nearly all records maintained by a governmental agency.

The Department's initial reference to this exemption fails first because the Department must identify an actual ongoing investigation, not merely assert a hypothetical use for potential future investigations. See *Deseret News Publ'g Co. v. Salt Lake Cnty.*, 2008 UT 26, ¶ 44, 182 P.3d 372. The Department's position evolved in its subsequent appeal denial, however, and on page 4 Mr. Pehrson emphasized that the Department, itself, does have "current actual and ongoing" investigations of COVID-19 outbreaks on mink farms in Utah.

First, it seems inconsistent that the Department can simultaneously allege that the records in its possession all originated from outside entities that shared their records pursuant to 63G-2-206, and that the Department *itself* has "current actual and ongoing" investigations related to this matter. Surely, the Department has its own records that originated within the Department and are maintained by the agency related to the agency's own "current actual and ongoing" investigations.

The Department's denial also fails because it has not explained how these subsections apply in even a general or hypothetical sense. It is not likely that the Department is serious about pursuing any meaningful investigation or enforcement action against these farms, and it is unclear by what statutory authority it could even do so. Even in its November 24, 2020 denial, the Department has still failed to articulate such a legal framework. Even if the Department were actively pursuing an enforcement action or investigation, it is unclear how release of the information sought by UARC would interfere with an investigation. All of the fur farms with ongoing COVID outbreaks are obviously already aware that they have had outbreaks on their farms. The information sought by UARC will not reveal any material information that these farms (presumably, the subjects of these

investigations) were not already privy to. There is no information in the documents sought by UARC which would thwart or undermine a hypothetical enforcement proceeding by the Department if they were disclosed. Because the Department has failed to outline with any greater detail how this exemption applies to the records sought by UARC, this basis for denial should be rejected.

In its November 24, 2020 appeal denial, the Department introduces a new, one-sentence, argument that releasing the records “would jeopardize the investigations themselves, as well as risk the safety of the public and animals in the state.” The Department has failed to provide any rationale at all for how releasing the records at issue would pose any unique risk to the safety of the public or animals. They would merely shed meaningful light on what the state is doing to combat the crisis of COVID-19 on Utah mink farms.

Additionally, even if the SRC does conclude that (1) there is an ongoing investigation, not merely a hypothetical future use of the information, and (2) that the records sought by UARC fall under one of the three subsections of Utah Code § 63G-2-305(10) that Mr. Pehrson claims are “most relevant,” you should still order disclosure of this information. Utah Code § 63G-2-406 authorizes disclosure of records protected by Utah Code § 63G-2-305(10), if it can be established “by a preponderance of the evidence, that the public interest favoring access is equal to or greater than the interest favoring restriction of access.” Clearly, given the ongoing COVID-19 crisis facing Utah and the nation, the threat posed by the state’s mink farms, and the state’s apparent inept and deceitful response to this threat, there is a significant public interest in disclosing this information to shed light on the severity of the threat facing Utah communities and to better understand how public officials have responded, or failed to respond. These records will substantially increase awareness and understanding of a matter of significant public concern. The public interest in disclosure far outweighs any interest in keeping the records secret.

#### Utah Code § 63G-2-305(49)

The Department also cited 63G-2-305(49) in its denial. This exemption applies to “records of the Department of Agriculture and Food that provides for the identification, tracing, or control of livestock diseases, including any program established under Title 4, Chapter 24, Utah Livestock Brand and Anti-Theft Act, or Title 4, Chapter 31, Control of Animal Diseases.” This statute does not apply for one simple reason: there is no established state program for the control of COVID-19, caused by a novel coronavirus, on Utah mink farms. The word “mink” does not appear in Chapters 24 & 31 of Title 4 of Utah Code, which are expressly referenced in this exemption. These chapters deal primarily with existing state programs for

controlling diseases of dairy cattle, poultry, swine, waterfowl. The Department was not able to cite an established program for surveilling and containing any mink disease, let alone the novel SARS-CoV-2, because one does not exist. On page 5 of its November 24, 2020 denial, the Department concedes that it does not have a program to control the spread of COVID-19 on Utah mink farms.

Unlike cattle, swine, sheep, and other livestock species, mink on fur farms are not branded or ear-tagged, and they are not entered into any voluntary government identification system, such as the USDA's National Animal Identification System (NAIS). The exemption that was carved out under Utah's GRAMA statutes was to assuage ranchers to persuade them to participate in a voluntary reporting & surveillance system. Because some livestock diseases can affect the marketing of their finished products – unlike COVID-19 in mink – ranchers would have refused to make voluntary disclosures if their reports ended up disclosed to the public, thereby creating possible market panics. None of these dynamics or interests are present with respect to COVID-19 on mink farms.

The absence of such a program is one reason why the records UARC requests and the ongoing COVID-19 crisis on mink farms are a matter of significant public concern. Subsection (49) of GRAMA was added during the 2005 Utah Legislature's General Session by House Bill 226, titled "Government Records Access and Management Act Requirements Regarding Animal Identification Program."<sup>37</sup> Its stated intent was to protect the records of "the National Animal Identification System (NAIS) and state programs providing for the identification, tracing, or control of livestock diseases." Mink are not part of the NAIS, a federal program administered by USDA-APHIS, and there are no existing programs on the state level aimed at tracking COVID-19 on mink farms. Additionally, COVID-19 is not strictly a "livestock disease;" it is a zoonotic disease with transmissibility to and between human beings. Therefore, this exemption does not apply.

## **Conclusion**

Under GRAMA, "[a] record is public unless otherwise expressly provided by statute." *See* Utah Code § 63G-2-201(2). For all of the reasons stated above, the statutes cited by the Department are not applicable to the records sought by UARC and thus should be released in their entirety. We ask that the SRC issue such an order. It should also be noted that the Department has still made no attempt to segregate any non-public information out of the records UARC requested and release the remainder. This is a requirement under GRAMA. *See* Utah Code § 63G-2-308.

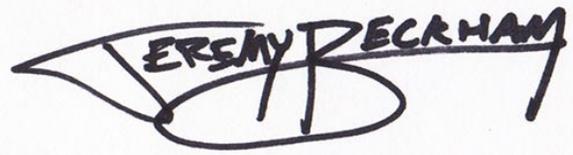
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<sup>37</sup> Utah House Bill 226. GRAMA Requirements Regarding Animal Identification Program. 2005 General Session. Available at <https://le.utah.gov/~2005/bills/static/HB0226.html>.

As a non-profit organization, UARC has no private or commercial interest in these records and intends to use these records to enhance public understanding of this important issue and to disseminate information to the news media and the public at large. UARC therefore believes that the release of these records “primarily benefits the public rather than a person” and accordingly we re-assert or request for a waiver of fees should you order additional records be disclosed. *See* Utah Code Ann. §63G-2-203(4)(a).

Thank you for your time and careful consideration. If I may be of assistance, please reach out using the contact information provided below. Email is preferred.

Sincerely,

A handwritten signature in black ink that reads "JEREMY BECKHAM". The signature is stylized, with the first letter of each word being significantly larger and more prominent than the others. The ink is dark and the background is a light, slightly textured paper.

Jeremy Beckham, MPA, MPH  
Executive Director  
Utah Animal Rights Coalition  
385-401-4301 (office)  
385-227-7034 (mobile)  
[jeremy@uarc.io](mailto:jeremy@uarc.io)

# **Exhibit A**



✉ P.O Box 3451  
SALT LAKE CITY, UT 84110  
☎ 385-401-4301  
🌐 uarc.io  
🐦 @uarc

October 14, 2020

Amanda Price, Records Officer  
Utah Department of Agriculture and Food  
350 North Redwood Road  
PO Box 146500  
Salt Lake City, UT 84114-6500

**Sent via e-mail: [udaf-commissioner@utah.gov](mailto:udaf-commissioner@utah.gov), [kwpehrson@utah.gov](mailto:kwpehrson@utah.gov), [agriculture@utah.gov](mailto:agriculture@utah.gov), [amandaprice@utah.gov](mailto:amandaprice@utah.gov)**

Dear Amanda Price:

On behalf of Utah Animal Rights Coalition (UARC), a 501(c)(3) non-profit organization, I write pursuant to the Government Records and Management Act (GRAMA), Utah Code Ann. §63G-2-101 to -901 to request records related to cases of SARS-CoV-2 in mink.

According to press accounts, at least nine farms in three counties in Utah have had COVID-19 outbreaks among their mink.<sup>1</sup> Thousands of mink have reportedly died from the disease. It remains unclear what, if any, requirements state authorities have implemented on these operations in response to the growing number of farms with outbreaks.

UARC requests the following records:

- **Records identifying any and all Utah mink farms which have had positively identified cases of SARS-CoV-2 and/or COVID-19, including (but not limited to) those nine farms referenced in public media reports.**
- **Necropsy reports and diagnostic test reports for any mink from the two Utah mink farms which later had confirmed positive cases of SARS-CoV-2 (March 1, 2020 – present).**
- **Correspondence between Utah Department of Agriculture and Food (UDAF) representatives and representatives of the U.S. Department of Agriculture (USDA) regarding SARS-CoV-2 cases in mink, or efforts to identify such cases (March 1, 2020 – present).**

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<sup>1</sup> Associated Press. Thousands of mink dead in COVID-19 outbreak on Utah farms. 6 Oct 2020. Available at <https://kutv.com/news/local/thousands-of-minks-dead-in-covid-19-outbreak-on-utah-farms>.

- **Correspondence between Utah Department of Agriculture and Food (UDAF) representatives and representatives of the Utah Department of Health (UDOH) or any county or district health department located in the state of Utah regarding SARS-CoV-2 cases in mink, or efforts to identify such cases (March 1, 2020 – present).**
- **Correspondence between any UDAF representatives and any representatives of the mink farming industry, including the Utah Farm Bureau, Fur Commission USA, and/or representatives of Utah fur farms, regarding the COVID-19 epidemic and its impact on Utah’s fur farming industry (March 1, 2020 – present).**
- **Any protocols or documents reflecting precautions being taken or recommended be taken for Utah mink farms to reduce transmission of SARS-CoV-2 (March 1, 2020 – present).**
- **Records revealing the nature of the “stringent biosecurity measures” implemented on fur farms in response to the latest COVID-19 outbreaks, as indicated by a UDAF spokesperson in recent public media reports.<sup>2</sup>**

If you are not the custodian of these records, or if these records are not maintained by your organization, I respectfully request that you refer me to the proper custodian or entity, if known.

As you may be aware, animal welfare and ongoing COVID-19 pandemic are matters of significant and growing public concern. The recent positive cases of SARS-CoV-2 on mink farms in Utah has already garnered substantial media coverage in both the local and national press. Growing evidence of bidirectional transmission of COVID-19 to and from mink and humans is a matter of significant public concern.

Issues relating to COVID-19 are of significant concern to the local media and public. The information UARC sought will shine a light on the conduct of state officials in responding to COVID-19 outbreaks in our state, promoting transparency and preserving accountability.

UARC, a non-profit organization, has no private or commercial interest in these records and intends to use these records to enhance public understanding of this important issue and to disseminate information to the news media and the public at large. UARC therefore believes that the release of these records “primarily benefits the public rather than a person” and accordingly requests a waiver of fees. *See* Utah Code Ann. §63G-2-203(4)(a).

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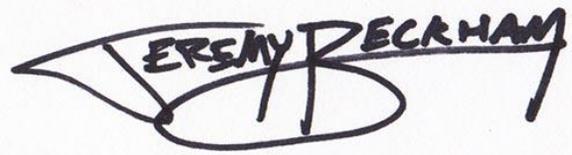
<sup>2</sup> See, for instance: <https://www.foxbusiness.com/lifestyle/coronavirus-outbreaks-on-utah-farms-leave-10000-minks-dead>

If you choose to deny this request for a fee waiver, please inform me of estimated costs prior to processing this request so that UARC may decide whether to proceed or examine our options for appeal. If you deny this request, in whole or in part, please provide a notice of denial. *See* Utah Code Ann. §63G-2-205.

In light of the ongoing COVID-19 pandemic, I prefer to receive electronic copies of the requested records, if possible, which can be emailed to me at [jeremy@uarc.io](mailto:jeremy@uarc.io). I look forward to receiving your response, to be sent no later than 10 business following your receipt of this request. *See* Utah Code Ann. §63G-2-204(3)(b).

If I may be of assistance, please reach out using the contact information provided below. Email is preferred.

Sincerely,

A handwritten signature in black ink that reads "JEREMY BECKHAM". The signature is stylized, with the first letters of each name being larger and more prominent. The signature is written over a light gray background.

Jeremy Beckham, MPA, MPH  
Executive Director  
Utah Animal Rights Coalition  
385-401-4301 (office)  
385-227-7034 (mobile)  
[jeremy@uarc.io](mailto:jeremy@uarc.io)

# **Exhibit B**



## State of Utah

GARY R. HERBERT  
Governor

SPENCER J. COX  
Lieutenant Governor

## Department of Agriculture and Food

R. LOGAN WILDE  
Commissioner

KELLY PEHRSON  
Deputy Commissioner

LEANN HUNTING  
Director, Animal Industry

October 19, 2020

Jeremy Beckham, MPA, MPH  
Executive Director  
Utah Animal Rights Coalition  
PO Box 3451  
Salt Lake City, UT 84110  
[jeremy@uarc.io](mailto:jeremy@uarc.io)

Re: GRAMA Request for the Utah Animal Rights Coalition

Dear Mr. Beckham,

The Utah Department of Agriculture and Food (Department) Division of Animal Industry received your request for:

- *Records identifying any and all Utah mink farms which have had positively identified cases of SARS-CoV-2 and/or COVID-19, including (but not limited to) those nine farms referenced in public media reports.*
- *Necropsy reports and diagnostic test reports for any mink from the two Utah mink farms which later had confirmed positive cases of SARS-CoV-2 (March 1, 2020 – present).*
- *Correspondence between Utah Department of Agriculture and Food (UDAF) representatives and representatives of the U.S. Department of Agriculture (USDA) regarding SARS-CoV-2 cases in mink, or efforts to identify such cases (March 1, 2020 – present).*
- *Correspondence between Utah Department of Agriculture and Food (UDAF) representatives and representatives of the Utah Department of Health (UDOH) or any county or district health department located in the state of Utah regarding SARS-CoV-2 cases in mink, or efforts to identify such cases (March 1, 2020 – present).*
- *Correspondence between any UDAF representatives and any representatives of the mink farming industry, including the Utah Farm Bureau and/or representatives of Utah fur farms, regarding the COVID-19 epidemic and its impact on Utah's fur farming industry (March 1, 2020 – present).*
- *Any protocols or documents reflecting precautions being taken or recommended be taken for Utah mink farms to reduce transmission of SARS-CoV-2.*
- *Records revealing the nature of the "stringent biosecurity measures" implemented on fur farms in response to the latest COVID-19 outbreaks, as indicated by a UDAF spokesperson in recent public media reports.*

The Department has conducted a thorough search of its records based on your GRAMA request. The Department must partially deny your request for the following reasons:

1. Some of the records you have requested, such as necropsy and other diagnostic test reports from state and federal veterinary diagnostic laboratories, as well as correspondence originating from other government agencies, are not prepared, owned, or maintained by the Department. These records are owned by the Utah Veterinary Diagnostic Laboratory, the USDA National Veterinary Services Laboratory, the Centers for Disease Control

and Prevention, and UDOH. Pursuant to Utah Code, 63G-2-204 (2), a person making a request for a record shall submit the request to the governmental entity that prepares, owns, or retains the record; and Subsection (2)(c) “if a governmental entity is prohibited from providing a record it shall, deny the records request and inform the person making the request that records requests must be submitted to the governmental entity that prepares, owns, or retains the record.”

2. All documents related to the identity of the mink farms or the ongoing investigation are considered protected under Sections 63G-2-305(10) and Section 63G-2-305(49), which state that the following records are protected:

63G-2-305(10) – “records created or maintained for civil, criminal, or administrative enforcement purposes or audit purposes, or for discipline, licensing, certification, or registration purposes, if release of the records:

- (a) reasonably could be expected to interfere with investigations undertaken for enforcement, discipline, licensing, certification, or registration purposes;
- (b) reasonably could be expected to interfere with audits, disciplinary, or enforcement proceedings;
- (c) would create a danger of depriving a person of a right to a fair trial or impartial hearing;
- (d) reasonably could be expected to disclose the identity of a source who is not generally known outside of government and, in the case of a record compiled in the course of an investigation, disclose information furnished by a source not generally known outside of government if disclosure would compromise the source; or
- (e) reasonably could be expected to disclose investigative or audit techniques, procedures, policies, or orders not generally known outside of government if disclosure would interfere with enforcement or audit efforts.

63G-2-305(49) – “records of the Department of Agriculture and Food that provides for the identification, tracing, or control of livestock diseases, including any program established under Title 4, Chapter 24, Utah Livestock Brand and Anti-Theft Act, or Title 4, Chapter 31, Control of Animal Disease;”

The Department has distributed one piece of guidance to mink farmers that is not a record of the Department and is publicly available. It is:

**Response & Containment Guidelines: Interim Guidance for Animal Health and Public Health Officials Managing Farmed Mink and other Farmed Mustelids with SARS-CoV-2** (available at: [https://www.aphis.usda.gov/publications/animal\\_health/sars-cov-2-mink-guidance.pdf](https://www.aphis.usda.gov/publications/animal_health/sars-cov-2-mink-guidance.pdf))

The Department is granting your request for a fee waiver for this information.

If you believe that the attached response is incomplete or deficient, you may appeal the GRAMA Officer’s decision to the Chief Administrative Officer for the Department: Kelly Pehrson, 350 N Redwood Rd, Salt Lake City, UT 84116, (801) 982-2200. Any appeal must be within thirty (30) days of the above date of determination and must be by filing a “notice of appeal” compliant with Utah Code 63G-2-401; Appeal to Head of Governmental Entity. Thank you for your cooperation, and if you have any questions, please feel free to contact our counsel Melissa Ure at 801-982-2200.

Sincerely yours,



Amanda Price, DVM, MS  
GRAMA Officer, Division of Animal Industry

# **Exhibit C**



✉ P.O Box 3451  
SALT LAKE CITY, UT 84110  
☎ 385-401-4301  
www.uarc.io  
@uarc

November 12, 2020

Kelly Pehrson  
Chief Administrative Officer  
Utah Department of Agriculture & Food  
350 N. Redwood Rd.  
Salt Lake City, UT 84116

**Sent via U.S. Mail & Email: [kwpehrson@utah.gov](mailto:kwpehrson@utah.gov)**

Dear Kelly Pehrson:

Pursuant to the Government Records and Management Act (GRAMA), Utah Code § 63G-2-401, I write on behalf of Utah Animal Rights Coalition (UARC), a 501(c)(3) non-profit organization, to appeal a denial of access to information. This is in regards to UARC's October 14, 2020 request,<sup>1</sup> which was denied by the Department on October 19, 2020.<sup>2</sup> UARC's request was for records related to outbreaks of COVID-19 on several Utah mink farms. Because the records requested by UARC cannot properly be classified as private, controlled, or protected under GRAMA, there is no legal basis for the Department's refusal to release the records, and we respectfully ask that you reverse the Department's denial. UARC is also re-asserting its request for a fee waiver pursuant to Utah Code § 63G-2-203(4)(a), should you order additional records released.

**COVID-19 is a matter of significant public concern**

On March 11, 2020, the World Health Organization (WHO) officially declared the rapidly spreading Coronavirus Disease 2019 ("COVID-19") outbreak a pandemic. The causative pathogen was identified as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The COVID-19 pandemic has upended life around the globe, including in Utah. As of November 12, 2020, Utah has had more than 138,000 cases of COVID-19, with 672 deaths. The epidemic is worsening, with Utah reporting more than 2,000 new daily infections of COVID-19 for 7 continuous days, and 410 current hospitalizations due to COVID-19. Today, November 12, 2020, the state of Utah shattered its previous record, reporting more than 3,900 cases of COVID-19.

In March 2020, Governor Gary Herbert issued what would be the first of many state public health emergency orders in an attempt to control the spread and impact of

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<sup>1</sup> UARC's October 14, 2020 GRAMA request is attached as Exhibit A.

<sup>2</sup> The Department's October 19, 2020 denial is attached as Exhibit B.

COVID-19.<sup>3</sup> These measures have had enormous reach, heavily restricting commerce, social activity, as well as the professional and personal lives of nearly all Utahns. Understanding the patterns of transmission of COVID-19, as well as the rationale and judgment behind our public officials' ongoing efforts to combat the pandemic, is a matter of paramount public concern affecting the lives of all Utahns.

### **Zoonoses, “the spillover effect,” and viral mutation**

Like many infectious diseases, SARS-CoV-2, the virus that causes COVID-19, is a zoonotic pathogen, meaning it originated as an endemic disease in nonhuman animals before jumping the species barrier and infecting humans, a process known as the “spillover effect.”<sup>4</sup> While most pathogens that spillover to humans fail to result in widespread secondary transmission, occasionally such pathogens can result in serious pandemics, because humans represent a large social population of hosts who have not previously encountered the novel virus and are thus immunologically naïve. SARS-CoV-2 is one such case.<sup>5</sup>

A growing body of research also reveals that humans infected with SARS-CoV-2 can, in some cases, transmit the virus to nonhuman populations, a process sometimes called the “spillback effect,” or “reverse zoonoses.” Domesticated animals who are intensively confined in laboratories or on agricultural operations are particularly susceptible to reverse zoonotic outbreaks, and these environments often have various biosecurity measures to prevent such incidents. SARS-CoV-2 infections have been identified in a handful of nonhuman species, but mink appear to be particularly susceptible to contracting the virus. To date, mink are the only species known to readily transmit the virus both to and from humans, a process known as bidirectional zoonoses.<sup>6</sup>

Bidirectional zoonotic viral transmission is particularly dangerous. Each time a virus enters a host and uses its cellular machinery to replicate copies of itself, there is a potential for viral mutation, or changing of the genetic code of the virus. The vast majority of viral mutations are harmless or self-limiting. However, on occasion, a virus can mutate in such a way that the virus becomes more transmissible or impactful to the host organism. It can also mutate to become more evasive of a host's immune system, a biological process known as “antigenic drift.” The influenza

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<sup>3</sup> Governor Gary Herbert. Executive Order 2020-1. Dated March 6, 2020. Available at <https://rules.utah.gov/wp-content/uploads/Utah-Executive-Order-No.-2020-1.pdf>. Attached as Exhibit C.

<sup>4</sup> Plowright RK, Parrish CR, McCallum H, et al. Pathways to zoonotic spillover. *Nat Rev Microbiol.* 2017;15(8):502-510. doi:10.1038/nrmicro.2017.45. Available at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5791534/>. Attached as Exhibit D.

<sup>5</sup> Munir K, Ashraf S, Munir I, et al. Zoonotic and reverse zoonotic events of SARS-CoV-2 and their impact on global health. *Emerg Microbes Infect.* 2020;9(1):2222-2235. doi:10.1080/22221751.2020.1827984. Available at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7594747/>. Attached as Exhibit E.

<sup>6</sup> Gorman, James. Mink and the coronavirus: what we know. *The New York Times.* November 11, 2020. Available at <https://www.nytimes.com/article/mink-coronavirus-mutation.html>. Attached as Exhibit F.

virus is a classic example of a familiar virus that routinely mutates in ways that result in antigenic drift, which explains why new forms of the flu vaccine must be developed and distributed each flu season. Antigenic drift is a serious obstacle to vaccine development and efficacy. When a virus finds a new species to infect, this novel organism's different immune system also acts upon the virus in unique ways, further increasing the chances of virus developing "antibody escape mutants." This is why bidirectional viral transmission is a particularly dangerous phenomenon for viral mutation.<sup>7,8</sup>

With a larger reservoir of hosts contracting and replicating the virus, there is greater risk for mutation, including mutations that result in increased transmissibility, lethality, or antigenic drift. On an operation with intensive animal confinement, a viral mutation that causes the disease to spread more readily would also find fertile ground for quick and widespread transmission to thousands of hosts. This is one reason why infectious disease experts and veterinarians, such as those with the U.S. Department of Agriculture's Animal and Plant Health Inspection Service (USDA-APHIS), conduct regular surveillance of some domesticated animal populations (although, notably, not mink), and maintain voluntary reporting systems. It is critically important to quickly identify and respond to emerging threats.

### **SARS-CoV-2 first identified on Dutch mink fur farms**

Following unusual widespread mortality events on two different mink farms in the Netherlands, SARS-CoV-2 infections were first identified in mink by researchers in April 2020.<sup>9</sup> It is believed that in both cases, infected workers on these operations first gave the virus to the mink, who then spread it to one another. The researchers also found evidence that seven feral cats who lived near these two mink farms had also been recently infected. Mink appear to transmit SARS-CoV-2 much the same way humans do, via respiratory droplets, and when one mink is infected, it can quickly and easily spread throughout the whole farm. Mink on fur farms are typically confined in tiny shoebox-sized wire cages, in close quarters with one another, with one shed containing hundreds, if not thousands, of mink. There is no social distancing for these cruelly confined animals.<sup>10</sup>

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<sup>7</sup> He, Shanshan and Han, Jie, A Dreadful Loop: Can Reverse Zoonosis of COVID-19 Seed Unrestrained Spread and Mutations in Wild Species and Transmission of Novel Strains to Humans?. *SSRN*. Published 2020 Oct 27. Available at <https://ssrn.com/abstract=3721791>. Attached as Exhibit G.

<sup>8</sup> Olival KJ, Cryan PM, Amman BR, et al. Possibility for reverse zoonotic transmission of SARS-CoV-2 to free-ranging wildlife: A case study of bats. *PLoS Pathog*. 2020;16(9):e1008758. Published 2020 Sep 3. doi:10.1371/journal.ppat.1008758. Available at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7470399/>. Attached as Exhibit H.

<sup>9</sup> Oreshkova N, Molenaar RJ, Vreman S, et al. SARS-CoV-2 infection in farmed minks, the Netherlands, April and May 2020. *Euro Surveill*. 2020;25(23):2001005. doi:10.2807/1560-7917.ES.2020.25.23.2001005. Available at <https://pubmed.ncbi.nlm.nih.gov/32553059/>. Attached as Exhibit I.

<sup>10</sup> Representative photographs from mink farms are attached as Exhibit J.

By August, more than one-third of all Dutch mink farms had active COVID-19 outbreaks. Dutch public health officials soon concluded that “[i]t is undesirable that the virus continues to circulate on mink farms as there is a risk that, in the long term, this will lead to infections – via employees – of people outside the mink farm.”<sup>11</sup> The Dutch government ordered the industry be shuttered at the end of the next pelting season, which begins in November 2020 but can run as late as March 2021. Prior to this order, the Netherlands had been the world’s fourth largest mink producing country, with 130 active farms and annual exports valued at \$101 million.<sup>12</sup>

### **Danish fur farm outbreaks and identified viral mutation**

Prior to the COVID-19 pandemic, the Danish fur industry was the largest producer of mink pelts in the world, with an estimated 40% of the world’s market share.<sup>13</sup> But similar to the experience in the Netherlands, the fur industry has been ravaged by COVID-19, with at least 216 out of 1,139 farms now coping with outbreaks. Most troublingly, using genomic sequencing, researchers have now identified several mutant strains of SARS-CoV-2 that arose on Danish mink farms, including one that has now resulted in an outbreak in the general human population, with more than 200 identified cases of human infection of this mutated virus.<sup>14</sup> More than a quarter million Danes in the region of Denmark where this mutant strain arose have now gone into lockdowns as a result of this new mutated virus, and the UK has banned all travel with Denmark.

This disease cluster has been called “cluster 5,” and is the result of a “mink variant strain” of the virus. The mutation has led to changes in the virus’s “spike protein,” a kind of “identification marker” on the surface of the virus that plays a crucial role in our body’s immune response.<sup>15</sup> This means that antibodies generated in humans by

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<sup>11</sup> U.S. Department of Agriculture Foreign Agriculture Service. Dutch mink industry to close in 2021 due to coronavirus. Report Number NL2020-0042 dated Sep. 2, 2020. Available at [https://apps.fas.usda.gov/newgainapi/api/Report/DownloadReportByFileName?fileName=Dutch%20Mink%20Industry%20to%20Close%20in%202021%20Due%20to%20Coronavirus%20\\_The%20Hague\\_Netherlands\\_08-28-2020](https://apps.fas.usda.gov/newgainapi/api/Report/DownloadReportByFileName?fileName=Dutch%20Mink%20Industry%20to%20Close%20in%202021%20Due%20to%20Coronavirus%20_The%20Hague_Netherlands_08-28-2020). Attached as Exhibit K.

<sup>12</sup> Reuters. Netherlands to close mink farms after coronavirus outbreaks. Aug. 27, 2020. Available at <https://www.reuters.com/article/us-health-coronavirus-netherlands/netherlands-to-close-mink-farms-after-coronavirus-outbreaks-idUSKBN25N2W2>. Attached as Exhibit L.

<sup>13</sup> Olsen, Jan M. North Denmark in lockdown over mutated virus in mink farms. *Associated Press*. Nov. 6, 2020. Available at <https://apnews.com/article/mutated-virus-mink-farm-denmark-lockdown-98ede7f921eb6ef3b312e53743fc3edb>. Attached as Exhibit M.

<sup>14</sup> Murphy, Simon and Beaumont, Peter. Travel to UK from Denmark banned amid worries over COVID in mink. *The Guardian*. Nov. 7, 2020. Available at <https://www.theguardian.com/world/2020/nov/06/coronavirus-mutation-danish-mink-spreads-to-214-people>. Attached as Exhibit N.

<sup>15</sup> Baylis, Matthew. The COVID-carrying Danish mink are a warning sign – but is anyone heeding it? *The Guardian*. Nov. 10, 2020. Available at <https://www.theguardian.com/commentisfree/2020/nov/10/the-covid-carrying-danish-mink-are-a-warning-sign-but-is-anyone-heeding-it>. Attached as Exhibit O.

prior COVID-19 infections will likely “miss” this new variant strain. Additionally, the viral spike protein is the target of most COVID-19 vaccines currently in development, including the Pfizer vaccine that may be nearing FDA market approval. If new mink variant strains continue to evolve and spread in the community, this will undermine the billions of dollars and months of intensive research and development for a COVID-19 vaccine, and will likely lead to additional lockdowns and social distancing requirements.

Public health researchers and authorities across the globe are profoundly alarmed by this development. The WHO stated on November 6, 2020:

Minks were infected following exposure from infected humans. Minks can act as a reservoir of SARS-CoV-2, passing the virus between them, and pose a risk for virus spill-over from mink to humans. People can then transmit this virus within the human population. Additionally, spill-back (human to mink transmission) can occur. It remains a concern when any animal virus spills in to the human population, or when an animal population could contribute to amplifying and spreading a virus affecting humans. As viruses move between human and animal populations, genetic modifications in the virus can occur. These changes can be identified through whole genome sequencing, and when found, experiments can study the possible implications of these changes on the disease in humans.<sup>16</sup>

Danish authorities immediately recognized the gravity of the threat, with the state epidemiologist stating there is a potential that we will have “a pandemic that will start all over again, starting from Denmark.” Authorities have already issued an order to cull all of the mink and shut down their large mink farming industry. Danish Prime Minister Mette Frederiksen gave an emergency press conference about the situation, where he stated:

We have a great responsibility towards our own population, but with the mutation that has now been found we have an even greater responsibility for the rest of the world. The mutated virus in minks could pose a risk that future vaccines won’t work as they should. It risks being spread from Denmark to other countries. The eyes of the world are on us.<sup>17</sup>

The fur farming industry has itself admitted the severity of the crisis. At the September 28, 2020 annual convention of Fur Commission USA, Dr. John Easley, DVM, Director of Research, stated:

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<sup>16</sup> World Health Organization. SARS-CoV-2 mink-associated variant strain – Denmark. Nov. 6, 2020. Available at <https://www.who.int/csr/don/06-november-2020-mink-associated-sars-cov2-denmark/en/>. Attached as Exhibit P.

<sup>17</sup> Dyer O. Covid-19: Denmark to kill 17 million minks over mutation that could undermine vaccine effort. *BMJ*. 2020;371:m4338. Published 2020 Nov 9. doi:10.1136/bmj.m4338. Attached as Exhibit Q.

[Researchers are] extremely confident that they've been able to demonstrate that [COVID-19] was brought on to farms by humans, the virus changed in the mink, and that changed virus was then transmitted back to people, and the people that got infected, transmitted that virus to other people. This is new information that is out now, so that is extremely important to the industry. It shows that mink can potentially be a reservoir for the virus, for the human population.<sup>18</sup>

If this mutated mink variant strain spreads further, or if we develop our own mutant strain on Utah mink farms, it may extinguish the promising hopes of a COVID-19 vaccine in 2021, and lead to further lockdowns, disease, and death.

### **COVID-19 & Utah's Mink Farming Industry**

For many years, Wisconsin and Utah have led the nation as the #1 and #2 leading producers of mink pelts. Even prior to COVID-19, the domestic mink farming industry, has been in a state of precipitous decline. According to USDA figures, for the period of 2014 – 2019, we have seen the following evidence of decline:<sup>19</sup>

- The market price of a mink pelt has decreased by 62%.
- The number of mink killed for their fur has decreased by 28% nationwide. In Utah, the number of mink killed has decreased 42%.
- Overall industry profits have decreased by 73%.

In August, Clayton Beckstead, mink farmer and spokesperson with the Utah Farm Bureau, told *The Washington Post* that half of all mink farms in Utah have closed in the past year, with only 38 farms remaining.<sup>20</sup> A variety of causes explain the mink industry's decline, but significant factors include states passing laws that prohibit the sale of fur products and a growing sentiment among consumers that fur products represent unnecessary cruelty to animals.

Utah was the first location of known COVID-19 cases on United States mink farms, with at least two farms having identified outbreaks in August 2020. Almost immediately, UARC recognized the serious risk of this situation, and wrote a letter of concern to the Governor's Office, which is coordinating the state's response, and urged him to implement a moratorium on additional breeding on these mink farms. We also launched a public call to action. More than 250 of our members and supporters in Utah subsequently wrote letters of concern to Governor Gary Herbert.

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<sup>18</sup> Video of this statement is available at <https://www.youtube.com/watch?v=o9dvnHcP2n0>.

<sup>19</sup> USDA Economics, Statistics and Market Information System. *Mink*. Data derived from reports dated July 2015 & July 2019. Available at <https://usda.library.cornell.edu/concern/publications/2227mp65f>. Attached as Exhibit R.

<sup>20</sup> Brulliard, Karin. First U.S. cases of coronavirus in minks found at Utah fur farms. *The Washington Post*. Aug. 17, 2020. Available at <https://www.washingtonpost.com/science/2020/08/17/coronavirus-mink-first-us-cases/>. Attached as Exhibit S.

In October, media reports indicated that the problem had worsened, with 10,000 mink dead due to COVID-19 outbreaks and quarantines at nine separate fur farms.<sup>21</sup> Just as in Denmark and the Netherlands, these mink likely contracted the virus from workers before spreading the virus amongst themselves.

The state of Utah's response to this crisis on our mink farms has, at best, been appallingly inept. At worst, the state, and in particular the Department, appears to have been disseminating misleading information to allay legitimate worries about the COVID-19 crisis on mink farms. As recently as October, Dr. Dean Taylor, state veterinarian with the Department, told the *Associated Press* that “[the Department] genuinely [doesn't] feel like there is much of a risk going from the mink to people”<sup>22</sup> and other media organizations that the virus only follows a “unidirectional path” [from humans to mink].<sup>23</sup> Dr. Taylor's public statements are simply at odds with the overwhelming evidence from news media, government reports, and peer-reviewed literature, which, even at that time, had demonstrated that bidirectional zoonotic transmission was and is occurring. For example:

- On May 20, 2020, the U.S. Department of Agriculture's Global Agricultural Information Network circulated a public report stating that the Dutch government had conducted genomic sequencing research of its mink farm outbreaks and found that at least one employee was likely infected by a mink.<sup>24</sup>
- As early as June 11, 2020, research in the publicly accessible disease surveillance publication *Eurosurveillance* demonstrated evidence, via genomic sequencing, that SARS-CoV-2 viral particles were present on inhalable dust on Dutch mink farms, and that the disease had been transmitted from mink to humans on these farms.<sup>25</sup>

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<sup>21</sup> Bekiempis, Victoria. Nearly 10,000 mink dead from COVID-19 outbreak at Utah fur farms. *The Guardian*. Oct. 11, 2020. Available at <https://www.theguardian.com/world/2020/oct/11/utah-10000-minks-dead-from-coronavirus>. Attached as Exhibit T.

<sup>22</sup> Aleccia, JoNel. Thousands of mink dead in COVID outbreak on Utah farms. *Associated Press*. Oct. 5, 2020. Available at <https://apnews.com/article/virus-outbreak-utah-animals-archive-2863345161adeebb318a3276e35e9501>. Attached as Exhibit U.

<sup>23</sup> Mossburg, C. At least 8,000 mink dead in Utah after contracting COVID-19. CNN. 8 Oct 2020. Available at [https://www.cnn.com/world/live-news/coronavirus-pandemic-10-08-20-intl/h\\_b1b17737445ac5cb60f54df4b0467c5d](https://www.cnn.com/world/live-news/coronavirus-pandemic-10-08-20-intl/h_b1b17737445ac5cb60f54df4b0467c5d). Attached as Exhibit V.

<sup>24</sup> U.S. Department of Agriculture Foreign Agriculture Service. Additional control measures for Dutch mink industry in response to COVID-19. Report Number NL2020-0019 dated May 20, 2020. Available at <https://apps.fas.usda.gov/newgainapi/api/Report/DownloadReportByFileName?fileName=Additional%20Control%20Measures%20for%20Dutch%20Mink%20Industry%20In%20Response%20to%20COVID-19%20The%20Hague%20Netherlands%2005-19-2020>. Attached as Exhibit W.

<sup>25</sup> Oreshkova N, Molenaar RJ, Vreman S, *et al.* SARS-CoV-2 infection in farmed minks, the Netherlands, April and May 2020. *Euro Surveill*. 2020;25(23):2001005. doi:10.2807/1560-7917.ES.2020.25.23.2001005. Available at <https://pubmed.ncbi.nlm.nih.gov/32553059/>. Attached as Exhibit X.

- In a September 1, 2020 manuscript partially titled “Jumping back and forth,” European public health researchers investigated COVID-19 outbreaks on 16 mink farms, and found that 68% of the tested mink farm residents, employees, or contacts had evidence of SARS-CoV-2 infection. Using whole genome sequencing, they concluded that there was “widespread circulation” of the virus among the mink, and that there had been “animal to human transmissions of SARS-CoV-2 in mink farms.”<sup>26</sup> These researchers’ findings were later published in *Science*,<sup>27</sup> often considered the most prestigious peer-reviewed scientific publication in the United States.
- The University of Minnesota’s Center for Infectious Disease Research and Policy (CIDRAP) published a news article titled “COVID-19 likely spreading from people to animals – and vice versa” on September 18, 2020, that largely concerned the spread of the disease from mink to humans.<sup>28</sup> CIDRAP is widely considered a global leader in addressing public health preparedness and emerging infectious disease response. CIDRAP also wrote on November 6, 2020 that when SARS-CoV-2 “is introduced to mink farms from humans, it can spread quickly, and possibly due to biological differences between minks and people, can accumulate mutations, which result in variants with the potential to jump back into humans.”<sup>29</sup>

Despite the available evidence, on October 14, 2020, in an email to *The Salt Lake Tribune* obtained by UARC via a GRAMA request, Dr. Taylor re-asserted the claim that SARS-CoV-2 does not transmit from mink to humans, claiming that “ALL studies so far indicated that the spread was from humans to mink and none indicate the reverse.”<sup>30</sup> There is no charitable way to interpret Dr. Taylor’s October 14, 2020 statement. He was simply either uninformed or being deceptive. UARC submitted a GRAMA request for information related to local studies or evaluations of SARS-CoV-2 on Utah mink farms, but the Department’s response appears to indicate that the state is not currently conducting or reviewing any such studies or

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<sup>26</sup> Oude Munnink BB et al. Jumping back and forth: anthropozoonotic and zoonotic transmission of SARS-CoV-2 on mink farms [Internet]. Cold Spring Harbor Laboratory; 1 Sep 2020. Available from: <http://dx.doi.org/10.1101/2020.09.01.277152>. Attached as Exhibit Y.

<sup>27</sup> Oude Munnink BB, Sikkema RS, Nieuwenhuijse DF, et al. Transmission of SARS-CoV-2 on mink farms between humans and mink and back to humans [published online ahead of print, 2020 Nov 10]. *Science*. 2020;eabe5901. doi:10.1126/science.abe5901. Available at <https://science.sciencemag.org/content/early/2020/11/09/science.abe5901>. Attached as Exhibit Z.

<sup>28</sup> Van Beusekom, Mary. COVID-19 likely spreading from people to animals – and vice versa. *CIDRAP News*. Sep. 18, 2020. Available at <https://www.cidrap.umn.edu/news-perspective/2020/09/covid-19-likely-spreading-people-animals-and-vice-versa>. Attached as Exhibit AA.

<sup>29</sup> Schnirring, Lisa. Global COVID-19 total clears 49 million, experts weigh in on mink variant. *CIDRAP News*. Nov. 6, 2020. Available at <https://www.cidrap.umn.edu/news-perspective/2020/11/global-covid-19-total-clears-49-million-experts-weigh-mink-variant?fbclid=IwAR3ibB400Pjplwh6MCiLKjK-ehbtW243JBv6ZbwRF9Ihii8XfDfqw78bek>. Attached as Exhibit BB.

<sup>30</sup> Taylor, Dean. Email communication with *The Salt Lake Tribune*. Oct. 14, 2020. Obtained via GRAMA. Attached as Exhibit CC.

surveillance.<sup>31</sup> It doesn't appear that there are, in fact, any "studies" upon which the Department ostensibly based its public statements downplaying the possibility of mink-to-human transmission. This is incredibly troubling.

It must be pointed out that the Department's Mission Statement is to "promote the healthy growth of Utah agriculture," and the bulk of the Department's activities are geared towards protecting the financial interests of the agriculture industry in Utah.<sup>32</sup> The Department's failure to handle this crisis and publicly convey an accurate assessment of the public health risk posed by Utah mink farms may be fundamentally at odds with the Department's mission and ethos. Greater transparency may help provide insight as to why the Department's response has been so deficient.

### **UARC's GRAMA Request & the Department's Denial**

In response to new additional media reports, UARC submitted a GRAMA request dated October 14, 2020 for records concerning Utah's ongoing and growing mink farm COVID-19 crisis and the state's response to this problem. Despite the profound implications on public health and oversight of government employees, the Department denied access to the vast majority of the records UARC requested, shrouding this crisis and the Department's response in secrecy. For reasons explained below, each denial by the Department was based on an incorrect reading or misapplication of state statute. Accordingly, UARC's request should be granted in full and a fee waiver granted.

#### **Utah Code § 63G-2-204(2) & Subsection (2)(c)**

First, the Department denied UARC's request for necropsy and diagnostic test reports, as well as for correspondence with various relevant outside entities. The Department erroneously cites "63G-2-204(2)" in denying access to these records, quoting language that simply does not appear in the statute. Because the Department relies on non-existent statutory language, its basis for denying access to these records ought to be rejected outright.

In any case, the Department's answer to this portion of UARC's request appears to obfuscate whether or not the requested records are, in fact, actually in possession of the Department, and if so, upon what statutory basis the Department denying access. The title of the Section cited by the Department, 63G-2-204, is "Record request." This section of GRAMA outlines only the necessary elements for a GRAMA *request* and basic procedural issues for how an entity is required to

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<sup>31</sup> Price, Amanda. Reply to GRAMA Request for the Utah Animal Rights Coalition. Oct. 19, 2020. Attached as Exhibit DD.

<sup>32</sup> Utah Department of Agriculture and Food. UDAF Mission, Values, and Priorities. Jun. 18, 2019. Available at <https://ag.utah.gov/about/>. Attached as Exhibit EE.

respond, including statutory deadlines and required response times. Nowhere in this section of Utah Code is there any statutory guidance for determining whether or not a particular record is actually subject to disclosure.

UARC has fulfilled all of its obligations under this provision GRAMA. It has properly submitted a request and has described the records it seeks with reasonable specificity. The statute then only asks whether the Department “retains” the record sought by UARC. *See* Utah Code § 63G-2-204(1)(a). Contrary to the thin rationale in the Department’s letter, it is irrelevant, *per se*, whether or not the records in question are “originating from other government agencies.” If the Department does retain the records identified by UARC, there is a presumption of disclosure under GRAMA, unless the Department can cite specific statutory authority to deny access to these records. *See* Utah Code § 63G-2-201(2). The Department has failed to do so.

In this portion of its denial letter, the Department also cites “[63G-2-204] Subsection(2)(c).” Once again, it erroneously quotes language that does not appear in the statute. This Section of Utah Code does not even have a Subsection (2)(c). Even if the language quoted in the Department’s letter did exist in the statute, it would not be a sufficient basis for denial, as the language appears to simply outline the procedural steps a governmental entity must follow for handling a response “[i]f a governmental entity is prohibited from providing a record,” it does not, itself, provide a statutory basis for such denial. Therefore, this portion of the Department’s response is an empty exercise of question-begging.

#### Utah Code § 63G-2-305(10)

Next, the Department denied access to “documents related to the identity of the mink farms or the ongoing investigation,” which, presumably, also includes “protocols or documents reflecting precautions being taken or recommended be taken for Utah mink farms to reduce transmission of SARS-CoV-2” as well as “records revealing the ‘stringent biosecurity measures’ implemented on fur farms in response to the latest COVID-19 outbreaks.” These records were requested by UARC, but not explicitly addressed in the Department’s response.

The Department first cites 63G-2-305(10), reproducing all subsections (a) through (e) in its letter, to deny access to this information. Broadly, this subsection exempts “records created or maintained for civil, criminal, or administrative enforcement purposes or audit purposes, or for discipline, licensing, certification, or registration purposes,” before listing five separate conditions, one of which *must* be met to satisfy this broad exemption. The Department did not make clear which subsection(s), specifically, the Department is relying upon to deny access to the records sought by UARC, which hinders our ability to directly respond to their basis for denial in this appeal.

Generally speaking, all five subsections cited by the Department clearly pertain to disclosures which could reasonably be expected to jeopardize the integrity of pending or future governmental proceedings, for example, identifying confidential human sources or requiring the government to reveal information that would “tip off” the subject of an ongoing investigation or audit, allowing them to take preparatory steps to thwart such investigation. It must be stressed, this exemption was clearly not intended to be a catch-all provision to exempt all records related to any enforcement purpose, as such an exemption would swallow nearly all records maintained by a governmental agency.

The Department’s reference to this exemption fails first because the Department must identify an actual ongoing investigation, not merely assert a hypothetical use for potential future investigations. See *Deseret News Publ’g Co. v. Salt Lake Cnty.* , 2008 UT 26, ¶ 44, 182 P.3d 372.

The Department’s denial also fails because it has not explained how these subsections apply in even a general or hypothetical sense. It is not likely that the Department is serious about pursuing any meaningful investigation or enforcement action against these farms, and it is unclear by what statutory authority it could even do so. Even if the Department were actively pursuing an enforcement action or investigation, it is unclear how release of the information sought by UARC would interfere with an investigation. All of the fur farms with ongoing COVID outbreaks are obviously already aware that they have had outbreaks on their farms. The information sought by UARC will not reveal any material information that these farms were not already privy to. There is no information in the documents sought by UARC which would thwart or undermine a hypothetical enforcement proceeding by the Department if they were disclosed. Because the Department has failed to outline with any greater detail how this exemption applies to the records sought by UARC, this basis for denial should be rejected.

Additionally, even if you do conclude that (1) there is an ongoing investigation, not merely a hypothetical future use of the information, and (2) that the records sought by UARC fall under one of the five subsections of Utah Code § 63G-2-305(10), you should still order disclosure of this information. Utah Code § 63G-2-406 authorizes disclosure of records protected by Utah Code § 63G-2-305(10), if it can be established “by a preponderance of the evidence, that the public interest favoring access is equal to or greater than the interest favoring restriction of access.” Clearly, given the ongoing COVID-19 crisis facing Utah and the nation, the threat posed by the state’s mink farms, and the state’s apparent inept response to this threat, there is a significant public interest in disclosing this information to shed light on the severity of the threat facing Utah communities and to better understand how public officials have responded, or failed to respond. These records will substantially increase awareness and understanding of a matter of significant public concern. The

public interest in disclosure far outweighs any interest in keeping the records secret.

#### Utah Code § 63G-2-305(49)

The Department also cited 63G-2-305(49) in its denial. This exemption applies to “records of the Department of Agriculture and Food that provides for the identification, tracing, or control of livestock diseases, including any program established under Title 4, Chapter 24, Utah Livestock Brand and Anti-Theft Act, or Title 4, Chapter 31, Control of Animal Diseases.” This statute does not apply for one simple reason: there is no established state program for the control of COVID-19, caused by a novel coronavirus, on Utah mink farms. The word “mink” does not appear in Chapters 24 & 31 of Title 4 of Utah Code, which are expressly referenced in this exemption. These chapters deal primarily with existing state programs for controlling diseases of dairy cattle, poultry, swine, waterfowl. The Department was not able to cite an established program for surveilling and containing any mink disease, let alone the novel SARS-CoV-2, because one does not exist.

Unlike cattle, swine, sheep, and other livestock species, mink on fur farms are not branded or ear-tagged, and they are not entered into any voluntary government identification system, such as the USDA’s National Animal Identification System (NAIS). The absence of such a program is one reason why the records UARC requests and the ongoing COVID-19 crisis on mink farms are a matter of significant public concern. Subsection (49) of GRAMA was added during the 2005 Utah Legislature’s General Session in order to protect the records of “the National Animal Identification System (NAIS) and state programs providing for the identification, tracing, or control of livestock diseases.”<sup>33</sup> Mink are not part of the NAIS, a federal program administered by USDA-APHIS, and there are no existing programs on the state level aimed at tracking COVID-19 on mink farms. Additionally, COVID-19 is not strictly a livestock disease; it is a zoonotic disease with transmissibility to and between human beings. Therefore, this exemption does not apply.

#### **Conclusion**

Under GRAMA, “[a] record is public unless otherwise expressly provided by statute.” *See* Utah Code § 63G-2-201(2). For all of the reasons stated above, the statutes cited by the Department are not applicable to the records sought by UARC and thus should be released in their entirety. We ask that you issue such an order. It should also be noted that the Department made no attempt to segregate any non-

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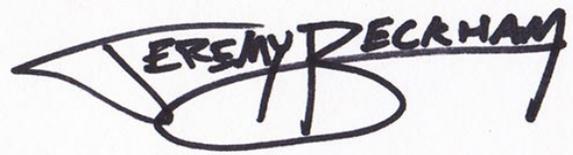
<sup>33</sup> Utah House Bill 226. GRAMA Requirements Regarding Animal Identification Program. 2005 General Session. Available at <https://le.utah.gov/~2005/bills/static/HB0226.html>.

public information out of the records UARC requested and release the remainder. This is a requirement under GRAMA. *See Utah Code § 63G-2-308.*

As a non-profit organization, UARC has no private or commercial interest in these records and intends to use these records to enhance public understanding of this important issue and to disseminate information to the news media and the public at large. UARC therefore believes that the release of these records “primarily benefits the public rather than a person” and accordingly we re-assert or request for a waiver of fees should you order additional records be disclosed. *See Utah Code Ann. §63G-2-203(4)(a).*

Thank you for your time and careful consideration. I look forward to receiving your decision within 10 business days. *See Utah Code Ann. §63G-2-401(5)(a).* If I may be of assistance, please reach out using the contact information provided below. Email is preferred.

Sincerely,

A handwritten signature in black ink that reads "JEREMY BECKHAM". The signature is stylized with a large, sweeping underline that loops back under the first part of the name.

Jeremy Beckham, MPA, MPH  
Executive Director  
Utah Animal Rights Coalition  
385-401-4301 (office)  
385-227-7034 (mobile)  
[jeremy@uarc.io](mailto:jeremy@uarc.io)

# **Exhibit D**

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BEFORE THE DEPUTY COMMISSIONER OF THE  
UTAH DEPARTMENT OF AGRICULTURE AND FOOD  
STATE OF UTAH

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UTAH ANIMAL RIGHTS COALITION  
(UARC),

Petitioner,

vs.

DEPARTMENT OF AGRICULTURE AND  
FOOD,

Respondent.

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**DECISION AND ORDER**

By this appeal, Petitioner, UARC, through Mr. Jeremy Beckham, seeks access to various records related to Utah mink farms which have identified cases of SARS-CoV-2 and/or COVID-19, including diagnostic test reports, necropsy reports, correspondence, and documents related to protocols or biosecurity measures implemented or recommended as a response to COVID-19 outbreaks on mink farms.

**FACTS**

On or about October 14, 2020, UARC made a records request of the Utah Department of Agriculture and Food (The Department), Respondent.

In response, the Department denied the request in part and granted it in part. Specifically, the Department provided UARC with a link to public guidance for animal health and public health officials managing farmed mink and other farmed mustelids with SARS-CoV-2 in response to

UARC's request for information regarding biosecurity measures implemented on fur farms and protocols or documents dealing with precautions being taken or recommended to Utah mink farms. The Department denied the request for additional records and correspondence.

UARC now appeals the Department's denial to the Chief Administrative Officer for the Department. In an appeal letter dated November 12, 2020, UARC through Mr. Beckham, disputed the Department's reasoning in denying the request and argued that the information they have requested should be released because it relates to areas of significant public health concern, particularly with regard to the risk of bidirectional zoonotic transmission of SARS-Cov-2 or COVID-19 which UARC argued has been shown during prior mink outbreaks. While the Department does not dispute the evidence UARC provided in the exhibits to their appeal letter, current evidence does not support the existence of animal to human transmission within mink populations in the State of Utah, which is consistent with State Veterinarian Dr. Dean Taylor's statements related to the COVID outbreak at mink farms in the state.

The Department's Chief Administrative Officer, having reviewed the materials requested and the arguments submitted, now issues the following Decision and Order.

#### **STATEMENT OF REASONS FOR DECISION**

1. GRAMA specifies that "all records are public unless otherwise expressly provided by statute." Utah Code Section 63G-2-201(2). Records that are not public are designated as either "private," "protected," or "controlled." See, Utah Code Sections 63G-2-302, -303, -304 and -305.

2. Every person has the right to inspect a public record free of charge, and the right to take a copy of a public record during normal working hours, subject to Sections, 63G-2-203 and 204. See Utah Code Section 63G-2-201(1)
3. A governmental entity shall provide a person with a certified copy of a record if the person identifies the record with reasonable specificity. See, Utah Code Section 63G-2-201(7)(b).
4. Utah Code Subsection 63G-2-204(1) states that “A person making a request for a record shall submit [the request] to the entity that retains the record.” In Subsection 63G-2-204(2)(a) the statute goes on to state that “a governmental entity may not provide a record that it has received under Section 63G-2-206 as a shared record” and that a request for such a record should be denied. See Subsection 63G-2-204(2)(b).
5. Utah Code Subsection 63G-2-305(10) states that “records created or maintained for civil, criminal, or administrative enforcement purposes or audit purposes, or for discipline, licensing, certification, or registration purposes” should be considered protected records if one of five listed conditions are present. See Subsection 63G-2-305(10)(a-e).
6. Utah Code Subsection 63G-2-305(49) provides that “records of the Department of Agriculture and Food that provide for the identification, tracing, or control of livestock diseases, including any program established under Title 4, Chapter 24, Utah Livestock Brand and Anti-Theft Act, or Title 4, Chapter 31, Control of Animal Diseases.”
7. Except as provided in Section 63G-2-406, the chief administrative officer may, upon consideration and weighing of the various interests and public policies pertinent to the

classification and disclosure or nondisclosure, order the disclosure of information properly classified as protected under Subsection 63G-2-305 if the interests favoring access are greater than or equal to the interests favoring restriction of access.

8. After reviewing arguments and reviewing the records in question, the Chief Administrative Officer finds that based upon a preponderance of the evidence:

- (1) UARC has failed to show that Utah Code Subsections 63G-2-204(2)(a) and 63G-2-206 are not applicable to this request. Necropsy reports and diagnostic test reports that the Department has received from the USDA National Veterinary Services Laboratory, the Centers for Disease Control and Prevention, and Utah Department of Health, as well as correspondence between the Department and these outside entities that are not retained by the Department cannot be released by the Department because they have been classified as “private, controlled, or protected” by another governmental entity and qualify as shared records under Section 63G-2-206. If UARC seeks these records, they must be requested from the entity that retains them under Subsection 63G-2-204(2)(b)(ii).

- (2) Pursuant to Utah Code Section 63G-2-305(10), the records in question in this appeal that are related to the identity of mink farms are properly classified as protected records because they relate to the Department’s **current actual and ongoing** investigation of SARS-Cov-2 and COVID-19 outbreaks in mink farms in the State of Utah. Specifically, Subsection 63G-2-305(10)(a-e) could all apply, although subsection a, b, and c are most relevant to this request because release of records that relate to the identity of mink farms “(a) reasonably

could be expected to interfere with investigations undertaken for enforcement, discipline licensing certification, or registration purposes; (b) reasonably could be expected to interfere with audits, disciplinary, or enforcement proceedings; [and] (c) would create a danger of depriving a person of a right to a fair trial or impartial hearing.” The Department is not obligated to provide the specific details of their ongoing investigations, as doing so would jeopardize the investigations themselves, as well as risk the safety of the public and animals in the state.

(3) Pursuant to Subsection 63G-2-305(49) correspondence related to the identity of mink farms subject to outbreak as well as diagnostic or necropsy reports of the Utah Veterinary Diagnostic Laboratory are properly classified as protected because they relate to the “identification, tracing, or control of livestock diseases,” by the Department. While the statute mentions programs that track diseases under Chapter 4-24 and Chapter 4-31, the protected status does not apply only to programs under these statutes. The Department is not required to have a program in place to control COVID-19 caused by novel coronavirus in mink farms in order for the status to apply. Indeed, it would be fairly impossible for the Department to have created and implemented such a program at this point in time. It is the Department’s position, rather, that Subsection 49 applies more broadly to any records linked to the Department’s “identification, tracing, or control of livestock disease.” Livestock is defined under Section 4-1-109 as cattle, sheep, goats, swine, horses, mules, poultry, domesticated elk as defined in Section 4-39-102, or any

other domestic animal or domestic furbearer raised or kept for profit.” While mink are not specifically mentioned in the definition of livestock they are reasonably classified as protected under this subsection because they are a furbearing animal raised for profit.

(4) In considering and weighing the various interests and public policies pertinent, the interests favoring access are not greater or equal to the interests favoring restriction. The Department does not dispute the significant public health threat associated with the COVID-19 pandemic, however, UARC has not provided sufficient evidence of a current threat posed by Utah’s mink farms or how the release of the information requested would lessen that threat.

**ORDER**

THEREFORE, IT IS ORDERED THAT Petitioner’s appeal is Denied.

**RIGHT TO APPEAL**

You may appeal this Decision and Order to the District Court or to the State Records Committee. The petition for review must be filed no later than thirty (30) days after the date of this order. The petition for judicial review must be a complaint. The complaint and the appeals process are governed by the Utah Rules of Civil Procedure and Utah Code Section 63G-2-404. The court is required to make its decision *de novo*. In order to protect its rights on appeal, a party may wish to seek advice from an attorney.<sup>1</sup>

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<sup>1</sup>This notice is required by Utah Code Section 63G-2-403(12)(d).

Entered this 24 day of November 2020.

BY

  
\_\_\_\_\_  
KELLY PEHRSON, Deputy Commissioner  
and Chief Administrative Officer, Utah  
Department of Agriculture and Food

**CERTIFICATE OF MAILING**

I hereby certify that I sent a true and correct copy of the foregoing Decision and Order  
via email, this \_\_\_\_ day of November 2020, to the following:

UARC, through Mr. Jeremy Beckham  
PO Box 3451  
Salt Lake City, UT 84110

A copy has also been sent by email to:  
UARC, through Mr. Jeremy Beckham  
jeremy@uarc.io

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# **Exhibit E**

## EXECUTIVE ORDER

Declaring a State of Emergency Due to Infectious Disease COVID-19 Novel Coronavirus

**WHEREAS**, On January 21, 2020, the Utah Department of Health activated its Department Operations Center in response to the evolving the global outbreak of novel coronavirus;

**WHEREAS**, The Utah Department of Health recognizes COVID-19 as a threat to the health and safety of the residents of Utah;

**WHEREAS**, Although no confirmed cases have been diagnosed in the state, the Utah Department of Health, local health departments, and health and medical partners have activated response plans and protocols to prepare for the likely arrival of the virus in Utah;

**WHEREAS**, These partners have also worked to identify, contact, and test individuals in the State of Utah who have been potentially exposed to COVID-19 in coordination with the United States Centers for Disease Control and Prevention (CDC);

**WHEREAS**, Proactively implementing mitigation measures to slow the spread of the virus is in the best interests of the state of Utah and its people;

**WHEREAS**, COVID-19, a respiratory disease that can result in serious illness or death, is caused by the SARS-CoV-2 virus, which is a new strain of coronavirus that had not been previously identified in humans and can easily spread from person to person;

**WHEREAS**, The CDC identifies the potential public health threat posed by COVID-19 both globally and in the United States as "high," and has advised that person-to-person spread of COVID-19 will continue to occur globally, including within the United States;

**WHEREAS**, On January 31, 2020, the United States Department of Health and Human Services Secretary Alex Azar declared a public health emergency for COVID-19, beginning on January 27, 2020;

**WHEREAS**, As of March 6, 2020, the CDC indicates there are over 100,000 confirmed cases of COVID-19 worldwide, with over 200 of those cases in the United States;

**WHEREAS**, On February 28, 2020, the State Emergency Operations Center raised its activation level to Level 3 - Elevated Action and the Utah Division of Emergency Management and Department of Health activated a Joint Information System for public information;

**WHEREAS**, The Utah Department of Public Safety, Division of Emergency Management, State Emergency Operations Center, is coordinating resources across state government to support the Utah Department of Health and local officials in alleviating the impacts to people, property, and infrastructure, and is assessing the magnitude and long-term effects of the incident with the Utah Department of Health;

**WHEREAS**, The State of Utah has implemented the Utah COVID-19 Community Task Force to coordinate the response to the incident throughout the entire state and among all levels of government;

**WHEREAS**, the circumstances of this outbreak may exceed the capacity of the services, personnel, equipment, supplies and facilities of any single city, county, or city and county, and require the combined forces of a mutual aid region or regions to combat; and

**WHEREAS**, these conditions do create a "State of Emergency" within the intent of the Disaster Response and Recovery Act found in Title 53, Chapter 2a of the Utah Code Annotated 1953, as amended:

**NOW, THEREFORE**, I, Gary R. Herbert, Governor of the State of Utah, declare a "State of Emergency" due to the aforesaid circumstances requiring aid, assistance, and relief available from State resources and hereby order:

The continued execution of the State Emergency Operations Plan;

Assistance from State government to political subdivisions as needed and coordinated by the Utah Department of Health, the Utah Department of Public Safety, and other state agencies as necessary;

The continued dissemination of timely and accurate information by state agencies to the public that will slow the spread of COVID-19, prevent unnecessary confusion and alarm, and mitigate impacts to the economy;

The continued outreach and assistance to the populations most vulnerable to COVID-19; and

Coordination with local authorities and the private sector to maximize access to appropriate medical care while preserving critical services for those most in need.

**IN WITNESS WHEREOF**, I have hereunto set my hand and caused to be affixed the Great Seal of the State of Utah. Done in Salt Lake City, Utah, on this, the 6th day of March, 2020.

(State Seal)

**Gary R. Herbert**  
**Governor**

ATTEST:

**Spencer J. Cox**  
**Lieutenant Governor**

2020/001/EO

# **Exhibit F**

# PERSPECTIVES

## OPINION

### Pathways to zoonotic spillover

Raina K. Plowright, Colin R. Parrish, Hamish McCallum, Peter J. Hudson, Albert I. Ko, Andrea L. Graham and James O. Lloyd-Smith

**Abstract** | Zoonotic spillover, which is the transmission of a pathogen from a vertebrate animal to a human, presents a global public health burden but is a poorly understood phenomenon. Zoonotic spillover requires several factors to align, including the ecological, epidemiological and behavioural determinants of pathogen exposure, and the within-human factors that affect susceptibility to infection. In this Opinion article, we propose a synthetic framework for animal-to-human transmission that integrates the relevant mechanisms. This framework reveals that all zoonotic pathogens must overcome a hierarchical series of barriers to cause spillover infections in humans. Understanding how these barriers are functionally and quantitatively linked, and how they interact in space and time, will substantially improve our ability to predict or prevent spillover events. This work provides a foundation for transdisciplinary investigation of spillover and synthetic theory on zoonotic transmission.

The phenomenon of cross-species spillover is the defining characteristic of pathogens that transmit from vertebrate animals to humans (zoonoses). The public health burden that is presented by zoonoses includes outbreaks of pathogens such as Ebola virus, influenza A virus (H1N1) pdm09 and Middle East respiratory syndrome coronavirus (MERS-CoV), as well as the ongoing transmission of endemic pathogens, such as *Salmonella* spp., *Leptospira* spp., *Trypanosoma* spp., *Mycobacterium* spp. and West Nile virus<sup>1–6</sup>.

Spillover transmission is promoted by successive processes that enable an animal pathogen to establish infection in a human. The probability of zoonotic spillover is determined by interactions among several factors, including disease dynamics in the reservoir host, pathogen exposure and the within-human factors that affect susceptibility to infections. These factors can be partitioned into three functional phases that describe all major routes of transmission (FIG. 1). In the first phase, the amount of pathogen available to the human host at a given point in space and time, known as the pathogen pressure, is determined by interactions among reservoir

host distribution, pathogen prevalence and pathogen release from the reservoir host, followed by pathogen survival, development and dissemination outside of the reservoir hosts. Second, human and vector behaviour determine pathogen exposure; specifically, the likelihood, route and dose of exposure. Third, genetic, physiological and immunological attributes of the recipient human host, together with the dose and route of exposure, affect the probability and severity of infection.

Each phase presents multiple barriers to the flow of a pathogen from a reservoir host to a recipient host. Spillover requires the pathogen to pass every barrier and thus can only occur when gaps align in each successive barrier within an appropriate window in space and time (FIG. 2). Consequently, zoonotic spillover is a relatively rare event, and although humans are continually exposed to many potentially infectious pathogens that are derived from other species, most of these microorganisms cannot infect or cause disease in humans<sup>7–10</sup>.

This Opinion article focuses on spillover transmission, strictly defined as the processes that enable a pathogen from a vertebrate animal to establish infection in a human.

Although many recent articles have examined the fields of zoonoses or emerging pathogens<sup>2,3,10–15</sup>, a synthetic mechanistic understanding of animal-to-human transmission is lacking<sup>14,16</sup>. Much attention has been dedicated to the characterization of emerging infections<sup>3,11,12,15</sup>; for example, the high frequency of zoonoses among emerging infections<sup>3,12</sup>, their socio-economic, environmental and ecological drivers<sup>2,13,17,18</sup>, and their phylogenetic and geographical distribution<sup>3</sup>. Similarly, the phases of zoonotic emergence in the human population<sup>11,14,18</sup>, adaptation and compatibility of zoonoses in humans<sup>10,11,19</sup>, and approaches to modelling the transmission of zoonoses<sup>14,16</sup>, have also been addressed in the literature. However, a comprehensive understanding of the processes that enable a pathogen from a vertebrate animal to establish infection in a human, and how these processes are hierarchically, functionally and quantitatively linked, remains a fundamental deficit in research on zoonoses<sup>14,16</sup>. In this Opinion article, we present a mechanistic structure that integrates the determinants of spillover and the interactions among them (FIG. 1). However, we do not address broader determinants of pathogen emergence or factors that affect disease severity or onward transmission in humans.

Although many of the individual determinants of spillover are subjects of intensive study, each is usually addressed in isolation in a specialized discipline (FIG. 2). Accordingly, the better-characterized factors become the focus of public health interventions. For example, reservoir hosts or vectors are often targeted for control before the concatenation and relative influence of processes that lead to spillover are understood, which sometimes leads to inefficient or even counterproductive interventions<sup>20</sup>. In other cases, multiple mechanisms are aggregated in analyses that obscure the interactions or heterogeneities that drive risk. Although the aggregation of mechanisms may be appropriate at times, identifying discrete mechanisms and how they interact to drive spillover is essential to recognize the assumptions that are implicit in simpler models, and to clarify which processes must be modelled explicitly and

which can be combined. For example, does assessment of the risk of acquiring a zoonotic infection require the measurement of the pathogen burden carried by individual reservoir hosts, or is it sufficient to estimate the cumulative abundance of a pathogen in the environment over time? This is a key question for pathogens such as *Leptospira interrogans*, *Giardia* spp., and *Escherichia coli* O157, and the answer may depend on modes of contact and dose–response relationships in humans (see below). Models that integrate data from experiments, the field and epidemiological studies, even if only partially parameterized, may be necessary to make such determinations.

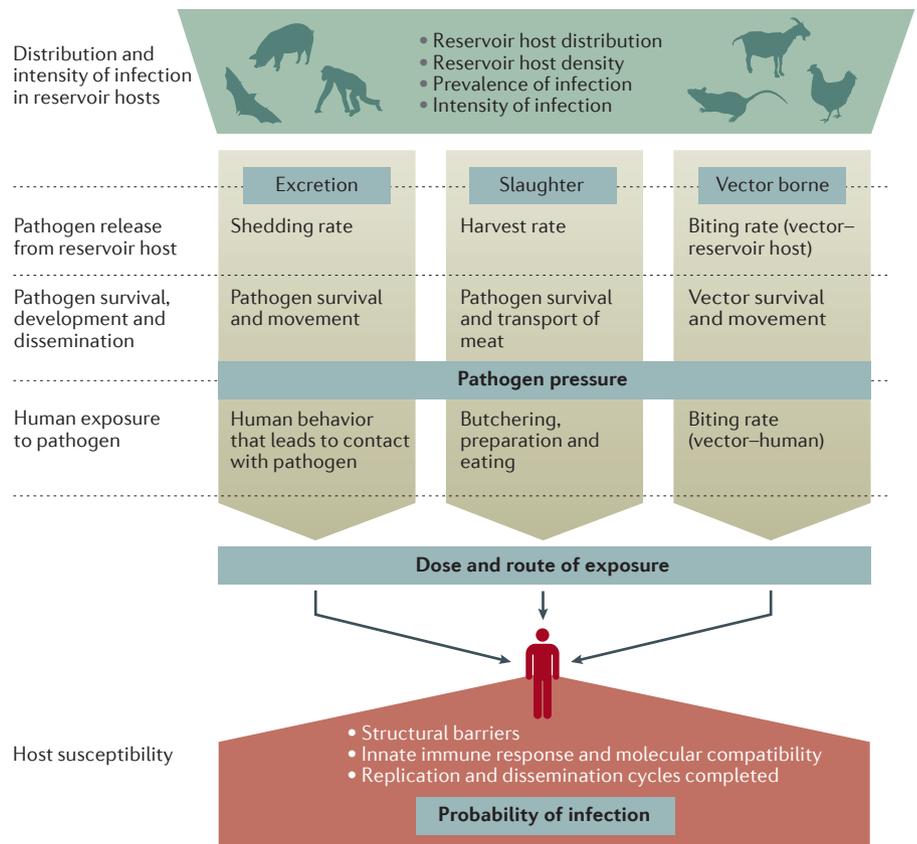
We describe how pathogens overcome a series of barriers to pass from reservoir hosts to humans. Crucially, nonlinear interactions among the barriers create bottlenecks in the flow of a pathogen between species. Such bottlenecks provide opportunities for public health interventions that could lead to substantial reductions in the risk of spillover. Alternatively, changing environmental or social conditions can alleviate these bottlenecks, which can cause surges in spillover infections. Our framework provides the foundation for operational models that are required for quantitative evidence-based risk analysis, preparedness, surveillance and control.

### Barriers to spillover

The probability of spillover is determined by the interactions among the barriers and the associated bottlenecks that might prevent cross-species transmission. Many of these interactions are nonlinear and dynamic in space and time.

**Pathogen pressure.** The series of processes that culminate in pathogen pressure (the amount of a pathogen that is available to humans at a given point in time and space) includes pathogen dynamics in reservoir hosts, pathogen release from reservoir hosts, and pathogen survival or dispersal outside of reservoir hosts.

Pathogen dynamics in reservoir hosts can be represented as three variables that determine the distribution and intensity of infection in time and space: the density of reservoir hosts, the prevalence of infection among reservoir hosts, and the average intensity of infection in an infected reservoir host in time and space ([Supplementary information S1](#) (box)). Many ecological and physiological factors influence these variables in communities of reservoir animals; however, two sets of factors are dominant.



**Figure 1 | Pathways to spillover.** The risk of spillover is determined by a series of processes that link the ecological dynamics of infection in reservoir hosts, the microbiological and vector determinants of survival and dissemination outside of reservoir hosts, the epidemiological and behavioural determinants of exposure, and the within-host biological factors that shape the susceptibility of recipient hosts. The distribution and intensity of infection in reservoir hosts, followed by pathogen release, movement, survival and possible development to infectious stage, determine the pathogen pressure, which is defined as the amount of pathogen available to the recipient host at a given point in space and time. Pathogen pressure then interacts with the behaviour of the recipient host (and vector for vector-borne pathogens) to determine the likelihood, dose and route of exposure. A series of within-host barriers then determine host susceptibility, and, therefore, the probability and severity of infection for a given pathogen dose.

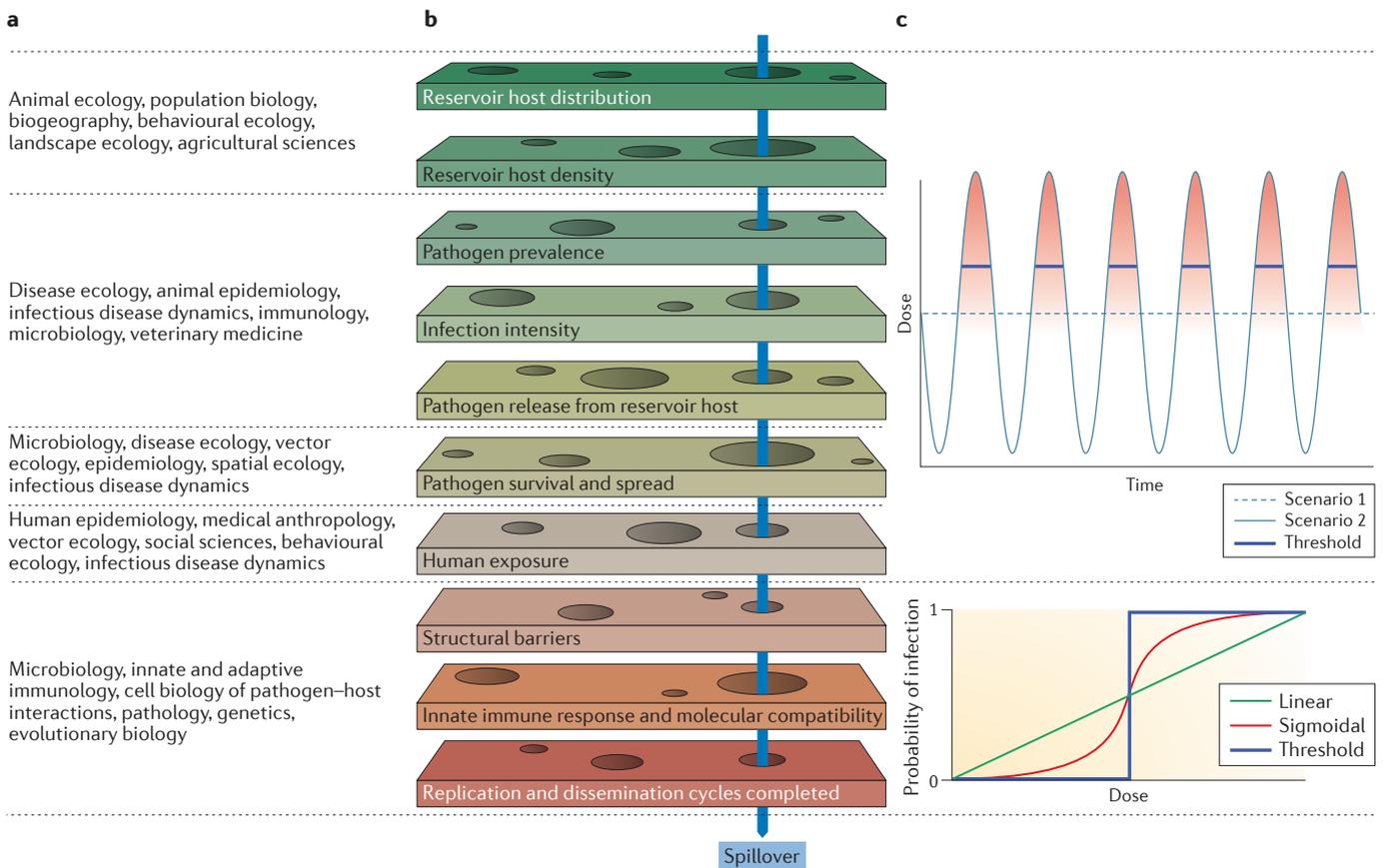
The first set is the natural history of infection in hosts, which includes the duration, intensity and severity of infection and the level of shedding. Second, the movement and behaviour of hosts affect contact and the likelihood of exposure within and between species. These factors interact with the abundance, density, demographic turnover, spatial distribution and physiological state of hosts to determine the efficiency of spread<sup>21</sup>. Collectively, these processes determine how the pathogen is distributed across reservoir host populations. Such pathogen distribution can be highly variable (for example, pulses of Sin Nombre virus infections in deer mice (*Peromyscus maniculatus*) populations in response to climate-driven increases in population density)<sup>22</sup>, or stable (as illustrated by *Mycobacterium bovis* infections in populations of livestock and wildlife)<sup>23</sup>.

The mode of pathogen release from reservoir hosts determines the major routes of transmission. Pathogens may be released in host excretions, through slaughter or through an arthropod vector (FIG. 1). The probability of a pathogen being released from a reservoir host is affected by its presence and viability in relevant tissues, such as the blood for many vector-borne pathogens, tissues contacted or consumed during butchering and eating for some food-borne pathogens, and tissues through which external shedding occurs for direct or environmental routes. For example, the viral load and excretion rates in the salivary glands are key determinants for the transmission of rabies virus from carnivores, whereas viral loads in the intestinal and respiratory tracts affect the transmission of avian influenza virus from poultry<sup>24–26</sup>. Likewise, the release of pathogenic *Leptospira*

spp. from animal hosts requires colonization of the renal tubules<sup>27</sup>. The excreted pathogen load depends on the quantity of leptospire that effectively colonize the tubules<sup>28</sup>, the rate of release and the urinary output of the host<sup>29</sup>. Moreover, the pathogen undergoes several changes in its lipopolysaccharide content and proteome during colonization and shedding in the urine<sup>30,31</sup>, which suggests that priming in the renal milieu is required to adapt for survival and infectivity in the external environment. The rate of pathogen release is a crucial determinant of spillover risk, and care must be taken to appropriately formulate models that represent the rate of release for each route of transmission (BOX 1; Supplementary information S1 (box)).

Following the release of a pathogen from its reservoir host, the opportunity for spillover transmission is influenced by the duration of pathogen survival outside of its host, the extent of spatial dispersal through passive transport (for example, through water, on fomites or in the air), and possible pathogen reproduction or obligate developmental stages outside of the primary host (for example, *Yersinia pestis*, the causative agent of plague, must multiply within flea vectors before it can be transmitted to humans<sup>32</sup>). These processes can be represented as the probability that the pathogen (shed, harvested or colonized in a vector) survives and is infectious at a given point in time, and is dispersed or transported to a particular location (Supplementary

information S1 (box)). Spillover of pathogens that have short survival times (for example, influenza A virus when transmitted through the respiratory route)<sup>33,34</sup> may require close interactions between reservoir and recipient hosts. Consequently, spillover patterns in recipient hosts correspond to the prevalence patterns in reservoir hosts. By contrast, if pathogens survive for sufficient periods of time outside of their reservoir hosts, they may be dispersed beyond the home range of the host through fomites or environmental transport. In this case, the release of a pathogen from its reservoir host and human exposure to the pathogen may become disconnected in space and time. An example is the spread of aerosolized *Coxiella burnetii*



**Figure 2 | Barriers to spillover and dose–response relationships.** **a** | Determinants of spillover are being studied by researchers in many disciplines. **b** | A pathogen must overcome a series of barriers to transmit from one species to another. If any of these barriers is impenetrable, spillover cannot occur. Spillover of some pathogens requires that gaps (depicted as holes) in all of the barriers align within a narrow window in space and time (indicated by the blue arrow, see Supplementary information S2 (movie)). For other pathogens, protracted survival in the environment (for example, *Bacillus anthracis* spores<sup>109</sup>), or wide dissemination (for example, the spread of aerosolized *Coxiella burnetii* by wind<sup>35</sup>), may stagger the alignment of barriers to spillover. **c** | Top panel: hypothetical dose available over time for a given pathogen. In scenario 1 (dashed light blue line), the pathogen is excreted consistently from infected reservoir hosts. In scenario 2 (solid light blue line), the pathogen is excreted in regular but short high-intensity pulses over time. In

both scenarios, the mean dose over the time interval is the same. Bottom panel: the likelihood that this dose will translate into infection depends on the functional form of the dose–response relationship. If the dose–response relationship is linear (green line), these two excretion scenarios generate the same total probability of spillover over the time interval shown. However, for non-linear dose–response relationships, the total probability of spillover differs between scenarios. If the relationship is sigmoidal (red line), there is some probability of spillover whenever the dose exceeds zero (indicated by the intensity of the red shading in the top panel), but the total spillover probability in scenario 2 is markedly higher. In the extreme case in which the recipient host can be infected only by a dose that exceeds a sharp threshold, as suspected for *Bacillus anthracis*<sup>67,68,79</sup>, the pathogen in scenario 2 will spill over when the dose peaks above the threshold (blue solid line near peak), but the pathogen in scenario 1 will never spill over.

by wind, which can lead to outbreaks of Q fever in humans that live several kilometres from the livestock reservoir hosts<sup>35</sup>.

As illustrated by rabies virus, pathogenic *Leptospira* spp. and *E. coli* O157 (FIG. 3), the bottlenecks that hinder the transfer of pathogens between species depend on the ecology of the reservoir host and the pathogen, and the interactions among the determinants of spillover. For example, the primary driver of pathogen pressure for rabies virus is the prevalence of infection in key hosts (such as domestic dogs<sup>36</sup>). Nonlinearities in rabies transmission generate a threshold effect in susceptible host density below which the pathogen cannot persist. These thresholds can be used to set vaccination targets for disease elimination<sup>37</sup>. By contrast, pathogen pressure of *L. interrogans* is also affected by fluctuations in reservoir host density (such as rodents<sup>29</sup>), and prevalence and shedding from infected animals<sup>29</sup>. However, if human exposure occurs through mechanisms that aggregate and disperse pathogens shed by many individuals (through accumulation in the environment, sustained survival after exiting the host<sup>38</sup>, and dispersal through rain, rivers and flood waters<sup>39</sup>), the detailed dynamics in reservoir hosts do not matter because they get integrated out by the environmental reservoir. In this scenario, spillover risk is determined by the aggregate pathogen pressure, human behaviours that determine exposure and the integrity of within-human barriers to infection. For example, when flooding mobilizes *Leptospira* spp. during the wet season in Brazil, human exposures can become widespread and epidemics of spillover infection can occur<sup>40</sup>. During these extreme environmental events, control efforts must focus on preventing exposure to contaminated sources (for example, by wearing protective clothing and boots<sup>41</sup>) and reducing the infectious inoculum rather than reducing the source of pathogen shedding, as the release of *Leptospira* spp. into the environment by animal reservoirs occurs before the extreme precipitation. Similarly, pathogen pressure of *E. coli* O157 is affected by the density of its cattle host population<sup>42</sup>, by variation in shedding among individuals and by prevalence in herds<sup>43</sup>. Each of these factors can be highly skewed and seasonal<sup>44,45</sup>. If spillover events are driven by contact between humans and cattle, then variation in pathogen load among animals would interact with nonlinear dose–response functions to determine spillover risk (see below). However, this individual variation matters less if human exposure

### Box 1 | The mathematics of spillover

The opportunities for cross-species transmission are influenced by processes that occur at scales from molecules to landscapes (FIG. 1). These processes are subjects of intense study, and their characterization is complicated by their variability in space and time, nonlinear responses and interactions with outside factors. Consequently, it is impossible to integrate all of the determinants of spillover transmission — or to assess the effects of gaps in our knowledge about these determinants — without appropriate tools, such as mathematical and computational models<sup>107</sup>.

In Supplementary information S1 (box), we present a general mathematical model of the spillover process, which provides a template for integrating our knowledge of processes for specific disease systems. This model framework essentially translates FIG. 1 into mathematical expressions. It allows for variation in space and time, and uses different formulations for transmission through pathogen excretion, slaughter or arthropod vectors.

The mathematical model reflects the modular nature of the spillover process, as emphasized in the main text, while highlighting dependencies among factors in ways such as the following:

- Factors that are linked to disease ecology of the reservoir host and the mode of pathogen release determine the amount of pathogen released to the environment or vector.
- Pathogen survival and transport outside of the animal host, which give rise to pathogen pressure at a particular place and time, are modelled with simple probability kernels.
- Human risk behaviours determine how this pathogen pressure translates to exposure dose.
- The probability of infection for a given dose and route of exposure is encapsulated in the dose–response relationship (FIG. 2c).

Mathematically, the focal point of this process is the dose to which the recipient host is exposed. All upstream factors come together, with appropriate functional dependencies, to shape this dose. To a reasonable approximation, which is consistent with current practice in quantitative microbial risk assessment<sup>108</sup>, the consequent risk of infection can be modelled independently through the dose–response relationship.

occurs after human-mediated dispersal of the pathogen through irrigation, meat processing and food transportation<sup>46–48</sup>. In this instance, outbreaks of *E. coli* O157 are determined by the pathogen pressure on vegetables or in hamburger meat, potentially derived from many sources. As the dose that is required for *E. coli* O157 spillover is thought to be very low<sup>49,50</sup>, public health policies aim to completely eliminate pathogen pressure in food that is processed for human consumption<sup>50</sup>. To achieve this goal, interventions are focused on creating successive bottlenecks in several barriers to spillover, including decreasing cattle density, preventing faecal contamination during meat processing and increasing cooking temperatures to reduce exposure dose in ground beef<sup>43,47,51</sup>. Cumulatively, these efforts are usually successful, but high levels of shedding from cattle during summer can sometimes overwhelm interventions<sup>47</sup>.

**Exposure.** The next phase of spillover — exposure — bridges the upstream processes that generate pathogen pressure and the within-host processes in the recipient that determine whether a given dose generates a spillover infection (see below). The interaction between recipient hosts and pathogen pressure determines both the dose and the route of exposure. Different behaviours of the recipient host are relevant

to exposure through different routes of transmission<sup>52</sup>. Human behaviours, such as occupational interactions with reservoir host animals, the consumption of certain animal products or the use of particular environments, may increase the risk of infection<sup>53</sup>.

Exposure is often conceptualized as a simple point of contact. However, nonlinear interactions between pathogen pressure, human risk behaviour and environmental factors can lead to unexpected complexity, especially for vector-borne diseases. For example, in rats, both a high prevalence of *Y. pestis* and high mortality may be necessary to drive outbreaks of bubonic plague in humans. Widespread exposure of humans through flea bites occurs only after a decrease in the abundance of rats, which are the primary hosts of *Y. pestis* in peridomestic settings<sup>54</sup>. Indeed, historically, high rat mortality ('rat-fall') was an indication of an imminent human plague epidemic<sup>32</sup>. Thus, killing rodents in response to cases of bubonic plague in humans could inadvertently increase the severity of the epidemic<sup>54</sup>. Conversely, and controversially, zooprophylaxis, which involves diverting vector bites from humans by increasing the local population density of another animal host, may decrease the risk of human exposure<sup>55</sup>. For example, the presence of chickens and dogs in rural areas of Argentina

# PERSPECTIVES

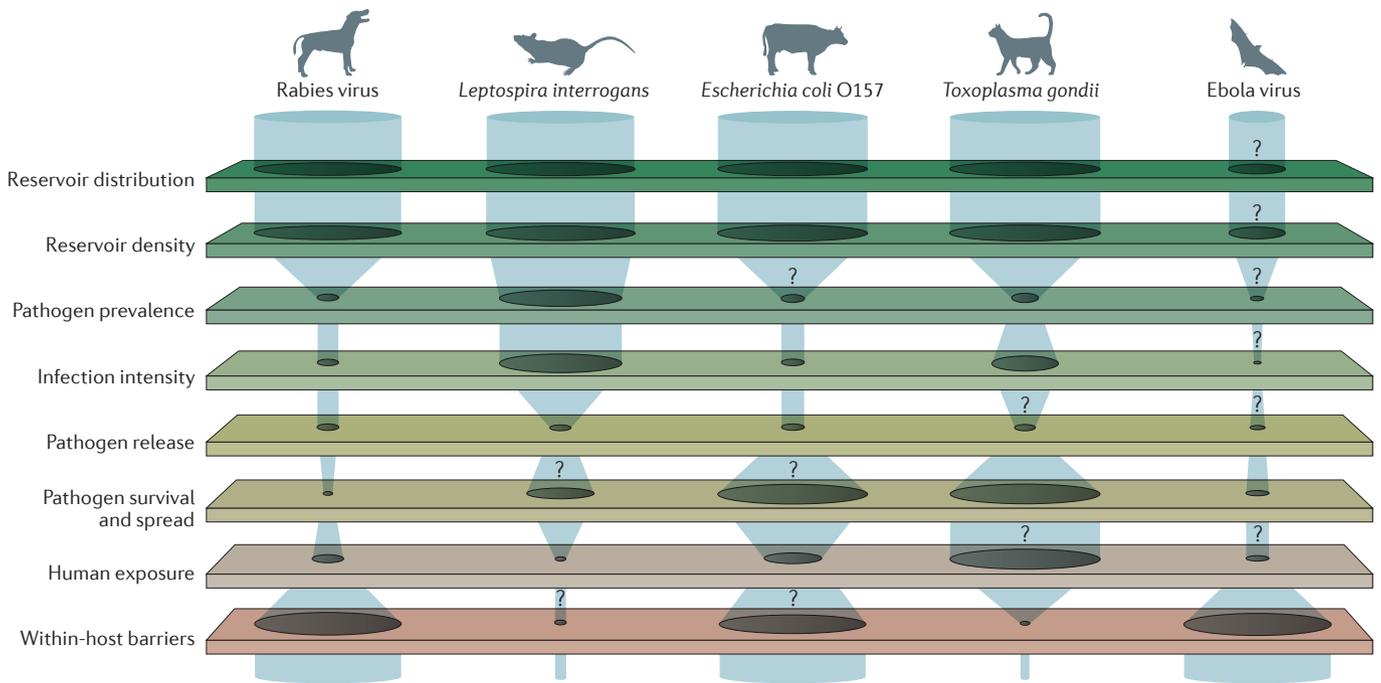
decreased the rate at which *Triatoma infestans* transmitted *Trypanosoma cruzi*, the causative agent of Chagas disease, to humans<sup>56</sup>. However, increasing the population density of reservoir hosts may also affect vector survival, vector abundance and pathogen prevalence in reservoir hosts, which, in turn, increases pathogen pressure and offsets reductions in human–vector contact rates<sup>56,57</sup>. These complexities highlight the need to understand the mechanisms that contribute to particular routes of spillover.

All of the factors that precede human exposure, mediated by human behaviour and environmental factors (FIG. 1), cumulate

in the dose to which a host is exposed at a given location and time (the integral of the pathogen pressure in space and time to which the host has been exposed (Supplementary information S1 (box)).

**Probability of infection.** Following cross-species exposure of a recipient host, the within-host barriers and their interactions with the strain of pathogen determine the functional relationship between the pathogen dose and the likelihood that an infection will establish. Within-host barriers to infection vary widely and depend on the specific combinations of pathogen, host species and

individual receptivity<sup>58</sup>. Physical barriers include the skin, mucous membranes, mucus, stomach acid or the absence of functional receptors that enable the pathogen to enter its target cells or tissues<sup>10</sup>. Interferon-induced and other innate immune responses may be triggered after the initial infection of a cell, resulting in protective mechanisms such as apoptosis or the induction of interferon-induced resistance in surrounding cells<sup>59</sup>. In addition, interfering defensive proteins in the host cell cytoplasm may block the replication of intracellular pathogens. In other cases, cells lack functional host factors that are required for the replication of the



**Figure 3 | Bottlenecks to spillover.** Different barriers permit or constrain the flow of pathogens from one species to another. The figure is illustrative, owing to the lack of sufficient data for more than one or two barriers for any given system. The width of the gaps in barriers represents the ease with which a pathogen can flow through the barriers and will vary depending on context. The question marks represent points at which the barriers are especially poorly understood and highlight gaps in our knowledge of some pathogens that are of global concern (for example, the lack of information on disease dynamics in reservoir hosts of Ebola virus). Many rabies virus reservoirs, such as domestic dogs, are widely distributed. The prevalence of rabies virus is generally low and the incidence of spillover closely tracks the prevalence of infection in the reservoir host. Rabies virus is almost always fatal to spillover hosts<sup>25</sup>. Interventions are usually aimed at reducing the prevalence in reservoir hosts through vaccination<sup>37</sup>. *Leptospira interrogans* survives in water and soil after being shed in the urine of a wide range of rodents and other reservoir hosts<sup>29</sup>. Key bottlenecks to the zoonotic spillover of this pathogen are exposure and within-host barriers. For example, during floods in Brazil, many humans that are exposed do not become infected, probably because the initial within-host barrier, the skin, is not penetrated<sup>41</sup>. However, once *L. interrogans* penetrates the skin (for example, through skin wounds), 1–10 leptospires may be sufficient to cause systemic infection<sup>110</sup>. Therefore, wearing protective clothing and boots is an effective control measure<sup>41</sup>. Important bottlenecks to *Escherichia coli* O157 spillover include

heterogeneous shedding from cattle<sup>43,44</sup> (although it is still unknown whether super-shedding is a characteristic of particular individuals or is a transient phase that occurs in most cattle<sup>42</sup>). In some contexts, exposure is an important bottleneck; for example, when the pathogen is eliminated from food through cooking. Widespread dispersal leads to uncertainties about the source of many outbreaks<sup>46,47</sup>, and weak within-human barriers enable low doses of *E. coli* to cause infection<sup>49,50</sup>. Humans are frequently exposed to *Toxoplasma gondii* carried by domestic cats and intermediate hosts, but the parasite rarely causes disease because most humans have strong within-host immunological barriers. Cats are widely and densely distributed, but the prevalence of *T. gondii* is low and cats shed oocysts only once in their lifetime<sup>111</sup>. However, sporulated oocysts survive in the environment for long periods of time<sup>112</sup>. Limiting exposure to oocysts may prevent spillover; however, this is challenging when it is unclear whether cats or the environment are the major sources of infection in humans<sup>111,113</sup>. Ebola virus has not been isolated from bats and the definitive reservoir bat species is unknown<sup>114</sup>; therefore, characteristics of infection in bats are unknown<sup>114,115</sup>. The pathogen is released through excretion or slaughter, then survives for up to a week, depending on the environmental conditions<sup>116</sup>. The most tractable bottlenecks for intervention may be the zoonotic exposure of humans through interaction with bats, bushmeat or the carcasses of other species<sup>97,117,118</sup>, because once exposed, the within-host barriers to Ebola virus may be extremely low<sup>119</sup>.

pathogen<sup>60,61</sup>. Even when pathogens can replicate within cells, several barriers can prevent their transmission to other cells<sup>62,63</sup> and thus the establishment of an infection. For example, avian influenza virus must pass through a series of within-host barriers to infect a human, including mucins in respiratory tract excretions, specific receptor molecules that constrain virus entry into cells and have different distributions in the respiratory tracts of different host species, suboptimal viral polymerase that restricts the ability of the virus to replicate in cells of the human respiratory tract, viral neuraminidase that is inefficient in its role in the release of influenza viruses from infected cells, and innate immune responses that are initiated early and that block infection in both infected and neighbouring cells<sup>63,64</sup>.

From an epidemiological perspective, these within-host interactions between zoonotic pathogens and hosts can be encapsulated by the functional relationship between pathogen dose and the probability of an infection. Although there is much to learn about dose–response relationships, they are expected to be nonlinear as, at minimum, they must saturate at high doses because the probability of infection cannot exceed one<sup>65</sup>. This nonlinearity imposes a filter on the dynamics of pathogen pressure and exposure (FIG. 2c). If the dose–response relationship is highly nonlinear, such that small changes in dose lead to large changes in the probability of an infection, then variation in any of the upstream factors that culminate in an exposure dose (including released dose, pathogen survival and human behaviour) may have disproportionate effects on the probability of spillover. Such effects could generate opportunities for targeted control measures. Moreover, nonlinear dose–response relationships may imply that infrequent high-intensity exposures are more likely to cause spillover infections than continuous low-intensity excretion. This phenomenon has been reported for occupational exposure to *Bacillus anthracis* aerosols; tannery workers who were exposed to infrequent high doses of *B. anthracis* spores in imported goat hair were more likely to die of anthrax than those who were exposed to frequent low doses of *B. anthracis* spores<sup>66–68</sup>. Conversely, if doses are far below the inflection point on the dose–response curve (FIG. 2c), then the system may be insensitive to changes in dose. If the dose–response function is close to linear, the total exposure dose over time is equal and host responses do not change as a consequence of early exposures, then longer-term exposure

to a low but constant dose may generate the same probability of infection as intermittent high-intensity exposures (FIG. 2c).

The genetic, immunological and physiological state of the host also can modulate the dose–response relationship. Immunosuppression (for example, due to AIDS, immunosuppressive drugs, co-infections or malnutrition) increases gaps in within-host barriers, which shifts dose–response curves and increases susceptibility<sup>69,70</sup>. For example, in immunosuppressed hosts, the decreased number or activity of lymphocytes can reduce the dose that is required to establish an infection with the widespread pathogen *Toxoplasma gondii*, or cause the loss of control of *T. gondii* infections that are usually kept in check by sustained immune pressure<sup>71</sup> (FIG. 3). Seasonality in human immune function (for example, enhanced baseline inflammation and altered cellular composition of the immune system in winter compared with summer) may also alter the permeability of within-host barriers by altering the magnitude and speed of immune responses<sup>72</sup>. Finally, the probability and severity of infection at a given dose are shaped by host genetics<sup>73</sup>; triathletes with a particular gene polymorphism were at increased risk of leptospirosis after swallowing lake water compared with athletes who lacked this polymorphism<sup>74</sup>.

Many of the interactions at the crossroads of exposure, inoculum dose and host response are poorly understood. Therefore, very little is known about the interactions between dose, timing of exposure and probability of infection. The current dose–response paradigm is based on discrete transient exposures, but the effects of protracted or cumulative exposure to environmental pathogens (for example, to low concentrations of *Leptospira* spp. in floodwater) are unclear<sup>75</sup>. Repeated low-dose exposure can increase host immunity to infection (for example, as postulated for poultry handlers who are exposed to avian influenza<sup>76</sup>, dairy farmers who are exposed to *E. coli* O157 (REF. 77) and mice that are exposed to continuous infections of parasites<sup>78</sup>). However, increases in immunity are not always observed; for example, such effects on immunity were not observed in tannery workers who were exposed to *B. anthracis*<sup>67,68,79</sup>. Moreover, it may be difficult to differentiate between a cumulative dose effect and the increasing opportunity to initiate an infection with each additional low-dose exposure (if each infectious unit has a probability of causing an infection that is above zero)<sup>20,80</sup>.

Once a pathogen has penetrated the within-host barriers to replicate and disseminate in the new host, the outcome of the infection may range from subclinical elimination of the microorganism to the death of the new host, and from dead-end spillover infection to sustained human-to-human transmission. For many important zoonotic pathogens, such as HIV or Zika virus, the transmission that drives the current public health crisis is human-to-human<sup>81,82</sup> and the events that led to spillover are long past. Although understanding disease severity and onward transmission is essential for understanding the consequences of emerging infectious diseases, these processes are beyond the scope of this article. Our current knowledge of the biological features of pathogens and characteristics of host–pathogen interactions that determine these outcomes are described elsewhere (for example, see REFS 83,84).

### Assessing zoonotic risk

When gaps in barriers to spillover are highly dynamic in time and space, they may vary asynchronously, so that the alignment of gaps in all barriers may be fleeting and spillover may seem random ([Supplementary information S2](#) (movie)). Research methods that group multiple barriers or integrate data over space and time may not capture these dynamics. For example, ecological niche models are often used to study zoonotic risk by assessing the distribution of reservoir hosts or vectors<sup>85</sup>, but this approach overlooks variation in downstream barriers that might drive risk. Alternatively, niche models that are based on the documented occurrence of spillover may capture the accumulated distribution of all conditions that enabled barriers to be breached over time (FIG. 1), but they cannot isolate the precise barriers that affect spillover risk (for example, see REF. 86). Therefore, niche models tend to overestimate the spatial range of spillover risk and do not readily enable extrapolation to novel conditions<sup>87</sup>. Examples of this include Hendra virus and Marburg virus, which can be excreted in discrete temporal and spatial pulses from their bat reservoir hosts<sup>20,88,89</sup>. However, for spillover, shedding must align with environmental and bat population conditions that generate levels of pathogen pressure that are sufficient to produce an infectious dose (FIG. 2), and with exposure behaviours and susceptibility of the recipient hosts. As some of these conditions vary among seasons and years, the pattern of outbreaks in livestock or humans has high spatial and temporal variability<sup>20,89</sup>. However,

as niche models often summarize risk across large areas and long durations, they overlook important heterogeneities and they lack the specificity that is required for public health intervention. Although niche models can help to identify regional-to-continental concentrations of risk<sup>90,91</sup>, risk assessments that are more quantitative and more precise with regard to space, time and which barriers they address are needed to guide concrete action.

Epidemiological investigations of spillover also need to account for conditions that are highly dynamic in space and time. If the alignment of gaps in all barriers is fleeting, delayed diagnoses or inconsistent case detection may delay outbreak investigations until the conditions that enabled spillover have changed. Similarly, investigations are sometimes triggered once the case count becomes high. These challenges differ among pathogens with different values of  $R_0$  (the basic reproductive number or expected number of secondary infections caused by a typical infected individual in a susceptible population). For supercritical pathogens with  $R_0 > 1$ , which can cause major epidemics through sustained transmission in human populations (for example, Ebola virus, Zika virus and the pandemic strain of severe acute respiratory syndrome coronavirus (SARS-CoV)<sup>4,81,92</sup>), spillover becomes challenging to study because a given human case is likely to be far removed in time or space from the spillover event that triggered an outbreak. Subcritical pathogens with  $0 < R_0 < 1$ , which cause self-limiting outbreaks or 'stuttering chains' in human populations (for example, monkeypox or avian influenza viruses<sup>93,94</sup>), raise distinct challenges because any given individual could have been infected by either an animal or a human source<sup>16</sup>. It is easiest to study the spillover of pathogens with  $R_0 = 0$  that are not transmitted between humans (for example, rabies virus or West Nile virus<sup>25,95</sup>), in which every case is an instance of spillover. The 2014–2015 Ebola virus epidemic in West Africa is a prime example whereby delayed response and investigation prevented researchers from reconstructing the conditions that initiated the human epidemic of a supercritical pathogen<sup>96,97</sup>. Ebola virus infection is an extreme example of spillover infection that only occurs during the rare alignment of gaps in barriers, and, accordingly, the precise determinants of risk are poorly understood (FIG. 3). By contrast, for other zoonoses, such as trypanosomiasis in some parts of Africa, incidence is high because the pathogen flows through consistently wide gaps in barriers to infection

(for example, common exposure to infected animal hosts and tsetse fly vectors, and low resistance in humans due to the ability of trypanosomes to neutralize or avoid human innate immune activity<sup>98,99</sup>). In all scenarios, irrespective of the frequency with which gaps align, the concept of hierarchical barriers can be used to organize and quantify the conditions that enable spillover.

The influence of particular barriers may vary in space and time, and this variation — coupled with data on realized spillover events — can help elucidate factors that shape infection risk, even in the absence of information on other barriers. In the westernmost province of the Democratic Republic of Congo, the observed lack of monkeypox spillover, despite high seroprevalence in the suspected reservoir hosts (*Heliosciurus* spp. and *Funisciurus* spp.), was attributed to cultural norms that forbade the consumption of small rodents<sup>100</sup>. The inconsistency between ecological data that suggested high pathogen pressure and epidemiological data that indicated a lack of spillover, focused attention on human behaviours that affect the probability of exposure. Research approaches that integrate data on multiple barriers are more likely to discern such behavioural effects.

Broad-scale discovery of novel microorganisms has the potential to characterize the pool of possible zoonotic pathogens and provide valuable baseline information<sup>101,102</sup>. However, each of the ~63,000 species of mammals, birds, reptiles, amphibians and fish<sup>103</sup> contains a multitude of infectious viruses, bacteria and parasites<sup>101,102,104–106</sup>. Although each of these microorganisms and parasites can be viewed as a potential pathogen, the vast majority may not cause disease in their natural hosts, and the extent to which they infect or cause pathology in other species, including humans, is unknown<sup>7,9,10</sup>. Therefore, discovery alone cannot address the potential risk of spillover. The translation of new discoveries of microorganisms into guidance for public health practitioners requires the identification of the barriers to microbial infection of humans, the conditions that facilitate the breaching of these barriers, and, therefore, the microbiological and environmental contexts that pose the greatest risk to human populations. For the foreseeable future, the greatest practical contribution of pathogen discovery and sequence characterization to the epidemiology of emerging pathogens is likely to be in the rapid post hoc identification of novel pathogens after spillover.

## Outlook

The framework presented in this Opinion article highlights that an important frontier in research on zoonotic spillover is to understand the functional and quantitative links among the determinants of spillover. To our knowledge, all of the processes that are necessary to achieve spillover have not been connected, compared and quantified for any single zoonotic pathogen. We address this gap, in part, by introducing a conceptual and quantitative model that can be used to integrate existing data, identify high-priority data gaps, investigate conditions that widen or align gaps in barriers to spillover, and identify the best gaps on which to focus intervention efforts. We suggest that future research focuses on developing case studies that contribute to fully quantifying the determinants of spillover and their linkages, with the goal of making operational contributions to risk assessment. We provide a mathematical framework that formalizes the ideas presented here to guide the formulation of mechanistic spillover models for particular zoonotic pathogens (BOX 1; [Supplementary information S1](#) (box)). We anticipate that this synthetic framework will provide a foundation for cross-scale data integration, transdisciplinary investigation, and a new body of theory on spillover that is necessary for risk assessment and public health planning.

*Raina K. Plowright is at the Department of Microbiology and Immunology, Montana State University, Bozeman, Montana 59717, USA.*

*Colin R. Parrish is at the Baker Institute for Animal Health, College of Veterinary Medicine, Cornell University, Ithaca, New York 14853, USA.*

*Hamish McCallum is at the Griffith School of Environment, Griffith University, Brisbane, Queensland 4111, Australia.*

*Peter J. Hudson is at the Center for Infectious Disease Dynamics, Pennsylvania State University, State College, Pennsylvania 16802, USA.*

*Albert I. Ko is at the Department of Epidemiology of Microbial Diseases, Yale School of Public Health, New Haven, Connecticut 06520–8034, USA.*

*Andrea L. Graham is at the Department of Ecology & Evolutionary Biology, Princeton University, Princeton, New Jersey 08544, USA.*

*James O. Lloyd-Smith is at the Department of Ecology & Evolutionary Biology, University of California, Los Angeles, Los Angeles, California 90095-7239, USA; and at Fogarty International Center, National Institutes of Health, Bethesda, Maryland 20892–2220, USA.*

*Correspondence to R.K.P. [raina.plowright@montana.edu](mailto:raina.plowright@montana.edu)*

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# **Exhibit G**

## Zoonotic and reverse zoonotic events of SARS-CoV-2 and their impact on global health

Khalid Munir<sup>a,b,†</sup>, Shoaib Ashraf<sup>b,c,†</sup>, Isra Munir<sup>d</sup>, Hamna Khalid<sup>e</sup>, Mohammad Akram Muneer<sup>b</sup>, Noreen Mukhtar<sup>a</sup>, Shahid Amin<sup>f</sup>, Sohaib Ashraf<sup>c,g</sup>, Muhammad Ahmad Imran<sup>g</sup>, Umer Chaudhry<sup>h</sup>, Muhammad Usman Zaheer<sup>i</sup>, Maria Arshad<sup>j</sup>, Rukhsana Munir<sup>k</sup>, Ali Ahmad<sup>l</sup> and Xin Zhao<sup>m</sup>

<sup>a</sup>PetLife Veterinary Professional Corporation, NJ, USA; <sup>b</sup>Department of Pathobiology, Riphah College of Veterinary Sciences, Riphah University, Lahore, Pakistan; <sup>c</sup>Wellman Center for Photomedicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA; <sup>d</sup>School of Dental Medicine, University of Pennsylvania, Philadelphia, PA, USA; <sup>e</sup>Department of Chemical and Biological Engineering, Villanova University, Villanova, PA, USA; <sup>f</sup>Animal Hospital of Loves Park, Loves Park, IL, USA; <sup>g</sup>Department of Microbiology, Shaikh Zayed Hospital Lahore, Lahore, Pakistan; <sup>h</sup>Royal (Dick) School of Veterinary Studies and Roslin Institute, Edinburgh, UK; <sup>i</sup>Food and Agriculture Organization of the United Nations, Country Office, Islamabad, Pakistan; <sup>j</sup>District Headquarter Hospital, Lahore, Pakistan; <sup>k</sup>Consultant Emergency Medicine, Russells Hall Hospital, Dudley Group of Hospitals NHS Trust, Dudley, UK; <sup>l</sup>CHU Sainte-Justine Research Center, Department of Microbiology, Infectious Diseases and Immunology, University of Montreal, Montreal, Canada; <sup>m</sup>Department of Animal Sciences, McGill University, Sainte-Anne-de-Bellevue, Canada

### ABSTRACT

Coronaviruses (CoVs) are enveloped, positive sense, single-stranded RNA viruses. The viruses have adapted to infect a large number of animal species, ranging from bats to camels. At present, seven CoVs infect humans, of which Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) is responsible for causing the Coronavirus Disease 2019 (COVID-19) in humans. Since its emergence in late 2019, SARS-CoV-2 has spread rapidly across the globe. Healthcare systems around the globe have been stretched beyond their limits posing new challenges to emergency healthcare services and critical care. The outbreak continues to jeopardize human health, social life and economy. All known human CoVs have zoonotic origins. Recent detection of SARS-CoV-2 in pet, zoo and certain farm animals has highlighted its potential for reverse zoonosis. This scenario is particularly alarming, since these animals could be potential reservoirs for secondary zoonotic infections. In this article, we highlight interspecies SARS-CoV-2 infections and focus on the reverse zoonotic potential of this virus. We also emphasize the importance of potential secondary zoonotic events and the One-Health and One-World approach to tackle such future pandemics.

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### Introduction

The novel coronavirus (2019-nCoV) was first detected in humans suffering from an atypical fatal pneumonia in early December 2019 in Wuhan, China. Although initial zoonotic transmission was suggested via the Huanan seafood market that also traded live wild animals [1, 2], the role of this market in spreading this virus remained unclear. Isolation of the virus from environmental samples collected from this market suggested the possibility of its crossing the species barrier from animal(s) to humans. On 7 January 2020, the 2019-nCoV was isolated from the nasal swab of a human patient [3], and re-named as SARS-CoV-2 by the *Coronaviridae* Study Group (CSG) of the International Committee on Taxonomy of Viruses (ICTV; [4]). The World Health Organization (WHO) named the resulting disease as COVID-19, an acronym derived from the

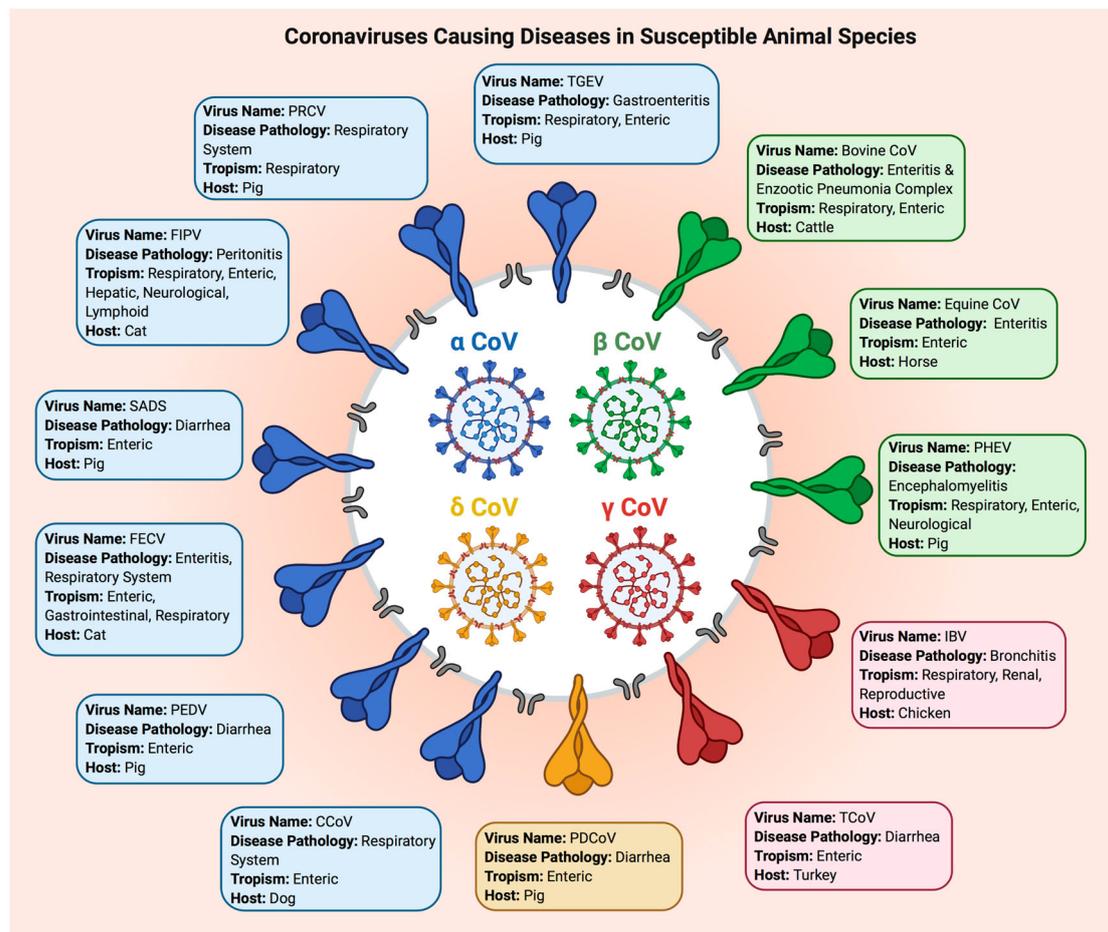
Coronavirus Disease of 2019. On 30 January 2020, the WHO declared the coronavirus outbreak as a Public Health Emergency of International Concern. With its rapid spread across continents, the WHO categorized the COVID-19 as a “Pandemic” on 11 March 2020. As of 24 August 2020, COVID-19 had caused over 816,535 deaths with more than 23,800,750 reported infections worldwide with a global case fatality rate (CFR) of 3.43% (covidvisualizer.com). Many countries including the USA and Canada have declared the COVID-19 epidemic as a “National Emergency” and have mobilized extra financial and public health resources to combat it.

### Animal coronaviruses

Coronaviruses (CoVs) are subdivided into four genera:  $\alpha$ ,  $\beta$ ,  $\gamma$  and  $\delta$ . Since late 1930s, different animal

**CONTACT** Shoaib Ashraf  [shoaib.ashraf@mail.mcgill.ca](mailto:shoaib.ashraf@mail.mcgill.ca); Ali Ahmad  [ali.ahmad@recherche-ste-justine.qc.ca](mailto:ali.ahmad@recherche-ste-justine.qc.ca); Xin Zhao  [xin.zhao@mcgill.ca](mailto:xin.zhao@mcgill.ca)  
#Authors contributed equally to the work and are joint first authors.

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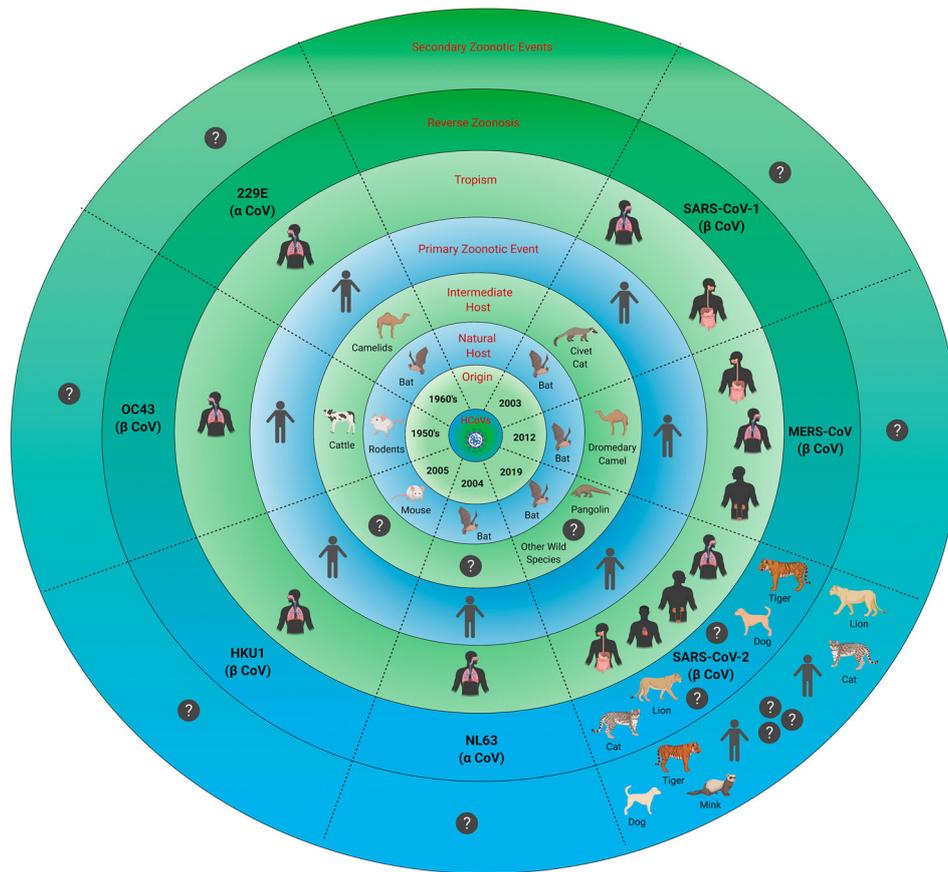
**Figure 1.** Selected important coronaviruses causing diseases in animal species. The figure shows different coronaviruses, their genera, main clinical symptoms, host species, and tissue/organ tropism. PEDV: Porcine Epidemic Diarrhea Virus; TGEV: Transmissible Gastroenteritis Virus; PRCV: Porcine Respiratory Coronavirus; FIPV: Feline Infectious Peritonitis Virus; FECoV: Feline Enteric Coronavirus; CCoV: Canine Coronavirus; PDCoV: Porcine Delta Coronavirus; TCoV: Turkey Coronavirus; IBV: Infectious Bronchitis Virus; PHEV: Porcine Hemagglutinating & Encephalomyelitis Virus; Equine CoV: Equine Coronavirus; BCoV: Bovine Coronavirus; Severe Acute Diarrhea Syndrome Coronavirus: SADS-CoV.

CoVs have been isolated from various infected animals and avian species including rodents, cattle, pigs, cats, camels, bats, dogs and chickens and turkeys [5–7]. The viruses cause respiratory, reproductive, gastrointestinal, hepatic, neurological and/or other systemic pathologies in a wide range of animal and avian species (Figure 1; [5–7]). Phylogenetic analyses of two porcine CoV, Porcine Respiratory Virus (PRCV) and Transmissible Gastroenteritis Virus (TGEV) revealed that the former originated from the latter through a deletion in a part of the Spike (S) protein that altered the tissue tropism of the virus from the gastrointestinal tract to the respiratory tract [5–10]. The deletion also resulted in reduced virulence of the new variant. It is noteworthy that all animal (and human) coronaviruses belong to the  $\alpha$  and  $\beta$  genera with the exception of one, the Porcine Delta CoV (PDCoV; Figure 1). The PRCV, porcine enteric diarrhea virus (PEDV) and the more recently emerged swine acute diarrhea syndrome coronavirus (SADS-CoV) [7] cause significant economic

losses to swine industry. The CoVs belonging to the  $\gamma$  genus mainly infect domestic birds. The avian infectious bronchitis virus (IBV), the first CoV detected in 1937 in chickens [7–9], affects the respiratory, renal and reproductive systems of chickens. Delta CoVs mainly infect wild birds, including bulbul coronavirus and sparrow coronavirus [6, 7, 10].

### Zoonotic origins of human coronaviruses

At present, seven species of CoVs are known to infect humans (Figure 2). Four of these human CoVs (HCoVs) namely 229E, OC43, NL63 and HKU1 are endemic, and cause 15–30% cases of common cold in humans, mostly during winter and early spring [5, 8–13]. The 229E strain B814 was the first HCoV identified in 1966 in the nasal swab of a human patient, who had contracted “common cold” [5, 8–15]. HCoV-OC43 was isolated in 1967 from the organ culture from an infected human [5, 8, 9, 13–15]. Comparative phylogenetic analyses of human and animal CoVs



**Figure 2.** Human coronaviruses. The figure shows seven human coronaviruses, their origins, natural reservoirs, intermediate hosts, tissue/organ tropism and reverse zoonosis along with primary and potential secondary and tertiary zoonotic events. An interrogative sign (?) indicates unknown or unidentified.

suggest that 229E and OC43 jumped their animal reservoirs (bats and cattle, respectively) to infect humans within the last 200 years ([8, 9, 11–15]; Figure 2). HKU1, isolated in 2004 from an elderly patient in Hong Kong, is believed to have originated from mice [5, 8, 9, 14, 15], while NL63, isolated in the same year from a seven-month old child in the Netherlands, jumped from bats to an unidentified intermediate host before crossing species barrier to humans ([5, 13, 14]; Figure 2). Within the last two decades, three  $\beta$ -CoVs have jumped from animal reservoirs directly or through intermediate hosts to cause severe diseases in humans; these are Severe Acute Respiratory Syndrome coronavirus (SARS-CoV-1) [14–21], Middle East Respiratory Syndrome coronavirus (MERS-CoV) [19–20] and the most recent being SARS-CoV-2 causing COVID-19 in humans ([4, 12, 13, 20, 21]; Figure 2). The first case of SARS, presenting with atypical pneumonia, was documented in late 2002 in the Guangdong province of China [5, 14, 17, 18, 20]. The SARS epidemic caused 8,096 reported cases with 774 deaths, in many countries of the world [17–20]. MERS, first reported in Saudi Arabia in the year 2012, caused only 2521 cases with 866 deaths. It proved more fatal than SARS-CoV-1 with CFR 34% versus 11% for MERS [17–20, 22]. SARS-CoV-1 evolved to jump the species barrier through

intermediate hosts “masked palm civets and raccoon dogs” causing epidemic, while MERS-CoV jumped through the intermediate host “dromedary camels” to infect humans ([5, 14, 19, 20]; Figure 2). MERS cases still occur periodically, likely resulting from occasional spill-over from the intermediate host “dromedary camels” [5, 12–14, 18–20, 22].

SARS-CoV-2 is more contagious compared to SARS-CoV-1 and MERS-CoV [5, 12, 20]. The basic reproductive number ( $R_0$  value) of SARS-CoV-2 is still controversial. The early estimates of  $R_0$  value for SARS-CoV-2 ranged from 2.2–3.1 [23, 24]. The recent estimates, however, indicate that the number of SARS-CoV-2 infected individuals doubles every 2.4 days during the early epidemic, and  $R_0$  is likely to range from 4.7–6.6 [25–28]. In a recent report,  $R_0$  of 3.54 was estimated for SARS-CoV-2 in the early outbreak in Wuhan, China [29] that is much higher than those reported for SARS-CoV-1 and MERS; the authors identified two key features of the outbreak in Wuhan: high covertness and high transmissibility of the SARS-CoV-2 infections [29]. Effective multi-pronged interventions and mitigation measures have considerable positive effects on controlling the outbreak i.e. decreasing the  $R_0$  value [29]. The higher transmission rates of the virus imply that short-term control measures (lockdowns, self-isolation and

quarantines) have to be replaced by long-term measures through effective prophylactic vaccine [25, 27–29].

Although bats are considered a natural reservoir of more than 5,000 diverse CoVs, only about 500 of them have been identified [5, 12, 14, 21, 30]. Based on comparative phylogenetic analyses, bats are considered the most likely natural reservoirs of SARS-CoV-1 and MERS-CoV. Bats have co-evolved with viruses for millions of years. The co-evolution has led bats to constitutively express higher levels of type I and type III interferons in their body cells. The interferons are known for inducing a large variety of antiviral genes, called Interferon-stimulated genes (ISG), which limit viral replication [5, 13, 16]. On the other hand, bats induce a very subdued tissue destructive and pathogenic inflammatory response to viruses. Viral infections in bats do not produce excessive amounts of cytokines and other pro-inflammatory mediators that are responsible for causing disease [5, 13, 16]. Furthermore, bats also exert attenuated responses to several pathogen-associated (e.g. viral RNA) and danger-associated molecular patterns (e.g. cytosolic DNA). It is noteworthy that a subset of ISG, such as RNA-dependent adenosine deaminases (ADARs) and apolipoprotein B mRNA editing enzyme catalytic polypeptide-like (APOBEC) family genes, promote mutations in the viral RNA leading to the emergence of novel viral strains, and at the same time attenuating host's innate immune responses to viral RNA [31, 32]. Thus, the persistence of viral infections, increased RNA editing, and longer life span of bats increase the probability of viral mutations and recombination events, which potentially contribute to the emergence of infectious and pathogenic CoV strains for other species. It is not surprising that bats act as reservoirs for CoVs as well as for many other highly pathogenic viruses, including rabies and hemorrhagic fever viruses [5, 11–14].

Unlike in bats, CoV infections in humans show a wide spectrum of disease severities. They may be asymptomatic, mild or severe, and may result in death [11, 16]. The severity of the disease depends upon the degree to which the infected host can mount an antiviral response without eliciting a self-destructive inflammatory response [11, 12]. The factors that determine nature of the host response could be both of viral and host origins [11, 16, 33]. A viral strain that has been circulating in the host and hence adapted to it, will be less pathogenic. Host's genetic propensity to exert excessive inflammatory response and the presence of pre-existing chronic inflammatory conditions (e.g. obesity, old age, cardiovascular disease, etc.) are known to aggravate the disease severity in COVID-19 patients [11, 12, 16]. Recent studies have shown that a prior exposure of humans to other Coronaviruses (SARS and/or

“common cold”-causing ones), induces cross-reactive antibodies and memory T cells that protect them when they contract SARS-CoV-2 infection [34]. About 20–50% of humans were shown to have such protection; they are likely to have no or mild clinical symptoms upon infection with SARS-CoV-2.

Similar to other RNA viruses, CoVs are prone to random mutations as they possess a relatively large RNA genome with a limited proof-reading activity. The mutation rate in SARS-CoV-2 (<25 mutations/year) is, however, less than that of influenza A virus ( $\geq 50$  mutations/year; [35, 36]). Recent studies suggest that SARS-CoV-2 continues to evolve as new mutation hotspots/ mutated strains of this virus are emerging in different parts of the world [35, 37]. The ultimate aim of viruses such as SARS-CoV-2 is to attain a point of equilibrium with their host and become endemic without causing high mortality in a susceptible host population. European, North American and Asian viral strains may possibly coexist, each characterized by a different mutation patterns in various viral genes, including RNA-dependent – RNA polymerase (RdRp) and Spike [35, 37]. The characterization of viral mutations is important not only for understanding viral drug resistance, immune evasion and pathogenesis-related mechanisms, but also for the development of vaccines, and designing antiviral drugs and diagnostic assays [35, 37].

### SARS-CoV-2 interspecies infections

Since the initial reports of mysterious pneumonia (COVID-19 pneumonitis) from Wuhan in China, there has been significant debate on why SARS-CoV-2 infects humans, and several hypotheses have been proposed. Through their Spike (S) protein, all CoVs bind their receptors on host cells and initiate the infection. The cleavage of S protein two segments (S1 and S2) by a host protease is essential for the infection. S1 carries the receptor-binding domain (RBD), which determines its specificity for the viral receptor on host cells. Mutations in S protein of SARS-CoV-2, due to natural selection, might have resulted in its higher affinity for human angiotensin converting enzyme-2 (ACE2) receptors [21]. The receptors are expressed in nasal mucosa, bronchus, lung, heart, esophagus, kidney, stomach, urinary bladder, testes and ileum [38], making these human organs highly vulnerable to infection with SARS-CoV-2.

It has been well known that the amino acid sequences of the cleavage peptide at the S1 and S2 junction determine the peptide's susceptibility to different host proteases, and contribute to viral tissue tropism, host range and pathogenesis. As mentioned above, the surface unit S1 binds to a cellular receptor, while the transmembrane unit S2 facilitates fusion of the viral membrane with cellular membrane. SARS-

CoV-2 has acquired a polybasic cleavage site containing arginine residues at the S1/S2 junction. The acquisition is an important evolutionary step necessary for the viral cross over to humans [21, 39, 40]. The polybasic site is important for several reasons. First, the site enables cleavage of S protein into S1 and S2 segments by furin, a ubiquitous protease, facilitating rapid viral dissemination from lungs to other tissues. Second, residues in the cleavage site influence 3D structure of S-protein, its furin binding affinity and alter viral virulence. Third, proteolytic cleavage of SARS-CoV-2 S-protein by furin is a prerequisite for subsequent activation (cleavage) of S2 by another host cell protease, the Transmembrane Serine Protease 2 (TMPRSS2), an essential step for viral entry into a host cell. Last but not the least, the SARS-CoV-2 S1/S2 cleavage site is identical to the furin-cleavage site present in the human epithelial sodium channel  $\alpha$ -subunit (ENaC- $\alpha$ ) [41]. In distal lung airways, ENaC is known to play a key role in controlling fluid reabsorption at the air-liquid interface. The proteolytic activation of ENaC- $\alpha$  by furin is required for the functional activation of this channel. It has been postulated that the viral S protein competes with ENaC- $\alpha$  for furin engagement leading to poor fluid reabsorption in the lungs of COVID-19 patients [41].

The importance of a polybasic furin cleavage site for tissue tropism and viral pathogenicity has been well documented in avian influenza A viruses. Analogous to the SARS CoV-2 S protein, the hemagglutinin (HA) of the Influenza viruses needs cleavage into HA1 and HA2 segments for their entry into host cells [42]. The viruses have been classified into low – or high-pathogenic avian influenza viruses (LPAIVs or HPAIVs, respectively) [42]. The LPAIVs cause asymptomatic or mild infections whereas HPAIVs cause severe systemic infections in poultry with high mortality. Remarkably, the LPAIVs possess a monobasic (usually a single arginine) cleavage site at the HA1/HA2 junction. The site is cleaved by trypsin and trypsin-like proteases, whose expression is restricted to avian respiratory and intestinal tract tissues [42]. On the other hand, the HA of HPAIVs contains a polybasic motif, which is cleaved by ubiquitously expressed proprotein convertases such as furin leading to severe systemic infections with high mortality. Interestingly, HPAIV strains emerge from LPAIV by insertion of multiple basic amino acids at the cleavage site loop. Thus, the acquisition of a polybasic cleavage site is an essential feature for the evolution of HPAIV from LPAIV.

Given the fact that SARS-CoV-2 is the only virus among SARS-related viruses whose S protein contains a peculiar furin cleavable polybasic cleavage site, the feature most likely contributes to the viral transmissibility, zoonotic potential, wide-spread tissue distribution and a wide spectrum of clinical symptoms. A

recent study suggests that a D614G mutation in the S-protein, which renders S protein more susceptible to cleavage by furin and TMPRSS2, is linked to a higher transmission rate of SARS CoV-2 [43, 44]. In addition to SARS CoV-2, many other human viruses of medical importance such as HIV-1, measles virus, respiratory syncytial virus, and Ebola virus require furin for cleavage and activation of their receptor-binding surface glycoproteins [42]. Unfortunately, because of its essential role in a wide array of cellular functions, furin cannot be targeted for devising antiviral strategies.

SARS-CoV-2 shares 96.2% identity at the nucleotide level with RaTG13, a CoV detected in horseshoe bat species, *Rhinolophus sinicus*; this virus, however, has not been detected in humans [21]. Although horseshoe bat has been proposed to be the natural host of SARS-CoV-2, no direct evidence on the existence of SARS-CoV-2 infection in the bats is documented to date. Despite the homology, the RaTG13 RBD is very divergent from that of the SARS CoV-2. Possibly due to selective pressure, the SARS-CoV-2 RBD, after evolving in horseshoe bats, has evolved further in a non-bat intermediate animal species before its zoonotic transfer to humans. In this regard, it is interesting to note that the SARS CoV-2 RBD is very similar to the one found in the SARS-related  $\beta$ -CoVs of Malayan pangolin [45–48], an endangered mammalian species. The viral sequences were found in archived samples of pangolins, who, similar to COVID-19 patients, had exhibited clinical symptoms such as cough and shortness of breath [46–48]. Moreover, there was evidence of vertical transmission of the SARS-related  $\beta$ -CoVs in pangolins, suggesting virus circulation in this natural population [48]. However, testing of throat and rectal swabs from 334 pangolins sampled from the market's upstream supply chain, did not yield any positive PCR results for this CoV's nucleic acid sequences [46], suggesting that positive samples from pangolins in the market may have resulted from exposure to infected humans, wildlife or other animals. Thus, the existing evidence does not conclusively support the hypothesis that RaTG13 or pangolin  $\beta$ -CoV is the immediate parental virus of SARS-CoV-2. A recent phylogenetic analysis indicates a strong purifying selection around SARS-CoV-2 RBD and other genes among bat, pangolin, and human CoVs through recombination event(s) with CoVs from pangolins giving SARS-CoV-2 surface protein the ability to infect human cells [49]. It is likely that SARS-CoV-2's RBD became optimized through pre-adaptation in pangolins for binding to human ACE2 receptors with high affinity. Biophysical and structural evidence suggests that the SARS-CoV-2's RBD is likely to bind human ACE2 with 10–20-fold higher affinity than that of SARS-CoV-1 [21, 45, 50–52]. To date, there is not enough scientific evidence to accurately explain the

original route of SARS-CoV-2 transmission to humans, which may involve an un-identified intermediate host. Further investigations are required to establish an evolutionary pathway of SARS-CoV-2 in bats, pangolins and/or other mammals. Since the cat ACE2 gene is the closest to the human's among non-primate animals, and can potentially bind with both SARS CoV-1 and SARS CoV-2 S proteins [53], it is important to monitor the presence of SARS-CoV-2 infection in cats because human patients with COVID-19 may potentially transmit this virus to cats.

The current concept is that parental viruses of HCoVs are archetypically non-pathogenic in their natural reservoir host(s) but become pathogenic after their transmission to a new host species. With further evolution, the viruses adapt to the new host and become more transmissible and less pathogenic [5, 43, 44]. It is therefore possible that a progenitor of SARS-CoV-2 jumped into humans and adapted from being more virulent to a more transmissible viral strain responsible for the current pandemic [21, 43, 44]. It is important to note that SARS-CoV-2 shows pathogenicity less than that of the SARS-CoV-1 and MERS-CoV but a transmissibility potential similar to or greater than that of the – community-acquired HCoVs (NL63, 229E, OC43, and HKU1) [5]. It is highly probable that the virus in humans will continue to evolve on this line and adapt further to humans and become less pathogenic unless intervened by therapeutics and/or prophylactic vaccines.

The dynamics of viral quasi-species resulting from genetic variation, competition and selection might have played a role in SARS-CoV2 adaptation to infect human cells. The quasi-species phenomenon has been reported for several RNA viruses including SARS CoV-1 and MERS-CoV [54, 55]. A recent genomic analysis of 103 viral isolates suggests that SARS-CoV-2 has evolved into S and L types [56], although the clinical significance of these two types is uncertain. It is possible that one strain type is more pathogenic than the other. Several genotypes, antigenic types and pathotypes of SARS-CoV-2 are possibly circulating among human populations. Future studies involving a large number of viral isolates might help to characterize genotypes and potential antigenic variants of this virus. The characterization will have important implications for the development of therapeutics, vaccines and diagnostic approaches.

### SARS-CoV-2: experimental infections

These infections are important to investigate pathogenic mechanisms of the virus, host immune response and efficacy of different drugs and vaccines. In this regard, structural modelling of the SARS-CoV-2 S protein and ACE2 receptors indicates that

the virus could bind and perhaps infect bat, civet, monkey and swine cells [57]. However, host range projections based on modelling are sometimes not correct and require *in-vivo* studies in animals to determine the host range of the virus [30]. Based on structural modelling of these proteins, Asian and African primates are likely more susceptible to SARS-CoV-2 compared to the South and Central American primates [51]. On the bases of viral genome sequence analyses, and structural and biochemical studies, it seems more likely that the SARS-CoV-2's RBD binds with high affinity to ACE2 from humans and ferrets [52, 57–59, 60–62]. In concordance with these findings, Macaques (*Macaca fascicularis* and *Macaca mulatta*), ferrets and Syrian golden hamsters were not only found to be highly susceptible to experimental infection with SARS-CoV-2 but these animals could also transmit the infection to their cage mates (Table 1; [51, 57–59]). Macaques develop respiratory signs very similar to those of COVID-19 patients [51] whereas in Syrian golden hamsters and ferrets, SARS-CoV-2 infections cause none or mild respiratory signs [57–59]. These animal species appear to be suitable animal models for investigations on COVID-19 [51, 58, 59]. Recently, North American deer mice (*Peromyscus maniculatus*) was also shown to be susceptible to experimental infection with SARS-CoV-2 [60]. ACE-2 receptors of these mice possess key amino acid residues that allow cell binding to SARS-CoV-2 S protein. However, the risk of reverse zoonosis and/or potential role of this animal species as a reservoir for SARS-CoV-2 needs further investigation. Initial findings suggest that chickens, ducks, turkeys and pigs are refractory to infection by SARS-CoV-2 under experimental conditions [57].

Recently, it was shown that the bat intestinal organoids (more specifically enteroids) were susceptible to infection with SARS CoV-2 and showed cytopathic effects [63]. This is not surprising considering 80.5% amino acid sequence similarity between human and horseshoe bat ACE-2 receptors. The establishment and characterization of the bat enteroids that simulate the cellular composition of the bat intestinal epithelium might allow rapid and robust isolation and study of SARS-CoV-2 isolates or its progenitor(s) with higher efficiency than Vero E6 cells; later being the most commonly used cell line for SARS-CoV-2 isolation and characterization [63]. In addition, the authors also reported active SARS-CoV-2 replication in human enteroids, suggesting that human intestinal tract might be an additional route for viral transmission [63]. Whether the intestinal epithelial cells are primarily infected with SARS-CoV-2 via the oral–fecal route or enteric infection occurs post-respiratory infection needs to be investigated.

**Table 1.** Animal Species Susceptibility to SARS-CoV-2.

Species	Susceptibility	Infection type	Clinical signs	Transmission	References
Lion/Tigers	High	Natural	None or mild (mild respiratory disease and dry cough)	Animal to animal, human to animals; virus shed in feces and perhaps respiratory secretions	[65, 66, 70]
Dogs	Low	Natural/ Experimental	None or very mild (respiratory signs possible; comorbidities may increase the susceptibility or severity of signs)	None reported; dogs may shed virus in nasal secretions	[57, 64–70]
Domestic Cats	High	Natural/ Experimental	None or mild (mild respiratory signs such as sneezing, transparent ocular discharge, and lethargy; presence of other respiratory pathogens or comorbidities may increase the severity of the signs)	Cat to cat; cats shed virus in their nasal secretions and feces; air-borne transmission reported among cage mates	[53, 57, 64–66, 68, 70–73]
Poultry (chickens and ducks)	None	Experimental	None	None	[57, 80]
Pigs	None	Experimental	None	None	[57, 80]
Ferrets	High	Experimental	None or mild (sneezing, elevated temperature, reduced activity and occasional cough)	Ferret to ferret; ferrets shed virus in nasal secretions, saliva, urine and feces; air-borne transmission among cage mates reported	[52, 57, 59, 80]
Rhesus Macaques ( <i>Macaca fascicularis</i> and <i>Macaca mulatta</i> )	High	Experimental	Moderate signs (irregular respiratory pattern, reduced appetite, hunched posture, pale appearance, dehydration, elevated temperature and weight loss as well as pulmonary infiltrates evident on lung radiograph)	Animal to animal; virus is shed in saliva, nasal secretions and feces	[51]
Fruit Bats ( <i>Rousettus aegyptiacus</i> )	High	Experimental	None or mild (rhinitis)	Bat to bat; fruit bats shed virus via respiratory, oral and fecal routes	[80]
Farmed Minks	High	Natural	None or moderate to severe signs (gastrointestinal and respiratory signs, pneumonia and increased mortality rate)	Human to mink, mink to mink, mink to cat possible, mink to human possible; minks shed virus in respiratory and oral secretions as well as in feces	[66, 74]
Golden Syrian Hamsters	High	Experimental	Mild (progressive weight loss, lethargy, ruffled furs, rapid breathing and hunched back posture)	Hamster to hamster; hamsters shed virus in respiratory secretions and feces	[58]
Deer Mice ( <i>Peromyscus maniculatus</i> )	High	Experimental	None or very mild (ruffled fur)	Mice to mice; mice shed virus in nasal secretions, saliva and feces	[60]

## Reverse zoonosis (Zooanthroponosis) and secondary zoonosis

Sporadic detection of natural SARS-CoV-2 infections together with successful experimental infections of certain animals raises concerns about reverse zoonosis (also termed as zooanthroponosis: transmission of the infection from humans to animals) as well as about secondary zoonotic events (transmission of the infection from animals back to humans). Several cases of dogs, cats and zoo animals have tested positive for SARS-CoV-2, mostly as a result of close contact with infected humans (Table 2; [64–66]). However, the occurrence of natural infections in these animal species has not been ruled out. There is a limited information available on clinical manifestations of SARS-CoV-2 in animals. The existing evidence suggests that the clinical manifestations may range from covert infections to symptomatic disease with signs that may include coughing, sneezing, respiratory distress, nasal discharge, ocular discharge, vomiting or diarrhea, fever, and lethargy, etc. (Table 1). The detection of asymptotically prevalent infections in companion animals, and estimation of their proportionate contribution in the spread of SARS-CoV-2 to humans and other animal species, if any, requires further investigations.

A report from Hong Kong in February 2020 suggested the possible presence of SARS-CoV-2 infection without any signs of illness in two dogs (Table 2; [67]); the owner of these dogs was previously diagnosed with COVID-19. The first case was a 17-year old Pomeranian breed dog, who tested positive for SARS-CoV-2 RNA by RT-PCR on multiple nasal and oral swabs. However, the virus could not be isolated from the dog's samples; mere presence of viral RNA does not decisively confirm active infection; serological testing, virus isolation and/or serial quantification of viral nucleic acids are required to confirm the infection. Although the dog tested negative on subsequent RT-PCR testing, seroconversion was noted in the initial sample, but additional testing was not possible due to unavailability of convalescent serum; the geriatric dog passed away three days later presumably due to some other underlying health problems. It was therefore concluded that the dog either had a low-level of infection or was contaminated with SARS-CoV-2 by close contact with and/or exposure to an infected person. The second case was a two-year old German Shepherd dog, who tested positive by RT-PCR in quarantine after its owner was confirmed to have COVID-19 [67, 68]. The first dog in the US reported to test positive for SARS-CoV-2 was a six-year old male German Shepherd, whose owner had confirmed COVID-19 (Table 2; [69]). The dog tested positive in mid-April 2020 and was euthanized on 11 July 2020. Although the dog

tested negative on RT-PCR for SARS-CoV-2 five days later, he did develop anti-SARS-CoV-2 antibodies indicating he had active infection. This dog showed signs of muco-purulent nasal discharge with laboured breathing and lethargy [69]. The additional signs noted were blood in the urine, clotted blood in the vomit, troubled walking and weight loss. This dog was also diagnosed with lymphoma and heart murmurs [69]. This case raised two important questions. First, what signs (if any) in this dog were due to SARS-CoV-2 infection, and second, whether comorbidities such as heart problems, or cancers, play any role in increasing the susceptibility of companion animals to SARS-CoV-2 infection. Research has shown that dogs exposed to SARS-CoV-2 could produce anti-SARS-CoV-2 antibodies without exhibiting symptoms of COVID-19 [57, 68, 70].

In March 2020, the SARS-CoV-2 RNA was detected in the feces and vomit contents of a cat by RT-PCR in Belgium (Table 2; [70]). The cat belonged to an owner who tested positive for SARS-CoV-2. The cat exhibited transient respiratory and gastrointestinal disease one week after the owner became symptomatic for COVID-19 [70]. Since no information on virus isolation, seroconversion and blood results was available at the time of this report, it was difficult to establish an association between the cat's clinical signs and active SARS-CoV-2 infection. On 1 April 2020, a pet cat tested positive for SARS-CoV-2 without showing any clinical signs of illness in Hong Kong after her owner was confirmed to have COVID-19 [70]. On April 05, 2020, a four-year old Malayan tigress at the Bronx Zoo in New York developed dry cough and tested positive for SARS-CoV-2 (Tables 1 and 2; [70]). Five other tigers and lions showed mild signs of respiratory illness and later recovered completely ([65, 66, 70]; Figure 2; Table 2). A zoo employee, an asymptomatic carrier of SARS-CoV-2, was deemed responsible for transmitting the virus to these zoo animals. On 22 April 2020, two domestic cats tested positive for SARS-CoV-2 in the USA, one cat contracted the infection from the virus-positive owner; the other cat presumably got infected from a covertly infected human [71]. As of 14 August 2020, 14 cases of dogs and 13 cases of domestic cats in the USA have tested positive for SARS-CoV-2 infection using RT-PCR or virus neutralization antibody tests. All these companion animals had exposure to either a covertly infected or confirmed human(s) with COVID-19 [65]. It has been shown that under experimental conditions, domestic cats are susceptible to infection with SARS-CoV-2 and can transmit the virus to other cats via droplet or short-distance aerosol ([57, 70]; Table 1); the susceptibility of cats to SARS-CoV-2 is explained by the fact that feline ACE-2 receptor differs only by three amino acids from that of humans [53]. According to a report, SARS-CoV-2

**Table 2.** Reverse zoonosis cases of SARS-CoV-2 reported in animals.

Case #	MM/DD/YYYY	Possible source of infection <sup>d</sup>	Animal	Region/Country	References
1	02/27/2020	Pet Owner	Dog <sup>ab</sup>	Hong Kong	[66–68, 70]
2	03/18/2020	Pet Owner	Dog <sup>abc</sup>	Hong Kong	[66–68, 70]
3	03/18/2020	Pet Owner	Cat <sup>a</sup>	Belgium	[66, 68, 70]
4	03/27/2020	Zoo Employee	Tiger <sup>a</sup>	NY, USA	[64–66, 70]
5	03/27/2020	Zoo Employee	Lion <sup>a</sup>	NY, USA	[64–66, 70]
6	03/30/2020	Pet Owner	Cat <sup>ab</sup>	Hong Kong	[66, 70]
7	04/01/2020	Pet Owner	Cat <sup>ab</sup>	NY, USA	[65, 66]
8	04/02/2020	Pet Owner	Cat <sup>b</sup>	China	[66]
9	04/04/2020	Zoo Employee	Tiger <sup>a</sup>	NY, USA	[64–66, 70]
10	04/06/2020	Pet Owner	Cat <sup>ab</sup>	NY, USA	[65, 66]
11	04/15/2020	Zoo Employee	Lion <sup>a</sup>	NY, USA	[66, 70]
12	04/22/2020	Pet Owner	Cat <sup>a</sup>	NY, USA	[65, 66]
13	04/22/2020	Pet Owner	Cat <sup>a</sup>	NY, USA	[65, 66]
14	04/26/2020	Farm Worker	Mink <sup>abc</sup>	The Netherlands	[66, 74]
15	04/28/2020	Pet Owner	Dog <sup>a</sup>	NC, USA	[65, 66]
16	05/01/2020	Pet Owner	Cat <sup>a</sup>	France	[66]
17	05/08/2020	Pet Owner	Cat <sup>a</sup>	Spain	[66]
18	05/08/2020	Farm Worker	Mink <sup>abc</sup>	The Netherlands	[66, 74]
19	05/12/2020	Pet Owner	Cat <sup>a</sup>	France	[66]
20	05/13/2020	Pet Owner	Cat <sup>a</sup>	Germany	[66]
21	05/15/2020	Farm Workers/Infected Minks	Cat <sup>ab</sup>	The Netherlands	[66]
22	05/15/2020	Human	Dog <sup>b</sup>	The Netherlands	[66]
23	05/18/2020	Pet Owner	Cat <sup>a</sup>	Russia	[66]
24	05/21/2020	Human	Cat <sup>a</sup>	Spain	[66, 73]
25	05/25/2020	Human	Cat <sup>b</sup>	The Netherlands	[66]
26	05/27/2020	Pet Owner	Dog	NC, USA	[65, 66]
27	06/01/2020	Pet Owner	Dog <sup>ab</sup>	NY, USA	[65, 66, 69]
28	06/01/2020	Pet Owner	Cat <sup>a</sup>	MN, USA	[65, 66]
29	06/02/2020	Farm Worker	Mink <sup>abc</sup>	The Netherlands	[66]
30	06/02/2020	Pet Owner	Dog <sup>a</sup>	NY, USA	[65, 66]
31	06/03/2020	Pet Owner	Cat <sup>ac</sup>	MN, USA	[65, 66]
32	06/04/2020	Pet Owner	Cat <sup>a</sup>	IL, USA	[65, 66]
33	06/24/2020	Pet Owner	Dog <sup>b</sup>	NY, USA	[65, 66]
34	06/24/2020	Pet Owner	Dog <sup>b</sup>	NY, USA	[65, 66]
35	07/01/2020	Pet Owner	Dog <sup>a</sup>	GA, USA	[65, 66]
36	07/08/2020	Pet Owner	Dog <sup>a</sup>	TX, USA	[65, 66]
37	07/08/2020	Pet Owner	Cat <sup>a</sup>	GA, USA	[65, 66]
38	07/09/2020	Pet Owner	Dog <sup>a</sup>	SC, USA	[65, 66]
39	07/15/2020	Pet Owner	Dog <sup>a</sup>	AZ, USA	[65, 66]
40	07/21/2020	Pet Owner	Cat <sup>a</sup>	TX, USA	[65, 66]
41	07/22/2020	Pet Owner	Cat <sup>b</sup>	UT, USA	[65, 66]
42	07/22/2020	Pet Owner	Cat <sup>b</sup>	UT, USA	[65, 66]
43	07/22/2020	Pet Owner	Dog <sup>b</sup>	UT, USA	[65, 66]
44	07/22/2020	Pet Owner	Dog <sup>b</sup>	WC, USA	[65, 66]
45	07/22/2020	Pet Owner	Dog <sup>b</sup>	WC, USA	[65, 66]
46	07/22/2020	Pet Owner	Dog <sup>b</sup>	NC, USA	[65, 66]
47	08/03/2020	Pet Owner	Dog <sup>a</sup>	LA, USA	[65, 66]
48	08/11/2020	Pet Owner	Dog <sup>a</sup>	NC, USA	[65, 66]
49	08/12/2020	Pet Owner	Cat <sup>b</sup>	NY, USA	[65]
50	08/17/2020	Farm Worker	Mink <sup>a</sup>	Utah, USA	[65]
51	08/17/2020	Farm Worker	Mink <sup>a</sup>	Utah, USA	[65]

<sup>a</sup>Positive by RT-PCR.<sup>b</sup>Positive by virus neutralizing antibodies.<sup>c</sup>Positive on virus isolation in cell culture.<sup>d</sup>SARS-CoV-2 positive (symptomatic or asymptomatic) pet owners, animal caretakers or farm workers most likely transmitted the virus to animals.

had infected cat population in Wuhan during the COVID-19 outbreak; 14.4% cat sera collected before and after the COVID-19 outbreak were positive for antibodies specific to the RBD of SARS-CoV-2 by indirect enzyme linked immunosorbent assay [72]. Among the 15 positive cat sera, 11 serum samples had various titers of SARS-CoV-2 neutralizing antibodies; the authors did not detect any serological cross-reactivity between the SARS-CoV-2 and FIPV. Recently, a large-scale study involving 500 companion animals (dogs and cats) living in COVID-19-positive and – negative households in Northern Italy reported measurable SARS-CoV-2 neutralizing antibody titers in 3.4% dogs and 3.9% cats [73]. These reports support the notion of human-to-animal

transmission (reverse zoonosis or zoonoanthroposis) of SARS-CoV-2.

In a recent report, minks showing signs of pneumonia and mortality were confirmed to be infected with SARS-CoV-2 at various farms in the Netherlands ([74]; Tables 1 and 2; Figure 2). It is believed that several farm workers, who developed symptoms consistent with COVID-19, transmitted the virus to the minks. It is also likely that infected minks might have transmitted the virus to some of the farm workers. The transmission was evident from similarity of viral sequences detected in infected individual to those found in minks. Additionally, seven of 24 cats at the mink farms also tested positive serologically for SARS-CoV-2-specific antibodies [66, 74], and at

least one seropositive cat tested positive for the SARS-CoV-2 RNA. Although, neither the source of the virus (infected minks or infected farm workers) in cats nor transmission of the virus from cat(s) to other animals or humans could be confirmed, the possibility of interspecies transmission of the virus, i.e. primary and secondary zoonotic events cannot be ruled out.

Given the evidence in this review, it is apparent that certain CoVs have crossed, and will continue to cross host species. A strong possibility exists that SARS-CoV-2 has been transmitted from humans to farmed minks and companion and zoo animals. The consequences of such zoonothonosis are unknown at the moment. The interspecies transmission among animals could make the pandemic control more difficult. It should, however, be noted that as of today, there is no conclusive evidence that cats, dogs, or zoo animals can transmit SARS-CoV-2 to humans. Based on the current information, the overall risk of SARS-CoV-2 transmission from companion and zoo animals to other animals or humans as well from humans to animals is low. However, uncertainty remains on how this virus will behave in various animal species. Thus, urgent and planned investigations and continuous monitoring as well as targeted proactive surveillance of specific animals and their caretakers, with known or suspected exposures to humans with COVID-19, are warranted at local and national levels.

Currently, there is not enough SARS-CoV-2 specific testing being done for companion and zoo animals. However, the situation may change in future. It is noteworthy that the USA IDEXX Laboratories have recently launched a test under the commercial name “SARS-CoV-2 (COVID-19) Real PCR Test” to test samples from companion animals [75]. Several other private and government veterinary laboratories are also in the process of developing and using serological assays and nucleic acid-based tests for SARS-CoV-2 detection in pet and zoo animals.

### The One-Health initiative and potential for secondary zoonotic events

The One-Health concept is based upon the premise that human health is intricately linked to, and dependent upon, the health of all the living creatures of this planet as well as of their habitats. Together they form an ecosystem, whose health ultimately affects human health (Figure 3). Therefore, it dictates that a collaborative, multisectoral, and transdisciplinary approach should be adopted at a global level for achieving the best possible health outcomes for people, animals, plants, and their shared environment. Over the last two decades, an alarming upsurge in newly emerging and certain re-emerging pathogens was observed [76]. During this period, three pathogenic

CoVs have struck humans, and the probability of another one is quite certain. This scenario leaves no option other than adopting One Health-One World approach. It is worth noting that about 60% of known infectious diseases in humans are zoonotic and about 70% of emerging infectious diseases in humans are also of zoonotic origin [77]. Several factors may account for the increases in infectious diseases of zoonotic origin. They include climate change, urbanization, rapid population growth, expansion of new geographic areas, lifestyle changes, eating habits, intensive farming systems, deforestation, land use changes, increased human national and international travel, and increased movements of animals and animal products across the globe for trade. These changes affect human and animal health, and the ecosystems, resulting in rapid spread of infectious diseases. They increase the probability of SARS-CoV-2 jumping not only from animals into humans through primary and secondary zoonotic events, but also from humans to animals through reverse spread. They also enhance the potential for emergence of new genotypes, pathotypes and/or antigenic types of SARS-CoV-2. Because of the ability of the virus to infect multiple host species, it could be quickly shipped via asymptomatic human carriers, infected animals and/or food products from one location to the other.



**Figure 3.** SARS-CoV-2 and the One-World – One-Health concept. It emphasizes that human health is dependent and intricately connected with that of animals (domestic and wild), birds and plants. A disturbance in the ecosystem results in human diseases (zoonotic or reverse-zoonotic). The letter X denotes a zoonotic event; the color red, white and yellow depict potential primary, secondary and tertiary zoonotic events, respectively.

The World Organization for Animal Health (Office International des Epizooties; OIE), the WHO and Food and Agriculture Organization (FAO) of the United Nations, the United States Department of Agriculture (USDA) and Center for Disease Control and Prevention (CDC), and many other global and local organizations are advocating and promoting the One-Health for One World approach. The occurrence of global epidemics such as HPAI, Ebola, SARS, MERS, and recently COVID-19 [33, 76–79] has provided stimulus to further strengthen the One-Health programme, especially in developing nations, and leveraging the expertise of veterinarians to support global public health community [79].

The One-Health approach recommends that veterinarians, medical doctors and human and animal health specialists be involved in inter-disciplinary collaboration to fight against not only COVID-19 but also against other newly emerging pathogens, which constantly threaten human and animal health as well as food safety and security. Adopting a One-Health strategy will not only help in developing and implementing effective strategic planning, policies, and procedures leading to timely disease agent detection and prevention but also in a coordinating emergency response and a solid contingency plan for future pathogens. The increased awareness on zoonotic and reverse zoonotic potential of SARS-CoV-2, and their mitigation measures should be communicated to the general public. The COVID-19 pandemic has also highlighted the importance of local provisions of essentials (e.g. food, medical equipment, and lifesaving drugs), and reduced dependency on global infrastructure. Veterinarians, microbiologists, epidemiologists and animal biologists might help to predict the emergence and potential source(s) of future outbreaks of infectious diseases. Surveillance of wild, food and domestic animal population is the key to preventing SARS-CoV-2 from establishing itself in another animal species, especially in companion and food animals. Future investigations on reverse zoonotic potential of SARS-CoV-2 should focus on disease transmission routes, prevalence, pathogenesis, and prevention mechanisms. It is unlikely that SARS-CoV-2 will be the last coronavirus to jump species barrier infecting human(s) and other animal species.

The lessons learned from COVID-19 pandemic could be used to create awareness for strengthening the veterinary and medical profession on modern grounds. This will aid veterinary professionals to effectively contribute to not only animal but also to public health at local, national, and global levels. The collective knowledge found, resources developed, and capacity built could be used for a more collaborated, rapid and effective emergency response that keeps in

check the future spread of emerging epidemics at a both national and international level.

## Conclusions

SARS-CoV-2 is a zoonotic disease that has crossed species barrier from its reservoir bat host, and infected humans via an unknown intermediate animal species. The disease, declared as a pandemic, has caused a great loss to human life and economy, and has disrupted our routine social life. The virus has clearly shown the potential of reverse zoonosis. During the last six months there have been consistent reports of the viral infections in companion, zoo and certain farm animals. The specter of primary and secondary zoonotic events, although not yet confirmed, has also been raised. We should continue to adhere to traditional measures of controlling the pandemic (lockdowns, physical distancing, testing and isolating the infected individuals, increased personal hygiene and protection of vulnerable) until effective therapies and vaccines are developed. The recommendations of the One-Health One-World should be implemented to prevent the emergence of future epidemic(s) and pandemic(s).

## Contributors

KM, SA, IM, HK MAK, NM, SOA, MAI, RM, AA and XZ wrote the manuscript with input from KM and SA. SHA, UC, MUZ, MA, AA and XZ provided intellectual input, did literature search and proofread the article. All authors revised the manuscript and approved the final report.

## Disclosure statement

No potential conflict of interest was reported by the author(s).

## ORCID

Shoab Ashraf  <http://orcid.org/0000-0002-1218-4877>

Ali Ahmad  <http://orcid.org/0000-0001-7689-7115>

Xin Zhao  <http://orcid.org/0000-0002-1078-7332>

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# **Exhibit H**

# *Mink and the Coronavirus: What We Know*

Mink are the only animal known to both catch the virus from people and transmit it to them.



By James Gorman

Nov. 11, 2020

Last week, Denmark announced its intention to cull all farmed mink, some 17 million, out of fear that a mutated version of the coronavirus might diminish the effectiveness of potential vaccines.

The decision has since been put on hold because of questions of legal authority. While the government seeks new legislation, culls of mink at infected farms continue, as does dismay in other countries and a debate among scientists about the validity of the concerns.

Six countries — Denmark, the Netherlands, Spain, Sweden, Italy and the United States — have reported cases of farmed mink infected with SARS-CoV-2, the virus that causes Covid-19. Mink catch the virus from humans and pass it on to each other. Unlike dogs, cats and some other animals, which express only mild symptoms, if any, mink can sicken and die from an infection.

Here are answers to basic questions about mink and the coronavirus:

## **Can mink infect people with the coronavirus?**

Yes. In Denmark, mink have contracted the virus and spread it to people. The same happened in the Netherlands this year.

## **Does the virus mutate in mink?**

Yes. In more than 200 people, Danish authorities have documented several variants of the virus that contain mutations originating in mink. The virus also mutates in people.

## **Is the mutated virus more dangerous?**

No. There is no evidence that any of the mutations that originated in mink make the coronavirus more transmissible in humans or make humans sicker.

## **Why did Denmark decide to kill all of its farmed mink?**

Danish health authorities were concerned that one set of mutations in a variant of the virus called cluster 5, which had infected at least 12 people, could make a potential coronavirus vaccine less effective.

One of the mutations occurs on a part of the virus — the spike protein — that is targeted by many potential vaccines. In lab studies, cells with this variant of the virus were exposed to antibodies, which did not act as strongly as they had with other coronavirus variants.

But this was a very preliminary test. The reaction to antibodies in laboratory cells does not necessarily indicate that the mutated virus would be resistant to vaccines; it merely raises that possibility.

## **Will the mutations diminish the value of vaccines?**

The World Health Organization and independent experts said there was no evidence so far that the cluster 5 variant would diminish the value of vaccines currently in development.

## **Did Denmark overreact?**

Scientists say that there are reasons beyond this particular mutated virus for Denmark to act. Mink farms have been shown to be reservoirs for the coronavirus, and mink are capable of transmitting the virus to humans. They are the only animal known to do so.

This set of mutations may not be harmful to humans, but the virus will doubtless continue to mutate in mink as it does in people, and the crowded conditions of mink farms could put evolutionary pressures on the virus different from those in the human population. The virus could also jump from mink to other animals. These are all worrisome possibilities, particularly in the midst of a resurgence of the virus in the human population.

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James Gorman is a science writer at large and the host and writer of the video series "ScienceTake." He joined The Times in 1993 and is the author of several books, including "How to Build a Dinosaur," written with the paleontologist Jack Horner.

# **Exhibit I**

# A dreadful loop: Can reverse zoonosis of COVID-19 seed unrestrained spread and mutations in wild species and transmission of novel strains to humans?

Shanshan He, Jie Han\*

Department of Environmental Science and Engineering, Xi'an Jiaotong University,  
Xi'an 710049, P.R. China

\*Corresponding author. E-mail: [jiehan@xjtu.edu.cn](mailto:jiehan@xjtu.edu.cn)

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The coronavirus disease (COVID-19) pandemic is becoming the greatest public health crisis since the influenza pandemic in 1918 (Sanders et al. 2020). At the time of writing (27 October 2020), there have been over 42 million confirmed cases around the globe, including over 1.1 million deaths (WHO 2020). The novel coronavirus (SARS-CoV-2) shares 79.6% of its genome sequences with SARS-CoV and 96.2% with those of a bat coronavirus isolated from *Rhinolophus affinis* (Zhou et al. 2020), suggesting bats may be the natural hosts of SARS-CoV-2 (Paraskevis et al. 2020; Lu et al. 2020). Cats, ferrets, minks, pangolins, snakes, and turtles have also been postulated as intermediate hosts of the novel coronavirus (Nabi et al. 2020; Li et al. 2020; Ji et al. 2020; Wu et al. 2020).

The infection of SARS-CoV-2 is effectuated by interactions between the SARS-CoV-2 receptor binding domain (RBD) and angiotensin-converting enzyme 2 (ACE2) receptor proteins (Santini and Edwards 2020; Wu et al. 2020; Zhou et al. 2020). Thus, an immense diversity of mammals can be potentially infected by SARS-CoV-2 via their ACE2 receptors (Damas et al. 2020; Wu et al. 2020). In a recent study, Wu et al. (2020) found that the ACE2 receptors of 26 species, including pets, domestic animals, and multiple wild animals, could bind to the SARS-CoV-2 RBD and facilitate the transduction of SARS-CoV-2 pseudoviruses. Real-life cases of SARS-CoV-2 infections have been reported on mammals, including cats, monkeys, ferrets, and hamsters (Santini and Edwards 2020). Studies have also shown that infected cats, ferrets, and hamsters were capable of spreading SARS-CoV-2 to other animals in laboratory settings (Kim et al. 2020; Shi et al. 2020; Sia et al. 2020).

Aggressive land reclamation, intensified livestock production, and increased wildlife hunting and trading activities are correlative with 70% of emerging infectious diseases and almost all recent pandemics caused by zoonoses (Di Marco et al. 2020). Conversely, regular or inadvertent

interactions between infected persons and wild or domestic animals allow the novel coronavirus to transmit in reverse direction, i.e. from humans to animals, creating a bidirectional path of interspecies infection. Anthroponosis, or reverse zoonosis, are more likely to occur in areas with community-wide spread of the novel coronavirus in the current pandemic. Recent incidents and studies provided direct evidence supporting this hypothesis. Domestic cats and dogs owned by infected individuals have been tested positive for SARS-CoV-2, with some showing no specific symptoms (Santini and Edwards 2020; Sit et al. 2020). In an earlier incident reported at the Bronx Zoo in New York city, the epidemiological data and genetic similarities of SARS-CoV-2 strains isolated from tigers and their keepers indicated direct human-to-animal transmission (McAloose et al. 2020). Minks infected with SARS-CoV-2 have also been identified on farms in the Netherlands, Denmark, Spain, and the United States, where infected farm workers were speculated as sources of infection (CDC 2020; Oreshkova et al. 2020). Human infection acquired from infected minks (i.e. reverse anthroponosis) was also suspected on two mink farms in the Netherlands reporting human-to-mink transmission (Oreshkova et al. 2020).

In addition to direct human-to-animal spread in zoos, farms, and other facilities with animal contact, wastes from infected households containing infectious body fluids or excreta (e.g. nasal discharge, phlegm, saliva, semen, vaginal fluids, blood, urine and feces) and personal protective equipment that is contaminated by the novel coronavirus and improperly disposed of may become secondary sources of COVID-19 infection for wild and stray animals (Franklin and Bevins 2020; Han and He 2020; Nabi et al. 2020). Under common ambient conditions, SARS-CoV-2 could survive for several days on face masks, tissues, and other common household materials (Chin et al. 2020; van Doremalen et al. 2020; Han et al. 2020). In response to the current pandemic, masks, face

coverings, gloves, tissues, and wipes are routinely used, creating enormous amounts of single-use items that could be potentially infected with the virus (UNEP 2020). When not managed timely and soundly, these could be subject to open dumping, which poses risks of infection for domestic and wild animals in surrounding environments.

Reverse zoonosis of SARS-CoV-2 may seed unrestrained spread and mutations in wild species and, at some stage, transmission of novel strains to humans. The genetic diversity of coronaviruses, caused by accumulation of point mutations and high-frequency homologous recombination, is the principal determinant of their competences in changing tissue tropism, hurdling interspecies barriers, and adapting to ecological variations (Amer 2018). Particularly, in-host genetic diversity could better position the virus to respond and adapt to a diverse array of selective pressures (e.g. host-switching events), causing different diseases and symptoms in hosts (Borucki et al. 2013). Members of the Coronaviridae family (e.g. SARS, MERS) have been shown to cross the interspecies barrier and induce different disease conditions in various animals (Amer 2018). In an earlier study, Graham and Baric (2010) found that the recombination of SARS in the spike glycoprotein genes might have mediated the initial cross-species transmission event from bats to other mammals. Recently, Ji et al. (2020) pointed out that a homologous recombination of SARS-CoV-2 may occur between a bat coronavirus and a coronavirus of an unknown origin within the viral spike glycoprotein gene. The study found that SARS-CoV-2 has most similar genetic information with bat coronavirus but most similar synonymous codon usage bias with snakes. In another study, Lau et al. (2020) showed that the entire genome of SARS-CoV-2 is most closely related to the SARSr-Ra-BatCoV RaTG13 from an intermediate horseshoe bat, except for its receptor-binding domain which is closest to pangolin-SARSr-CoVs, suggesting that SARS-CoV-2 is a recombinant virus. These findings indicated the

complex origin of SARS-CoV-2 where evolutionary recombination and strong purifying selection occurred between coronaviruses from distinct host species before the novel coronavirus spilled over to humans (Li et al. 2020; Wu et al. 2020).

Continuous movement of wildlife provides a window for the virus to adapt to new hosts and possibly develop into novel strains (Amer 2018). Without human intervention, the dense roosting behavior and long foraging range of some wild species may facilitate exchange of viruses and recombination. Lau et al. (2010) found that recombination events occurred between strains of Rousettus bat coronavirus (Ro-BatCoV HKU9) from different bat individuals, which might have allowed the same bat to be infected by at least two distinct genotypes. Likewise, different species co-infected with influenza A genotypes potentially facilitated genetic recombination of the virus, for instance, between human and avian virus strains. These activities can create new genotypes with substantial antigenic changes that can result in an influenza pandemic and produce a virulent strain (Carrat et al. 2007). It should be noted that genetic recombination is a key contributor to major shifts in influenza antigenicity. As antigenic changes continue to occur during the process of developing recommendations and applying the influenza season vaccine, mismatch can occur, which renders the vaccine less effective (Carrat et al. 2007). Similar risks exist in the case of the novel coronavirus. Once SARS-CoV-2 spills from human to wild species, the spontaneous behavior and uncontrolled movements of the latter can facilitate the pathogen to establish within and transmit between different species (Keesing et al. 2010). Foraging, predation, mating, and open defecation enable the spread of pathogens carried by infected animals to others in new terrestrial and aquatic environments, causing clustered and cross-species infections with the virus continuously evolving in wildlife reservoirs.

As of week 21, 2020, a total of 11,627 genomes (34.4%) of SARS-CoV-2 isolated from humans had shown single mutations, and the variations in 8,773 genomes (25.9%) were considered high risks affecting the reliability of nucleic acid testing (Peñarrubia et al. 2020). Since the first case reported in Hong Kong on August 24, 2020 (To et al. 2020), there have been at least six published cases of SARS-CoV-2 reinfections around the globe (Van Elslande et al. 2020; Larson et al. 2020; Mulder et al. 2020; Prado-Viviat et al. 2020; Tillett et al. 2020; To et al. 2020). In four of those cases, patients showed more severe symptoms than those resulted from their first infection, including one severe case where the individual died shortly after the reinfection. In all of the six cases, viral strains isolated from the reinfected individuals showed substantial genetic differences from those causing their first infection. There are considerable risks that novel strains of SARS-CoV-2 may emerge in wildlife reservoirs by accumulating point mutations and homologous recombination as it spreads in an uncontrolled manner between different hosts and species. Reverse anthroponosis of novel strains, once it occurs, can potentially render the current vaccines for COVID-19 – most of them still in a development stage – less effective, posing renewed risks of infection to the immunized population (Dai et al. 2020). Given that SARS-CoV-2 can potentially infect a vast range of animals, the virus may spill in two-way between humans and animals in the current pandemic, forming a dangerous “loop” with prolonged spread, recurrent infections and outbreaks, and continuing fights with evolved viral strains (**Fig. 1**).

Early intervention can be implemented to minimize the risks of forming a loop of zoonosis, anthroponosis, and reverse anthroponosis during the current pandemic. Since mid-October 2020, Denmark, the world’s largest producer of mink pelts, has opted to cull 2.5 million minks in the coming months as a precautionary measure to control the spread of COVID-19 in minks and farm

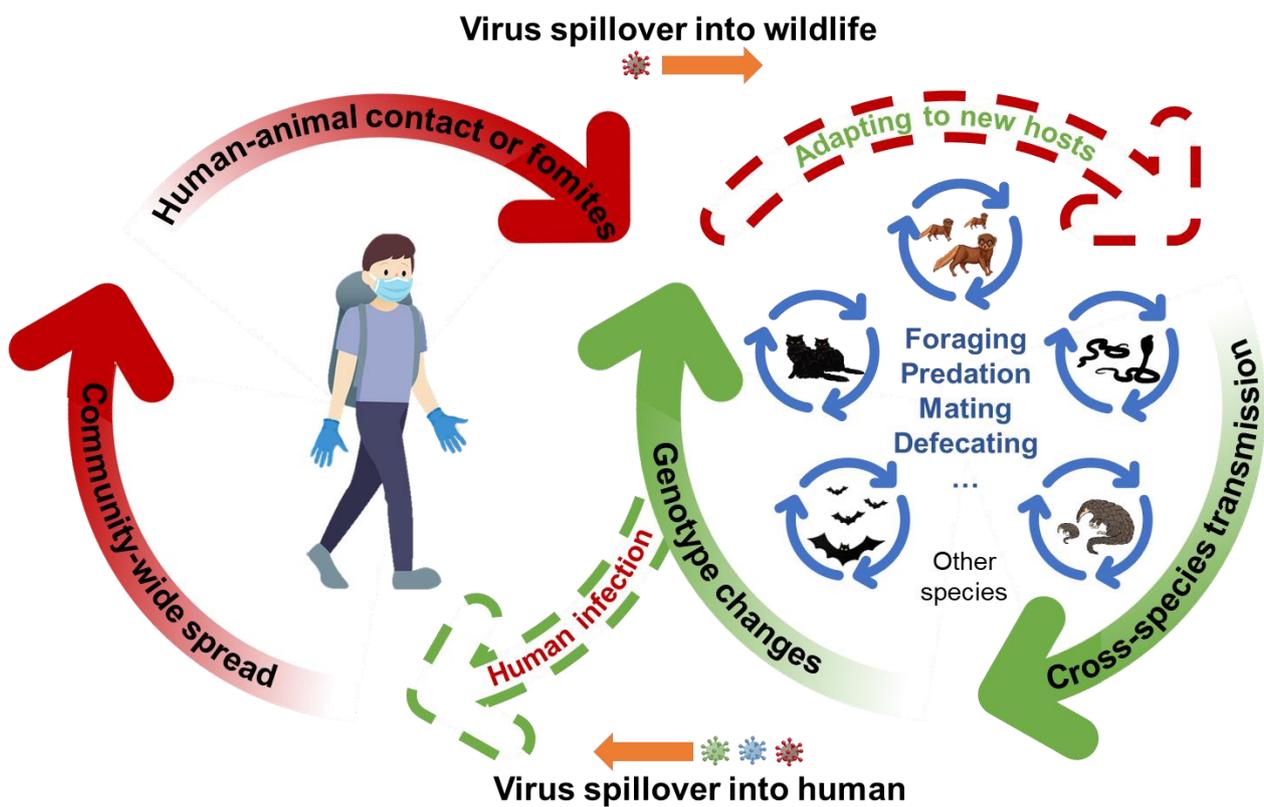
workers (Olsen and Scisłowska 2020). A series of control measures may be put in place, such as: 1) quarantining and safely disposing of domesticated animals or livestock with suspected SARS-CoV-2 infection; 2) advising the public to keep safe distances from wildlife, particularly species that are known to be susceptible to SARS-CoV-2 infections, for instance, by issuing emergency orders and temporary bans on hunting, trading, and other non-essential contact with wildlife; and 3) monitoring novel strains of SARS-CoV-2, including those emerged in animal hosts, and continually developing vaccines for mutated virus strains.

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### **Conflict of Interest**

The authors declare that they have no conflict of interest in this work.



**Fig. 1** A schematic diagram illustrating the two-way spillover of SARS-CoV-2 between human and wildlife. In the current pandemic with numerous locations of community-wide spread of the zoonotic agent, any intentional or inadvertent human-animal contacts or anthropogenic wastes carrying SARS-CoV-2 allows reverse zoonosis, namely the transmission of the virus from infected persons to wildlife species. With no human intervention, spontaneous behaviors of wild species such as foraging, predation, mating, and defecating enable both in-species and cross-species transmission, facilitating genotype changes and evolution of SARS-CoV-2 in various wildlife reservoirs. Mutated viruses may then spillover to humans through different natural or intermediate hosts, forming a dangerous loop of zoonosis, anthroponosis, and reverse anthroponosis of an evolving virus between human and other hosts. Once transmitted to humans, those novel strains will pose new challenges for future infection control by causing reinfections, re-emergent outbreaks, and rendering current vaccines less effective.

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# **Exhibit J**

REVIEW

# Possibility for reverse zoonotic transmission of SARS-CoV-2 to free-ranging wildlife: A case study of bats

Kevin J. Olival<sup>1</sup>✉\*, Paul M. Cryan<sup>2</sup>✉\*, Brian R. Amman<sup>3</sup>, Ralph S. Baric<sup>4</sup>, David S. Blehert<sup>5</sup>, Cara E. Brook<sup>6</sup>, Charles H. Calisher<sup>7</sup>, Kevin T. Castle<sup>8</sup>, Jeremy T. H. Coleman<sup>9</sup>, Peter Daszak<sup>1</sup>, Jonathan H. Epstein<sup>1</sup>, Hume Field<sup>1,11</sup>, Winifred F. Frick<sup>10,12</sup>, Amy T. Gilbert<sup>13</sup>, David T. S. Hayman<sup>14</sup>, Hon S. Ip<sup>5</sup>, William B. Karesh<sup>1</sup>, Christine K. Johnson<sup>15</sup>, Rebekah C. Kading<sup>7</sup>, Tigga Kingston<sup>16</sup>, Jeffrey M. Lorch<sup>5</sup>, Ian H. Mendenhall<sup>17</sup>, Alison J. Peel<sup>18</sup>, Kendra L. Phelps<sup>1</sup>, Raina K. Plowright<sup>19</sup>, DeeAnn M. Reeder<sup>20</sup>, Jonathan D. Reichard<sup>9</sup>, Jonathan M. Sleeman<sup>5</sup>, Daniel G. Streicker<sup>21,22</sup>, Jonathan S. Towner<sup>3</sup>, Lin-Fa Wang<sup>17</sup>



**1** EcoHealth Alliance, New York, New York, United States of America, **2** US Geological Survey, Fort Collins Science Center, Ft. Collins, Colorado, United States of America, **3** US Centers for Disease Control and Prevention, Atlanta, Georgia, United States of America, **4** Department of Epidemiology, University of North Carolina, Chapel Hill, North Carolina, United States of America, **5** US Geological Survey, National Wildlife Health Center, Madison, Wisconsin, United States of America, **6** Department of Integrative Biology, University of California Berkeley, Berkeley, California, United States of America, **7** Arthropod-borne and Infectious Diseases Laboratory, Department of Microbiology, Immunology & Pathology, College of Veterinary Medicine & Biomedical Sciences, Colorado State University, Ft. Collins, Colorado, United States of America, **8** Wildlife Veterinary Consulting, Livermore, Colorado, United States of America, **9** US Fish and Wildlife Service, Hadley, Massachusetts, United States of America, **10** School of Veterinary Science, University of Queensland, Gatton, Queensland, Australia, **11** Bat Conservation International, Austin, Texas, United States of America, **12** Department of Ecology & Evolutionary Biology, University of California Santa Cruz, Santa Cruz, California, United States of America, **13** US Department of Agriculture, National Wildlife Research Center, Ft. Collins, Colorado, United States of America, **14** School of Veterinary Science, Massey University, Palmerston North, New Zealand, **15** One Health Institute, School of Veterinary Medicine, University of California Davis, Davis, California, United States of America, **16** Department of Biological Sciences, Texas Tech University, Lubbock, Texas, United States of America, **17** Programme in Emerging Infectious Diseases, Duke-National University of Singapore Medical School, Singapore, **18** Environmental Futures Research Institute, Griffith University, Nathan, Australia, **19** Department of Microbiology & Immunology, Montana State University, Bozeman, Montana, United States of America, **20** Department of Biology, Bucknell University, Lewisburg, Pennsylvania, United States of America, **21** Institute of Biodiversity, Animal Health & Comparative Medicine, University of Glasgow, Scotland, United Kingdom, **22** MRC-University of Glasgow Centre for Virus Research, Glasgow, Scotland, United Kingdom

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✉ These authors contributed equally to this work.  
\* [olival@ecohealthalliance.org](mailto:olival@ecohealthalliance.org) (KJO); [cryanp@usgs.gov](mailto:cryanp@usgs.gov) (PMC)

## Abstract

The COVID-19 pandemic highlights the substantial public health, economic, and societal consequences of virus spillover from a wildlife reservoir. Widespread human transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) also presents a new set of challenges when considering viral spillover from people to naïve wildlife and other animal populations. The establishment of new wildlife reservoirs for SARS-CoV-2 would further complicate public health control measures and could lead to wildlife health and conservation impacts. Given the likely bat origin of SARS-CoV-2 and related beta-coronaviruses (β-CoVs), free-ranging bats are a key group of concern for spillover from humans back to

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wildlife. Here, we review the diversity and natural host range of  $\beta$ -CoVs in bats and examine the risk of humans inadvertently infecting free-ranging bats with SARS-CoV-2. Our review of the global distribution and host range of  $\beta$ -CoV evolutionary lineages suggests that 40+ species of temperate-zone North American bats could be immunologically naïve and susceptible to infection by SARS-CoV-2. We highlight an urgent need to proactively connect the wellbeing of human and wildlife health during the current pandemic and to implement new tools to continue wildlife research while avoiding potentially severe health and conservation impacts of SARS-CoV-2 "spilling back" into free-ranging bat populations.

## Spillover of pandemic viruses

The threat of emerging infectious diseases (EIDs) to wildlife health and biodiversity conservation is recognized [1], but cross-species transmission of novel pathogens, or spillover, is typically viewed in the specific context of originating in a wildlife reservoir and transmitting to humans [2]. Research assessing EID risk has typically focused on identifying geographic regions [3, 4] and wildlife species [5–7] whereby spillover of zoonotic diseases into humans is most likely. Among recent pandemic zoonotic viruses, some have no evidence of transmission back to wildlife or domestic animal populations after establishment in people (e.g., human immunodeficiency virus, which causes acquired immunodeficiency syndrome), while others have repeatedly crossed species boundaries (e.g., pandemic H1N1 influenza A virus) [8, 9]. Evidence of “reverse zoonotic” transmission, sometime referred to as “spillback,” from people to wildlife and domestic animals is widespread [9]; however, systematic surveys to determine the proportion of EIDs that spill back into novel wildlife hosts are lacking. Infection of bats by viruses of probable human origin has been recorded only twice [10, 11], and further transmission [12], or spread to a wider bat population, has not been recorded.

In December 2019, a novel coronavirus was detected from a cluster of 41 atypical pneumonia cases in Wuhan, China, and has since spread to cause a pandemic with significant global morbidity, mortality, and economic impact [13]. Phylogenetic evidence suggests that this virus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and the clade of SARS-related coronaviruses (SARSr-CoVs) that it belongs in evolved in Old-World bats of the family Rhinolophidae [14–16]. There is no epidemiological evidence of direct or indirect transmission of SARS-CoV-2 from bats to people, but a full genome of its closest known relative (with 96.2% sequence similarity) was reported from an Intermediate Horseshoe Bat (*Rhinolophus affinis*) sampled from Yunnan province, China, in 2013 [17]. The timing of SARS-CoV-2 spillover from bats and any involvement of intermediate host species remain undetermined [18, 19]. The United States currently has the highest number of confirmed human cases of COVID-19, the disease caused by SARS-CoV-2. The consequences of this pandemic are many and include the possibility of SARS-CoV-2 transmission from humans to free-ranging wildlife populations. Given the likely bat origin of SARS-CoV-2, free-ranging bats are a key group of concern for spillover from humans. Humans frequently handle and come into close contact with North American temperate-zone bats during the course of ecological research, wildlife rehabilitation, wildlife/pest control, and disease investigations. Anticipating the need for similar risk assessments across many potentially vulnerable species of wildlife and domesticated mammals globally, we here examine the possibility of humans inadvertently infecting free-ranging North American bats with SARS-CoV-2. We further discuss the possible public health and wildlife conservation consequences of SARS-CoV-2 becoming endemic in bats outside its natural host range.

## Threats of SARS-CoV-2 to North American bats

The pandemic spread of SARS-CoV-2 may directly or indirectly threaten North American bat populations in at least three different ways. First, SARS-CoV-2 might infect any of the diverse and historically isolated 40+ endemic species of temperate-zone North American bats, with or without causing disease, morbidity, and mortality. Second, SARS-CoV-2 might infect and become established in one or more North American bat species, creating novel reservoirs capable of causing human infections (e.g., bat rabies lyssaviruses in the New World [20]). Third, if SARS-CoV-2 infection persists in North American bats of one or more species, it could potentially evolve or recombine with endemic viruses [19, 21] to become more pathogenic or infectious to humans or other animals. In addition to new public health challenges, the latter outcomes could quickly shift public perception of bats from mostly beneficial wildlife with associated disease risks that are manageable to bats posing unacceptable disease risks to human and animal health. Such a shift could increase the likelihood of negative human–bat interactions and conflicts, as well as undermine decades of concerted science, conservation, and education efforts aimed at conserving these valuable animals [22–24]. The potential threat of SARS-CoV-2 transmission from humans to other animals applies to many species of wildlife and domesticated mammals, but the likely bat origin of SARS-CoV-2 and the current threats to bat populations due to another disease in North America influenced us to focus this review on bats.

## Lessons from an epizootic—Susceptibility of North American bats to an introduced pathogen

SARS-CoV-2 is not the first pathogen with the potential for inadvertent spread from people to North American bats. The COVID-19 pandemic follows the arrival of a fungal pathogen (*Pseudogymnoascus destructans*) that as early as 2006 began infecting hibernating bat populations in North America, spreading within and among species to alter the evolutionary trajectory of the continent's bats [25–28]. Genetic analyses indicate that *P. destructans* was introduced to North America [29], in our opinion likely by movement of humans or materials contaminated with fungal spores. White-nose syndrome (WNS), the disease caused by *P. destructans*, remains the only documented bat epizootic to cause multiyear, widespread mass mortality [30], although short-term bat die-offs have been also linked to Lloviu virus in Europe [31]. WNS has killed millions of North American bats, affected populations of at least 12 species of 3 genera, and has already spread across half of the US and Canada (whitenoosesyndrome.org, accessed 11 May 2020). Effective methods to mitigate WNS spread and impacts remain elusive despite substantial research effort, and targeted mitigation actions have had limited success against its impacts [32]. It took years of concerted international scientific effort to identify the cold-growing fungus, determine that it likely originated somewhere in the temperate zones of Europe or Asia, understand its mechanisms of infection and pathogenicity, develop strategies to limit accidental translocation, and track its rapid spread through an immunologically naïve continental assemblage of hibernating bats [33–35].

The devastating impact of WNS on a diverse group of North American bats likely resulted from evolutionary isolation of the continent's bat fauna from other parts of the world for millions of years, despite other species of *Pseudogymnoascus* being present. Bats in both Europe and Asia can become infected by *P. destructans* but do not suffer mass mortality from WNS [36, 37]. The bat fauna spanning the higher latitudes of North America (in the US and Canada) is composed almost entirely of endemic species belonging to the family Vespertilionidae. Vespertilionid bats occur globally but likely originated and diversified in North America tens of millions of years ago before dispersing to other continents [38, 39]. No extant species of bat in

the Americas also occurs outside of the Americas [40, 41], and no bats migrate across the Pacific or Atlantic Oceans [42, 43]. The WNS epizootic demonstrates that a large proportion of these historically isolated bats can be vulnerable to a pathogen introduced from another continent during a single event. Additionally, bats already in a physiologically stressed condition due to WNS or other pressures may be more susceptible to viral infection, experience exacerbated disease outcomes, and/or experience increased viral shedding [44, 45]. The COVID-19 pandemic resembles WNS with respect to potential spread of a pathogen from another continent through interconnected, multispecies assemblages of North American bats that might be immunologically naïve and highlights deficits in our understanding of temperate-zone bat pathogens in North America.

### **Gaps in understanding global patterns of Bat–CoV diversity, evolution, and host range**

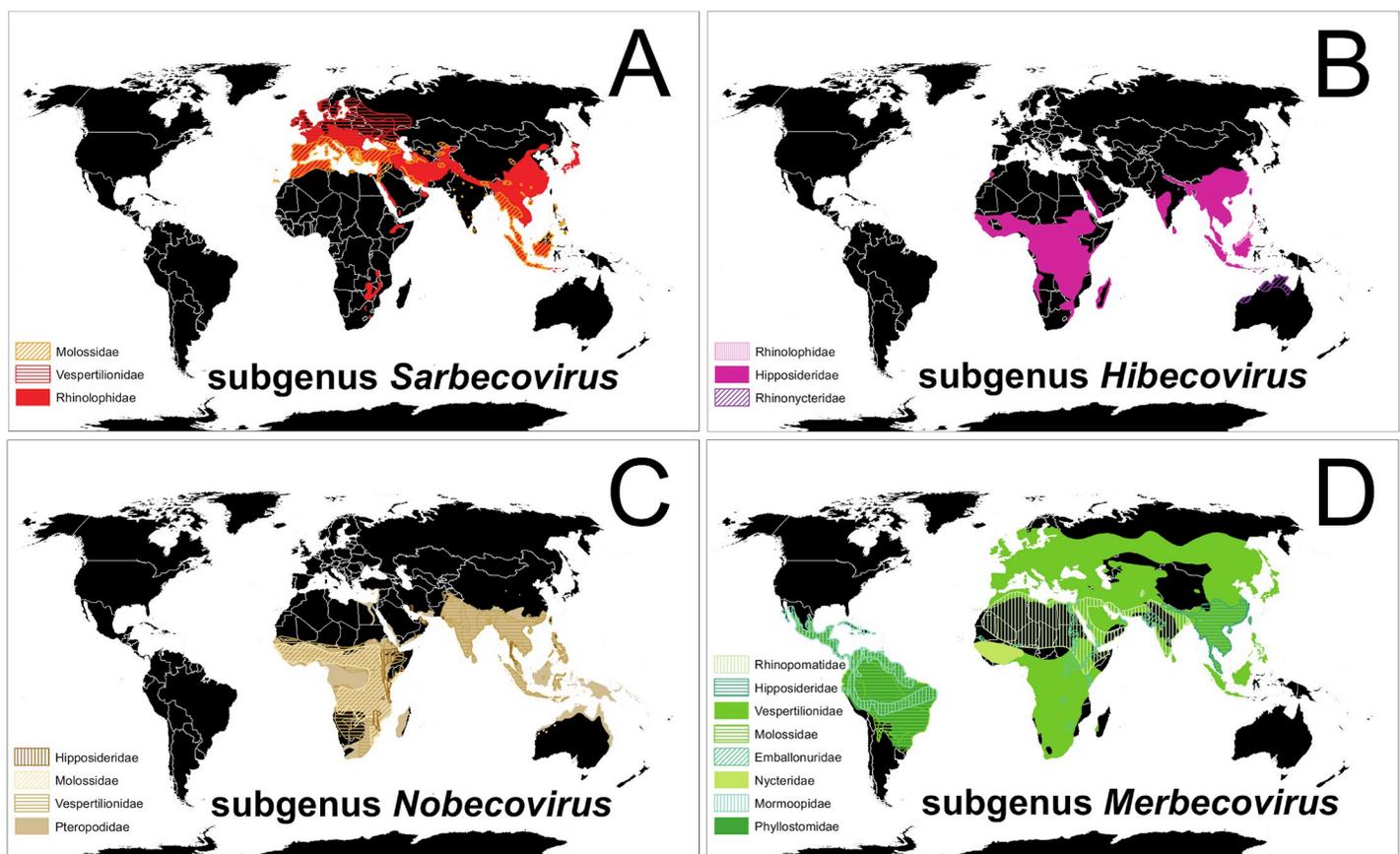
Bats are among the world's most diverse mammals (comprising approximately 1,400 species [46]), and the global distribution and diversity of CoVs in bats proportionally reflects that of their hosts [47, 48]. Available evidence indicates that bats are natural reservoirs of CoVs, some of which have the potential to cause diseases in humans, domesticated animals, and wildlife [17, 47, 49–59]. Coronaviruses appear to have ancient and ancestral relationships with bats, diversifying globally through a process of within-host evolution and cross-taxonomic host-switching events [47, 59–61]. Bats are the likely mammalian progenitor hosts of all alpha ( $\alpha$ -) and beta ( $\beta$ -) CoVs [58, 59, 62, 63] and potentially all coronaviruses [60]. Alpha-CoVs of likely bat origin include the causative agent of swine acute diarrhea syndrome (SADS), which caused mass mortality of over 25,000 piglets on farms in Guangdong province, China [57], and a variant strain of porcine epidemic diarrhea virus (PEDV) that spread rapidly from China in recent decades and caused mass piglet mortality in multiple US states [64]. Human CoVs NL63 and 229E also likely had their evolutionary origins in bats [59, 65]. Two recent human disease epidemics (severe acute respiratory syndrome [SARS] and Middle East respiratory syndrome [MERS]) and now the current COVID-19 pandemic are caused by viruses that probably originated from  $\beta$ -CoVs circulating in bat populations in regions where outbreaks occurred [17, 19, 50–54, 58, 66–68].

The emergence of diseases like SADS, PEDV, SARS, MERS, and now COVID-19 strongly indicates a close association between CoVs that become pathogenic in humans and the wildlife reservoirs from which they originate [17, 50–54, 67]. The evolutionary relationships of CoVs within bats are consistent with geographically structured transmission cycles, with occasional transmission among related bat species [47, 58, 69]. These phylogeographic factors are also universal determinants of viral sharing among all mammals [70]. However, bat–virus association patterns can be particularly difficult to discern because bats often roost together in multi-species aggregations that can facilitate viral sharing, with each species capable of harboring multiple CoV lineages [47, 58, 68, 71]. Host shifts from bats to more divergent taxa are more difficult to predict—firstly, because the potential host breadth for many CoVs is broad [55, 56, 60, 72], and secondly, because host susceptibility and onward transmission involve complex, multistage processes [2, 12]. Bat–CoV associations likely remain substantially undersampled and understudied in temperate-zone North America [47, 71, 73, 74].

### **Are viruses like SARS-CoV-2 already present in North American bats?**

Our examination of CoV evolutionary lineages and global distribution patterns of the diversity of bat species they infect suggests that temperate-zone North American bats could be

immunologically naïve to infection by viruses like SARS-CoV-2. Alpha and  $\beta$ -CoVs have been detected in bats on most continents, sometimes with both types occurring in bats of the same species [58, 68]. However, an exception to this pattern is the lack of published evidence that  $\beta$ -CoVs infect bats of temperate-zone North America, despite several search efforts which used methods suitable to detect both  $\alpha$ - and  $\beta$ -CoVs [59, 71, 74, 75]. Multiple novel  $\alpha$ -CoVs have been detected and described in vespertilionid bats of the US and Canada, infecting species both living in close contact with humans and in remote wild areas [59, 71, 74–76]. However, SARSr-CoVs and  $\beta$ -CoVs of the viral subgenus *Sarbecovirus* have thus far been detected almost exclusively in species of the Old-World Chiropteran suborder Yinpterochiroptera (Fig 1A) [47, 58, 69]. The few exceptions to this pattern are the detection of novel Clade 3 and Clade 1 *Sarbecovirus* (*sensu* [53]) viruses in the wrinkle-lipped free-tailed bat (*Mops plicatus*, family Molossidae) in China [77] and the vespertilionid Leisler's noctule (*Nyctalus leisleri*) cohabiting a Bulgarian cave during autumn with several species of rhinolophids in which other SARSr  $\beta$ -CoVs were concurrently detected, suggesting cross-species infections (Fig 1A) [78]. Putative detections of a Clade 1 *Sarbecovirus* were also reported from guano samples of the



**Fig 1. Global patterns of bats and associated  $\beta$ -CoVs.** (A) Red-shaded distributions of bat species in which SARS-related  $\beta$ -CoVs of the subgenus *Sarbecovirus* have been detected; (B) pink-shaded distributions of bat species known to host  $\beta$ -CoVs of the subgenus *Hibecovirus*; (C) brown-shaded distributions of bats in which  $\beta$ -CoVs of the *Nobecovirus* lineage have been detected; and (D) green-shaded distributions of bats known to host MERS-related  $\beta$ -CoVs of the subgenus *Merbecovirus*. Different colors and shade styles within each panel represent different families of bats. A data table that includes all known bat species associations for each  $\beta$ -CoVs subgenus and peer-reviewed citations is available at US Geological Survey data release <https://doi.org/10.5066/P9U461P>. Maps created using ArcMap (ESRI, Redlands, California, United States of America) and bat ranges derived from spatial data on terrestrial mammals from the International Union for the Conservation of Nature (IUCN 2020. The IUCN Red List of Threatened Species. January 2019 [version 6.2]. <https://www.iucnredlist.org>; Downloaded on 11 April 2020).  $\beta$ -CoV, beta-coronavirus; MERS, Middle East respiratory syndrome; SARS, severe acute respiratory syndrome.

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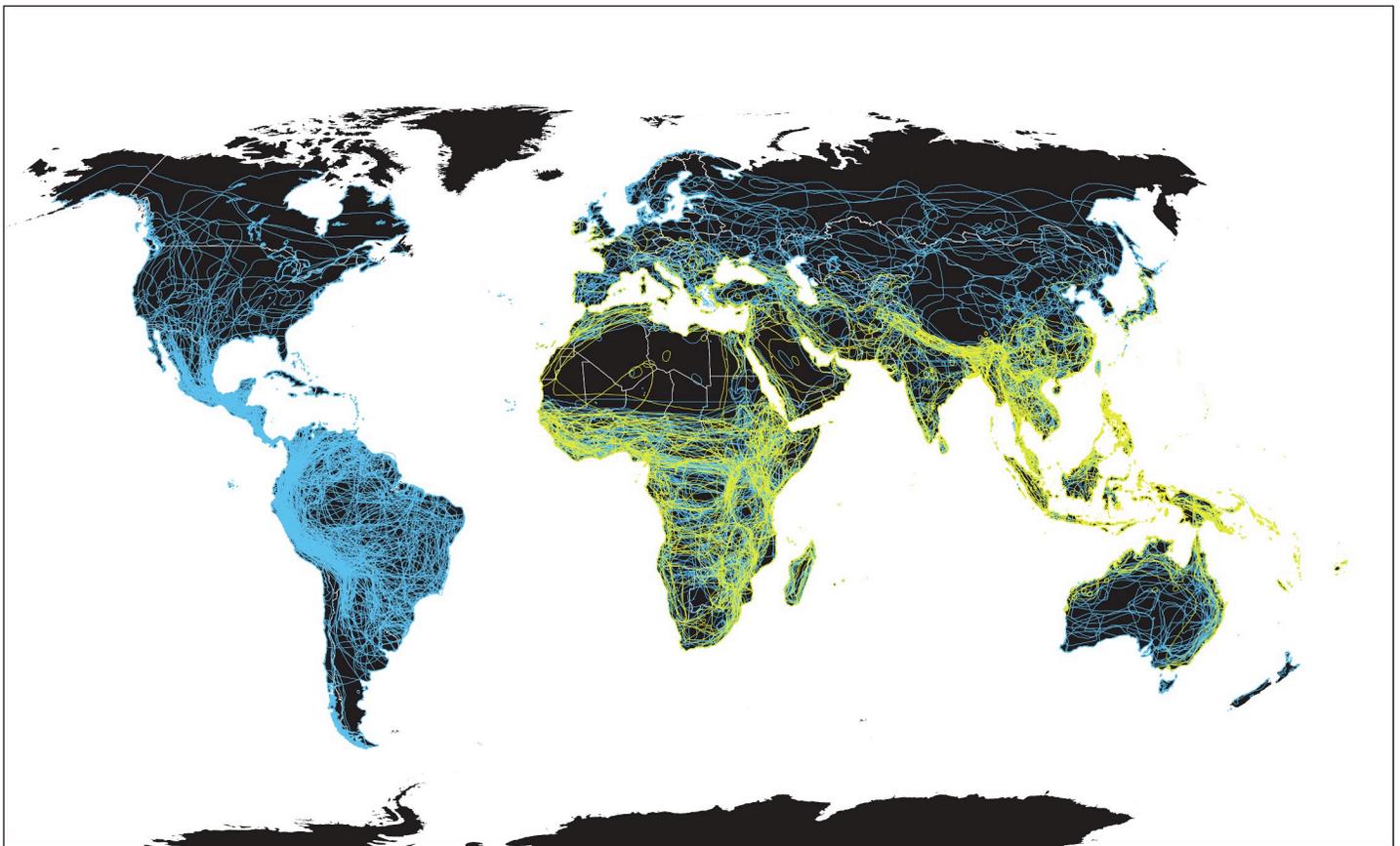
vespertilionid brown long-eared bat (*Plecotus auritus*) and the molossid European free-tailed bat (*Tadarida teniotis*) on Sardinia, where the same novel  $\beta$ -CoV was described in the greater horseshoe bat (*R. ferrumequinum*) [79].

Viruses in the  $\beta$ -CoV subgenera *Hibecovirus* and *Nobecovirus* also have been reported mostly from Old-World bat families Rhinolophidae, Hipposideridae, Rhinonycteridae, and Pteropodidae, except for novel viruses of the latter subgenus detected in four species of the vespertilionid genus *Scotophilus* in Asia and Africa (Fig 1B and 1C) [47, 58, 69].

Bat  $\beta$ -CoVs of the subgenus *Merbecovirus* (MERS-related lineages) occur in a greater diversity of bat families and across more global regions than the other subgenera (Fig 1D) [47, 58, 69]. These widely distributed MERS-like viruses can cause disease in humans (e.g., MERS) and notably appear to be the only bat  $\beta$ -CoVs to diversify among several families of the globally distributed suborder Yangochiroptera (Fig 1D) [47, 58, 69].

### Lack of evidence for $\beta$ -CoVs in temperate-zone North American bats

The several hundred species of extant bats spanning the Americas all belong to the suborder Yangochiroptera, which likely diverged from the Old-World suborder Yinpterochiroptera more than 50 million years ago (Fig 2) [80]. The only  $\beta$ -CoVs detected in the Americas to date



**Fig 2. Old-World and New-World bats.** Overlapping species distribution outlines of bats in the globally distributed suborder Yangochiroptera (blue) and Old-World Yinpterochiroptera (yellow). Maps created using ArcMap (ESRI, Redlands, California, USA) and bat ranges derived from spatial data on terrestrial mammals from the International Union for the Conservation of Nature Red List of Threatened Species, January 2019 [version 6.2]. <https://www.iucnredlist.org>; Downloaded on 11 April 2020.

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belong to the subgenus *Merbecovirus* and appear restricted to two exclusively Neotropical bat families (Phyllostomidae and Mormoopidae) and one that is globally distributed (Molossidae). Distinct CoV lineages in the subgenus *Merbecovirus* were described from three species of *Pteronotus* (family Mormoopidae), four species of *Artibeus*, and Seba's short-tailed bat (*Carollia perspicillata*; family Phyllostomidae) from tropical regions of Mexico [47, 81]. Novel  $\beta$ -CoVs of the subgenus *Merbecovirus* were detected in two neotropical bat species of the family Molossidae: Wagner's bonneted bat (*Eumops glaucinus*) in southern Brazil and the broad-eared free-tailed bat (*Nyctinomops laticaudatus*) in southern Mexico [81, 82]. In vitro infections have shown that primary kidney cells from the Jamaican fruit-eating bat (*Artibeus jamaicensis*) can be infected with MERS-CoV, and virus replication and shedding was reported in experimentally infected bats of this species but without obvious clinical signs of disease [83]. Similar to the evidence for natural invasion of bat rabies viruses among New World bats [84], available evidence suggests  $\beta$ -CoVs may have arrived through South America and have long been evolving in Neotropical bats. Although some bat hosts of *Merbecoviruses* overlap geographically with species of temperate-zone North American bats, none occur outside of the Neotropics. Sampling has been limited, but we are not aware of any published detections of *Merbecoviruses* or any other  $\beta$ -CoVs in temperate-zone North American vespertilionid bats.

Our inference of true patterns of CoV occurrence and distribution in bat populations is limited by uneven global sampling. Yet SARSr-CoVs (*Sarbecovirus* spp.), a focus of many surveillance efforts, have been almost exclusively documented in Old-World Yinpterochiroptera. SARSr-CoVs were only found in the ultra-diverse and globally distributed bat suborder Yangochiroptera under conditions with plausible transmission from co-roosting *Rhinolophus* sp. bats [53, 85]. This absence of evidence for SARS-like  $\beta$ -CoVs in yangochiropteran bats in general, and in temperate-zone vespertilionid bats of North America in particular, likely represents a unique biogeographic pattern driven by underlying factors of host susceptibility or life history. These observations also point to the susceptibility of vespertilionid bats under circumstances of SARSr-CoV environmental exposure and that they may not be naturally immune to these viruses.

Bats rank among the most ecologically important mammals and play varied roles in most of Earth's ecosystems; bats pollinate and disperse seeds of numerous plants in tropical regions, and all over the world, bats are primary nocturnal predators of flying insects [23, 24]. Across the Holarctic, chiropteran species diversity is greatest among hibernating vespertilionid bats. At least 25 of the ecologically diverse vespertilionid species of bats in the US and Canada hibernate [86], which might influence their susceptibility to or interactions with viruses, as has been postulated for common vespertilionids infected with  $\alpha$ -CoVs and rabies virus [44, 87–89]. Hibernation strategies vary among species of bats (e.g., degree of sociality, thermoregulatory behaviors, habitat selection) [90], but bat body temperatures during hibernation generally remain consistently below 10° C for periods lasting 7–9 months per year [91], providing a potential mechanism to limit viral replication and spread [92]. Experimental studies to assess the ability of SARS-CoV-2 or other  $\beta$ -CoVs to survive and replicate in bats (cell lines and individuals) at low temperatures [92, 93] would provide additional insight into risk of reverse zoonosis. However, appropriate tools for studying such possibilities are lacking, particularly immortalized cell lines from several hibernating, vespertilionid bats [59]. These tools would also enable interrogation of other physiological features of vespertilionids that may influence susceptibility, such as receptor-binding affinity and the expression of receptors across tissues. Scientists did not discover and isolate the obligately psychrophilic fungus that causes WNS until they collected samples in bat hibernation sites and moved culture dishes for incubation into laboratory refrigerators [25]. Similar innovative explorations outside the typical temperature conditions of laboratory experimentation could help assess the risk of SARS-CoV-2

infecting the more than two dozen species of bats in the US and Canada that hibernate to survive harsh temperate-zone winters.

## Proactively connecting the wellbeing of human and bat populations

Scientists have long recognized the risk of pathogen spillover from humans to bats [94–96], but bat researchers in North America have not systematically addressed this risk prior to WNS. Outside of reservoir host studies, few bat researchers studied infectious diseases in bats before WNS emerged in 2007 [73] nor studied bat viruses (other than rabies) before bats were retrospectively connected to the SARS epidemic [15, 66, 97]. Fortunately, bat and wildlife disease researchers recently began addressing these knowledge gaps in more detail [7, 97, 98]. Possible explanations for why bats might host particularly pathogenic viruses include characteristics of their life history (e.g., long-lived, wide ranging, multispecies aggregations, daily and seasonal heterothermy) [97], unique physiology for repairing their damaged DNA [99], unique ability to suppress some of their innate immunity pathways [100–105], high species diversity [48], and unmatched metabolic range and high body temperatures during flight [106]. Bats also cryptically come into close contact with humans, increasingly in urban and periurban settings as a result of native habitat loss, often crossing human–wildlife interfaces [107–113].

Except for *Lyssavirus* infections, bats rarely show substantial signs of sickness from the same pathogens that cause virulent disease in humans. Bats cope with viral infections in ways that we do not yet fully comprehend, but learning how they do so may reveal important insights to develop therapeutics and ultimately to protect human health [103–105]. In vitro and laboratory studies demonstrate that bats can specifically regulate naïve immunity pathways to effectively cope with viral infection [114]. For example, dendritic cells generated from the bone marrow of the Egyptian rousette (*Rousettus aegyptiacus*) infected with Marburg virus down-regulate immune-stimulatory pathways and maturation of cells targeted by the virus while up-regulating pathogen-sensing pathways [115]. Unique bat immune regulation may occur with MERS-CoV infection, at least under experimental conditions [101]. Egyptian rousette bats experimentally challenged with SARS-CoV-2 by intranasal inoculation became transiently infected, shed virus, and one cohoused bat became infected but showed no clinical signs of disease other than rhinitis [116]. Our potential lack of understanding of clinical signs of illness in bats and the cryptic habits of many species also generally inhibit our ability to easily detect spillover of pathogens from human to bat populations. This may add to uncertainty about cross-species transmission and dispersal of CoVs among human and animal communities. Laboratory findings suggest human viruses that likely originated in bats, such as HCoV-NL63, are capable of infecting bat cells, at least in vitro [59]. SARS-CoV-2 and other CoVs have some of the longest genomes among all RNA viruses, and despite having specialized RNA proofreading machinery [117, 118], they are still prone to recombination and copy errors in hosts, sometimes resulting in functional adaptations (e.g., altered receptor binding capacity or temperature adaptation of enzymes) [119]. CoVs can even recombine with functional fragments of other virus families, such as when a bat-derived CoV gained a functional gene from a reovirus [21]. Spillover of SARS-CoV-2 from infected humans to North American bats they handle or come in close contact with could lead to the virus becoming either less or more pathogenic to bats or other wildlife, domesticated animals, or humans through genetic mixing in one or more novel hosts. The public health and conservation consequences of a more virulent virus could be severe, whereas genetic mixing in a bat host that resulted in a less-virulent virus might go unnoticed.

## Need for an interdisciplinary response

Effectively managing risks of human disease caused by emerging zoonotic pathogens and ensuring the health and conservation of wildlife species that are potential reservoirs of those disease agents can be synergistic goals under a One Health framework. Spillover risk (from or to wildlife) is often greatest in disturbed ecosystems where there is an elevated frequency of human–wildlife interactions or disruption of ecological patterns [3, 120–124]. Thus, effective bat conservation and management requires understanding both pathogens that cause disease in bats, as well as human activities and ecological contexts that increase direct and indirect interactions with bats that could present health risks [2]. Furthermore, fear-based reactions to disease risk from wildlife, such as culling infected bat populations or indiscriminate killing, often have negative unintended consequences for the interconnected health of both humans and bats (e.g., culling of bats in a Uganda mine led to a more than doubling of Marburg virus prevalence in the bats living there) [30, 125–127]. Temperate-zone vespertilionid bats inhabiting human dwellings in the US and Canada represent a particularly relevant human–wildlife interface, in which conservation and management actions to proactively address the potential consequences for pathogen spillover are worth careful consideration [73].

Conservation-compatible surveillance of bat viruses has demonstrated the potential for mutually beneficial collaboration between public health scientists and conservation stakeholders [94, 113, 125, 128, 129]. Disease-focused studies that integrate ecological principles into a rigorous study design provide the most informative context to interpret bat–virus associations and patterns of richness globally [130–132]. Assessing the risks of SARS-CoV-2 spillover into North American bats presents a timely opportunity to form multidisciplinary scientific teams that include experts on emerging infectious diseases and ecologists with expertise on North American bats [128]. Scientists researching emerging infectious diseases can benefit from sampling opportunities and methods that bat researchers have developed for observing, counting, and noninvasively sampling bats [73, 133]. Bat researchers can learn about human and animal health monitoring and supporting laboratory methods, including biosafety, secure handling/transport of CoV-positive samples, and training in the proper use of personal protective equipment (PPE) from professionals with expertise in veterinary and medical sciences [113, 131, 134, 135]. A shared goal of all stakeholders is to identify and implement simple, widely available diagnostic tests for detecting SARS-CoV-2 infection that are species-independent, practical for field and laboratory use, highly specific and sensitive, and that do not require strict biosafety containment [136]. All investigators can also work together to develop mutually beneficial goals, such as joint risk communications to the public with effective and balanced messaging about bat populations and higher risk activities for human–bat contact.

Adopting a precautionary approach in the face of global COVID-19 transmission among human populations, national and international wildlife organizations have advised limiting capturing and handling of bats in the field to minimize the risk of humans infecting wild bats with SARS-CoV-2 until further assessment can be made [137, 138]. The emergence of WNS in 2007 prompted a similar surge in interdisciplinary collaboration that enabled the rapid advances already mentioned and introduced changes to guidance for PPE use and disinfection practices for bat researchers and recreational cavers. Similarly, the emergence of SARS-CoV-2 and other viruses will likely alter the status quo of bat research, emphasizing the need to carefully weigh risks and benefits of wildlife research in the context of population-altering diseases. For example, PPE, including respiratory protection, is a standard practice adopted by many bat virus researchers but by few others studying and regularly handling bats [134, 139]. The urgent research priority of a rapid, quantitative risk assessment and analysis of various mitigation options is currently underway [137, 140]. One key question is whether the proper use of

optimal PPE, including bidirectional N95 or equivalent masks, along with effective risk communication and adherence to other basic biosafety practices [134, 141, 142] during field work, can significantly reduce the transmission risk of SARS-CoV-2 from humans to bats. In the interim, until new guidelines are established for handling and for close-proximity work with bats, we have outlined gaps in our understanding of SARS-CoV-2 spillover risks at the interface between humans, domesticated animals, and free-ranging wildlife. Temporarily shifting to “hands-off” bat research methods also seems prudent, wherever possible, and could facilitate ongoing work with reduced risk.

### Examples of “hands-off” research strategies

Multiple research strategies that do not involve close contact with free-ranging bats already exist for addressing critical gaps in understanding CoV diversity, distribution, evolution, and potential health effects in temperate-zone bats. For example, a combination of host-cell receptor analyses and in vitro and in vivo experimental infections across a diversity of bat and other mammalian species have helped inform potential host range expansion for SARS-CoV-2. The receptors that many CoVs use to gain access to host cells, such as angiotensin-converting enzyme 2 (ACE2) and dipeptidyl peptidase-4 (DPP4/CD26), have undergone positive selection in bats, resulting in diverse and recombinant CoV strains [72, 143]. These strains can likely bind to numerous variants of a host receptor protein and facilitate spillover into other animal species [72, 144]. SARS-CoV-2 targets and strongly binds to mammalian ACE2 cell receptors [72, 145, 146]. Beta-CoVs of the subgenus *Merbecovirus* (like those known to occur in the Americas) are not known to target ACE2 cell receptors, instead using as a receptor DPP4/CD26 or possibly other receptors [53, 144]. Current in silico predictions that bats will likely have low susceptibility to SARS-CoV-2 based on ACE2 structural analyses conflict with in vitro evidence and do not comprehensively account for ACE2 amino acid sequence variation (including intraspecific variation) that occurs within bats [17, 72, 145]. Assessing SARS-CoV-2 host range will require additional virus-host receptor binding assays in silico and in vitro [17, 53, 72, 144, 145], together with future experimental infection studies for confirmation of Koch’s postulates. In addition, in vitro studies could evaluate species variability in innate immune responses. These investigations will help quantify the potential for North American bat infection and transmission among free-ranging populations.

Examples of other “hands-off” methods applicable to both bat disease and conservation research include the following: virus discovery and characterization focused on existing specimens archived in scientific museums or through partnerships and collaboration with established national bat disease monitoring or surveillance programs [147, 148]; monitoring echolocation calls to determine the occurrence, distributions, and seasonal or nightly activity patterns of bats [133, 149]; digital imaging methods for counting bats and studying physiology and behaviors in the context of disease [90, 108]; sampling guano from below bat roosts to determine bat species and individual identity, population dynamics, and daily or seasonal patterns of bat occupancy and pathogen shedding [71, 150–152]; and mathematical modeling to predict susceptible host species, virus sharing among hosts, spread patterns, or to estimate mortality in affected populations [5, 70, 122, 135]. Promising areas for innovation include making technologies for bat research more accessible to a broader global user base, less expensive, easier to use, and scientifically reproducible through open-source hardware, software, and laboratory methods [153, 154]. In addition to research, standardized field protocols and probabilistic sampling strategies are needed for monitoring bats and their viruses at continental scales ([www.nabatmonitoring.org](http://www.nabatmonitoring.org)) [155, 156], as are longitudinal studies across multiple sites to better understand the ecological drivers of CoV dynamics and spillover [157].

Developing simple management tools and methods for rapidly assessing risks of virus spillover from humans to wildlife, while maintaining scientific rigor, could also help with future disease response. It might also be useful to prepare a suite of tools, protocols, and risk communication strategies for natural resource managers and public health officials to immediately deploy while risks are being assessed. Such prepared management resources could include public outreach material and guidelines for enhanced use of PPE for those in closest contact with potentially susceptible wildlife.

## Conclusion

Many questions remain about the risk of SARS-CoV-2 to naïve wildlife populations, the influences of human behavior on those risks, and the potential for establishment of new CoV reservoirs. Cross-species virus transmission events are relatively rare, requiring an infectious reservoir host to be in contact with a recipient host when conditions concurrently favor susceptibility and onward transmission [12, 113, 114]. The currently unknown, but possible and potentially high-consequence, risk of SARS-CoV-2 transmission and establishment in North American bats (or other free-ranging mammals) warrants precaution [116, 140]. Strategically managing interactions between people and potentially susceptible or at risk species can decrease the probability of cross-species virus spillover [113]. Humans that frequently handle and come into close contact with North American temperate-zone bats, such as bat researchers, wildlife rehabilitators, wildlife/pest control workers, and disease investigators, can help decrease any chances of spillover by adopting basic PPE and biosafety practices and carefully evaluating how their actions might adversely affect bat populations. We are at a critical nexus of biosecurity and natural resource conservation that will require ingenuity and diligence to continue important research on bats whilst simultaneously evaluating the ecological future of SARS-CoV-2. Our actions during this current pandemic could profoundly influence and protect the health of both humans and wildlife in North America.

## Supporting information

**S1 Table. Global patterns of betacoronavirus ( $\beta$ -CoV) associations in bats.** The table lists bat species in which betacoronaviruses ( $\beta$ -CoVs) were detected, organized by viral subgenera and clade (for Sarbecorviruses), bat family, bat suborder, and general global region where the species of bat occurs. Reference to the published literature sources of information for each row are listed in the last column. Provided in comma-separated value (.csv) format at <https://doi.org/10.5066/P9U461PJ>. (XLSX)

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# **Exhibit K**

# SARS-CoV-2 infection in farmed minks, the Netherlands, April and May 2020

Nadia Oreshkova<sup>1</sup>, Robert Jan Molenaar<sup>2</sup>, Sandra Vreman<sup>1</sup>, Frank Harders<sup>1</sup>, Bas B Oude Munnink<sup>3</sup>, Renate W Hakze-van der Honing<sup>1</sup>, Nora Gerhards<sup>1</sup>, Paulien Tolsma<sup>4</sup>, Ruth Bouwstra<sup>2</sup>, Reina S Sikkema<sup>3</sup>, Mirriam GJ Tacke<sup>1</sup>, Myrna MT de Rooij<sup>5</sup>, Eefke Weesendorp<sup>1</sup>, Marc Y Engelsma<sup>1</sup>, Christianne JM Brusckhe<sup>6</sup>, Lidwien AM Smit<sup>5</sup>, Marion Koopmans<sup>3</sup>, Wim HM van der Poel<sup>1</sup>, Arjan Stegeman<sup>7</sup>

1. Wageningen Bioveterinary Research, Wageningen University and Research, Lelystad, the Netherlands
2. GD Animal Health, Deventer, the Netherlands
3. Department of Viroscience, Erasmus University Medical Center, Rotterdam, the Netherlands
4. Regional Public Health Service Brabant-Zuid-Oost, Eindhoven, the Netherlands
5. Institute for Risk Assessment Sciences (IRAS), Utrecht University, Utrecht, the Netherlands
6. Ministry of Agriculture, Nature and Food Quality, The Hague, the Netherlands
7. Department of Farm Animal Health, Faculty of Veterinary Medicine, Utrecht University, the Netherlands

Correspondence: Wim H.M. van der Poel ([wim.vanderpoel@wur.nl](mailto:wim.vanderpoel@wur.nl))

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**Respiratory disease and increased mortality occurred in minks on two farms in the Netherlands, with interstitial pneumonia and SARS-CoV-2 RNA in organ and swab samples. On both farms, at least one worker had coronavirus disease-associated symptoms before the outbreak. Variations in mink-derived viral genomes showed between-mink transmission and no infection link between the farms. Inhalable dust contained viral RNA, indicating possible exposure of workers. One worker is assumed to have attracted the virus from mink.**

Currently, humanity is facing a pandemic of a new coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The virus is spreading efficiently among people, causing predominantly respiratory disease with varying degree of severity. The virus has also been shown to infect a number of animal species under experimental conditions. Rhesus and cynomolgus macaques, ferrets, cats and golden Syrian hamsters supported viral replication in respiratory tract and some of those species (rhesus macaques, juvenile cats and hamsters) displayed a mild to moderate clinical disease [1-9]. Besides the experimental infections, occasional spillover from humans to domestic or captive animals has been reported. In a few isolated cases, cats and dogs owned by infected individuals tested positive for SARS-CoV-2 RNA and occasionally, cats also displayed clinical disease [10,11]. Recently, several tigers in the Bronx zoo (New York City, United States (US)) with respiratory symptoms were confirmed positive for SARS-CoV-2 [10]. In all cases, a direct correlation with infected humans was established or at least other sources of infection were excluded [10].

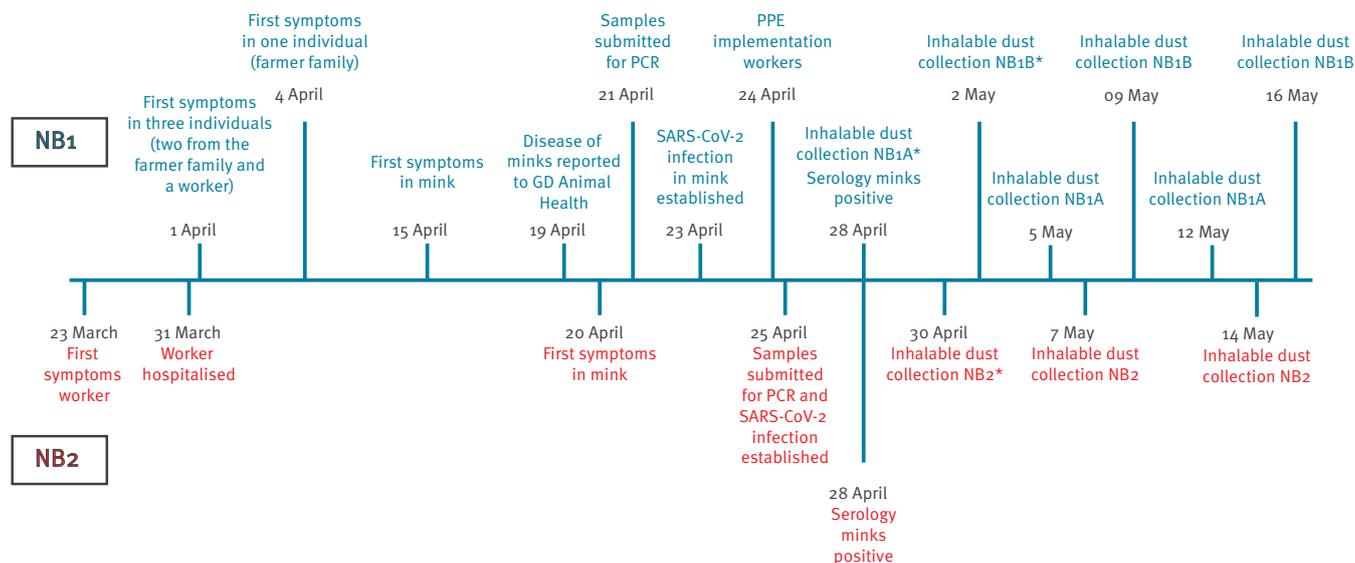
Here, we report SARS-CoV-2 infection of minks on two farms in the Netherlands and describe the associated clinical signs, pathological and virological findings. Sequence analysis of mink-derived viruses pointed at humans as the probable source of the initial infection and demonstrated transmission between minks. Furthermore, the presence of viral RNA in inhalable dust collected from the farms indicated a possible exposure of workers to virus excreted by minks.

## Mink farming background

Minks are farmed for their fur. In the Netherlands, there are around 125 mink farms, with an average of 5,000 female breeding animals. In 2019, 4 million minks were produced. The sector has around 1,200 full-time and 400 part-time employees [12]. On two mink farms (NB1 and NB2) situated in the south of the Netherlands, province North Brabant (NB), an increased mink mortality was observed mid-April 2020, which coincided with display of respiratory signs in some animals. On NB1, 13,700 animals are housed in two separate, but closely situated houses (house A and house B, 115 m apart), which are served by the same personnel and vehicles. NB2 has 7,500 animals. Farms NB1 and NB2 are 14 km apart from each other. There was no connection of workers, vehicles or animal transports, between these two farms. On both farms, minks are individually housed in wire netting cages with a nest box. The cages are arranged in long single rows, separated by feeding alleys. The two cage sides that border other cages are solid, made of wood or plastic, ensuring that there is no direct animal-to-animal contact. The cage rows are situated inside halls, which provide a roof, but are largely open to the wind from the sides. Both farms are family-owned and besides the four (NB1) and

**FIGURE 1**

Schematic representation of the time-line of events in the first month of a SARS-CoV-2 outbreak on two mink farms, the Netherlands, April 2020



Covid-19: coronavirus disease; NB1/NB2: Farms 1 and 2 in North Brabant; PPE: personal protective equipment; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2.

Dates of significant events are shown with the corresponding findings. Cases of (suspected) human Covid-19 infections in farm workers that coincided with the SARS-CoV-2 infection of the minks are excluded from this report. Analysis of those cases is currently being performed and will be reported in a subsequent publication. Asterisks indicate the dates on which dust samples collected inside the mink farm buildings were found positive for viral RNA.

**TABLE 1**

Gross pathology and cause of death of necropsied minks, SARS-CoV-2 outbreak on two mink farms, the Netherlands, April 2020 (n = 36)

Farm NB1				Farm NB2			
Animal number	Date of death	Date of necropsy	Cause of death	Animal number	Date of death <sup>a</sup>	Date of necropsy	Cause of death
1	28 Apr	28 Apr	Interstitial pneumonia	1	27 Apr	27 Apr	Sepsis and lung oedema with congestion
2 <sup>b</sup>	28 Apr	28 Apr	Interstitial pneumonia	2 <sup>b</sup>	27 Apr	27 Apr	Interstitial pneumonia
3	28 Apr	28 Apr	Interstitial pneumonia	3	27 Apr	27 Apr	Aleutian disease
4	28 Apr	28 Apr	Interstitial pneumonia	4	27 Apr	27 Apr	Aleutian disease
5	28 Apr	28 Apr	Interstitial pneumonia	5	27 Apr	27 Apr	Sepsis
6	28 Apr	28 Apr	Interstitial pneumonia	6	27 Apr	27 Apr	Dystocia
7	28 Apr	28 Apr	Interstitial pneumonia	7 <sup>b</sup>	27 Apr	27 Apr	Interstitial pneumonia
8	28 Apr	28 Apr	Interstitial pneumonia	8 <sup>b</sup>	27 Apr	27 Apr	Interstitial pneumonia
9	28 Apr	28 Apr	Aleutian disease	9	26 Apr	27 Apr	Interstitial pneumonia
10	28 Apr	28 Apr	Interstitial pneumonia	10	26 Apr	27 Apr	Interstitial pneumonia
11	28 Apr	28 Apr	Interstitial pneumonia	11	26 Apr	27 Apr	Interstitial pneumonia
12	28 Apr	28 Apr	Interstitial pneumonia	12	26 Apr	27 Apr	Interstitial pneumonia
13 <sup>b</sup>	28 Apr	28 Apr	Interstitial pneumonia	13	26 Apr	27 Apr	Interstitial pneumonia
14 <sup>b</sup>	28 Apr	28 Apr	Interstitial pneumonia	14	26 Apr	27 Apr	Interstitial pneumonia
15	28 Apr	28 Apr	Interstitial pneumonia	15	26 Apr	27 Apr	Interstitial pneumonia
16 <sup>b</sup>	28 Apr	28 Apr	Interstitial pneumonia	16	26 Apr	27 Apr	Interstitial pneumonia
17	28 Apr	28 Apr	Interstitial pneumonia	17	26 Apr	27 Apr	Interstitial pneumonia
18	28 Apr	28 Apr	Interstitial pneumonia	18	26 Apr	27 Apr	Sepsis

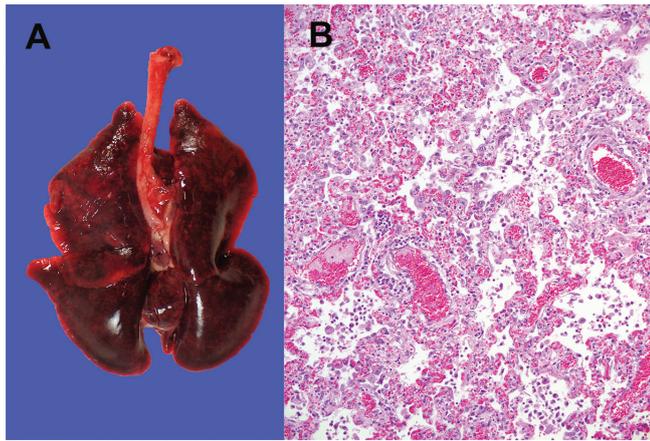
SARS-CoV-2: severe acute respiratory syndrome coronavirus 2.

<sup>a</sup> Date when the animals were found dead (animals are inspected daily).

<sup>b</sup> Organs from those animals were collected for SARS-CoV-2 qPCR.

## FIGURE 2

Lung from a necropsied mink, SARS-CoV-2 outbreak on two mink farms, the Netherlands, April 2020



SARS-CoV-2: severe acute respiratory syndrome coronavirus 2.

Panel A: Representative macroscopic image of an affected lung. Panel B: Representative microscopic image (objective 20x) of a section of the lung, fixed in 10% formalin and stained with haematoxylin and eosin, showing interstitial pneumonia.

two (NB2) members of the farmer family, one and six employees were working on the farms, respectively.

### Disease history and clinical observations

Signs of respiratory disease in the animals were reported on 19 and 20 April 2020 (Figure 1) on NB1 and NB2, respectively. The symptoms were mostly limited to watery nasal discharge, but some animals showed severe respiratory distress. The exact numbers of animals that displayed symptoms, as well as the severity of the symptoms, were not registered. On both farms, the veterinarian was consulted when severe respiratory disease symptoms were observed by the farmer. Animals that had died were necropsied and tested for SARS-CoV-2, influenza A, adenoviral infection, *Escherichia coli* and *Pseudomonas aeruginosa*. All tests except SARS-CoV-2 were negative. Overall mortality between date of reporting and 30 April was 2.4% at NB1 and 1.2% at NB2, while ca 0.6% would have been expected, based on observations from previous years, in the same period. Affected animals were not concentrated in a specific location, but rather scattered throughout the buildings of each farm. At this time of the year, the mink populations consist mainly of pregnant females. In the few litters that were already present, no increase in pup mortality was noticed.

Lungs from three recently died animals per farm were collected and submitted for qPCR analysis on 21 (NB1) and 25 (NB2) April. One sample per farm was also sequenced (index samples). In the following week, 36 recently dead animals were collected (18 per farm) and necropsied. A throat and rectal swab were taken from each animal for qPCR analysis.

## Pathological analysis

### Macroscopic findings

The necropsies revealed that 16 of 18 animals from NB1 and 12 of 18 from NB2 had diffusely dark to mottled red, wet lung lobes that did not collapse when opening the thoracic cavity, indicating interstitial pneumonia (Table 1 and Figure 2A). Other investigated organs displayed no significant macroscopic changes. Minks without the described lung findings had macroscopic changes consistent with either chronic Aleutian disease, septicæmia, or dystocia. From seven animals with clear macroscopic lung changes, organs were harvested for histopathological and virological investigation.

### Histological findings

A severe diffuse interstitial pneumonia with hyperaemia, alveolar damage and loss of air containing alveolar lumina was detected in all the seven harvested lungs (Figure 2B). Bacterial cultures from the organs of the seven animals were negative.

### Virus detection and sequencing

Presence of viral RNA was determined by qPCR against the SARS-CoV-2 E gene (Table 2) [13]. Viral RNA was detected in the conchae, lung, throat swab and rectal swab of all seven minks from which organs were collected. In addition, viral RNA was detected in the liver of one, and in the intestines of three animals. Splens of all seven animals were negative for viral RNA (Table 2). In the swabs collected from all 36 necropsied animals, viral RNA was detected in all throat swabs and 34 of the 36 rectal swabs. The cycle threshold (Ct) values varied, but were on average lower in the throat swabs than in the rectal swabs (average Ct = 21.7 and 31.2, respectively), indicating higher viral loads in the throat swabs.

The viral sequences of the index samples and from additional four and five animals from NB1 and NB2, respectively, were determined by next generation sequencing and deposited in GenBank (MT396266 and MT457390–MT457399). Phylogenetic analysis of the sequences suggests separate virus introductions to each of the farms (Figure 3). The index sequences show nine (NB1) and 15 (NB2) nucleotide substitutions across the complete genome in comparison with Wuhan-Hu-1 (NC\_045512.2, EPI\_ISL\_402125). The two index sequences diverge at 22 nucleotide positions, but the sequences from each farm cluster together (Figure 3). Mink-specific single nucleotide polymorphisms were found in ORF1a, ORF1b, spike, ORF3, ORF7a and 3'UTR (Supplementary Table 2).

### History of coronavirus disease in farm workers

Farm owners and their families were interviewed by the public health service for possible history of disease. Four persons on farm NB1 have had respiratory disease symptoms compatible with Covid-19 since beginning of April, including three members of the farmer's family

**TABLE 2**

Virus titres, determined by qPCR in organs and swabs of necropsied minks, SARS-CoV-2 outbreak on two mink farms, the Netherlands, April 2020 (n = 36)

	Animal number	Conchae	Lung	Spleen	Liver	Distal large intestines	Throat swab	Rectal swab
Farm NB1	2	8,25	4,54	Not detected	Not detected	4,22	6,87	3,30
	13	9,16	5,17	Not detected	Not detected	3,56	6,81	3,01
	14	8,08	3,83	Not detected	Not detected	Not detected	7,04	3,95
	16	7,08	3,90	Not detected	Not detected	4,97	6,47	4,47
Farm NB2	2	8,19	5,77	Not detected	Not detected	Not detected	8,03	2,58
	8	8,55	5,55	Not detected	3,45	Not detected	7,30	3,84
	7	8,46	5,98	Not detected	Not detected	Not detected	6,69	5,42

SARS-CoV-2: severe acute respiratory syndrome coronavirus 2.

Titres were calculated based on a calibration curve of a virus stock with a known infectious virus titre and are expressed as log<sub>10</sub> (median tissue culture infectious dose (TCID<sub>50</sub>)/g of tissue (organ material) or log<sub>10</sub> TCID<sub>50</sub>/mL of swab material (swabs were always submerged in 2 mL of cell culture medium)).

and a worker (Figure 1). These people were not investigated for SARS-CoV-2 infection. At NB2, one worker had been diagnosed with SARS-CoV-2 infection and hospitalised on 31 March (Figure 1). A clinical sample was retrieved, but the viral load was too low for sequencing analysis. At farm NB1, one person who stayed on the farm, showed mild respiratory disease and was diagnosed with SARS-CoV by 28 April. Based on preliminary sequencing results, this person was assumed to have attracted the virus from mink. A further detailed investigation focusing on the transmission of the virus between humans and mink on the farms is ongoing.

### Sampling of the environment and stray cats

Inhalable dust samples were collected three times between 28 April and 16 May (Figure 1) by active stationary air sampling during 5–6 h, using Gilian GilAir 5 pumps (Sensidyne, St. Petersburg, US) at 3.5 L/min, total dust sampling system (Gesamtstaubprobenahme; GSP) sampling heads (JS Holdings, Stevenage, United Kingdom) and Teflon filters (Pall Corporation, Ann Arbor, US). In each mink house, sampling was conducted at three different locations. Viral RNA was detected in two of the three samples from NB1, house A (Ct = 35.95 and 38.18) and in one of three samples from NB1, house B (Ct = 35.03) and from NB2 (Ct = 35.14) on the first sampling moment, but all samples were negative on the second and third sampling moments.

A total of 24 stray cats found in the surroundings of the farms NB1 and NB2 were sampled for SARS-CoV-2 infection by collecting serum and oropharyngeal swabs. Seven cats had antibodies against SARS-CoV-2, detected by an in-house virus microneutralisation assay, and one cat was positive for viral RNA. However, the amounts of viral RNA were very small, and we were unable to generate a sequence from this cat. The sampled stray cats inhabit the surroundings of the farms, but do not come into the houses of people.

### Discussion

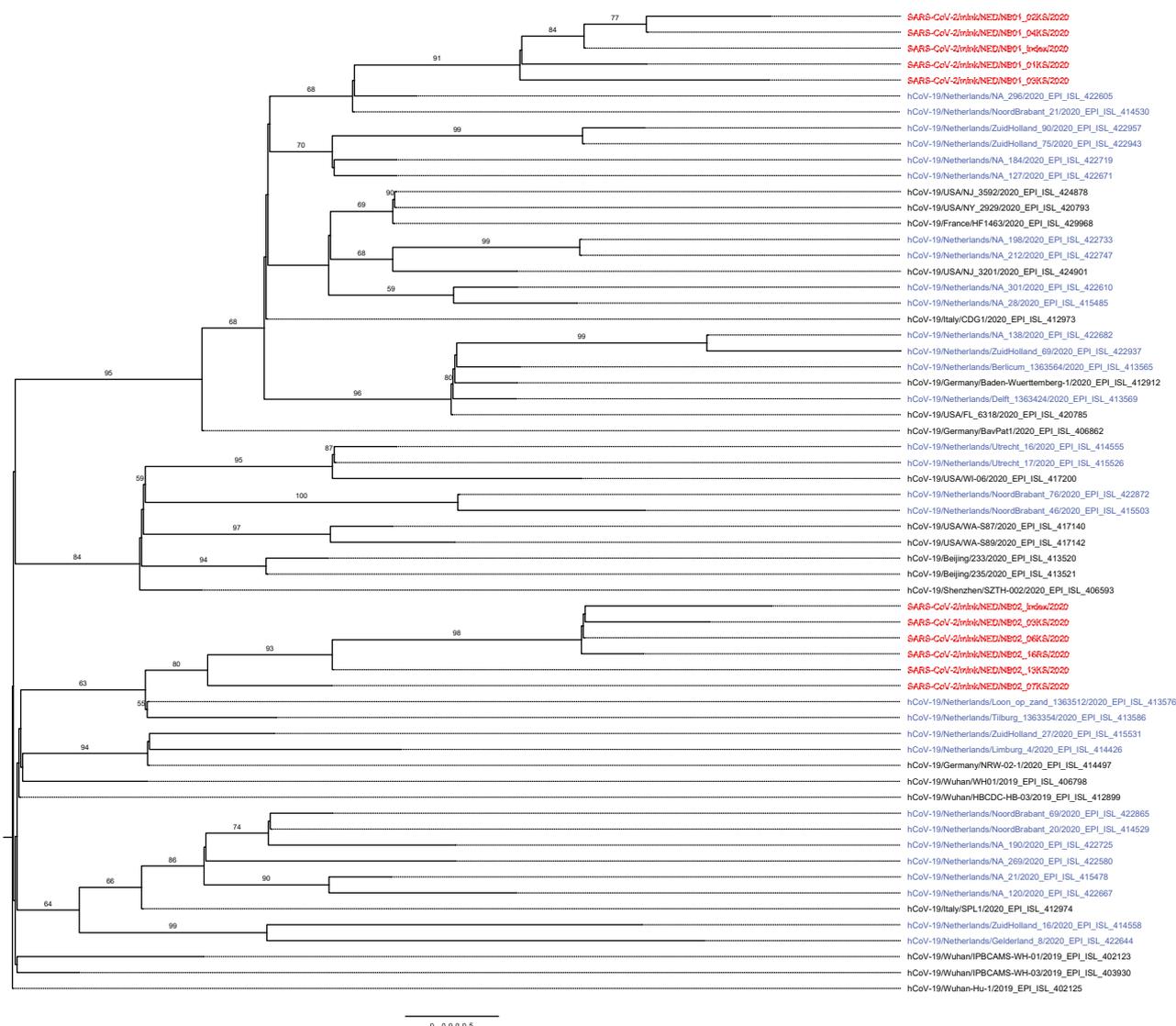
Here we present a report of infection of two mink farms with SARS-CoV-2. While this manuscript was being

prepared, similar SARS-CoV-2 outbreaks occurred on another nine farms in the Netherlands, eight in the province Noord Brabant and one in the province Limburg. On farms NB1 and NB2 described here, coronavirus disease (COVID-19)-like symptoms were present in people working on the farms before signs were seen in the minks, and SARS-CoV-2 infection was confirmed in one hospitalised person. The viral sequences obtained from the mink samples were closely related to sequences of human-derived isolates. The distance between the two sequence clusters originating from the two farms suggests separate introductions, arguing against an epidemiological connection between the two farms. Whether the outbreaks on the rest of the farms were connected to the first two cases and between each other is being investigated. The most likely explanation for the widespread infection on the mink farms is introduction of the virus by humans and subsequent transmission among the minks. Ferrets, which are closely related to minks, were also able to transmit the virus to other ferrets under experimental conditions; transmission was observed under both direct and indirect contact (animals were housed in cages with a permeable partition separating infected from uninfected animals) [5]. Minks can be housed in cages with permeable separation between them, which could have explained animal-to-animal transmission. On the mink farms in question however, animals are caged separately with non-permeable partition between cages, precluding direct contact as a mode of transmission. Indirect transmission between minks could either be through fomites (e.g. by feed or bedding material provided by humans), by infectious droplets generated by the infected animals, or by (faecally) contaminated dust from the bedding.

Detection of viral RNA in the airborne inhalable dust on the mink farms clearly suggests dust and/or droplets as means of transmission between the minks and occupational risk of exposure for the workers on the farms. While the exact occupational hazard for humans is currently being determined, to anticipate the exposure risk for personnel working on the mink farms with confirmed

**FIGURE 3**

Maximum likelihood phylogenetic tree of SARS-CoV-2 sequences from minks and selected full-length sequences from the GISAID EpiCoV database



GISAID: Global Initiative on Sharing All Influenza Data; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2.

Red: sequences from minks described in this report; blue: Dutch sequences from GISAID; black: international sequences from GISAID.

Details on the sequences from GISAID (<https://www.gisaid.org/>) used for this analysis, based on proposed lineages [14], are listed and acknowledged in Supplementary Table 1). The collected sequences were aligned using MAFFT v7.427 [15] and the evolutionary history was inferred by RAxML version 8.2.12 [16] using the maximum likelihood method based on the general time reversible model with a gamma-distributed variation of rates and 1,000 bootstrap replicates. The tree is rooted at Wuhan-Hu-1. Bootstrap support values above 50 are indicated at the corresponding branch.

SARS-CoV-2 infections, the public health authorities in the Netherlands have issued an advice for all workers on infected mink farms to wear personal protective equipment including face masks, goggles, gloves and overalls, while fulfilling their work duties [17]. Visitors are prohibited to enter those farms. Mink farm workers who have COVID-19 symptoms are advised to stay at home. Mandatory screening of all Dutch mink farms was started on 28 May and is aimed to be completed by 15 June. On 3 June, the Dutch Ministry of Agriculture

decided to cull all minks of SARS-CoV2 infected farms, starting on 5 June [18].

Mink farms are present in other countries in Europe, China and the US but so far, SARS-CoV-2 infections in these animals have been reported only in the Netherlands. The purpose of the current report is to raise awareness in the scientific community and in the mink industry that minks are susceptible for SARS-CoV-2. Infected animals developed respiratory disease

with typical pathological findings of viral pneumonia and were able to transmit the virus among each other. While this manuscript was in preparation, also serological surveillance was performed on the farms NB1 and NB2. Sixty random serum samples were collected from the minks of each farm and were all found positive for SARS-CoV-2 neutralising antibodies, except one sample from NB1. These findings coincided with the disappearance of symptoms and mortality on the farms and were followed by inability to detect viral RNA in inhalable dust, suggesting that the SARS-CoV-2 outbreaks were widely spread within the farms and resolved on their own when the majority of animals had seroconverted. There are still a lot of questions to address, especially regarding possible transmission from mink to human and exposure risks for the public outside the farms. In this report, we showed that humans can become a source of infection for minks, which results in a disease outbreak. Human infections acquired from mink are also suspected and data on exposure risk for humans as well as samples of potentially Covid-19-infected people on the farms are being collected and analysed; forthcoming results will be published in the future.

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### Conflict of interest

None declared.

### Authors' contributions

Nadia Oreshkova - combination of the data and writing of the manuscript. Robert Jan Molenaar, Sandra Vreman, Ruth Bouwstra - field work, obtaining of mink material and pathological work. Frank Harders, Bas B Oude Munnink, Reina S Sikkema, Marc Engelsma - sequencing and sequence analysis. Renate Hakze, Nora Gerhards, Mirriam Tacken, Eefke Weesendorp - sample preparations and PCR analysis. Paulien Tolsma - interviewing of the farm workers and providing the human-related data. Myrna MT de Rooij, Lidwien AM Smit - environmental sampling and analysis. Christianne Bruscke - commissioner advice. Marion Koopmans, Wim HM van der Poel, J Arjan Stegeman - coordination between the different institutions, supervision and advice.

All authors contributed to the writing by providing information about their work and by reviewing the manuscript.

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# **Exhibit L**









# **Exhibit M**

**Voluntary Report** – Voluntary - Public Distribution

**Date:** September 02,2020

**Report Number:** NL2020-0042

**Report Name:** Dutch Mink Industry to Close in 2021 Due to Coronavirus

**Country:** Netherlands

**Post:** The Hague

**Report Category:** Agricultural Situation, Agriculture in the News, Livestock and Products

**Prepared By:** Marjolein Selten

**Approved By:** Christopher Riker

**Report Highlights:**

The government has elected to put an end to Dutch mink farming three years ahead of schedule due to the recent coronavirus (COVID-19) outbreaks on the country's mink farms. More than one-third of all Dutch mink farms have been infected by COVID-19, to date. The 'fur period' starts in November and once all minks have been stripped of their fur, the breeders will not longer be permitted to place new animals in their cages (effectively shuttering the industry by the end of March 2021). In the meantime, additional control measures have been imposed on the industry, and a mandatory buyout scheme will be established to buyout the industry before it was scheduled to close in 2024.

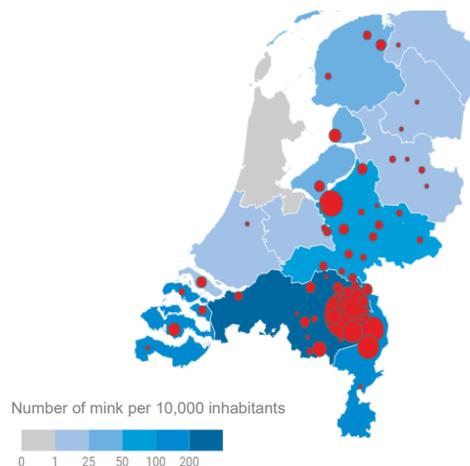
## General

Although the Dutch mink industry was scheduled to cease operations on January 1, 2024 (pursuant to the [Fur Animal Husbandry Act](#)<sup>1</sup>), Ministers Schouten (Agriculture, Nature and Food Quality) and de Jonge (Health, Welfare and Sport) have ordered all mink farms in the Netherlands to end their breeding programs by the end of March 2021 due to the rapid spread of the coronavirus (COVID-19) on these farms. The Ministers made this decision based on a recommendation from the Zoonotic Outbreak Management Team (known by its Dutch Acronym of OMT-Z).<sup>2</sup> In an official press release, the Government stated:

“despite the limited risk to public health at the moment, it is desirable to stop the spread of the virus via mink farming. It is undesirable that the virus continues to circulate on mink farms as there is a risk that, in the long term, this will lead to infections - via employees - of people outside the mink farm. The OMT-Z therefore recommends a mandatory buyout scheme for mink farms. The Cabinet is adopting this advice.”<sup>3</sup>

To date, more than one-third of Dutch mink farms have been infected by COVID-19. Most of the farms, including those that have been infected, are located in the southeastern part of the country -- in the provinces of Brabant and Limburg (see, e.g., Figure 1). All farms where mink were found to be infected by COVID-19 have been cleared by the Netherlands Food and Consumer Product Safety Authority (known by its Dutch acronym of NVWA). Since the beginning of the COVID-19 crisis (as of September 1, 2020), more than 1.5 million mink<sup>4</sup> have been culled by the NVWA across 43 farms.

**Figure 1. Mink Farms in the Netherlands**



Source: [Brabants Dagblad](#), based on figures of Statistics Netherlands

<sup>1</sup> Since 2013, there has been [a ban on opening new mink farms or expanding existing operations](#) (in Dutch) in the Netherlands, and mink farming originally would have to be completely phased out by January 1, 2024.

<sup>2</sup> If there is a cross-regional outbreak of infectious disease in the Netherlands, or if there is an international threat of infectious disease, the Dutch National Institute for Public Health and the Environment can convene an Outbreak Management Team (OMT).

<sup>3</sup> <https://www.rijksoverheid.nl/actueel/nieuws/2020/08/28/kabinet-neeomt-omt-z-advies-verplichte-stoppersregeling-voornertsenfokkerij-over>

<sup>4</sup> <https://www.dutchnews.nl/news/2020/08/coronavirus-spreads-to-39th-fur-farm-no-moves-yet-on-total-cull/>

According to Government sources, the measures will cost roughly 180 million euros: 40 million for the culls and 140 million for a “mandatory buyout scheme.” In November, the “fur period” begins (i.e., when mink are stripped of their fur). Afterwards, the breeders will no longer be permitted to put new animals in their cages (effectively ending the industry by the Government’s new target).

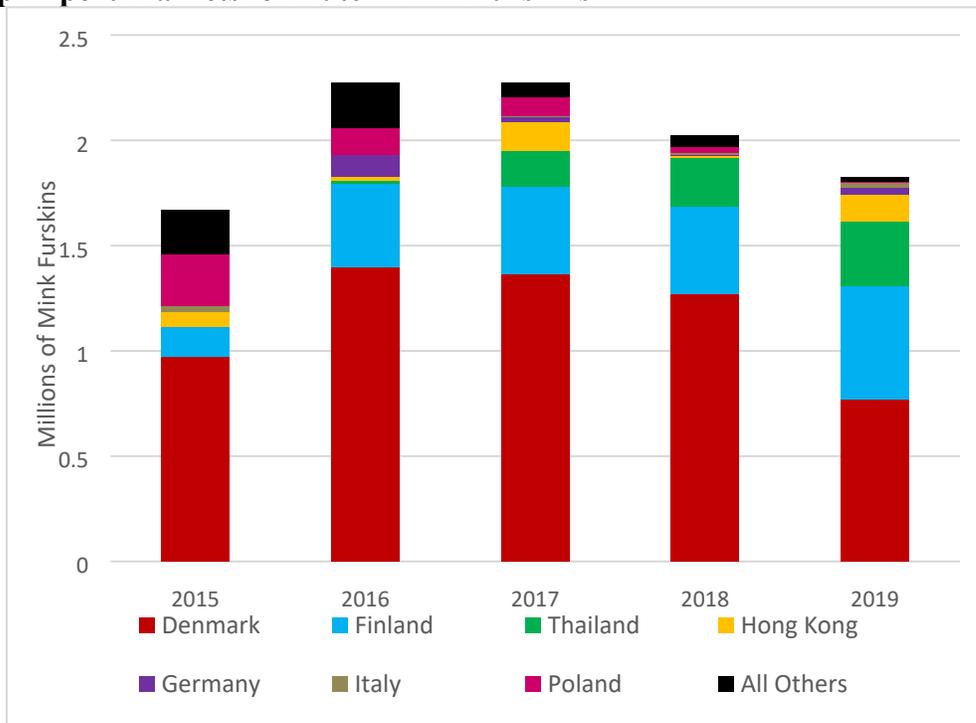
In addition to the buyout scheme, Minister Schouten has also strengthened the COVID-19 control measures on mink farms to help mitigate the further spread of the virus. According to the OMT-Z, humans are the most likely source of contamination on Dutch mink farms. The measures are therefore aimed at preventing this ‘contamination route through, for example, stricter registration of who works when and where. For employees who work at multiple locations, a waiting period of ten days will be imposed before they can start working on another farm. The Minister has also requested an investigation into the industry's compliance with the initial control measures imposed on the sector.

The plans for the termination of the mink industry in the Netherlands have been approved by the Cabinet and further details on the compensation scheme (including the exact amount of compensation that mink farmers will receive) are expected in the coming weeks.

Dutch Exports of Mink Furskins

In 2019, the Netherlands exported \$50 million of raw, whole mink furskins. Denmark (the world’s largest producer of mink furskins) was the Dutch industry’s leading export market, accounting for 42 percent of exports, followed by Finland (29 percent), Thailand (17 percent) and Hong Kong (7 percent).

**Figure 2. Top Export Markets for Dutch Mink Furskins**



Source: Trade Data Monitor, HS Code 4301.10

Related Reports:

- [NL2020-0016 - COVID-19 Found on Dutch Mink Farms](#)
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- [NL2020-0036 - Coronavirus Continues to Challenge Dutch Mink Farms](#)

**Attachments:**

No Attachments.

# **Exhibit N**



HEALTHCARE & PHARMA

AUGUST 27, 2020 / 1:36 PM / UPDATED 3 MONTHS AGO

# Netherlands to close mink farms after coronavirus outbreaks

By Reuters Staff

1 MIN READ



NOW READING Netherlands to close mink farms after coronavirus outbreaks

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FILE PHOTO: People with and without masks in the Red Light District in Amsterdam, Netherlands August 5, 2020. REUTERS/Eva Plevier

AMSTERDAM (Reuters) - More than 100 mink farms in the Netherlands will be ordered closed by March after animals at dozens of locations contracted the coronavirus, Dutch news agency ANP reported on Thursday.

Hundreds of thousands of the ferret-like animals, which are bred for their fur, have been culled in the Netherlands and other European countries since the virus outbreak.

The Netherlands had already intended to halt its mink breeding industry by 2024, but decided to bring forward the closures after several farm employees contracted COVID-19.

The government has set aside 180 million euros (\$212 million) to compensate farmers, the ANP report said, citing sources.

According to the Dutch Federation of Pelt Farmers, the Netherlands exports around 90 million euros

(\$101 million) worth of fur a year for use in China and globally. The country had roughly 900,000 mink at 130 farms, Statistics Netherlands data said.

Reporting by Anthony Deutsch; Editing by Leslie Adler

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# North Denmark in lockdown over mutated virus in mink farms

By JAN M. OLSEN November 6, 2020



COPENHAGEN, Denmark (AP) — More than a quarter million Danes went into lockdown Friday in a northern region of the country where a mutated variation of the coronavirus has infected minks being farmed for their fur, leading to an order to kill millions of the animals.

Prime Minister Mette Frederiksen said the move was meant to contain the

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virus, and it came two days after the government ordered the cull of all 15 million minks bred at Denmark's 1,139 mink farms.

by Taboola

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The coronavirus evolves constantly and, to date, there is no evidence that any of the mutations pose an increased danger to people. But Danish authorities were not taking any chances.

“Instead of waiting for evidence, it is better to act quickly,” said Tyra Grove Krause, head department at Statens Serum Institut, a government agency that maps the spread of the coronavirus in Denmark.

In seven northern Danish municipalities with some 280,000 residents sport and cultural activities have been suspended, public transportation has been stopped and regional borders have been closed. Only people with so-called “critical functions” such as police and health officials and different authorities are being permitted to cross municipal boundaries.

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People in the region have been urged to be tested. As of Saturday, restaurants must close and school students from fifth grade and up will switch to remote learning Monday.

“We must knock down completely this virus variant,” Health Minister Magnus Heunicke said Thursday, adding that the mutated virus had been found in 12 people.

Last month, Denmark started culling millions of minks in the north of the country after COVID-19 infections were reported among the stock there. Nationwide, at least 216 out of the 1,139 fur farms in Denmark have now been

infected.

Kaare Moelbak of Statens Serum Institut said the virus variant was registered in August and September, and no mutations have been found since, so it was not known if it still exists. The mutated virus was found in five mink farms, according to the government body.

WHO officials said each case needs to be evaluated to determine if any of the changes mean the virus behaves differently.

“We are a long, long way from making any determination of that kind,” said Mike Ryan, the WHO emergencies chief. He said that such mutations happen all the time in viruses.

“Right now the evidence that we have doesn’t suggest that this variant is in any way different in the way it behaves,” he said in Geneva.

Peter Ben Embarek, a WHO expert on food safety, said that initial studies on pigs, chickens and cattle “show that these species are not at all susceptible in the same way that mink are, for example. So even if these animals were infected, they would not be able to sustain and spread the disease in the same way.”

Britain on Friday said that people coming from Denmark must self-isolate for 14 days, adding the country to a list of countries it deems risky.

The Danish government said a mutation of the virus had been found in 12 people infected by minks, which farmers have been ordered to cull en masse, but experts said the significance of any variant strain and its effect on humans was unclear because it was yet to be studied.

Denmark, the world’s largest mink fur exporter, produces an estimated 17 million furs per year. Copenhagen Fur, a cooperative of 1,500 Danish breeders,

accounts for 40% of the global mink production. Most of its exports go to China and Hong Kong.

The pelts of the mink will be destroyed and Danish fur farmers have said the cull, which is estimated to cost up to 5 billion kroner (\$785 million), may spell the end of the industry in the country.

Overall, Denmark has reported 53,180 cases of coronavirus and 738 deaths.

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Jamey Keaten in Geneva contributed to this report.



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LONDON (AP) —  
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# **Exhibit P**

# The Guardian

## Travel to UK from Denmark banned amid worries over Covid in mink

**All non-British national or resident travellers who have been in Denmark in past 14 days will be denied entry into UK**

**Coronavirus - latest updates**  
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**Simon Murphy and Peter Beaumont**

Sat 7 Nov 2020 03.13 EST



Minks are seen at Hans Henrik Jeppesen's farm near Soroe, Denmark, after the Danish government's decision to cull his entire herd. Photograph: Jacob Gronholt-Pedersen/Reuters

Travel to the UK from Denmark has been banned amid mounting concern over an outbreak in the country of a mutation of coronavirus linked to mink, the British government has announced.

Downing Street had already taken action to remove Denmark from the travel corridor, forcing arrivals to quarantine for two weeks from Friday at 4am.

But following a Covid committee meeting on Friday afternoon, the UK government is halting inbound travel from Denmark.

All non-British national or resident travellers who have been in or transited through Denmark in the past 14 days will be denied entry into the UK.

British nationals or residents returning from Denmark will still be allowed entry into the UK. Freight and hauliers are also excluded from the ban.

The rule came into force as of 4am on Saturday.

Unveiling the move in a series of tweets at 2.18am on Saturday - less than two hours before the ban took effect - the transport secretary, Grant Shapps, wrote: "This decision to act quickly follows on from health authorities in Denmark reporting widespread outbreaks of coronavirus in mink farms. Keeping the UK public safe remains our top priority."

The chief medical officer, Chris Whitty, is understood to be particularly concerned by developments in Denmark. It follows the discovery of a new strain of the disease in mink bred for fur in Denmark's northern regions which has spread to humans. It is feared the new strain could prove to be more resistant against a vaccine.

Anyone who has been in Denmark over the past fortnight will be asked to isolate, including their household. Meanwhile, NHS test and trace will prioritise contacting all those who have recently returned from Denmark.

A spokeswoman from the Department for Transport said: "Unlike other travel to the UK, there will be no exemptions to this quarantine policy."

"The UK government is working closely with international partners to understand the changes in the virus that have been reported in Denmark and we are conducting a programme of further research here in the UK to inform our risk assessments."

The travel ban and extra requirements will be reviewed after a week, the department added.

Danish government experts have insisted they are acting with an "abundance of caution" in imposing restrictions in the northern Jutland region in response to the outbreak and ordering the cull of 17 million mink on its commercial farms.

Several variants of Covid-19 that have infected mink have been detected in more than 200 human cases in Denmark, but it has been the one cluster of 12 cases that has caused particular concern.

The country's prime minister, Mette Frederiksen, had said the measures were being put in place since the mutation of the virus could potentially have an impact on the efficacy of vaccines in development, but the experts stressed on Friday there was as yet no hard evidence to suggest it would.

The World Health Organization also offered a circumspect assessment of the risk from the new mink variant. Soumya Swaminathan, the WHO's chief scientist, said on Friday it was too early to jump to conclusions about the implications of mutations in the virus found in mink.

“We need to wait and see what the implications are but I don’t think we should come to any conclusions about whether this particular mutation is going to impact vaccine efficacy,” she said. “We don’t have any evidence at the moment that it would.”

Frederiksen’s comments that the strain “could pose a risk that future vaccines won’t work”, however, attracted international attention as she called for immediate action, adding that the “eyes of the world are on us”.

Dr Tyra Grove Krause of the Danish State Serum Institute told reporters on Friday that while researchers did not have “complete evidence”, they were determined to act on the information they had acquired quickly as a precaution while they continued their research.



Mink farmers protest in Holstebro in western Jutland on Friday. Photograph: Bo Amstrup/EPA

Responding to whether recent statements and actions had generated “panic”, she added: “There is always a balance of risk. In this case ... you need to act in time instead [of] waiting [to] get all the evidence. You need to act in time and stop transmission.”

Frederiksen had told a news conference on Thursday: “From tonight, citizens in seven areas of north Jutland are strongly encouraged to stay in their area to prevent the spread of infection.. We are asking you in north Jutland to do something completely extraordinary. The eyes of the world are on us.”

After Frederiksen’s statement, the UK government announced that Denmark would be removed from its safe travel list. The UK’s transport secretary, Grant Shapps, the transport secretary, announced in an “urgent” 4am update that the country had lost its quarantine-free status.

The WHO said on Friday it was looking at biosecurity in other countries where mink were farmed, adding that it was important to prevent the animals and farms becoming reservoir for the disease.

Maria van Kerkhove, the WHO’s technical lead for Covid-19, told a WHO news briefing in Geneva that the transmission of the virus between animals and humans was “a concern”, with a second expert saying the risk of such transmission was higher with mink than it was with other animals.

“Mutations [in viruses] are normal. These type of changes in the virus are something we have been tracking since the beginning. We are working with regional offices ... where there are mink farms, and looking at biosecurity and to prevent spillover events,” Van Kerkhove said.

However, concern is centring on the fact that most mutations of the virus so far identified have been similar enough for vaccines in development to be hoped to work on them while this reportedly diverges more.

While the emergence of the mutation has sparked alarm, scientists were divided over the implications for a virus that has infected dozens of species of mammals so far.

. This article was amended on 7 November 2020 to replace the graph showing Covid-19 cases. An early version was inadvertently displaying figures only for the self-governing territory of the Faroe Islands, whose small number of cases form part of the total for Denmark now shown.

#### Topics

- Coronavirus
- Denmark
- Animals
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# **Exhibit Q**

# The Guardian

The Covid-carrying Danish mink are a warning sign - but is anyone heeding it?

*Matthew Baylis*

Tue 10 Nov 2020 07:19 EST

Sars, Mers, now this: we must think hard about how we farm animals that are known hosts of human coronaviruses



'A more alarming situation has recently emerged in Denmark, where the virus appears to have mutated in farmed mink and re-entered the human population.' Photograph: Mads Claus Rasmussen/Ritzau Scanpix/AFP/Getty Images

**T**wo decades ago, a seminal study from the University of Edinburgh compiled a list of all known human infectious diseases. It found a total of 1,415 different human pathogens, and claimed that 61% were capable of spreading between humans and animals. Today, with the world put on hold by a deadly disease that seems likely to have spread first from bats to humans, we know the dangerous effects of such pathogens all too well.

The group of diseases that spread from animals to humans are collectively known as zoonoses. The term encompasses diseases such as measles, which first spread from cattle to humans

thousands of years ago but now transmits exclusively between people, and Ebola, which periodically passes from bats to humans, where it then spreads from person to person. It can also refer to food-borne diseases caused by bacteria such as salmonella and campylobacter that we only get from the consumption of animal products and almost never pass from person to person.

Very occasionally, diseases pass the other way, from humans to animals. We call these “reverse zoonoses”. Covid-19 is both a zoonosis and a reverse zoonosis: it originally spread from animals to humans, before transmitting from humans back to domesticated animals such as cats. We know the virus multiplies in felines and can spread from cat to cat, although there is no evidence so far of it spreading from cats to people.

We also know that Covid-19 has passed between people and farmed mink. This was first reported in April, in the North Brabant region of the Netherlands, where mink were, until recently, still farmed for their fur. Analysis of the genetic code of the virus from mink suggested that it had passed from infected farm workers to animals, where it then spread from mink to mink. Scientists also suspect that the virus passed from mink back to one worker.

A more alarming situation has recently emerged in Denmark, where the virus appears to have mutated in farmed mink and re-entered the human population. Thousands of mink are now being culled. The country has the largest mink-farming industry in the world, and so far over 200 people have reportedly been infected with a mink-associated strain of the virus. Twelve of those people were infected with a unique mink-related variant that hasn't been seen before.

Mutations in viruses are expected during an outbreak. They occur more frequently in those with genomes made from RNA (a large group which includes coronaviruses), compared with those with genomes made from DNA, because RNA replication is more prone to error than DNA replication. In most cases, these mutations are “silent” - they do not change the amino acids that make up the virus's proteins, so have no effect on any of its properties - but they have a signature that can be used to track the outbreak.

The mutations in Danish mink, however, have led to changes in the sequence of amino acids that make up the virus's “spike protein”. This is the key that allows the virus to fit into a human's (or other animal's) lock. In the virus that causes Covid-19, the lock is a protein called ACE2 which straddles cell membranes. When the spike protein fits to ACE2, the virus gains entry to the cell and can begin to replicate. Because the spike protein and the ACE2 receptor are close fitting, changes to the amino acid sequence of either affect the virus's ability to enter the cell.

Mink ACE2 is slightly different from human ACE2, so mink-to-mink transmission may have favoured a mutated virus with a change to its spike protein key that better fits the mink ACE2 lock. As the antibodies that humans generate to fight off Covid-19 target the spike protein on the external surface of the virus, this mink-adapted virus, which has a mutation in its spike protein, may be better able to circumvent our defences.

Danish researchers report that one of the variants of the virus found in mink isn't as easily defeated by the antibodies that humans produce against Covid-19. One risk is that people who

have recovered from Covid-19 may have antibodies that are less able to fight off the mink strain of the virus, leaving them open to reinfection. And most of the vaccines under development, on which we are pinning so much hope, are intended to induce antibodies that target the spike protein in the virus that causes Covid-19 in humans. While it's too early to say for certain, one possibility is that these vaccines could be less effective against the mink virus, because it has a different spike protein.

A close relative of the mink, the ferret, has a similar respiratory tract physiology to humans, and experiences respiratory diseases such as Sars, Covid-19 and influenza much as we do. This is why they can be used in laboratories to study human respiratory diseases. But the fact that ferrets experience these diseases in a similar way to humans raises serious questions about keeping large numbers of mink confined in close quarters. Indeed, these conditions provide the perfect environment for respiratory viruses to spread.

In this age of zoonotic epidemics, with Sars, Mers and now Covid-19 all emerging in the past 20 years, we must think carefully about how we intensively farm mammals that are known hosts of human coronaviruses. Before the pandemic, the Netherlands was already in the process of stopping intensive mink farming. But many dangerous types of animal farming still continue. Consider the palm civet. This animal was implicated in the emergence of Sars in 2003, acting as a probable intermediary between the bats in which the Sars virus originated, and the people whom it later infected.

As an animal that might have helped to trigger a pandemic, are we now keeping the palm civet at a safe distance? Quite the opposite. In parts of Asia the palm civet is farmed intensively, fed coffee cherries, and the beans collected from its faeces are used to make the world's most expensive coffee, kopi luwak.

Given the huge human, social and economic costs of pandemics, there's a compelling argument that in order to prevent future catastrophes, we can no longer afford to take such risks.

. Matthew Baylis is the Oxenhale chair of veterinary epidemiology at the University of Liverpool

## Topics

- Coronavirus
- Opinion
- Farming
- Sars
- Infectious diseases
- Denmark
- Europe
- comment

# **Exhibit R**



## Emergencies preparedness, response

### SARS-CoV-2 mink-associated variant strain – Denmark

Disease Outbreak News

6 November 2020

Since June 2020, 214 human cases of COVID-19 have been identified in Denmark with SARS-CoV-2 variants associated with farmed minks, including 12 cases with a unique variant, reported on 5 November. All 12 cases were identified in September 2020 in North Jutland, Denmark. The cases ranged in age from 7 to 79 years, and eight had a link to the mink farming industry and four cases were from the local community.

Initial observations suggest that the clinical presentation, severity and transmission among those infected are similar to that of other circulating SARS-CoV-2 viruses. However, this variant, referred to as the "cluster 5" variant, had a combination of mutations, or changes that have not been previously observed. The implications of the identified changes in this variant are not yet well understood. Preliminary findings indicate that this particular mink-associated variant identified in both minks and the 12 human cases has moderately decreased sensitivity to neutralizing antibodies. Further scientific and laboratory-based studies are required to verify preliminary findings reported and to understand any potential implications of this finding in terms of diagnostics, therapeutics and vaccines in development. In the meantime, actions are being taken by Danish authorities to limit the further spread of this variant of the virus among mink and human populations.

SARS-CoV-2, the virus which causes COVID-19, was first identified in humans in December 2019. As of 6 November, it has affected more than 48 million people causing over 1.2 million deaths worldwide. Although the virus is believed to be ancestrally linked to bats, the virus origin and

intermediate host(s) of SARS-CoV-2 have not yet been identified.

Available evidence suggests that the virus is predominantly transmitted between people through respiratory droplets and close contact, but there are also examples of transmission between humans and animals. Several animals that have been in contact with infected humans, such as minks, dogs, domestic cats, lions and tigers, have tested positive for SARS-CoV-2.

Minks were infected following exposure from infected humans. Minks can act as a reservoir of SARS-CoV-2, passing the virus between them, and pose a risk for virus spill-over from mink to humans. People can then transmit this virus within the human population. Additionally, spill-back (human to mink transmission) can occur. It remains a concern when any animal virus spills in to the human population, or when an animal population could contribute to amplifying and spreading a virus affecting humans. As viruses move between human and animal populations, genetic modifications in the virus can occur. These changes can be identified through whole genome sequencing, and when found, experiments can study the possible implications of these changes on the disease in humans.

To date, six countries, namely Denmark, the Netherlands, Spain, Sweden, Italy and the United States of America have reported SARS-CoV-2 in farmed minks to the World Organisation for Animal Health (OIE).

### **Public health response**

Danish authorities have announced the following planned or ongoing public health actions:

- Culling of all farmed mink (more than 17 million) in Denmark, including its breeding stock;
- Enhancing surveillance of the local population to detect all COVID-19 cases, including through population-wide mass PCR testing for the region of North Jutland;
- Expanding the percentage of sequencing of human and mink SARS-CoV-2 infections in Denmark;
- Rapid sharing of the full genome sequences of the mink-variant SARS-CoV-2; and
- Introducing new movement restrictions and other public health measures to affected areas in North Jutland to reduce further transmission, including movement restrictions between municipalities.

### **WHO risk assessment**

All viruses, including SARS-CoV-2, change over time. SARS-CoV-2 strains infecting minks, which are subsequently transmitted to humans, may have acquired unique combinations of mutations. In order to fully understand the impact of specific mutations, advanced laboratory studies are required. These investigations take time and are done in close collaboration between different research groups.

The recent findings reported by the Danish Public Health Authority (Statens Serum Institut) in Denmark related to the novel variant of SARS-CoV-2 identified in humans need to be confirmed and further evaluated to better understand any potential implications in terms of transmission, clinical presentation, diagnostics, therapeutics and vaccine development.

Furthermore, detailed analyses and scientific studies are needed to

better understand the reported mutations. The sharing of full genome sequences of human and animal strains will continue to facilitate detailed analyses by partners. Members of the WHO SARS-CoV-2 Virus Evolution Working Group are working with Danish scientists to better understand the available results and collaborate on further studies. Further scientific and laboratory-based studies will be undertaken to understand the implications of these viruses in terms of available SARS-CoV-2 diagnostics, therapeutics and vaccines in development.

Actions taken by the Danish authorities will limit continued spread of mink-associated variants of SARS-CoV-2 in Denmark, and in particular have been implemented to contain the unique variant reported to WHO. These actions include restricting movement of people, culling animals, widespread testing of people living in affected areas and increased genomic sequencing of SARS-CoV-2 viruses across the country.

## **WHO advice**

This event highlights the important role that farmed mink populations can play in the ongoing transmission of SARS-CoV-2 and the critical role of strong surveillance, sampling and sequencing SARS-CoV-2, especially around areas where such animal reservoirs are identified.

The preliminary findings by Denmark are globally relevant and WHO recognises the importance of sharing epidemiological, virological and full genome sequence information with other countries and research teams, including through open-source platforms.

WHO advises further virological studies should be conducted to understand the specific mutations described by Denmark and to further investigate any epidemiological changes in function of the virus in terms of its transmissibility and the severity of disease it causes. WHO advises all countries to increase the sequencing of SARS-CoV-2 viruses where possible and sharing the sequence data internationally.

WHO advises all countries to enhance surveillance for COVID-19 at the animal-human interface where susceptible animal reservoirs are identified, including mink farms.

WHO also reminds countries to strengthen farming biosafety and biosecurity measures around known animal reservoirs in order to limit the risk of zoonotic events associated with SARS-CoV-2. This includes infection prevention and control measures for animal workers, farm visitors and those who may be involved in animal husbandry or culling.

The basic principles to reduce the general risk of transmission of acute respiratory infections are as follows:

- Avoiding close contact with people suffering from acute respiratory infections;
- Ensuring frequent hand-washing, especially after direct contact with ill people or their environment;
- For people with symptoms of acute respiratory infection, practicing cough etiquette, such as maintain distance, cover coughs and sneezes with disposable tissues or clothing, and wash hands; use of masks where appropriate; and
- Enhancing standard infection prevention and control practices in hospitals in health care facilities, especially in emergency departments.

WHO advises against the application of any travel or trade restrictions for Denmark based on the information currently available on this event.

WHO has issued guidance for [Public health considerations while resuming international travel](#), recommending a thorough risk assessment, taking into account country context, the local epidemiology and transmission patterns, the national health and social measures to control the outbreak, and the capacities of health systems in both departure and destination countries, including at points of entry. In case of symptoms suggestive of acute respiratory illness either during or after travel, the travellers are encouraged to seek medical attention and share their travel history with their health care provider. Health authorities should work with travel, transport and tourism sectors to provide travellers with information to reduce the general risk of acute respiratory infections via travel health clinics, travel agencies, conveyance operators, and at points of entry.

For more information, see:

- [WHO Health Topics page on COVID-19](#)
- [WHO Scientific brief on the transmission of SARS-CoV-2: implications for infection prevention precautions](#)
- [WHO Public health considerations while resuming international travel](#)
- [OIE Update 6 on the COVID-19 situation in mink in Denmark](#)
- [OIE Technical factsheet, infection with SARS-CoV-2 in animal](#)
- [OIE Questions and Answers on COVID-19](#)
- [FAO Exposure of humans or animals to SARS-CoV-2 from wild, livestock, companion and aquatic animals](#)

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## Related links

[WHO Health Topics page on COVID-19](#)

[WHO Scientific brief on the transmission of SARS-CoV-2: implications for infection prevention precautions](#)

[WHO Public health considerations while resuming international travel](#)

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# **Exhibit S**



Montreal

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## Covid-19: Denmark to kill 17 million minks over mutation that could undermine vaccine effort

Owen Dyer

Scientists at the World Health Organization and around the world are studying a mutated variant of the novel coronavirus that is infecting humans after spreading through mink farms in the north of Denmark.

One strain of mutated SARS-CoV-2, found in 12 humans in Denmark, appeared in laboratory tests to exhibit “decreased susceptibility” to antibodies from previously infected people, the country’s State Serum Institute said in a preliminary report.<sup>1</sup> This variant, if it spread, might be less easily controlled by covid-19 vaccines currently under development, the report warned.

The only safe option, said Danish prime minister Mette Frederiksen, is to cull all 17 million minks kept by the Danish fur industry. Denmark is the world’s biggest mink fur exporter, supplying about a third of global demand.

“We have a great responsibility towards our own population, but with the mutation that has now been found we have an even greater responsibility for the rest of the world,” Frederiksen told a press conference on 6 November.

“The mutated virus in minks could pose a risk that future vaccines won’t work as they should. It risks being spread from Denmark to other countries. The eyes of the world are on us.”

Frederiksen announced local lockdowns in seven districts of North Jutland, where the fur industry is concentrated. Mink farmers took to the roads in tractors to protest as public health teams began a cull that is expected to last two weeks. Germany and the UK added Denmark to their quarantine lists in response.

Like many mammals, minks are susceptible to infection by the novel coronavirus, and it spread rapidly through Denmark’s densely caged mink farm populations this summer. Similar outbreaks have already triggered smaller culls at mink farms in Spain, the Netherlands, and the US.

Five different virus strains have since been detected in Danish patients that first passed through the farmed mink population and underwent changes in the process. The mutations involve changes to the spike protein that the virus uses to penetrate human cells. This protein is also the main focus of vaccine efforts.

Among 5102 samples of virus taken from Danish patients since June, five infection clusters affecting 214 people involved mink variant virus. One of these, known as cluster 5, is the problematic variant believed less susceptible to antibodies. This cluster affected 11 people in North Jutland and one on the

island of Zealand. In North Jutland nearly half of recent human covid-19 cases involved a mink variant, while elsewhere in Denmark the proportion is under 1%.

The mink variant viruses show no sign of spreading faster or causing more severe symptoms than other strains of SARS-CoV-2, and many experts have expressed scepticism over Danish government claims that these mutations could seriously undermine vaccine efforts. Danish authorities have begun uploading genetic sequences onto public databases for other scientists to study.

The cluster 5 variant has “moderately decreased sensitivity to neutralising antibodies,” a WHO statement acknowledged.<sup>2</sup> “[It] had a combination of mutations, or changes that have not been previously observed. The implications of the identified changes in this variant are not yet well understood.”

This was a “concern,” said Maria van Kerkhove, WHO’s technical lead on covid-19. But “mutations are normal,” she added. “I don’t think we should come to any conclusions about whether this particular mutation is going to impact vaccine efficacy.”

“We need to wait and see what the implications are,” said WHO chief scientist Soumya Swaminathan.

1 Statens Serum Institut. Mutations in the mink virus. 5 Nov 2020. <https://www.ssi.dk/aktuelt/nyheder/2020/mutationer-i-minkvirus>

2 World Health Organization. SARS-CoV-2 mink-associated variant strain—Denmark. Disease Outbreak News, November 6, 2020. <https://www.who.int/csr/don/06-november-2020-mink-associated-sars-cov-2-denmark/en>.

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# **Exhibit T**

# Detection of new SARS-CoV-2 variants related to mink

12 November 2020

## Summary

Since April 2020, when the first SARS-CoV-2 infection was reported in the Netherlands in a mink and subsequently in a mink farm worker, it has been established that human-to-mink and mink-to-human transmission can occur [1]. Since then, infections in mink have been reported in Denmark, Italy, Spain, Sweden and the United States [2].

On 5 November 2020, Denmark reported 214 human COVID-19 cases infected with SARS-CoV-2 virus variants related to mink, as well as infected mink at more than 200 mink farms. Most human and animal cases reported since June 2020 have been in the North Jutland Region. The SARS-CoV-2 variants detected in these cases were part of at least five closely-related clusters; each cluster was characterised by a specific mink-related variant, identified in humans and animals from infected mink farms. Denmark has implemented robust response measures to control the outbreaks in mink and decrease the spill-over between the human and the animal reservoir.

One of the clusters (Cluster 5), which was reported as circulating in August and September 2020, is related to a variant with four genetic changes, three substitutions and one deletion, in the spike (S) protein. Since the S protein contains the receptor-binding domain, and is a major target for immune response, such mutations could, in theory, have implications for viral fitness (ability to infect humans and animals), transmissibility, and antigenicity. As a consequence, the evolution of viruses with increasing changes in functional domains of the S protein could affect treatment, certain diagnostic tests and virus antigenicity. It could also have an impact on the effectiveness of developed vaccine candidates, and possibly require them to be updated. Investigations and studies are ongoing to clarify the extent of these possible implications.

## What is the risk to human health posed by SARS-CoV-2 mink related variants?

### *Transmissibility*

Current evidence available from Denmark and the Netherlands on SARS-CoV-2 variants related to mink indicates that these variants are able to circulate rapidly in mink farms and the human communities close to the farms, however, they do not appear to be more transmissible than other circulating SARS-CoV-2 variants. Thus, the probability of infection with mink-related variant strains is assessed as low for the general population, moderate for populations in areas with a high concentration of mink farms and very high for individuals with occupational exposure.

### *Severity*

Patients reported to be infected with mink-related variants, including the Cluster 5 variant in Denmark, do not appear to have more severe clinical symptoms than those infected with non-mink-related variants. Therefore the current impact of COVID-19 on disease severity in patients infected with any mink-related variant appears to be similar to those infected with non-mink-related variants. This impact was previously assessed as low for the general population and very high for individuals with risk factors for severe COVID-19 disease, such as the elderly.

### **Immunity, reinfection, vaccination and treatment**

Of all mink-related variants analysed so far, only the Cluster 5 variant has raised specific concern due to its effect on antigenicity. Further investigations are needed to assess whether this may have any impact on i) the risk of reinfection, ii) reduced vaccine efficacy or iii) reduced benefit of treatment with plasma from convalescent patients or with monoclonal antibodies. It should be noted that continued transmission of SARS-CoV-2 in mink farms may eventually give rise to other variants of concern.

### **Cross-border spread**

The cross-border spread of SARS-CoV-2 variants related to mink in EU/EEA countries and the UK through humans has not been observed so far, but there is no indication that the potential for cross-border spread is different to that for other SARS-CoV-2 variants. Genetic adaptation in mink populations could give rise to a selective advantage in regions with mink farming activity. The mutation Y453F, defining mink-related variants, has also been detected outside of Europe, indicating the potential for circulation of such strains. In the past few months, community transmission has occurred in Denmark and, to some extent, in the Netherlands, which could lead to cross-border spread.

The cross-border spread of SARS-CoV-2 variants related to mink in EU/EEA countries and the UK through animals and animal products appears very low.

### **Conclusion**

Based on the information currently available on transmissibility, severity, immunity and cross-border spread, the overall level of risk to human health posed by SARS-CoV-2 mink-related variants can be determined as:

- low for the general population and moderate for medically-vulnerable individuals, which is no different to other SARS-CoV-2 strains (not related to mink);
- low for the general population in areas with a high concentration of mink farms and moderate-to-high for medically-vulnerable individuals living in the same areas;
- moderate for non-medically vulnerable individuals with occupational exposure and very high for medically-vulnerable individuals with occupational exposure.

If the concerns raised in relation to immunity, reinfection, vaccination and treatment are confirmed, the risk assessment will be immediately reviewed to re-assess the overall level of risk to human health and the potential implications for COVID-19 diagnosis, treatment and vaccine development. This also applies to any further mink-related variants with mutations in the S protein that may arise and spread in the EU/EEA and the UK.

## **Options for response**

To decrease the risk posed to public health, national authorities should consider implementing measures aimed at mink farms, mink farm workers and communities in contact with mink farms along the lines below.

**Human testing, sequencing and characterisation of antigenic properties and virus infectivity** – national authorities should implement a systematic approach to testing and sequencing, particularly in mink farm workers and nearby communities. Outbreak investigations, comprehensive testing of workers and contact tracing, isolation and quarantine should be immediately initiated if a human case is identified related to a mink farm. Mutations of concern should be reported and assessments of antigenicity and viral infectivity should be developed.

**Infection prevention and control measures for mink farm workers and visitors** – the number of people in contact with mink and mink farms should be limited and farm workers with COVID-19-compatible symptoms should not have access to the farms. Appropriate technical and organisational measures should be taken to ensure the health and safety of workers in the workplace. Workers should be informed, trained and provided with appropriate personal protective equipment, including respiratory and eye protection. The possibility of language barriers for seasonal workers at mink farms needs to be considered when implementing hygiene and prevention measures on the farms.

**Animal testing and prevention of spread from animals** – monitoring and surveillance of mink farms (repetitive surveys and/or testing of dead mink on weekly basis) should be undertaken for as long as SARS-CoV-2 exposure from humans to mink cannot be excluded. It is recommended that isolated SARS-CoV-2 strains be genotyped systematically according to validated protocols and genome sequences from all infected animals, in particular mink, should be shared. This will enable the rapid identification of possible clusters and related variants. Culling of mink and destruction of raw pelts from infected farms should be considered in accordance with appropriate biosecurity measures.

**Development of One Health preparedness and response strategies** – enhanced coordination between the agricultural, animal health, and human health (including occupational health and safety) sectors is essential for a timely and effective response. It is also important to increase public awareness of mink-related SARS-CoV-2 prevention and control strategies specifically targeting mink producers, mink farm workers, veterinarians and veterinary staff working with mink farms and partners in the fur industry.

## Event background

As of 5 November 2020, Denmark had reported 214 human COVID-19 cases infected with SARS-CoV-2 related to mink (all carrying the mutation Y453F in the spike (S) protein, referred to as mink-related variants). These cases are part of an ongoing spread with both zoonotic and anthroponotic transmission. The 214 cases represent 4.2% of the 5 102 human samples sequenced in Denmark from week 24 (8–14 June) to week 42 (12–18 October) 2020, when many mink farm outbreaks in the north-west of the country were reported. The 5 102 sequenced strains accounted for 13% of the total number of 37 967 cases reported in Denmark during the period in question.

Of the 214 human cases infected with mink-related virus variants, 12 human cases were infected with strains showing four genetic changes in the S protein; three substitutions and one deletion. This cluster is referred to in the Danish risk assessment as Cluster 5 [1]. The 12 human cases were reported in the North Jutland Region in August and September 2020 and not all of them had a direct link to a mink farm.

Statens Serum Institut (SSI) in Denmark has developed and validated a wild-type virus microneutralisation antibody assay, to investigate possible antigenic changes related to the genomic changes identified in the S protein. Preliminary results, using a panel of convalescent sera from humans (n=9), infected with common circulating SARS-CoV-2 strains during spring 2020 with low, medium and high neutralising antibody titers, exhibited an average of 3.58-fold (range 0–13.5) reduction [3]. However, only three of the strains exhibited a 4-fold reduction when tested with the virus isolate from a patient with the Cluster 5 virus variant, compared to the unmutated common wild-type SARS-CoV-2 strain. A 4-fold reduction is commonly required for an assessment of significant antigenic changes in new influenza strains [4], however as yet there is no similar agreement for SARS-CoV-2 strains since no set of reference sera has been established. These findings indicate that there could be a potential impact on antibody-mediated immunity provided by SARS-CoV-2 infection or vaccines. It should be noted that these findings are preliminary and have to be confirmed before any conclusions can be drawn. Further studies, using more virus isolates from humans infected by mink-related strains with different genomic changes, have been initiated and confirmation from other investigators is being sought in Denmark and internationally. The Danish risk assessment stresses that if these new SARS-CoV-2 variants with lower susceptibility to neutralising antibodies spread widely in the population it might have an impact on the level of vaccine effectiveness for the vaccines currently under development. Furthermore, the establishment of a virus reservoir among mink may give rise to problematic virus variants in the future.

## Mink-related SARS-CoV-2 variants in Denmark and the Netherlands

The 214 mink-related cases reported by Denmark all involve strains with the S protein mutation Y453F. The mutation Y453F has been observed in several clusters related to mink farms in the Netherlands [5]. The strains from the Netherlands and Denmark are not closely related and fall into different genetic clades, which excludes a direct link between farms in the two countries. From the sequence data available from Denmark so far it is not possible to determine the extent to which mink-to-human transmission is currently contributing to transmission chains. Some of the strains from mink in the Netherlands lack Y453F, which demonstrates that it is not a prerequisite for infecting mink, but probably a selected mutation in the mink population [6,7]. Variants with Y453F, unrelated to the Danish and Dutch variants, have also been reported sporadically from other countries (the Russian Federation, South Africa, Switzerland, and the United States) in the GISAID EpiCoV sequence database [6]. These variants have come from human cases without a known link to mink farms, which suggests that the strain may not always be related to mink, unless there was undetected mink-to-human transmission.

About half of the mink-related strains reported by Denmark additionally carry a deletion of two amino acids (69-70) in the S protein. This mutation is not present in any of the mink strains from the Netherlands but has been widely reported in unrelated human cases without Y453F in the GISAID EpiCoV database (from Australia, Canada, Côte d'Ivoire, France, Germany, Malaysia, New Zealand, Norway, Sweden, and the United Kingdom). The Cluster 5 variant strains carry two additional mutations in the S protein (I692V, M1229I) for a total of four S protein mutations, one of which (Y453F) is located in the receptor binding domain (RBD).

The Danish health authorities have not observed changes in the human-to-human transmissibility of the virus or severity of disease for any of the mink-related variants in Denmark. The Cluster 5 variant was last observed in Denmark on 14 September 2020, which may suggest that it is no longer circulating. However, viruses with the S protein Y453F mutation have become increasingly common and are now causing approximately 40% of the COVID-19 cases in the North Jutland Region. In the Netherlands, the viruses with the Y453F mutation related to mink farms did not continue to circulate.

The sequences of the mink-related viruses from Denmark and the Netherlands have been deposited with GISAID EpiCoV by the national sequencing laboratories [6]. These include representative sequences from Denmark with Y453F only (EPI\_ISL\_618040), with additional del 69-70 (EPI\_ISL\_616269) and from Cluster 5 (EPI\_ISL\_616695). Denmark is also expanding sequencing capacity for human and mink SARS-CoV-2 infections.

## Outbreaks of SARS-CoV-2 infections in mink farms

According to the World Organisation for Animal Health (OIE), SARS-CoV-2 infections in animals are notifiable [8,9]. As of 6 November 2020, six countries had reported SARS-CoV-2 infections in farmed mink to OIE: Denmark, Italy, the Netherlands, Spain, Sweden and the United States [2]. Outbreaks affecting mink-farms have been observed in large numbers due to the apparent high susceptibility of mink to SARS-CoV-2 infection, coupled with the highly intensive characteristics of mink farming [10,11].

Denmark is one of the largest mink fur producers in the world. On 17 June 2020, Danish authorities reported the first identification of SARS-CoV-2 in mink at a farm in the North Jutland Region [1,12]. Since early-August 2020, large SARS-CoV-2 infection outbreaks have been reported in mink farms in Denmark. Despite intensive efforts to contain the outbreaks, as of 8 November 2020 the virus had been detected in 229 (20%) of the 1 140 mink farms in the country [13]. Affected farms are located in northern, central and western Jutland regions. In the majority of the infected farms, the PCR and sero-prevalence in mink were close to 100% by the time the outbreak was detected. Links between human cases and mink outbreaks were found, although it was often not possible to determine whether mink or humans were infected first. To contain the spread of mink farm outbreaks, a range of measures have been implemented at various stages during the epidemic. Measures include the culling of infected mink, enhanced surveillance of the local human population, including population-wide mass RT-PCR testing in the North Jutland Region, movement restrictions in the affected areas, limited access to the farms (for employees only), and application of strict hygiene routines - e.g. hand washing and changing clothes before and after entering farms. Local restrictions, including restricted movement of people between municipalities, have been implemented for the period 9 November 2020 to 3 December 2020 in the North Jutland Region [14,15]. Since 4 November 2020, the government of Denmark has been discussing a cull of all mink in the country [16].

The Netherlands reported SARS-CoV-2 infections at 69 mink farms in three regions during the period 23 April to 5 November 2020 [17]. At the time of the first identification, a mink-related variant was reported in a farm employee, suggesting the first possible case of animal-to-human SARS-CoV-2 transmission [5]. Since 20 May 2020, mink farmers, veterinarians and laboratories have been obliged to report clinical signs and SARS-CoV-2 infections in mink to the Netherlands Food and Consumer Product Safety Authority (NVWA). In addition, an early warning system is in place whereby animals are tested and results reported every week. Since 28 May 2020, national measures have been in place for all mink farms. On 3 June 2020, the national authorities decided to cull mink at the affected farms. On 28 August 2020, it was announced that the effective date of a ban on mink farming in the Netherlands will be brought forward from 1 January 2024 to early 2021 [18]. Following the first SARS-CoV-2 infection outbreaks at mink farms in the Netherlands, an epidemiological investigation concluded that the most likely explanation for the infection at the mink farms is the introduction of the virus by humans and subsequent transmission among the mink.

Mink are housed in adjoining cages made of wire netting, allowing free airflow and contact between animals in adjacent cages, which explains the rapid animal-to-animal transmission. Furthermore, the presence of viral RNA in inhalable dust collected from inside the farms indicates the possibility of workers having been exposed to the virus in mink excretions. Following outbreaks of SARS-CoV-2 infection at mink farms in the Netherlands during 2020, the points below should be borne in mind.

- Mink-to-mink transmission is very efficient.
- No link has been identified between infected farms.
- A proportion of farm animals had clinical symptoms suggestive of acute respiratory illness for about four weeks, but some animals were still RT-PCR-positive for SARS-CoV-2 in throat swabs after clinical symptoms had disappeared. This may vary, as seen recently in Danish outbreaks, where clinical symptoms were observed for shorter periods.
- The high diversity in the sequences from some mink farms can probably be explained by the existence of many generations of infected animals before an increase in mortality was observed.
- The current estimates are that the substitution rate of SARS-CoV-2 is one mutation per two weeks. There was also a relatively high sequence diversity observed in farms, which still tested negative one week prior to the outbreak, implying that the virus evolves more quickly in the mink population. This can indicate that the virus might replicate more efficiently in mink or that it may have acquired mutations which make it more virulent in mink [5].

Italy reported one mink (weakly) positive for SARS-CoV-2 at a farm in the Lombardy region on 10 August 2020. No lesions were found in this mink. The detection came after the identification of a case of COVID-19 in a worker from the farm. In response, around 1 500 mink were tested and no further cases were detected. Surveillance activities are ongoing at mink farms [19].

Spain reported SARS-CoV-2 infections at a mink farm in the Aragon region. On 21 May 2020, seven asymptomatic infections were reported among workers at a mink farm in Aragon, according to media quoting the Spanish health authorities [20]. Hygiene and biosecurity measures were put in place and the movements restricted in relation to the farm. No clinical symptoms were observed among the animals at the farm. On 22 June 2020, one animal tested positive by RT-PCR for SARS-CoV-2. On 7 July 2020, 78 of the 90 animals tested were found positive by RT-

PCR. The Government of the Autonomous Community of Aragon decided to proceed with the safe disposal of the carcasses and other potentially infected materials, after which the facilities were cleaned and disinfected [21].

As of 6 November 2020, Sweden had reported ten SARS-CoV-2-positive mink at farms in Blekinge county, where the first detection in one mink occurred on 16 October 2020. Several mink that had been found dead also tested positive. Sequences from two mink and two human cases have been reported without any S protein mutations. Surveillance at the 40 mink farms in Sweden is ongoing. There are no plans to cull at present. However, movement restrictions are in place and strict biosecurity measures have been imposed on all mink farms in Sweden [22-24].

As of 30 October 2020, 11 outbreaks in commercial mink farms have been reported in three states of the United States. These outbreaks occurred between 26 July and 29 September 2020. Several people that were in contact with mink from these farms also tested positive for SARS-CoV-2. In total, 12 231 mink died as a result of contracting the virus. In response to these outbreaks, state officials quarantined the premises and worked with One Health partners to dispose of deceased mink, and are continuing to monitor the situation. No mink were culled as a result.

## Disease and virus background

For information on the latest scientific evidence relating to COVID-19, please visit ECDC's website:

<https://www.ecdc.europa.eu/en/2019-ncov-background-disease>

### Mink farming and susceptibility of mink to respiratory viruses and viral adaptation in infected mink

SARS-CoV-2 can infect several species of domesticated animals, the most highly susceptible are felines (cats, tigers, lions), ferrets, mink, Golden Syrian hamsters, Egyptian fruit bats (*Rousettus aegyptiacus*) and Macaques (*Macaca fascicularis* and *Macaca mulatta*) [26-28]. Susceptibility of several species within the family Mustelidae (such as mink and ferret) to respiratory viruses (e.g. influenza) has been demonstrated in natural and experimental conditions. Cross-species transmission, particularly of influenza viruses, has been reported from companion animals and captive wild animals. In Danish mink farms, the median daily mortality observed in mink during the peak of SARS-CoV-2 epidemic has been 0.14% (5th-95<sup>th</sup> percentiles: 0–0.74%), compared to a baseline mortality close to zero (e.g. 1-4 animals /month per farm with an average size of 10 000 mink per farm). Therefore, in mink farms any increased mortality is easily detected, although the virus may have already entered the farm some time before.

The introduction of species-specific adaptation mutations and reassortment events of influenza virus in infected mink populations have been described. This underlines the importance of the species for the acquisition of mutations and generation of antigenically diverse viruses, mainly respiratory, which spread quickly between mink at the densely-populated farms. Ferrets are the standard model for assessing the potential of airborne transmission of influenza viruses, particularly those viruses with pandemic potential, and these animals have been used as a model to test transmissibility of SARS-CoV-2 [29,30]. Ferrets and mink belong to the same family of animals, but are not directly or closely related [31]. The American mink (*Neovison vison*) is mainly used to produce fur and large outbreaks of respiratory viruses at farms have been described. However, such infections have also been observed in free living European mink (*Mustela lutreola*). In recent decades, mink escaping or being released from breeding farms in Europe has led to the establishment of a feral population of American mink in several European countries [32].

At mink farms, the whole production cycle (including breeding, lactation, weaning, growing and finally r pelting) occurs in a closed system on the same farm over a period of one year. The close proximity of mink housing may facilitate efficient animal-to-animal transmission of diseases. Three main breeding periods can be defined: from pelting to mating, from mating to separation, from separation to pelting. Conditioning and breeding take place in the period December–March, followed by whelping and weaning (April–June), growth and furring (July–October) and grading and slaughter (November–December). The pelting season begins in November/December. During the pelting process, the pelt is prepared in such a way that it can be kept for up to a year without being dressed. The pelts are placed on drying boards to maintain their shape during the drying process. The rest of the carcass is recycled for use in the production of bio-diesel, fertilisers, among other products.

Europe is the global leader in fur production, with more than 27 million mink pelts produced annually (2019) at more than 2 750 mink farms, 1 100 of which are in Denmark [33] (Annex 1, Figure 1, 2 and 3).

Mink farms often employ seasonal workers who come from abroad during the periods of mating, whelping, vaccination and pelting for various lengths of time during the year [25].

## SARS-CoV-2 spike protein variants and their impact on viral infectivity and antigenicity

SARS-CoV-2 has accumulated mutations since its emergence in the human population in 2019. On average a genome from a virus collected in October 2020 had around 20 accumulated mutations compared to the first strain sequenced in January 2020 (Wuhan-Hu-1) [34,35]. Most of these mutations are expected to be neutral or detrimental to the virus fitness in the human population, while a few may provide some selective advantage, such as increased infectivity [36,37]. When a virus switches host species, an increased mutation rate can be observed due to the virus adapting to its new host [38]. Mutations in the structural proteins of the virus, altering the antigenic properties of the strain, can lead to reduced effectiveness of the immune response if the immunity was acquired through infection by a strain, or a vaccine derived from a strain, without these mutations [39].

Thanks to laboratories sharing genomic data in databases, such as GISAID EpiCoV [6] and the COVID-19 data portal [40], and visualisations provided by free online platforms [35,41,42], the evolution of SARS-CoV-2 can be followed.

For SARS-CoV-2, the most important structural protein in this context is the S protein as it binds to the ACE-2 receptor during the entry of the virus particle into human cells; the part of the protein that directly binds to the receptor is called the receptor binding domain (RBD) [43,44]. The RBD has been shown to be less conserved than the rest of the S protein in circulating SARS-CoV-2 [45].

It is not possible to predict accurately what effect individual structural protein mutations will have on antigenic properties from the virus sequence data alone. The location of mutations in genes coding for the structural proteins can provide an indication [46], but experimental evidence is needed to provide a better estimate of the effect on the immune response. A common method used to assess antigenic properties is neutralisation assays, where the mutated virus is grown in the laboratory in the presence of serum from humans or animals that have been infected by a strain, or vaccinated with a vaccine derived from a strain without the mutations [47].

The ability of SARS-CoV-2 to infect an animal depends on several factors that are not fully understood, including compatibility between the S protein of the virus and the host receptor ACE-2. Mink can be infected by SARS-CoV-2 and they can also transmit the virus to humans [48]. It is rare that a novel variant becomes successful and gives rise to a new genetic clade that can spread globally. When this happens, it can be due to spurious founder effects and/or selective advantages [49]. If the spread among mink is not controlled and there is recurrent spill-over into the human population, variants that provide a selective advantage in mink populations could become widespread in humans, even without any selective advantage in the human population.

During the summer and autumn of 2020, S protein mutations unrelated to mink have emerged and become widespread in the EU/EEA and the UK. These include amino acid substitutions A222V and S477N, which are increasing in proportion, although no selective advantages or changes in antigenic properties have been demonstrated [50], and N439K, for which reduced neutralisation effect by convalescent sera has been demonstrated [45].

The impact of mutations in the SARS-CoV-2 S protein on viral infectivity and antigenicity have been assessed for eighty natural variants and twenty-six glycosylation spike variant strains using a pseudovirus assay [51]. Most variants observed with amino acid change in the receptor binding domain were less infectious, while some variants - including A475V, L452R, V483A and F490L - were resistant to some neutralising antibodies.

Virus mutations can affect the sensitivity of diagnostic assays that detect nucleic acid, antigen or antibodies. None of the mink-related variants reported by Denmark [52] are known to cause any issues with existing RT-PCR assays as none of the mutations defining the mink-related clusters are located within the amplicons of RT-PCR assays recommended by WHO, and such assays generally do not target the S gene. The variants could potentially affect antigen and antibody detection assays and further investigations are needed to assess this.

## Development of immunity including neutralising antibodies to SARS-CoV-2 viruses in humans

In most infected individuals, antibody responses to SARS-CoV-2 can be detected 10–15 days after onset of COVID-19 symptoms.

Sequential serum samples collected up to 94 days after onset of symptoms in laboratory-confirmed human cases show that antibodies, including IgM, IgA, IgG and neutralising antibodies, develop in more than 95% of cases [53]. A wide range of SARS-CoV-2 neutralising antibody titres have been reported after infection and these vary depending on the length of time from infection and the severity of disease [54–56]. Neutralising antibodies can be assessed using either wild-type SARS-CoV-2 virus or a pseudotype neutralisation assay, and a correlation between the two has been shown [57]. A surrogate neutralisation assay using soluble RBD which can be performed at biosafety level 2 has also been described [58]. In the study mentioned above using a pseudotype neutralisation assay, the kinetics of the neutralising antibody responses were characterized over time and an initial peak was observed, which subsequently declined. The height of this peak at 3–4 weeks post onset of symptoms, with titres ranging from 98–32 000, and the subsequent rate of decline over time to levels still above or at base-level with no neutralising antibodies, was shown to be dependent upon disease severity.

The neutralising antibody titre required for protection from reinfection and/or a new symptomatic disease in humans is not yet understood. In animal challenge models it has been shown that selected highly-potent neutralising monoclonal antibodies isolated from SARS-CoV-2 infected individuals can protect in a dose-dependent manner [59-61].

First results from immunogenicity, assessed in phase 1/2 clinical trials testing vaccine candidates that may possibly become available in the EU, have shown peak median neutralising antibodies ranging from 100 to 3 900 titres for various vaccine candidate constructs [62-65]. However, it is acknowledged that different assays and formats were used, making any direct comparison problematic [66].

Further characterisation of the correlates of protection and longevity of vaccine-induced protection is needed, including the role of T-cell-mediated immunity. For assessment of B- and T-cell immunity, further standardisation is necessary to allow for comparability. To support these efforts, the Coalition for Epidemic Preparedness Innovations (CEPI) recently set up a centralised laboratory network to standardise methods for assessment of COVID-19 vaccine candidates [67].

## Risk assessment

This assessment is based on information available to ECDC at the time of publication and, unless otherwise stated, the assessment of risk refers to the risk that existed at the time of writing. It follows the ECDC rapid risk assessment methodology, with relevant adaptations [68]. The overall risk is determined by a combination of the probability of an event occurring and its consequences (impact) for individuals or the population [68].

### What is the risk to human health posed by SARS-CoV-2 variants related to mink?

#### *Transmissibility*

Human cases of SARS-CoV-2 infection originating from variants related to mink have been identified in Denmark and the Netherlands. In Denmark, viruses from around 13% of human cases have been sequenced so far. Of these viruses, 214 have been identified as mink-related variants since the first outbreak at a mink farm was reported in June 2020 [1]. Some of these cases have no known link to mink farms. COVID-19 incidence of human cases in the North Jutland Region is higher than in the neighbouring regions. In this region, from June to October 2020, around 40% of cases where the virus was sequenced were caused by a mink-related variant. However, the sampling strategy applied is not the same as in other regions and therefore the incidence cannot be directly compared [69]. The Cluster 5 variant has not been identified since September. Nevertheless, undetected circulation cannot be ruled out, as not all cases are detected and not all viruses sequenced.

In the Netherlands, at least 66 of 97 farm employees tested were positive for SARS-CoV-2 and at least 47 human cases infected with mink-related variants were confirmed by whole genome sequencing. However, only limited human transmission has been reported outside of mink farms since the first mink farm outbreak was identified in April 2020.

Different patterns of transmission after spill-over events in a variety of settings could be due to prevention and control measures at farm and/or country level, surveillance and sequencing capacities, or the inherent transmissibility of the strain.

The information available to date from outbreaks of mink-related strains in Denmark and the Netherlands does not demonstrate increased transmissibility of mink-related variants compared to other variants of SARS-CoV-2, even though uncertainties remain.

On the basis of the evidence available, the probability of infection with mink-related variant strains is assessed as low for the general population, moderate for the populations in areas with a high concentration of mink farms and very high for individuals with occupational exposure.

#### *Severity*

Patients reported to be infected with mink-related variants, including Cluster 5 variant in Denmark, do not appear to have more severe clinical symptoms than those infected with non-mink related variants, either in Denmark, or in the Netherlands. However, there is still a high level of uncertainty due to the small number of cases reported so far.

On the basis of the information available, the current impact of COVID-19 on disease severity in patients infected with mink-related variants appears to be similar to that for patients infected with non-mink variants. This has previously been assessed by ECDC [70] as low for the general population and very high for medically-vulnerable groups (individuals with risk factors for severe COVID-19 disease, such as the elderly) [71]).

#### *Immunity, re-infection, diagnostic tests, vaccination and treatment*

Of all the mink-related variants analysed so far, only the Cluster 5 variant has raised specific concern due to its effect on antigenicity and this requires specific assessment. In preliminary studies, this variant showed reduced sensitivity to neutralising antibodies from COVID-19 patients during the spring of 2020. Antibodies generated by

natural infection with other variants and the antibodies generated by vaccines may potentially exhibit reduced neutralisation in individuals infected with this variant. T-cell mediated immune responses have not yet been investigated for this variant. It should be noted that these findings are preliminary and need to be confirmed before any conclusions can be drawn. Further investigations are needed to assess the impact on i) the risk of reinfection, ii) reduced vaccine efficacy or iii) reduced benefit from treatment with plasma from convalescent patients or with monoclonal antibodies. If any of these concerns are confirmed, given the extent of spread of the mink-related strains in the human population, the current assessment will be immediately reviewed to increase the overall level of risk to human health.

If SARS-CoV-2 transmission among mink affects a very large number of animals and/or is sustained over long periods of time, there is a risk that variants with significantly different antigenic properties or variants causing increased severity of disease could eventually emerge. The likelihood of this risk and the consequences are unclear, but such a scenario should be taken into consideration.

The sensitivities of diagnostic RT-PCR assays are not affected by the Cluster 5 variant or other Danish mink-related S protein variants as RT-PCR assays do not target the spike gene. The variants could potentially have an effect on the sensitivities of antigen and antibody detection assays, including rapid antigen tests (RATs), although any effect will probably be small. Further investigations are needed to determine such effects.

### ***Cross-border spread of SARS-CoV-2 variants related to mink in EU/EEA countries and the UK through humans***

It is rare that a novel variant becomes successful and gives rise to a new genetic clade that can spread globally, but adaptation to transmission in mink populations could establish a selective advantage in regions with mink farming activity.

The mutation Y453F, found both in Denmark and the Netherlands and linked to mink, which is believed to confer a selective advantage in mink-to-mink transmission, has also been detected sporadically in Russian, South African, Swiss and US sequences with no link to the variants found in Denmark or the Netherlands. This could be an indication that this mutation can also arise in humans, or that there is undetected sporadic mink-to-human transmission of SARS-CoV-2 in these countries. It is also possible that low level circulation of these strains is already occurring unnoticed in some places due to the lack of comprehensive sequencing information for all confirmed human cases. The geographically uneven sequencing coverage and delay between sampling and upload of sequence data to international databases is delaying the overall availability of information and limiting the assessment of geographical spread of the new variants beyond affected areas.

Workers employed at mink farms which are not fully compliant with hygiene measures could also introduce the mink-related variants to the community in the vicinity of the farm, new areas or other countries when travelling or returning home while infected. Such events could contribute to the cross-border spread of new variants.

In summary, the probability of cross-border spread of SARS-CoV-2 variants related to mink in EU/EEA countries and the UK through humans appears to be high, in the same way as it is for other SARS-CoV-2 strains.

Increased surveillance, involving collaboration and communication between animal and public health authorities, testing and sequencing of samples from mink farm workers and populations living near mink farms may help prevent the introduction of SARS-CoV-2 into mink farms and identify cases of SARS-CoV-2 infection early.

Response measures currently implemented to control the COVID-19 pandemic have reduced population movement as well as travel and may help to lower the possibility of new variants spreading rapidly to other countries. With the increasing incidence of COVID-19, it is becoming very challenging to detect and characterise specific clusters or outbreaks. However, increased testing, sequencing, contact tracing, isolation of cases, and the general strengthening of public health measures currently being implemented in many countries may help identify clusters of cases due to newly emerging mink-related variants early on to prevent spread in the community.

### ***Cross-border spread of SARS-CoV-2 variants related to mink in EU/EEA countries and the UK through animals and animal products***

It is also important to consider that cross-border transmission of SARS-CoV-2 variants is possible through the trade of infected animals or animal products. The possible pathways for transboundary circulation of mutated SARS-CoV-2 linked to movement of mink or mink products are discussed below.

#### ***Transport of live mink***

Around 1% of the annual production (mainly breeding animals) are transported alive [72]. Transport of infected mink not displaying clinical symptoms and without prior testing can contribute to the spread of infection between mink farms. Given the seasonality of mink production, live mink are mainly transported during the period December-March. Thus, the many outbreaks occurring from April to November 2020 were probably not caused by mink transport. Given the events reported in 2020 and the awareness of the risk of SARS COV-2 in mink, along with the fact that surveillance and a ban on movement is now in place in most Member States, putting a stop to the transport of live mink will reduce the probability of transboundary spread of SARS-CoV-2. For example, the Netherlands will end mink production by the end of 2020. Denmark, the largest mink fur producer in the world, has introduced robust response measures to limit the movement of mink, thus drastically reducing the transport of live mink. As a consequence, the risk of transboundary spread of SARS-CoV-2 out of Denmark will become negligible. Transport of pet mink is extremely rare as mink are usually not kept as pet.

### **Accidental escape from farms**

Release of farmed mink into the wild has been reported, either as a result of accidental escape or intentional release by animal welfare activists. Denmark adopted new containment measures in 1999 which reduced the number of farm-originated mink in the wild (from a hunting bag of 8 000 mink in 2000 to 2 000 mink in 2016 and 1 638 in 2018) [73,74]. A variety of containment measures adopted across Europe have reduced the risk of accidental escapes. However, deliberate releases still occur occasionally in Europe as an act of protest against mink farming by animal welfare activists (in Denmark several thousand per year) [74]. In Spain, around 200–300 feral mink (farmed mink escaped into the wild) are caught each year, mainly in the areas of Burgos and Catalonia [75,76]. If infected mink escape into the wild there may be a risk of SARS-CoV-2 spreading to other susceptible wild or domestic species (e.g. cats), although the exposure to humans is limited. The probability of a wild animal being exposed to infected with SARS-CoV-2 from farmed (infected) mink is probably low. Mink farms generally have a perimeter fence and traps within compounds, which are meant to keep wildlife out and prevent mink from escaping. If infection were to occur among wild mink the spread would be limited and transient. The solitary and territorial nature of mink means that widespread transmission would be unlikely. Overall, the probability of cross-border spread of mutated SARS-CoV-2 through the movement of infected mink having escaped or been released from farms is considered very low.

### **Mink-derived products**

In SARS-CoV-2 infected mink farms, mink pelt can be contaminated by the virus through faeces, respiratory droplets and saliva. Based on a study by Riddel et al. (2020)[77], it is probable that SARS-CoV-2 on the pelt of live mink can remain viable for 1–2 weeks. SARS CoV-2 persists on surfaces for up to 28 days, depending on environmental conditions and surface material [77]. Persistence is reduced in hot and dry environments, while only minimal reduction in virus concentration has been observed after 21 days at 4°C and -80°C [78].

After skinning, raw fur pelts are blow-dried for a few hours at room temperature and stored refrigerated or frozen at the farms where the animals are bred. In rare cases, where very small farms have limited pelting capacity, carcasses are transferred to pelting centres where they are stored frozen until they are processed. After drying, pelts are stored at farms for a few days before being transported to auction houses. When mink are pelted, the drying process and the storage period will reduce the virus load on pelts [79], although this may not completely inactivate the virus, which may remain viable on the raw pelts transported to other areas for further processing [78]. Additional contamination of raw pelts by an infected person cannot be excluded.

Processed pelts are considered to be safe, as SARS-CoV-2 is inactivated in the chemical tanning processing [80]. In the tanning process detergents, antibacterial agents, potassium alum and other salts dissolved in water are used. The tanning process lasts 4–5 days during which the leather undergoes washing, fattening and other mechanical operations to improve its quality, often in acidic pH baths. The procedures applied, carried out by trained and protected personnel, the acidity of the baths and the execution times do not favour the survival, proliferation and transmission of bacteria or viruses. The storage, drying and/or tanning process, requiring many washes and the further drying of the product, will ensure that all trace of the virus is removed. Based on these data, processed pelts are not considered a source of SARS-CoV2, and therefore the probability of spread of SARS-CoV-2 variants from processed pelts is considered very low.

Similarly, other products derived from mink carcasses after pelting (mink oil, fertilisers, bio-fuels, etc.) also undergo rendering treatments [81] which inactivate the virus, meaning that there is no probability of mink-related variants being spread.

In summary, the probability of cross-border spread of SARS-CoV-2 variants related to mink in EU/EEA countries and the UK through animals or animal products appears very low, although stronger evidence is needed, to determine whether raw mink pelts from infected mink may represent a source of viable virus when transported to other areas.

### **Conclusion**

Based on the information currently available on transmissibility, severity, immunity and cross-border spread, the overall level of risk to human health posed by SARS-CoV-2-mink-related variants can be stratified as follows:

- low for the general population and moderate for medically-vulnerable individuals, which is the same as for other SARS-CoV-2 strains (not related to mink);
- low for the general population in areas with a high concentration of mink farms and moderate-to-high for medically-vulnerable individuals living in the same areas;
- moderate for non-medically-vulnerable individuals with occupational exposure to mink farms and very high for medically-vulnerable individuals with the same occupational exposure.

It is important to note that if the concerns raised in relation to immunity, reinfection, vaccination and treatment are confirmed, the risk assessment will immediately be reviewed to re-assess the overall level of risk to human health and the potential implications for COVID-19 diagnosis, treatment and vaccine development. This also applies to any further mink-related variants with mutations in the S protein that may arise and spread in the EU/EEA and the UK.

## Options for response

The risk control measures set out below should be considered in response to this event.

### Human testing, sequencing and characterisation of antigenic properties and virus infectivity

Close collaboration between animal and public health authorities under the One Health approach is crucial for the early detection of SARS-CoV-2 infection outbreaks at mink farms and human cases related to mink farms, to allow timely response and control measures. Information on human and animal cases needs to be shared as quickly as possible to prevent COVID-19 being introduced into mink farms and the SARS-CoV-2 virus circulating undetected. This will also prevent human infection in people exposed to positive cases or farms, and further spread in the community. Information should also be shared with occupational safety and health authorities, to ensure appropriate measures are taken to inform and adequately protect workers at these farms.

Member States should consider a systematic and possibly incremental approach to the proportion of SARS-CoV-2 positive specimens to be sequenced in order to expand the representativeness of the geographical distribution in the population, and to improve the early detection of mutations to better understand the spread. ECDC will continue to support SARS-CoV-2 sequencing for human cases at the request of the Member States.

If a mutation of concern is detected, this should immediately be reported to national and European authorities (through the Early Warning and Response System - EWRS) and the international community. Sharing sequences regularly in open databases and early communication of epidemiological and microbiological investigation results is encouraged in order to improve knowledge of SARS-CoV-2 variants.

Testing and sequencing of suspected SARS-CoV-2 infection cases in mink, farm workers or visitors to mink farms during the incubation period is advised.

Health authorities should consider regularly testing for SARS-CoV-2, irrespective of COVID-19-like symptoms, in farm workers and people with access to premises where mink are kept in order to identify human infections early, prevent introduction into farms and animal populations and avoid further spread in the community/among co-workers. The use of RT-PCR is advised over antigen tests to avoid false negative test results which could increase the risk of community spread. In the event of a positive RT-PCR, sequencing is advised. With a positive detection in a worker, an outbreak investigation should be initiated immediately, and the testing of all workers considered. Exposed workers and visitors should be quarantined as quickly as possible. Appropriate measures also need to be taken to avoid the spread of infection in seasonal workers' accommodation. Workers should be informed and advised, as well as receiving appropriate support to prevent further infections and spread to other countries or geographical areas. Contact tracing should be rapidly implemented and enhanced testing and sequencing of the surrounding population is advised to identify possible circulating mink-related variants.

If COVID-19 community clusters/outbreaks are identified in an area with mink farms, enhanced testing of the population and sequencing of positive specimens is also encouraged, in order to identify possible circulating mink-related variants.

Triggers should be developed for when to initiate assessment of antigenicity and viral infectivity in viral isolates that exhibit genomic changes in areas of the genome that may influence induction of neutralising antibodies. This would facilitate preparation or agreement with reference laboratories of how and when to conduct such studies. Although genome-wide sequencing is becoming standard in all EU/EEA Member States and the UK, further development to agree upon and standardise methods for assessing antigenic changes using neutralisation antibody assays and viral infectivity is urgently needed. The ECOVID-LabNet (European COVID-19 reference laboratory network) is the forum for sharing experiences and method developments on antigenic characterisation and neutralisation assays. Panels of antibody standards and convalescent sera from naturally-infected and vaccinated individuals should be made available. To initiate monitoring of the antigenic properties of SARS-CoV-2 variants, ECDC will discuss with ECOVID-LabNet the possibility of using standardised protocols or centralised virus characterisation, including the testing of antigenic properties, in order to be able to compare results. Sera from humans or animals immunised with current vaccine candidates could be used to assess the relative effect on different vaccine candidates.

### Infection prevention and control measures for mink farm workers and visitors

It is advised to limit the number of people in contact with mink and mink farms, including the avoidance of unnecessary visits, as a measure for reducing the risk of SARS-CoV-2 being introduced into the mink population and re-introduced from the mink population into the human population.

In June 2020, SARS-CoV-2 was classified as risk group 3 according to the biological agents directive<sup>1</sup>. Employers therefore have an obligation to keep a list of exposed workers as well as a record of exposures, accidents and incidents for at least 10 years following the end of exposure, in accordance with national laws and/or practice.

Farm workers or visitors with COVID-19 compatible symptoms should not go to the premises of mink farms.

At the facilities, including areas where there are no mink (e.g. offices) all mink farm workers and visitors (e.g. inspectors) should follow the general recommendations for the prevention of COVID-19, whether or not they have had direct contact with mink. These recommendations include hand and respiratory hygiene, physical distancing, avoiding crowded settings and wearing a face mask, especially in indoor settings where physical distancing cannot be guaranteed. Farm facilities should be well ventilated.

In accordance with the respective EU legislation, appropriate measures [82-86] should be taken by employers to ensure the health and safety of workers after a workplace risk assessment, not only for their own protection but also to help prevent the spread of the virus, and avoid contamination of non-contaminated areas, such as communal break-time and housing facilities and means of transport. Such measures should be in accordance with the legislation governing risks from biological agents at work, in particular Directive 2004/54/EC on the protection of workers from exposure to biological agents which has been implemented into national legislation in all Member States [87].

Workers should be informed, trained and provided with any additional equipment, including appropriate personal protective equipment (PPE), washing facilities or disinfectants. Given that SARS-CoV-2 has been identified in inhalable dust [48], measures to protect against dust and aerosols are indispensable and farm facilities should have appropriate ventilation in place [48,88].

The possibility of language barriers for seasonal workers at mink farms needs to be considered when hygiene and prevention measures are being implemented on the farms in general, but particularly in relation to outbreaks and follow-up activities. It should be ensured that seasonal workers receive timely information and training in a manner that makes it accessible for them.

At mink farms with suspected or confirmed outbreaks, a workplace risk assessment should be revised by employers in coordination with the health and safety committee where it was established. Appropriate measures need to be taken that include all additional risks (e.g. increased physical and mental workload due to additional tasks such as culling and the use of PPE, chemical and physical risks) and any alterations to the work process that might have an impact on the risks workers are exposed to. Workers should be informed and consulted on these measures.

PPE needs to be provided and appropriate storage facilities for PPE should be ensured. It is essential that all mink farm workers are trained in the proper use of PPE and know how to follow the procedures for putting on and safely removing PPE in the correct sequence. Hands should be washed immediately before and after removing PPE.

In addition to the application of specific preventive measures, such as dust and aerosol avoidance, appropriate ventilation and the use of appropriate cleaning methods, workers should wear respiratory protection (filtering face piece (FFP) 2/3 respirator) and eye protection (tightly-fit goggles) and wash their hands when working closely with the animals (e.g. feeding) and when cleaning farm premises [89].

Access to appropriate facilities for hand-washing, as well as disinfectants where necessary, needs to be ensured by employers. The preventive measures and PPE used by mink farm workers involved in culling should be in accordance with the national recommendations and laws relating to culling operations. The following hygienic measures should also be considered: 1) changing to clean clothes and footwear before entering the breeding (black) area, 2) taking a shower after work and 3) washing work clothes at a temperature of minimum 60°C and washing and disinfecting footwear. Appropriate procedures need to be set up to avoid any contamination of non-contaminated (white) areas. This includes the separate storage of work and street clothing, and infection prevention measures in communal break areas and housing, in particular where workers are housed on site or in shared facilities provided by employers. Measures should also be foreseen if communal transport is used.

Pelting in infected farms represents a high risk of occupational infection. During culling operations, infected animals need to be safely destroyed and farms where infections have been confirmed need to be disinfected to minimise human exposure. All operations should follow standard procedures in the respective countries in line with national occupational safety and health requirements. All disinfection needs to include measures to cover animal products and excretions.

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<sup>1</sup> Commission Directive (EU) 2020/739 of 3 June 2020 amending Annex III to Directive 2000/54/EC of the European Parliament and of the Council as regards the inclusion of SARS-CoV-2 in the list of biological agents known to infect humans and amending Commission Directive (EU) 2019/1833, <https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32020L0739>, to be transposed by Member States by 24 November 2020.

## Animal testing and prevention of spread

Intensively-reared animal species, susceptible to SARS-CoV-2, such as mink may act as an amplifier of the virus, leading to an increased virus biomass in the environment, and a greater risk of virus mutations and transmission within farmed mink and between mink and humans. Therefore, increased health surveillance should be considered for mink and mink farm workers and any other people in close contact with mink, especially at farms with a previous/current history of personnel with COVID-19.

National authorities should consider increasing and continuing clinical surveillance at mink farms and laboratory testing of suspected infected mink (dead or with respiratory clinical symptoms). This should include:

- farms where mink have clinical symptoms, direct detection of SARS-CoV-2 infection via throat swabs in combination with histopathology of the lungs;
- farms without clinical symptoms, where the options for testing are PCR of throat swabs from mink that have died recently, even in the absence of lesions.

Ongoing monitoring and surveillance of mink farms (repetitive testing and/or testing of dead mink on a weekly basis) should be considered, if SARS-CoV-2 exposure from humans to mink has not been excluded.

Active serological surveillance is an option for understanding if and to what extent the virus is circulating at mink farms.

The systematic genotyping of isolated SARS-CoV-2 strains in accordance with validated protocols and the sharing of genome sequences from all infected animals, in particular mink, is recommended in order to identify clusters and related variants as soon as possible. Cats and dogs, and mustelids other than minks within the fenced area, or owned by farm personnel at infected mink farms, should be considered for testing in combination with surveillance for clinical symptoms.

National authorities should consider culling mink from infected farms and destroying raw pelts in accordance with appropriate biosecurity measures. A ban on the movement of live mink and raw pelts processed in 2020 within the EU and worldwide should also be considered for as long as SARS-CoV-2 exposure from humans to mink is occurring.

## Development of One Health preparedness and response strategies

Enhanced coordination between agricultural, animal health, and human health (including occupational health and safety) sectors is essential for a timely and effective response [90]. Jurisdictions with mink farms where SARS-CoV-2 is circulating – or has the potential to circulate – in animal populations should consider developing coordinated surveillance and response plans based on timely and effective information sharing. These could include joint outbreak investigation protocols and should also take into account the measures described above relating to human and animal testing, sequencing and infection prevention and control.

There is a need to increase public awareness of mink related SARS-CoV-2 prevention and control strategies. The following groups should be specifically targeted: mink producers, mink farm workers, veterinarians and veterinary staff working with mink farms and partners in the fur industry.

## Limitations

The overall assessment of this event, and particularly the assessment of the public health risk of the mutations related to Cluster 5, is limited by the low number of human cases with mink-related variants reported to date. Further investigations are needed to provide better evidence. The assessment of severity is limited by the low number of cases reported and the case-based data available in order to understand the respective circumstances of the exposures and the course of the disease.

Only a small proportion of human isolates have been sequenced worldwide and therefore it might not be possible to identify a low-level spread of new mutations of concern (irrespective of whether these are mink-related) within a population at a sufficiently early stage. Sequence analysis and virus characterisation requires time to identify new virus mutants and might not be available quickly enough and therefore general response and control measures are needed to control viral spread.

There is limited laboratory information available about phenotypic properties of the variants.

The issue of mutation of SARS-CoV-2 posing a risk for vaccine efficacy and effectiveness still has to be confirmed, and further studies are needed.

## Source and date of request

ECDC internal decision, 6 November 2020.

## Consulted experts

ECDC experts (in alphabetic order): Cornelia Adlhoch, Erik Alm, Julien Beaute, Eeva Broberg, Orlando Cenciarelli, Margot Einöder-Moreno, Catherine Fleming, Céline Gossner, Kari Johansen, Grazina Mirinaviciute, Angeliki Melidou, Nathalie Nicolay, Diamantis Plachouras, Emily Scott, Ettore Severi, Therese Westrell.

### Public health experts

Denmark: Kåre Mølbak (Statens Serum Institut - SSI).

The Netherlands: Aura Timen (National Institute for Public Health and the Environment - RIVM), Bas Oude Munnink and Marion Koopmans (Erasmus Medical Centre).

Sweden: Mia Brytting (Folkhälsomyndigheten).

European Medicines Authority (EMA): Marco Cavalieri.

European Agency for Safety and Health at Work (OSHA): Elke Schneider.

### Veterinary Public Health Experts

Denmark: Anette Ella Boklund, and Søren Saxmose Nielsen (University of Copenhagen); Anette Bøtner (University of Copenhagen and Statens Serum Institut - SSI).

European Food Safety Authority (EFSA): Alessandro Broglia, Nikolaus Kriz, Yves Van der Stede.

All experts have submitted declarations of interest, and a review of these declarations did not reveal any conflict of interest.

## Disclaimer

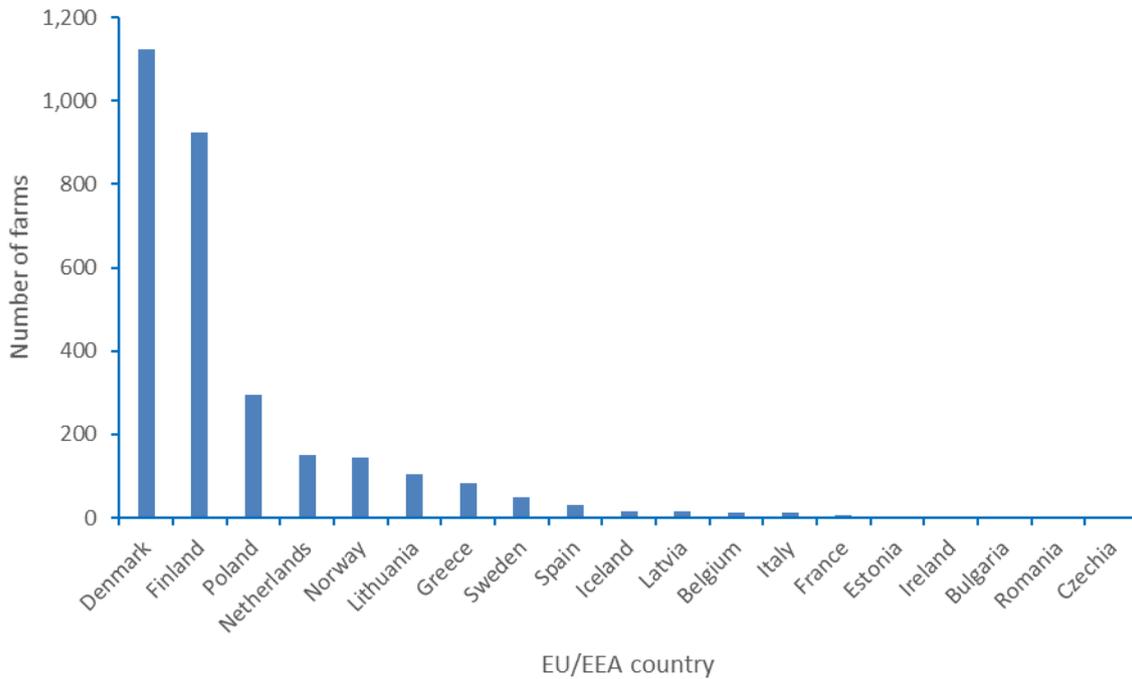
ECDC issues this risk assessment document based on an internal decision and in accordance with Article 10 of Decision No 1082/13/EC and Article 7(1) of Regulation (EC) No 853/2004 establishing a European centre for disease prevention and control (ECDC). In the framework of ECDC's mandate, the specific purpose of an ECDC risk assessment is to present different options on a certain matter. The responsibility on the choice of which option to pursue and which actions to take, including the adoption of mandatory rules or guidelines, lies exclusively with the EU/EEA Member States. In its activities, ECDC strives to ensure its independence, high scientific quality, transparency and efficiency.

This report was written with the coordination and assistance of an Internal Response Team at the European Centre for Disease Prevention and Control. All data published in this risk assessment are correct to the best of our knowledge at the time of publication. Maps and figures published do not represent a statement on the part of ECDC or its partners on the legal or border status of the countries and territories shown.

# Annex 1

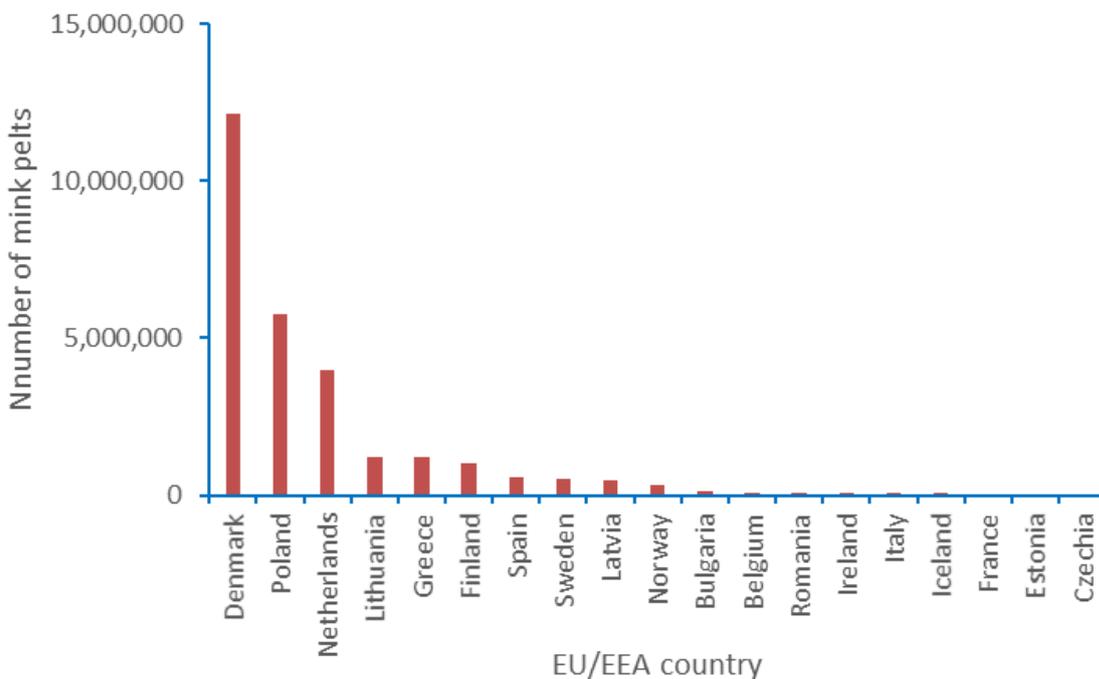
**Figure 1. Number of mink farms by EU/EEA country in 2019**

Note: The number of farms include a minority of fox and Finn raccoon farms.



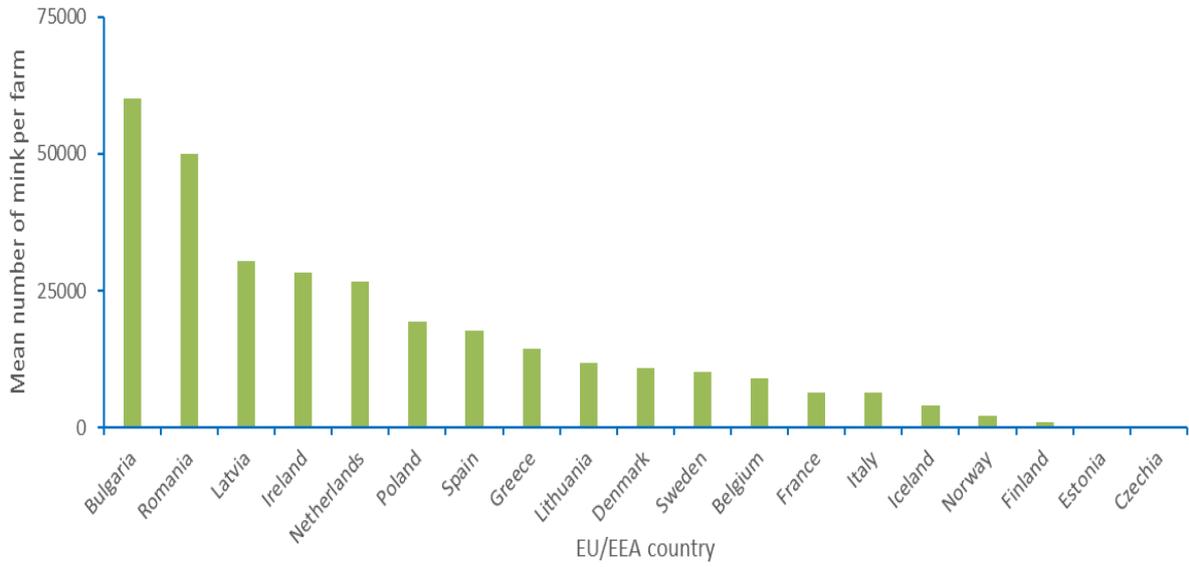
Source: EU Fur Association <https://www.sustainablefur.com/>

**Figure 2. Number of mink pelts produced by EU/EEA country in 2019**



Source: EU Fur Association <https://www.sustainablefur.com/>

**Figure 3. Mean number of animals per farm by EU/EEA country in 2019**



Source: EU Fur Association <https://www.sustainablefur.com/>

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Released July 24, 2015, by the National Agricultural Statistics Service (NASS), Agricultural Statistics Board, United States Department of Agriculture (USDA).

## **Pelt Production Up 6 Percent**

**Mink pelt production** in the United States in 2014 totaled 3.76 million pelts, up 6 percent from 2013. Wisconsin, the largest mink producing State, produced 1,268,760 pelts. Utah, the second largest producing State, produced 958,760 pelts.

The number of pelts by color class as a percent of the total United States production in 2014 is as follows: Black at 50 percent, Mahogany at 24 percent, and Blue Iris at 8 percent. The remaining color classes accounted for 18 percent.

**Value of pelts produced** during the 2014 crop year was \$217 million, up 9 percent from \$200 million a year ago. The average price per pelt for the 2014 crop year was \$57.70, up \$1.40 from \$56.30 in 2013.

**Female mink bred** to produce kits in 2015 totaled 853,140, up slightly from the previous year.

Percent of total females bred to produce kits in 2015 by color class is as follows: Black at 52 percent, Mahogany at 21 percent, and Blue Iris at 8 percent. The remaining color classes accounted for 19 percent.

# **Exhibit U**



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Released July 23, 2020, by the National Agricultural Statistics Service (NASS), Agricultural Statistics Board, United States Department of Agriculture (USDA).

## **Pelt Production Down 15 Percent**

**Mink pelt production** in the United States in 2019 totaled 2.70 million pelts, down 15 percent from 2018. Wisconsin, the largest mink producing State, produced 1.02 million pelts. Utah, the second largest producing State, produced 556,710 pelts.

The number of pelts by color class as a percent of the total United States production in 2019 is as follows: Black at 52 percent, Mahogany at 17 percent, White at 8 percent, and Sapphire at 6 percent. The remaining color classes accounted for 17 percent.

**Value of pelts produced** during the 2019 crop year was \$59.2 million, down 30 percent from \$84.3 million the prior year. The average price per pelt for the 2019 crop year was \$21.90, down \$4.70 from \$26.60 in 2018.

**Female mink bred** to produce kits in 2020 totaled 359,850, down 48 percent from the previous year.

Percent of total females bred to produce kits in 2020 by color class as is follows: Black at 52 percent, Mahogany at 20 percent, White at 6 percent, and Sapphire at 5 percent. The remaining classes accounted for 17 percent.

# **Exhibit V**

# First U.S. cases of coronavirus in minks found at Utah fur farms

By **Karin Brulliard**

August 17, 2020 at 4:13 p.m. MDT

Minks at two Utah fur farms have tested positive for the virus that causes covid-19 in humans, the Department of Agriculture said Monday, announcing the first U.S. cases in a species that has been widely culled in Europe after outbreaks there.

Employees at the farms in Utah, the second-largest producer of mink pelts used for coats and other luxury items, also tested positive for the coronavirus, the USDA said. Dean Taylor, Utah's state veterinarian, told reporters Monday state and federal agencies are conducting additional testing to determine whether the minks were infected by humans or vice versa, and whether minks at other farms are sick.

Minks were discovered to be susceptible to the virus in April, when the Netherlands reported outbreaks at several farms, and mink farms in Denmark and Spain were later affected. The three countries have since killed more than a million of the animals, according to the Associated Press, but the spread has continued: As of this month, at least 27 Dutch farms have been hit. Minks are related to ferrets, which laboratory experiments have shown are highly vulnerable to the virus.

A small number of novel coronavirus cases have been confirmed in dogs, cats, and other animals in the United States and other countries, and scientists and public health agencies say evidence suggests most animals are infected by people and play no meaningful role in the spread of covid-19. Taylor emphasized that on Monday, saying "the risk of animals spreading SARS-CoV-2 to humans is considered low," but he noted research has been "limited."

Dutch researchers, however, said genetic analysis strongly suggested minks sickened by humans there passed the virus back to two farmworkers, in the world's first reports of animal-to-human transmission. That conclusion has prompted calls by infectious diseases researchers for broader study of virus transmission between humans and animals.

In Utah, a state agriculture laboratory performed necropsies on several minks after “unusually large numbers of mink died at the farms,” the USDA said. A Washington State University lab found that samples of five animals were positive for the virus, and the USDA's veterinary lab confirmed the results. Taylor said the two farms — which he declined to identify — have been quarantined and there are no immediate plans for culling.

“We don't feel like we have enough information to make that decision at this point,” Taylor said. “Most of these farms have already got good biosecurity. I don't think they need to worry unduly, but all of us need to take it seriously.”

The report of the outbreak is the latest bad news for the U.S. mink industry, which has faced declining production and profits in recent years and has been hard-hit by President Trump's trade war with China, the top buyer of American mink. Production of pelts dropped 15 percent from 2018 to 2019, and the value of those sold dropped 30 percent to \$59.2 million, according to a July report from the USDA.

Clayton Beckstead, a mink farmer and regional manager for the Utah Farm Bureau, said in an interview that the declines were partially due to global overproduction of mink. But the pandemic has battered the state's mink farms, about half of which have closed this year. There are now 38 farms in the state, he said.

“Our main industry is in China. This started with the trade wars, and now nobody can travel, so we haven't been able to sell any product,” Beckstead said. Many fur farms have received federal paycheck protection grants, but they are ineligible for relief offered to farmers and ranchers, he said.

This year “has been terrible,” he said. “It's been one thing after another.”

The industry already stepped up biosecurity measures when the Dutch outbreaks began, he said, increasing the use of masks, gloves, rubber boots and other protective measures.

“This is our livelihood. We want to protect our animals. We want to protect our families and our employees. ... We want to stop [the virus] in its tracks.”

# **Exhibit W**

# The Guardian

This article is more than **1 month old**

## Nearly 10,000 mink dead from Covid-19 outbreak at Utah fur farms

**State's veterinarian says coronavirus had mostly affected older mink, 'wiping out 50% of the breeding colonies'**

**Victoria Bekiempis**

Sun 11 Oct 2020 12.21 EDT



Covid-19 infected minks were first discovered in the Netherlands, on multiple farms.  
Photograph: Henning Bagger/Ritzau Scanpix/AFP/Getty Images

Almost 10,000 mink in Utah have reportedly died due to Covid-19, spurring quarantines at nine fur farms impacted by the outbreak.

The state's veterinarian, Dean Taylor, reportedly said that coronavirus had mostly affected older mink, "wiping out 50% percent of the breeding colonies." Younger mink were largely unharmed, he said.

The first known Covid-19 cases among US minks were in Utah, with their diagnoses confirmed in mid-August, the federal Department of Agriculture (USDA) said. Authorities learned about mink contracting coronavirus after farm workers tested positive, Taylor told NBC News.

"After unusually large numbers of mink died at the farms, the Utah Veterinary Diagnostic Laboratory completed necropsies on several of the affected animals," the USDA said. Samples

from the procedures were sent to two laboratories, and Covid-19 was ultimately confirmed.

Earlier this month, authorities also confirmed coronavirus cases among mink in Wisconsin and Michigan.

Dutch mink were first infected with coronavirus by their handlers in April. The government identified two cases in which humans had been infected by sick animals in May, the only animal-to-human transmissions known since the global outbreak began in China.

Research indicates that persons with Covid-19 can infect animals, and some cases of the reverse have been identified in Europe. In May, the government identified two cases in which humans had been infected by sick animals. At that time, they were the only animal-to-human transmissions known since the global outbreak began in China.

Utah agriculture authorities have maintained that animal-to-human infection is unlikely, however, stating: “There is currently no evidence that animals, including mink, play a significant role in transmitting the virus to humans. As it now stands, due to limited information and research, the risk of animals spreading SARS-CoV-2 to humans is considered low.”

Humans and mink exhibit similar symptoms from Covid-19 - respiratory distress. More than 214,000 humans have died after contracting the coronavirus in the US, and more than 7.7 million people across the country have been infected.

“Mink show open mouth breathing, discharge from their eyes and nose, and are not sick for several days before they pass away,” Taylor explained. “They typically die within the next day.”

Taylor said that no mink were euthanized in the Utah outbreak. Agriculture and public health officials - including the Centers for Disease Control - were coordinating with mink farm employees to stop coronavirus from spreading, he said.

“Once final testing is done, we’re going to create a state plan to stop this virus from spreading to more farms,” Taylor told the NBC News. “It’s far easier to prevent it from happening, then stopping it from happening all at once.”

According to Fur Commission USA, the nation’s largest association of mink farmers, there are at least 245 mink farms in 22 states. Utah is the country’s second biggest producer for pelts, according to the publication Science.

Covid-19 infected mink were first discovered in the Netherlands, on multiple farms which “also experienced an increase in mink deaths”, the USDA said. There were subsequent outbreaks in Spain and Denmark. These countries have since killed more than 1 million farmed mink as a precautionary measure.

The number of animals worldwide reported to have Covid-19 is “small ... mostly after close contact with people with Covid-19,” USDA officials said.

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# **Exhibit X**

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# Thousands of minks Dead in COVID outbreak on Utah farms

By JoNEL ALECCIA October 5, 2020



Thousands of minks at Utah fur farms have died because of the coronavirus in the past 10 days, forcing nine sites in three counties to quarantine, but the state veterinarian said people don't appear to be at risk from the outbreak.

The COVID-19 infections likely were spread from workers at the mink ranches to the animals, with no sign so far that the animals are spreading it to

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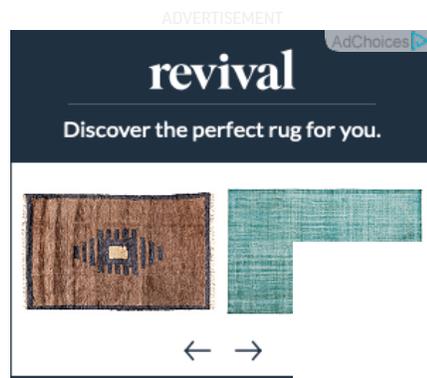
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humans, said Dr. Dean Taylor, the state veterinarian, who is investigating the outbreak.

“We genuinely don’t feel like there is much of a risk going from the mink to the people,” he said Thursday.

Between 7,000 and 8,000 minks have died since the disease swept through the ranches that produce the animals, valued for their luxurious pelts. So far, no animals in Utah have been euthanized because of the disease, and it doesn’t appear to be necessary, Taylor said.



Fur from the dead infected animals will be processed to remove any traces of the virus and then used for coats and other garments, according to Fur Commission USA, a mink farming trade group. The U.S. produces more than 3 million mink pelts each year.

Taylor declined to name the farms or the counties where the affected minks were found.

With minks, as with humans, COVID-19 is less deadly for the young.

“It’s going through the breeding colonies and wiping out the older mink and leaving the younger mink unscathed,” Taylor said. Most of the deaths have been in minks between the ages of 1 and 4 years.

In addition to the minks, more than 50 animals in the U.S. had tested positive for the coronavirus as of Sept. 2,

according to the U.S. Department of Agriculture. The infections have been detected in pet cats and dogs, as well as lions and tigers at a New York zoo.

Minks seem particularly susceptible to COVID-19, likely because of a protein in their lungs, the ACE2 receptor, which binds to the virus and appears to predict vulnerability to the infection, according to Wageningen University & Research in the Netherlands. Humans also have this protein in their lungs.

The COVID outbreak in Utah has surged since mid-August, when the first cases of the disease in the animals were confirmed by the USDA.

Minks were discovered to be susceptible to the SARS-CoV-2 virus, which causes COVID-19, in April, after outbreaks at several farms in the Netherlands, followed by outbreaks in Denmark and Spain. More than 1 million animals were culled in those countries, according to the Associated Press.

**AP**

## Thousands of minks Dead in COVID outbr...

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Several workers at the Utah mink farms have tested positive for COVID-19, including some who had no symptoms.

“Some of our mink ranchers have more than one facility, and that’s probably how it spread,” Taylor said.

A study in the Netherlands found that the virus appeared to jump back and forth between people and minks, but the data so far remains limited.

After the initial U.S. cases were confirmed, mink farms across Utah and

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the rest of the country implemented strict measures to prevent the disease from spreading, such as restricting access, conducting health checks on workers and disinfecting surfaces. The USDA and the Centers for Disease Control and Prevention have issued guidelines for farmed minks and other mustelids, a family of animals that also includes weasels and badgers.

“Obviously, it’s very concerning to have a species that is this susceptible with this high of a death rate,” Taylor said.

The outbreak has led to the quarantine of a quarter of Utah’s three dozen mink ranches and raised concerns across the state, said Clayton Beckstead, regional manager for the Utah Farm Bureau and a fourth-generation mink farmer.

“We’re certainly worried, but I think everybody’s taking pretty extreme biosecurity measures,” said Beckstead, whose own farm has not been affected.

Utah is one of the nation’s top mink producers. Overall, there are 245 fur farms in 22 states, part of an industry valued at \$82.6 million a year, according to Fur Commission USA.

Investigating an outbreak of a novel virus in a new species is “daunting,” Taylor said.

“We’re learning as quick as we can,” he said. “We’re scrambling to help these animals and protect this industry.”

—

is a reporter with Kaiser Health News.

Kaiser Health News (KHN) is a national health policy news service. It is an editorially independent program of the Henry J. Kaiser Family Foundation which is not affiliated with Kaiser Permanente.



# **Exhibit Y**



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pelts.

The virus first appeared in the creatures in August, shortly after farmworkers fell ill in July, according to Dr. Dean Taylor, state veterinarian of Utah. Initial research shows the virus was transmitted from humans to animals, and so far has not seen any cases of the opposite.

“Everything we’ve looked at here in Utah suggests it’s gone from the humans to the animals,” Taylor told CNN.

“It feels like a unidirectional path,” he said, adding that testing is still underway.

**Some context:** This is the first outbreak among mink in the United

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States, though other cases have been detected in the Netherlands, Spain and Denmark, according to the US Department of Agriculture.

Mink, which are closely related to weasels, otter and ferrets, appear to suffer similar symptoms to humans. Difficulty breathing and crusting around the eyes are usually seen, but the virus progresses rapidly, and most infected mink are dead by the next day, according to Taylor. It's unclear what makes mink such a susceptible species, while others appear to be unaffected.

Mink join only cats, dogs, a tiger and a lion to be the only confirmed animals with Covid-19 in the US, according to the USDA data.

The cluster of cases in Utah has spread to nine farms, but Taylor warns that "we're still in the middle of the outbreak." Each farm is under quarantine with only essential workers permitted on site. Farmworkers are being directed to use proper protective equipment at all times.

The pelts from most of the mink that have died from the virus have been either contained and buried

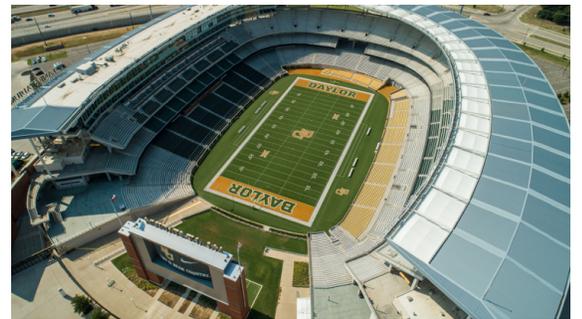
or incinerated. No pelts have left the state, according to Taylor.



6:10 p.m. ET, October 8, 2020

## **Baylor University football team suspends all activities due to Covid-19 test results**

From CNN's David Close



McLane Stadium at Baylor University in Waco, Texas Shutterstock

Baylor University, in Waco, Texas, has announced it is halting all football-related activities following positive results from recent coronavirus testing. The school did not reveal how many players and/or staff tested positive for Covid-19.

Last month, the team was forced to postpone a game versus the Houston Cougars due to Covid-19 cases on the Baylor team.

### **CNN Underscored**

These 5-star Amazon products make for the perfect holiday gifts

Traveling for Thanksgiving? Here's what to buy to stay safe

# **Exhibit Z**

**Voluntary Report** – Voluntary - Public Distribution

**Date:** May 20,2020

**Report Number:** NL2020-0019

**Report Name:** Additional Control Measures for Dutch Mink Industry In Response to COVID-19

**Country:** Netherlands

**Post:** The Hague

**Report Category:** Agricultural Situation, Agriculture in the News

**Prepared By:** FAS/The Hague Staff

**Approved By:** Christopher Riker

**Report Highlights:**

Based on research conducted by the Dutch government, it is now believed that mink which were infected with the coronavirus (COVID-19) may have transmitted the virus to a farm employee. The relevant study also shows that mink can have the virus without showing any disease symptoms. Based on these developments, the Minister of Agriculture, Nature and Food Quality and the Minister of Health, Welfare, and Sport will implement a number of control measures. Herein is an unofficial summary/translation of the Ministry of Agriculture, Nature and Food Quality's announcement.

## General Information

In late April and early May, four Dutch fur farms were found to have mink that were positive for the coronavirus (COVID-19). For additional information, see [NL2020-0016 - COVID-19 Found on Dutch Mink Farms](#).

Based on the results from the ongoing investigation, the Dutch government has determined that it is plausible that mink transmitted the virus to a farm employee.<sup>1</sup> The study also indicates mink may carry the disease without showing any disease symptoms. Based on these findings, Carola Schouten, the Minister of Agriculture, Nature and Food Quality, and Hugo de Jonge, the Minister of Health, Welfare and Sport, have instructed their respective Ministries to take a number of measures.<sup>2</sup>

As background, the Dutch Ministry of Agriculture, Nature, and Food Quality (MANFQ) notes the virus that causes COVID-19 mutates relatively quickly, but that these changes in the genetic code can be monitored. By comparing the genetic code of the virus of different animals and people with each other, a “family tree” can be created, and an image can be obtained of how people and animals have been infected in time and place. This type of research has also been done on infected mink and humans. Through this research the Dutch government has learned that one infected employee at an infected mink farm has been shown to have similarities with the virus found in mink on the same farm. Based on the comparison and the position of the virus in the family tree, it is concluded from this investigation that it is plausible that mink may have infected this employee.

To clarify this further, researchers are currently further mapping the 'genetic pedigree' of infected people from the environment of the infected mink farm in order to obtain the most complete picture possible. Despite this finding, the National Institute for Public Health and the Environment (RIVM) has reiterated that the risk of exposure to the virus outside of the mink house remains negligible.

## Control Measures

Based on these new findings, the Cabinet is taking a number of measures in addition to those that have already been introduced. For additional information on previously introduced measures, see [NL2020-0016 - COVID-19 Found on Dutch Mink Farms](#).

The screening of mink farms (for antibodies) is expanded to include all mink farms in the Netherlands (and will be mandatory). In the interest of the health of employees at the farms, MANFQ comments that it is important to get an overview of the situation for all mink farms. The Netherlands Food and Consumer Product Safety Authority (NVWA) will coordinate this screening.

If an infection is detected on a farm, the same measures will be applied as at other infected enterprises. There will also be a ban on visitors in the stables of the infected companies, and additional hygiene

<sup>1</sup> <https://www.rijksoverheid.nl/actueel/nieuws/2020/05/19/nieuwe-onderzoeksresultaten-covid-19-bij-nertsenbedrijven>

<sup>2</sup> By identifying COVID-19 in mink on mink farms as an infectious animal disease according to Article 15 of the Dutch Animal Health and Welfare Act, the government may require additional control measures for the industry.

requirements imposed. Additionally, employees are advised to use protective equipment during their work.

Minister Schouten previously instituted a notification obligation for mink farmers, veterinarians, and persons from research institutions, but these reporting obligations have now been extended to include all symptoms that may indicate a COVID-19 infection in mink. To prevent the possible spread of the virus to other farms, the requirement that animals and manure not leave an infected farm will remain in place.

### **Farm Cats**

MANFQ reports that current research indicates the virus on two of the infected mink farms is very similar. Because antibodies against the virus have been demonstrated in three out of eleven farm cats on one of the infected farms, MANFQ reports it is important to investigate the role farm cats may play in potential virus transmission between farms (which will include participation from the [Netherlands Centre for One Health](#)).<sup>3</sup> MANFQ advises that infected mink farms ensure that cats cannot enter or leave the premises.

### **Pets**

MANFQ comments that COVID-19 was previously known to occur in pets, but the risk of people becoming infected by their pets remains small. The existing advice from RIVM on COVID-19 and the handling of animals remains unchanged: keep your animal indoors if there are people in the household with complaints that are pertinent for COVID-19 and/or if the animal is also sick.

### **Attachments:**

[May 19 Letter to House of Representatives from Ministry of Agriculture, Nature and Food Quality \(in Dutch\).pdf](#)

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<sup>3</sup> MANFQ defines farm cats as cats that live in the yard and are not socialized.

# **Exhibit AA**

# SARS-CoV-2 infection in farmed minks, the Netherlands, April and May 2020

Nadia Oreshkova<sup>1</sup>, Robert Jan Molenaar<sup>2</sup>, Sandra Vreman<sup>1</sup>, Frank Harders<sup>1</sup>, Bas B Oude Munnink<sup>3</sup>, Renate W Hakze-van der Honing<sup>1</sup>, Nora Gerhards<sup>1</sup>, Paulien Tolsma<sup>4</sup>, Ruth Bouwstra<sup>2</sup>, Reina S Sikkema<sup>3</sup>, Mirriam GJ Tacken<sup>1</sup>, Myrna MT de Rooij<sup>5</sup>, Eefke Weesendorp<sup>1</sup>, Marc Y Engelsma<sup>1</sup>, Christianne JM Brusckhe<sup>6</sup>, Lidwien AM Smit<sup>5</sup>, Marion Koopmans<sup>3</sup>, Wim HM van der Poel<sup>1</sup>, Arjan Stegeman<sup>7</sup>

1. Wageningen Bioveterinary Research, Wageningen University and Research, Lelystad, the Netherlands
2. GD Animal Health, Deventer, the Netherlands
3. Department of Viroscience, Erasmus University Medical Center, Rotterdam, the Netherlands
4. Regional Public Health Service Brabant-Zuid-Oost, Eindhoven, the Netherlands
5. Institute for Risk Assessment Sciences (IRAS), Utrecht University, Utrecht, the Netherlands
6. Ministry of Agriculture, Nature and Food Quality, The Hague, the Netherlands
7. Department of Farm Animal Health, Faculty of Veterinary Medicine, Utrecht University, the Netherlands

Correspondence: Wim H.M. van der Poel ([wim.vanderpoel@wur.nl](mailto:wim.vanderpoel@wur.nl))

## Citation style for this article:

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Article submitted on 24 May 2020 / accepted on 04 Jun 2020 / published on 11 Jun 2020

**Respiratory disease and increased mortality occurred in minks on two farms in the Netherlands, with interstitial pneumonia and SARS-CoV-2 RNA in organ and swab samples. On both farms, at least one worker had coronavirus disease-associated symptoms before the outbreak. Variations in mink-derived viral genomes showed between-mink transmission and no infection link between the farms. Inhalable dust contained viral RNA, indicating possible exposure of workers. One worker is assumed to have attracted the virus from mink.**

Currently, humanity is facing a pandemic of a new coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The virus is spreading efficiently among people, causing predominantly respiratory disease with varying degree of severity. The virus has also been shown to infect a number of animal species under experimental conditions. Rhesus and cynomolgus macaques, ferrets, cats and golden Syrian hamsters supported viral replication in respiratory tract and some of those species (rhesus macaques, juvenile cats and hamsters) displayed a mild to moderate clinical disease [1-9]. Besides the experimental infections, occasional spillover from humans to domestic or captive animals has been reported. In a few isolated cases, cats and dogs owned by infected individuals tested positive for SARS-CoV-2 RNA and occasionally, cats also displayed clinical disease [10,11]. Recently, several tigers in the Bronx zoo (New York City, United States (US)) with respiratory symptoms were confirmed positive for SARS-CoV-2 [10]. In all cases, a direct correlation with infected humans was established or at least other sources of infection were excluded [10].

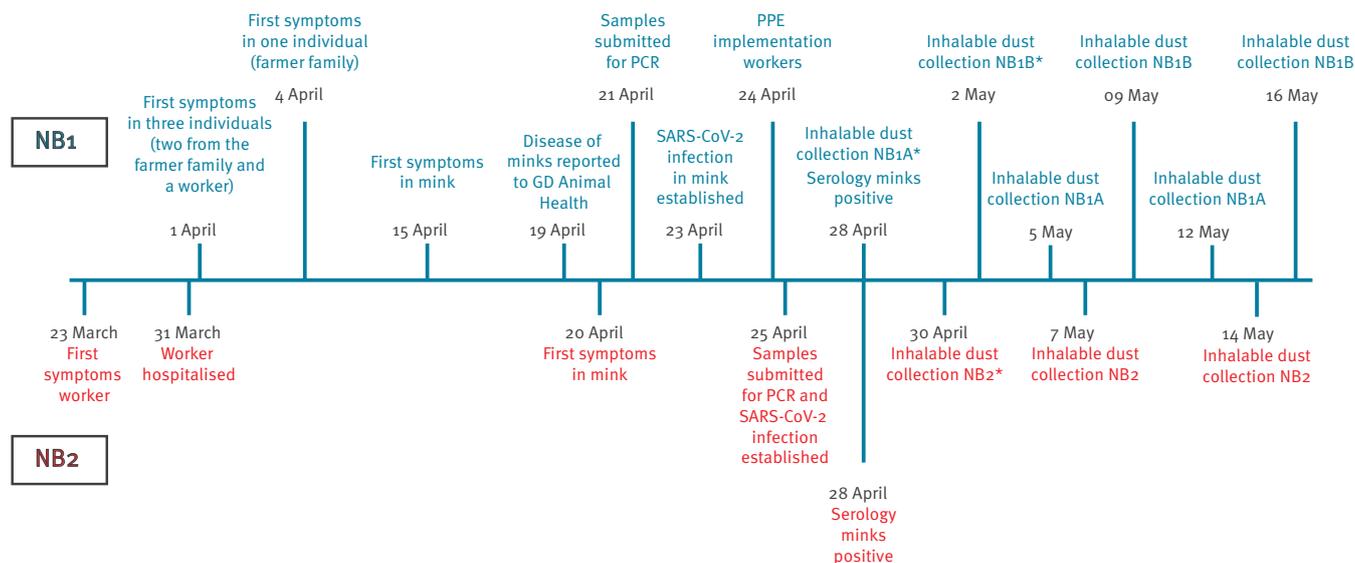
Here, we report SARS-CoV-2 infection of minks on two farms in the Netherlands and describe the associated clinical signs, pathological and virological findings. Sequence analysis of mink-derived viruses pointed at humans as the probable source of the initial infection and demonstrated transmission between minks. Furthermore, the presence of viral RNA in inhalable dust collected from the farms indicated a possible exposure of workers to virus excreted by minks.

## Mink farming background

Minks are farmed for their fur. In the Netherlands, there are around 125 mink farms, with an average of 5,000 female breeding animals. In 2019, 4 million minks were produced. The sector has around 1,200 full-time and 400 part-time employees [12]. On two mink farms (NB1 and NB2) situated in the south of the Netherlands, province North Brabant (NB), an increased mink mortality was observed mid-April 2020, which coincided with display of respiratory signs in some animals. On NB1, 13,700 animals are housed in two separate, but closely situated houses (house A and house B, 115 m apart), which are served by the same personnel and vehicles. NB2 has 7,500 animals. Farms NB1 and NB2 are 14 km apart from each other. There was no connection of workers, vehicles or animal transports, between these two farms. On both farms, minks are individually housed in wire netting cages with a nest box. The cages are arranged in long single rows, separated by feeding alleys. The two cage sides that border other cages are solid, made of wood or plastic, ensuring that there is no direct animal-to-animal contact. The cage rows are situated inside halls, which provide a roof, but are largely open to the wind from the sides. Both farms are family-owned and besides the four (NB1) and

**FIGURE 1**

Schematic representation of the time-line of events in the first month of a SARS-CoV-2 outbreak on two mink farms, the Netherlands, April 2020



Covid-19: coronavirus disease; NB1/NB2: Farms 1 and 2 in North Brabant; PPE: personal protective equipment; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2.

Dates of significant events are shown with the corresponding findings. Cases of (suspected) human Covid-19 infections in farm workers that coincided with the SARS-CoV-2 infection of the minks are excluded from this report. Analysis of those cases is currently being performed and will be reported in a subsequent publication. Asterisks indicate the dates on which dust samples collected inside the mink farm buildings were found positive for viral RNA.

**TABLE 1**

Gross pathology and cause of death of necropsied minks, SARS-CoV-2 outbreak on two mink farms, the Netherlands, April 2020 (n = 36)

Farm NB1				Farm NB2			
Animal number	Date of death	Date of necropsy	Cause of death	Animal number	Date of death <sup>a</sup>	Date of necropsy	Cause of death
1	28 Apr	28 Apr	Interstitial pneumonia	1	27 Apr	27 Apr	Sepsis and lung oedema with congestion
2 <sup>b</sup>	28 Apr	28 Apr	Interstitial pneumonia	2 <sup>b</sup>	27 Apr	27 Apr	Interstitial pneumonia
3	28 Apr	28 Apr	Interstitial pneumonia	3	27 Apr	27 Apr	Aleutian disease
4	28 Apr	28 Apr	Interstitial pneumonia	4	27 Apr	27 Apr	Aleutian disease
5	28 Apr	28 Apr	Interstitial pneumonia	5	27 Apr	27 Apr	Sepsis
6	28 Apr	28 Apr	Interstitial pneumonia	6	27 Apr	27 Apr	Dystocia
7	28 Apr	28 Apr	Interstitial pneumonia	7 <sup>b</sup>	27 Apr	27 Apr	Interstitial pneumonia
8	28 Apr	28 Apr	Interstitial pneumonia	8 <sup>b</sup>	27 Apr	27 Apr	Interstitial pneumonia
9	28 Apr	28 Apr	Aleutian disease	9	26 Apr	27 Apr	Interstitial pneumonia
10	28 Apr	28 Apr	Interstitial pneumonia	10	26 Apr	27 Apr	Interstitial pneumonia
11	28 Apr	28 Apr	Interstitial pneumonia	11	26 Apr	27 Apr	Interstitial pneumonia
12	28 Apr	28 Apr	Interstitial pneumonia	12	26 Apr	27 Apr	Interstitial pneumonia
13 <sup>b</sup>	28 Apr	28 Apr	Interstitial pneumonia	13	26 Apr	27 Apr	Interstitial pneumonia
14 <sup>b</sup>	28 Apr	28 Apr	Interstitial pneumonia	14	26 Apr	27 Apr	Interstitial pneumonia
15	28 Apr	28 Apr	Interstitial pneumonia	15	26 Apr	27 Apr	Interstitial pneumonia
16 <sup>b</sup>	28 Apr	28 Apr	Interstitial pneumonia	16	26 Apr	27 Apr	Interstitial pneumonia
17	28 Apr	28 Apr	Interstitial pneumonia	17	26 Apr	27 Apr	Interstitial pneumonia
18	28 Apr	28 Apr	Interstitial pneumonia	18	26 Apr	27 Apr	Sepsis

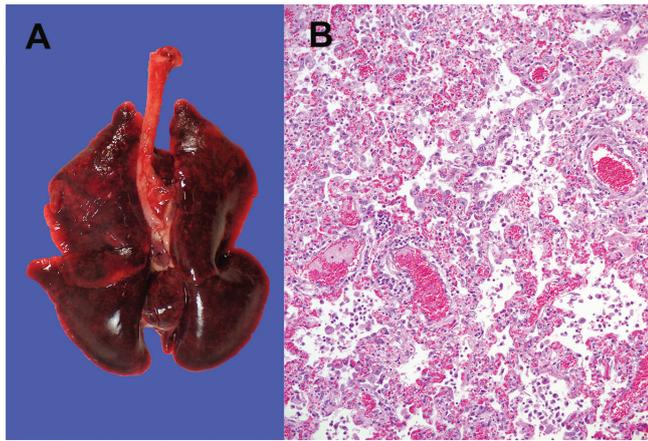
SARS-CoV-2: severe acute respiratory syndrome coronavirus 2.

<sup>a</sup> Date when the animals were found dead (animals are inspected daily).

<sup>b</sup> Organs from those animals were collected for SARS-CoV-2 qPCR.

## FIGURE 2

Lung from a necropsied mink, SARS-CoV-2 outbreak on two mink farms, the Netherlands, April 2020



SARS-CoV-2: severe acute respiratory syndrome coronavirus 2.

Panel A: Representative macroscopic image of an affected lung. Panel B: Representative microscopic image (objective 20x) of a section of the lung, fixed in 10% formalin and stained with haematoxylin and eosin, showing interstitial pneumonia.

two (NB2) members of the farmer family, one and six employees were working on the farms, respectively.

### Disease history and clinical observations

Signs of respiratory disease in the animals were reported on 19 and 20 April 2020 (Figure 1) on NB1 and NB2, respectively. The symptoms were mostly limited to watery nasal discharge, but some animals showed severe respiratory distress. The exact numbers of animals that displayed symptoms, as well as the severity of the symptoms, were not registered. On both farms, the veterinarian was consulted when severe respiratory disease symptoms were observed by the farmer. Animals that had died were necropsied and tested for SARS-CoV-2, influenza A, adenoviral infection, *Escherichia coli* and *Pseudomonas aeruginosa*. All tests except SARS-CoV-2 were negative. Overall mortality between date of reporting and 30 April was 2.4% at NB1 and 1.2% at NB2, while ca 0.6% would have been expected, based on observations from previous years, in the same period. Affected animals were not concentrated in a specific location, but rather scattered throughout the buildings of each farm. At this time of the year, the mink populations consist mainly of pregnant females. In the few litters that were already present, no increase in pup mortality was noticed.

Lungs from three recently died animals per farm were collected and submitted for qPCR analysis on 21 (NB1) and 25 (NB2) April. One sample per farm was also sequenced (index samples). In the following week, 36 recently dead animals were collected (18 per farm) and necropsied. A throat and rectal swab were taken from each animal for qPCR analysis.

## Pathological analysis

### Macroscopic findings

The necropsies revealed that 16 of 18 animals from NB1 and 12 of 18 from NB2 had diffusely dark to mottled red, wet lung lobes that did not collapse when opening the thoracic cavity, indicating interstitial pneumonia (Table 1 and Figure 2A). Other investigated organs displayed no significant macroscopic changes. Minks without the described lung findings had macroscopic changes consistent with either chronic Aleutian disease, septicæmia, or dystocia. From seven animals with clear macroscopic lung changes, organs were harvested for histopathological and virological investigation.

### Histological findings

A severe diffuse interstitial pneumonia with hyperaemia, alveolar damage and loss of air containing alveolar lumina was detected in all the seven harvested lungs (Figure 2B). Bacterial cultures from the organs of the seven animals were negative.

### Virus detection and sequencing

Presence of viral RNA was determined by qPCR against the SARS-CoV-2 E gene (Table 2) [13]. Viral RNA was detected in the conchae, lung, throat swab and rectal swab of all seven minks from which organs were collected. In addition, viral RNA was detected in the liver of one, and in the intestines of three animals. Splens of all seven animals were negative for viral RNA (Table 2). In the swabs collected from all 36 necropsied animals, viral RNA was detected in all throat swabs and 34 of the 36 rectal swabs. The cycle threshold (Ct) values varied, but were on average lower in the throat swabs than in the rectal swabs (average Ct = 21.7 and 31.2, respectively), indicating higher viral loads in the throat swabs.

The viral sequences of the index samples and from additional four and five animals from NB1 and NB2, respectively, were determined by next generation sequencing and deposited in GenBank (MT396266 and MT457390–MT457399). Phylogenetic analysis of the sequences suggests separate virus introductions to each of the farms (Figure 3). The index sequences show nine (NB1) and 15 (NB2) nucleotide substitutions across the complete genome in comparison with Wuhan-Hu-1 (NC\_045512.2, EPI\_ISL\_402125). The two index sequences diverge at 22 nucleotide positions, but the sequences from each farm cluster together (Figure 3). Mink-specific single nucleotide polymorphisms were found in ORF1a, ORF1b, spike, ORF3, ORF7a and 3'UTR (Supplementary Table 2).

### History of coronavirus disease in farm workers

Farm owners and their families were interviewed by the public health service for possible history of disease. Four persons on farm NB1 have had respiratory disease symptoms compatible with Covid-19 since beginning of April, including three members of the farmer's family

**TABLE 2**

Virus titres, determined by qPCR in organs and swabs of necropsied minks, SARS-CoV-2 outbreak on two mink farms, the Netherlands, April 2020 (n = 36)

	Animal number	Conchae	Lung	Spleen	Liver	Distal large intestines	Throat swab	Rectal swab
Farm NB1	2	8,25	4,54	Not detected	Not detected	4,22	6,87	3,30
	13	9,16	5,17	Not detected	Not detected	3,56	6,81	3,01
	14	8,08	3,83	Not detected	Not detected	Not detected	7,04	3,95
	16	7,08	3,90	Not detected	Not detected	4,97	6,47	4,47
Farm NB2	2	8,19	5,77	Not detected	Not detected	Not detected	8,03	2,58
	8	8,55	5,55	Not detected	3,45	Not detected	7,30	3,84
	7	8,46	5,98	Not detected	Not detected	Not detected	6,69	5,42

SARS-CoV-2: severe acute respiratory syndrome coronavirus 2.

Titres were calculated based on a calibration curve of a virus stock with a known infectious virus titre and are expressed as log<sub>10</sub> (median tissue culture infectious dose (TCID<sub>50</sub>)/g of tissue (organ material) or log<sub>10</sub> TCID<sub>50</sub>/mL of swab material (swabs were always submerged in 2 mL of cell culture medium)).

and a worker (Figure 1). These people were not investigated for SARS-CoV-2 infection. At NB2, one worker had been diagnosed with SARS-CoV-2 infection and hospitalised on 31 March (Figure 1). A clinical sample was retrieved, but the viral load was too low for sequencing analysis. At farm NB1, one person who stayed on the farm, showed mild respiratory disease and was diagnosed with SARS-CoV by 28 April. Based on preliminary sequencing results, this person was assumed to have attracted the virus from mink. A further detailed investigation focusing on the transmission of the virus between humans and mink on the farms is ongoing.

### Sampling of the environment and stray cats

Inhalable dust samples were collected three times between 28 April and 16 May (Figure 1) by active stationary air sampling during 5–6 h, using Gilian GilAir 5 pumps (Sensidyne, St. Petersburg, US) at 3.5 L/min, total dust sampling system (Gesamtstaubprobenahme; GSP) sampling heads (JS Holdings, Stevenage, United Kingdom) and Teflon filters (Pall Corporation, Ann Arbor, US). In each mink house, sampling was conducted at three different locations. Viral RNA was detected in two of the three samples from NB1, house A (Ct = 35.95 and 38.18) and in one of three samples from NB1, house B (Ct = 35.03) and from NB2 (Ct = 35.14) on the first sampling moment, but all samples were negative on the second and third sampling moments.

A total of 24 stray cats found in the surroundings of the farms NB1 and NB2 were sampled for SARS-CoV-2 infection by collecting serum and oropharyngeal swabs. Seven cats had antibodies against SARS-CoV-2, detected by an in-house virus microneutralisation assay, and one cat was positive for viral RNA. However, the amounts of viral RNA were very small, and we were unable to generate a sequence from this cat. The sampled stray cats inhabit the surroundings of the farms, but do not come into the houses of people.

### Discussion

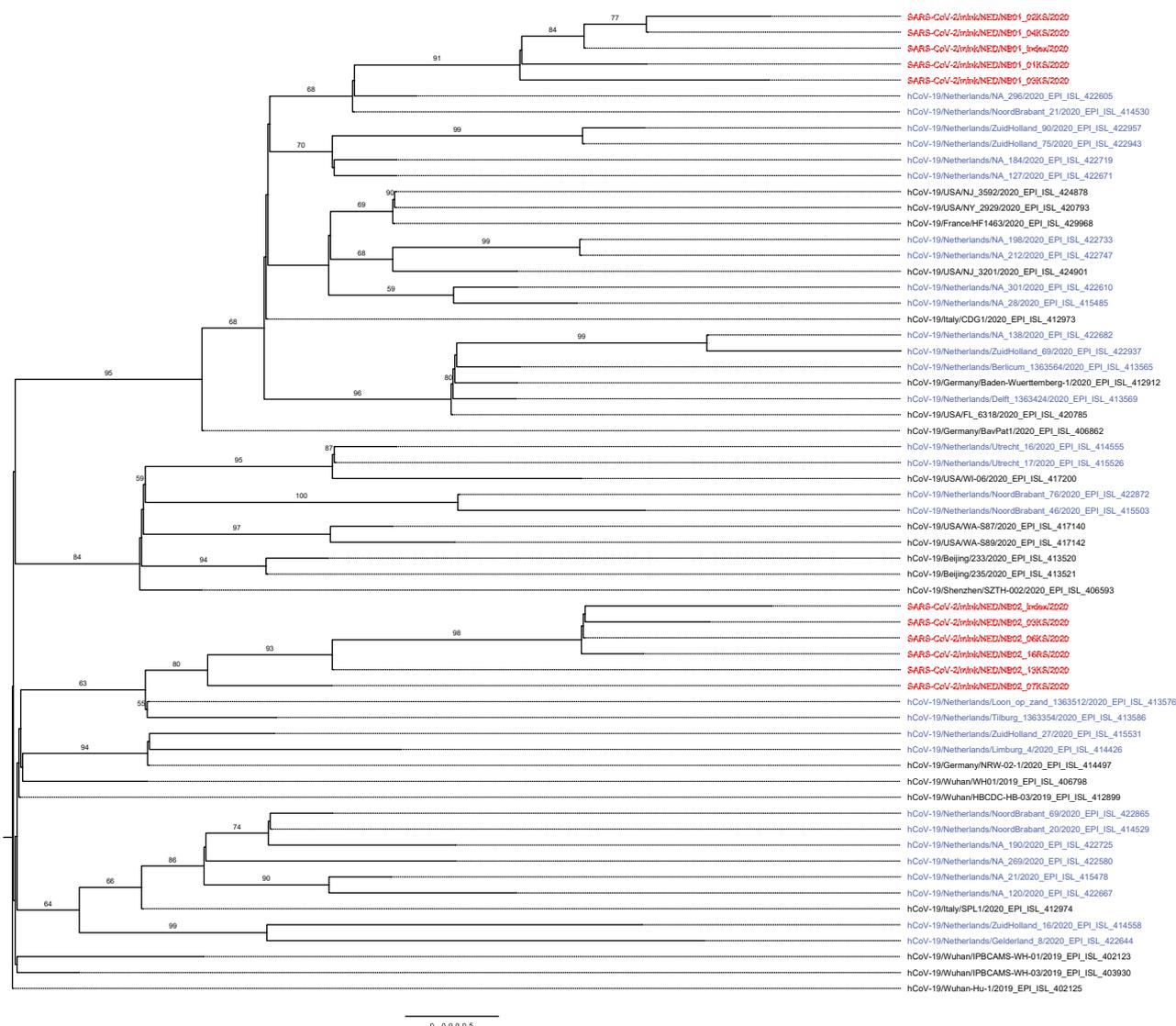
Here we present a report of infection of two mink farms with SARS-CoV-2. While this manuscript was being

prepared, similar SARS-CoV-2 outbreaks occurred on another nine farms in the Netherlands, eight in the province Noord Brabant and one in the province Limburg. On farms NB1 and NB2 described here, coronavirus disease (COVID-19)-like symptoms were present in people working on the farms before signs were seen in the minks, and SARS-CoV-2 infection was confirmed in one hospitalised person. The viral sequences obtained from the mink samples were closely related to sequences of human-derived isolates. The distance between the two sequence clusters originating from the two farms suggests separate introductions, arguing against an epidemiological connection between the two farms. Whether the outbreaks on the rest of the farms were connected to the first two cases and between each other is being investigated. The most likely explanation for the widespread infection on the mink farms is introduction of the virus by humans and subsequent transmission among the minks. Ferrets, which are closely related to minks, were also able to transmit the virus to other ferrets under experimental conditions; transmission was observed under both direct and indirect contact (animals were housed in cages with a permeable partition separating infected from uninfected animals) [5]. Minks can be housed in cages with permeable separation between them, which could have explained animal-to-animal transmission. On the mink farms in question however, animals are caged separately with non-permeable partition between cages, precluding direct contact as a mode of transmission. Indirect transmission between minks could either be through fomites (e.g. by feed or bedding material provided by humans), by infectious droplets generated by the infected animals, or by (faecally) contaminated dust from the bedding.

Detection of viral RNA in the airborne inhalable dust on the mink farms clearly suggests dust and/or droplets as means of transmission between the minks and occupational risk of exposure for the workers on the farms. While the exact occupational hazard for humans is currently being determined, to anticipate the exposure risk for personnel working on the mink farms with confirmed

**FIGURE 3**

Maximum likelihood phylogenetic tree of SARS-CoV-2 sequences from minks and selected full-length sequences from the GISAID EpiCoV database



GISAID: Global Initiative on Sharing All Influenza Data; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2.

Red: sequences from minks described in this report; blue: Dutch sequences from GISAID; black: international sequences from GISAID.

Details on the sequences from GISAID (<https://www.gisaid.org/>) used for this analysis, based on proposed lineages [14], are listed and acknowledged in Supplementary Table 1). The collected sequences were aligned using MAFFT v7.427 [15] and the evolutionary history was inferred by RAxML version 8.2.12 [16] using the maximum likelihood method based on the general time reversible model with a gamma-distributed variation of rates and 1,000 bootstrap replicates. The tree is rooted at Wuhan-Hu-1. Bootstrap support values above 50 are indicated at the corresponding branch.

SARS-CoV-2 infections, the public health authorities in the Netherlands have issued an advice for all workers on infected mink farms to wear personal protective equipment including face masks, goggles, gloves and overalls, while fulfilling their work duties [17]. Visitors are prohibited to enter those farms. Mink farm workers who have COVID-19 symptoms are advised to stay at home. Mandatory screening of all Dutch mink farms was started on 28 May and is aimed to be completed by 15 June. On 3 June, the Dutch Ministry of Agriculture

decided to cull all minks of SARS-CoV2 infected farms, starting on 5 June [18].

Mink farms are present in other countries in Europe, China and the US but so far, SARS-CoV-2 infections in these animals have been reported only in the Netherlands. The purpose of the current report is to raise awareness in the scientific community and in the mink industry that minks are susceptible for SARS-CoV-2. Infected animals developed respiratory disease

with typical pathological findings of viral pneumonia and were able to transmit the virus among each other. While this manuscript was in preparation, also serological surveillance was performed on the farms NB1 and NB2. Sixty random serum samples were collected from the minks of each farm and were all found positive for SARS-CoV-2 neutralising antibodies, except one sample from NB1. These findings coincided with the disappearance of symptoms and mortality on the farms and were followed by inability to detect viral RNA in inhalable dust, suggesting that the SARS-CoV-2 outbreaks were widely spread within the farms and resolved on their own when the majority of animals had seroconverted. There are still a lot of questions to address, especially regarding possible transmission from mink to human and exposure risks for the public outside the farms. In this report, we showed that humans can become a source of infection for minks, which results in a disease outbreak. Human infections acquired from mink are also suspected and data on exposure risk for humans as well as samples of potentially Covid-19-infected people on the farms are being collected and analysed; forthcoming results will be published in the future.

### Acknowledgements

We acknowledge the authors, originating and submitting laboratories of the sequences from GISAID's EpiCov Database on which the phylogenetic analysis was based (see Supplement). All submitters of data may be contacted directly via the GISAID website [www.gisaid.org](http://www.gisaid.org)

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### Conflict of interest

None declared.

### Authors' contributions

Nadia Oreshkova - combination of the data and writing of the manuscript. Robert Jan Molenaar, Sandra Vreman, Ruth Bouwstra - field work, obtaining of mink material and pathological work. Frank Harders, Bas B Oude Munnink, Reina S Sikkema, Marc Engelsma - sequencing and sequence analysis. Renate Hakze, Nora Gerhards, Mirriam Tacken, Eefke Weesendorp - sample preparations and PCR analysis. Paulien Tolsma - interviewing of the farm workers and providing the human-related data. Myrna MT de Rooij, Lidwien AM Smit - environmental sampling and analysis. Christianne Bruscke - commissioner advice. Marion Koopmans, Wim HM van der Poel, J Arjan Stegeman - coordination between the different institutions, supervision and advice.

All authors contributed to the writing by providing information about their work and by reviewing the manuscript.

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# **Exhibit BB**

# 1 **Jumping back and forth: anthroozoonotic and zoonotic** 2 **transmission of SARS-CoV-2 on mink farms**

3

4 Bas B. Oude Munnink<sup>1</sup>, Reina S. Sikkema<sup>1</sup>, David F. Nieuwenhuijse<sup>1</sup>, Robert Jan Molenaar<sup>2</sup>,  
5 Emmanuelle Munger<sup>1</sup>, Richard Molenkamp<sup>1</sup>, Arco van der Spek<sup>3</sup>, Paulin Tolsma<sup>4</sup>, Ariene  
6 Rietveld<sup>5</sup>, Miranda Brouwer<sup>5</sup>, Noortje Bouwmeester-Vincken<sup>6</sup>, Frank Harders<sup>7</sup>, Renate Hakze-  
7 van der Honing<sup>7</sup>, Marjolein C.A. Wegdam-Blans<sup>8</sup>, Ruth J. Bouwstra<sup>2</sup>, Corine GeurtsvanKessel<sup>1</sup>,  
8 Annemiek A. van der Eijk<sup>1</sup>, Francisca C. Velkers<sup>9</sup>, Lidwien A.M. Smit<sup>10</sup>, Arjan Stegeman<sup>9</sup>, Wim  
9 H.M. van der Poel<sup>7</sup>, Marion P.G. Koopmans<sup>1</sup>

10

## 11 **Affiliations**

12 <sup>1</sup> ErasmusMC, Department of Viroscience, WHO collaborating centre for arbovirus and viral  
13 hemorrhagic fever Reference and Research, Rotterdam, the Netherlands

14 <sup>2</sup> Royal GD, Deventer, the Netherlands

15 <sup>3</sup> Netherlands Food and Consumer Product Safety Authority (NVWA), Utrecht, the Netherlands

16 <sup>4</sup> Municipal health Services GGD Brabant-Zuidoost, Eindhoven, the Netherlands

17 <sup>5</sup> Municipal health Services GGD Hart voor Brabant, 's-Hertogenbosch, the Netherlands

18 <sup>6</sup> Municipal health Services GGD Limburg-Noord, Venlo, the Netherlands

19 <sup>7</sup> Wageningen Bioveterinary Research, Lelystad, the Netherlands

20 <sup>8</sup> Stichting PAMM, Veldhoven, the Netherlands

21 <sup>9</sup> Farm Animal Health, Utrecht University, Utrecht, the Netherlands

22 <sup>10</sup> Institute for Risk Assessment Sciences (IRAS), Utrecht University, Utrecht, the Netherlands

23

24 **One sentence summary**

25 SARS-CoV-2 transmission on mink farms.

26

27 **Abstract**

28 The zoonotic origin of the SARS-CoV-2 pandemic is still unknown. Animal experiments have  
29 shown that non-human primates, cats, ferrets, hamsters, rabbits and bats can be infected by  
30 SARS-CoV-2. In addition, SARS-CoV-2 RNA has been detected in felids, mink and dogs in the  
31 field. Here, we describe an in-depth investigation of outbreaks on 16 mink farms and humans  
32 living or working on these farms, using whole genome sequencing. We conclude that the virus  
33 was initially introduced from humans and has evolved, most likely reflecting widespread  
34 circulation among mink in the beginning of the infection period several weeks prior to  
35 detection. At the moment, despite enhanced biosecurity, early warning surveillance and  
36 immediate culling of infected farms, there is ongoing transmission between mink farms with  
37 three big transmission clusters with unknown modes of transmission. We also describe the  
38 first animal to human transmissions of SARS-CoV-2 in mink farms.

39

## 40 **Main text**

41 Late December 2019, SARS-CoV-2 was identified as the causative agent in a viral pneumonia  
42 outbreak, possibly related to a seafood and a live animal market in Wuhan, China (1). Since  
43 then, SARS-CoV-2 spread across the world and by August 31<sup>st</sup>, over 25,200,000 people had  
44 been infected with SARS-CoV-2 resulting in over 840,000 deaths (2). In the Netherlands, over  
45 72,000 infections have been confirmed, over 6,200 SARS-CoV-2 related deaths have been  
46 reported, and drastic measures have been put into place to prevent further spread of SARS-  
47 CoV-2 (3).

48 In view of the similarities with SARS-CoV-1, a zoonotic origin of the outbreak was  
49 suspected by the possible link with the Wuhan market where various animals were sold  
50 including fish, shellfish, poultry, wild birds and exotic animals. The finding of cases with onset  
51 of illness well before the period observed in the cluster, however, suggests the possibility of  
52 other sources (4). Although closely related coronaviruses in bats (5, 6) and pangolins (7, 8)  
53 have most sequence identity to SARS-CoV-2, the most likely diversion date of SARS-CoV-2  
54 from the most closely related bat sequence is estimated to date back to somewhere between  
55 1948-1982 (9). Therefore, the animal reservoir(s) of SARS-CoV-2 is (are) yet to be identified.

56 Experimental infections in dogs (10), cats (10, 11), ferrets (10, 12), hamsters (13, 14),  
57 rhesus macaques (15), tree shrew (16), cynomolgus macaques (17), grivets (18), common  
58 marmosets (19), rabbits (20), and fruit bats (21) have shown that these species are susceptible  
59 to SARS-CoV-2, and experimentally infected cats, tree shrews, hamsters and ferrets could  
60 transmit the virus. In contrast, experimental infection of pigs and several poultry species with  
61 SARS-CoV-2 proved to be unsuccessful (10, 21, 22). SARS-CoV-2 has also sporadically been  
62 identified in naturally infected animals. In the USA and in Hong Kong, SARS-CoV-2 RNA has  
63 been detected in dogs (23). In the Netherlands, France, Hong Kong, Belgium and the USA, cats

64 have tested positive by RT-PCR for SARS-CoV-2 (24–27). Furthermore, SARS-CoV-2 has been  
65 detected in four tigers and three lions in a zoo in New York (28). In Italy, the Netherlands and  
66 in Wuhan, antibodies to SARS-CoV-2 have been detected in cats (29–31). Recently, detected  
67 SARS-CoV-2 was detected in farmed mink (*Neovison vison*) that showed signs of respiratory  
68 disease and increased mortality (29, 32).

69         Thereafter, the Dutch national response system for zoonotic diseases was activated,  
70 and it was concluded that the public health risk of animal infection with SARS-CoV-2 was low,  
71 but that there was a need for increased awareness of possible involvement of animals in the  
72 COVID-19 epidemic. Therefore, from May 20<sup>th</sup> 2020 onwards, mink farmers, veterinarians and  
73 laboratories were obliged to report symptoms in mink (family *Mustelidae*) to the Netherlands  
74 Food and Consumer Product Safety Authority (NFCPSA) and an extensive surveillance system  
75 was set up (33).

76         Whole genome sequencing (WGS) can be used to monitor the emergence and spread  
77 of pathogens (34–37). As part of the surveillance effort in the Netherlands over 1,750 SARS-  
78 CoV-2 viruses have been sequenced to date from patients from different parts of the  
79 Netherlands (38). Here, we describe an in-depth investigation into the SARS-CoV-2 outbreak  
80 in mink farms and mink farm employees in the Netherlands, combining epidemiological  
81 information, surveillance data and WGS on the human-animal interface.

82

## 83 **Methods**

### 84 **Outbreak investigation**

85 Following initial detection of SARS-CoV-2 in mink on two farms on April 23<sup>rd</sup> and April 25<sup>th</sup>,  
86 respectively, as part of routine health monitoring done by the Royal GD Animal Health service  
87 and subsequent investigation by Wageningen Bioveterinary Research (WBVR), the national  
88 reference laboratory for notifiable animal diseases, a One Health outbreak investigation team  
89 was convened (39, 40). Subsequently, respiratory signs and increased mortality in mink was  
90 made notifiable by the Dutch Ministry of Agriculture, Nature and Food Quality and the farms  
91 were quarantined (no movements of animals and manure and visitor restrictions). On May 7<sup>th</sup>  
92 two other mink farms in the same region were confirmed to be infected. By the end of May  
93 the Dutch minister of Agriculture decided that all mink on SARS-CoV-2 infected farms had to  
94 be culled. Moreover, as the clinical manifestation of the infection was highly variable within  
95 and between farms, including asymptomatic infections, weekly testing of dead animals for  
96 SARS-CoV-2 infections became compulsory for all mink farms in the Netherlands. Moreover,  
97 a nation-wide transport ban of mink and mink manure, and a strict hygiene and visitor  
98 protocol was implemented. The first infected mink farms were culled from June 6<sup>th</sup> onwards.  
99 From the 10<sup>th</sup> infected farm (NB10) onwards, culling took place within 1-3 days after diagnosis.  
100 In this manuscript, the data up to June 26<sup>th</sup>, when a total of 16 mink farms in the Netherlands  
101 were found positive for SARS-CoV-2 infections, is presented.

102

### 103 **Veterinary and human contact tracing**

104 The Netherlands Food and Consumer Product Safety Authority (NVWA) traced animal related  
105 contacts with other mink farms. Backward and forward tracing of possible high-risk contacts  
106 was done in the framework of the standard epidemiological investigation by the NVWA (i.e.

107 focused on movement of vehicles, visitors such as veterinary practitioners, (temporary  
108 workers, sharing of equipment between farms and transport and delivery of materials, such  
109 as feed, pelts, carcasses and manure). Persons with possible exposure from this investigation,  
110 as well as farm owners and resident farm workers were asked to report health complaints to  
111 the municipal health service for testing and – in the case of confirmed infections – for health  
112 advice and further contact tracing. Farm owners and workers on infected mink farms were  
113 informed of potential risks and were given advice on the importance and use of personal  
114 protective equipment and hygiene when handling animals (41). The contact structure on the  
115 farms was assessed through in-depth interviews, to identify additional persons with possible  
116 exposure to mink. In order to provide an enhanced set of reference genome sequences,  
117 anonymized samples from patients that had been diagnosed with COVID-19 in the area of the  
118 same four-digits postal codes as farms NB1-NB4 in March and April 2020 were retrieved from  
119 clinical laboratories in the region.

120

### 121 **SARS-CoV-2 diagnostics and sequencing**

122 The presence of viral RNA in mink samples was determined using a RT-PCR targeting the E  
123 gene as previously described (42). For the human samples, diagnostic RT-PCR was performed  
124 for the E and the RdRp gene (42). In addition, serology was performed, using the Wantai Ig  
125 total and IgM ELISA, following the manufacturer's instructions(43). For all samples with a Ct  
126 value <32, sequencing was performed using a SARS-CoV-2 specific multiplex PCR for Nanopore  
127 sequencing, as previously described (3). The libraries were generated using the native barcode  
128 kits from Nanopore (EXP-NBD104 and EXP-NBD114 and SQK-LSK109) and sequenced on a R9.4  
129 flow cell multiplexing 24 samples per sequence run. Flow cells were washed and reused until  
130 less than 800 pores were active. The resulting raw sequence data was demultiplexed using

131 Porechop (<https://github.com/rrwick/Porechop>). Primers were trimmed after which a  
132 reference-based alignment was performed. The consensus genome was extracted and  
133 positions with a coverage <30 were replaced with an “N” as described previously (44).  
134 Mutations in the genome compared to the GISAID sequence EPI\_ISL\_412973 were confirmed  
135 by manually checking the mapped reads and homopolymeric regions were manually checked  
136 and resolved by consulting reference genomes. The average SNP difference was determined  
137 using snp-dists (<https://github.com/tseemann/snp-dists>). All sequences generated in this  
138 study are available on GISAID.

139

#### 140 **Phylogenetic analysis**

141 All available near full-length Dutch SARS-CoV-2 genomes available on 1<sup>st</sup> of July were selected  
142 (n=1,775) and aligned with the sequences from this study using MUSCLE (45). Sequences with  
143 >10% “Ns” were excluded. The alignment was manually checked for discrepancies after which  
144 IQ-TREE (46) was used to perform a maximum likelihood phylogenetic analysis under the  
145 GTR+F+I +G4 model as best predicted model using the ultrafast bootstrap option with 1,000  
146 replicates. The phylogenetic trees were visualized in Figtree  
147 (<http://tree.bio.ed.ac.uk/software/figtree/>). For clarity reasons all bootstrap values below 80  
148 were removed. To look at potential relationships with migrant workers, also all Polish  
149 sequences from GISAID (47) were included in the alignment (**Supplementary table 1**).

150

#### 151 **Mapping specific mutation patterns on mink farms and in mink farm employees**

152 Amino acid coordinates are described in relation to the Genbank NC\_045512.2 reference  
153 genome. Open reading frames were extracted from the genome alignment using the genome  
154 annotation as supplied with the reference genome. A custom R script was used to distinguish

155 synonymous from non-synonymous mutations and non-synonymous mutations were  
156 visualized using a tile map from the ggplot2 package (48).

157

### 158 **Geographical overview of mink farms in the Netherlands and SARS-CoV-2 positive farms**

159 To protect confidentiality, SARS-CoV-2 positive mink farms were aggregated at municipality  
160 level. The datasets "*Landbouw; gewassen, dieren en grondgebruik naar gemeente*" and "*Wijk-  
161 en Buurtkaart 2019*" from Statistics Netherlands (CBS) were used (49). Maps were created  
162 using R packages sp (50), raster (51) and rgdal (52) and ArcGIS 10.6 software by ESRI.

163

## 164 Results

165 SARS-CoV-2 was first diagnosed on two mink farms in the Netherlands on April 23<sup>rd</sup> (NB1) and  
166 April 25<sup>th</sup> (NB2), respectively. After the initial detection of SARS-CoV-2 on these farms an in-  
167 depth investigation was started to look for potential transmission routes and to perform an  
168 environmental and occupational risk assessment. Here, we describe the results of the  
169 outbreak investigation of the first 16 SARS-CoV-2 infected mink farms by combining SARS-CoV-  
170 2 diagnostics, WGS and in-depth interviews.

171

### 172 Screening of farm workers and contacts

173 Farm owners of the 16 SARS-CoV-2 positive mink farms were contacted by the municipal  
174 health services to conduct contact investigation and samples were taken for RT-PCR-based  
175 and serological SARS-CoV-2 diagnostics. In total, 97 individuals were tested by either  
176 serological assays and/or RT-PCR. In total, 43 out of 88 (49%) upper-respiratory tract samples  
177 tested positive by RT-PCR while 38 out of 75 (51%) serum samples tested positive for SARS-  
178 CoV-2 specific antibodies. In total, 66 of 97 (67%) of the persons tested had evidence for SARS-  
179 CoV-2 infection (**table 1**).

180

181 **Table 1.** Overview of human sampling on SARS-CoV-2 positive mink farms.

Farm:	First diagnosis in animals:	Date(s) of sampling employees and family members:	PCR positive (%)	Serology positive (%)	Employees and family members tested positive (PCR and/or serology)
NB1	24-04-2020	28-04-2020 – 11-05-2020	5/6 (83%)	5/5 (100%)	6/6 (100%)
NB2	25-04-2020	31-03-2020 – 30-04-2020	1/2 (50%)	8/8 (100%)	8/8 (100%)
NB3	07-05-2020	11-05-2020 – 26-05-2020	5/7 (71%)	0/6 (0%)*	5/7 (71%)
NB4	07-05-2020	08-05-2020	1/3 (33%)	2/2 (100%)	2/3 (66%)
NB5	31-05-2020	01-06-2020	2/7 (29%)	3/6 (50%)	3/7 (43%)
NB6	31-05-2020	01-06-2020	1/6 (17%)	4/6 (66%)	4/6 (66%)

<b>NB7</b>	31-05-2020	10-06-2020 – 01-07-2020	8/10 (80%)	NA**	8/10 (80%)
<b>NB8</b>	02-06-2020	03-06-2020	5/10 (50%)	5/9 (56%)	8/10 (80%)
<b>NB9</b>	04-06-2020	07-06-2020	1/7 (14%)	1/7 (14%)	2/7 (29%)
<b>NB10</b>	08-06-2020	11-06-2020	1/8 (13%)	3/8 (38%)	4/8 (50%)
<b>NB11</b>	08-06-2020	11-06-2020	1/3 (33%)	0/2 (0%)	1/3 (33%)
<b>NB12</b>	09-06-2020	11-06-2020	6/9 (66%)	2/8 (25%)	7/9 (78%)
<b>NB13</b>	14-06-2020	11-06-2020 – 18-06-2020	3/3 (33%)	0/2 (0%)	3/3 (33%)
<b>NB14</b>	14-06-2020	14-06-2020	1/3 (100%)	5/6 (83%)	5/6 (83%)
<b>NB15</b>	21-06-2020	10-06-2020 – 30-06-2020	2/2 (100%)	NA**	2/2 (100%)
<b>NB16</b>	21-06-2020	23-06-2020	0/2 (0%)	NA**	0/2 (0%)
<b>Total:</b>			<b>43/88 (49%)</b>	<b>38/75 (51%)</b>	<b>66/97 (68%)</b>

182 \* Serology was done approximately one week before the positive PCR test.

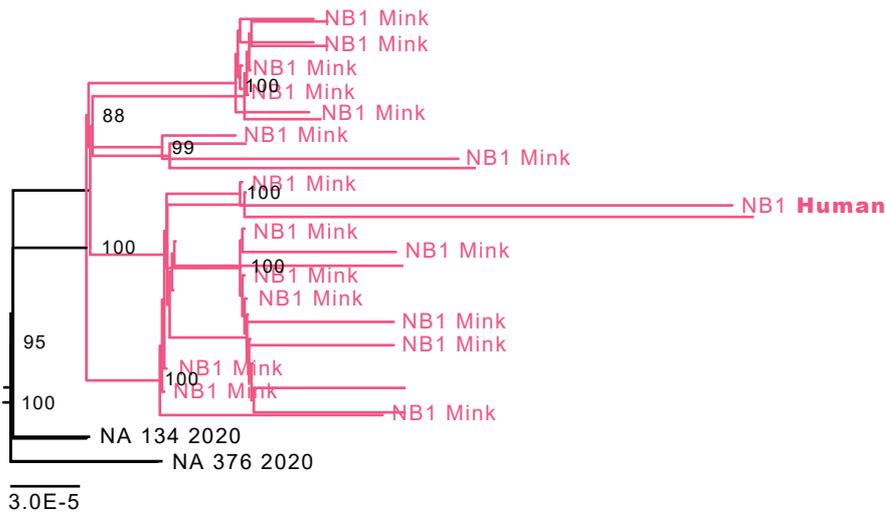
183 \*\* No serology was performed

184

### 185 **Anthropozoonotic transmission of SARS-CoV-2**

186 During the interview on April 28<sup>th</sup>, four out of five employees from NB1 reported that they  
 187 had experienced respiratory symptoms before the outbreak was detected in minks, but none  
 188 of them had been tested for SARS-CoV-2. The first day of symptoms of people working on NB1  
 189 ranged from April 1<sup>st</sup> to May 9<sup>th</sup>. For 16 of the mink, sampled on April 28<sup>th</sup>, and one farm  
 190 employee, sampled on May 4<sup>th</sup>, a WGS was obtained (hCov-  
 191 19/Netherlands/NoordBrabant\_177/2020). The human sequence clusters within the mink  
 192 sequences although it had 7 nucleotides difference with the closest mink sequence (**Figure 1**  
 193 and cluster A in **figures 2 and 3**). On farm NB2, SARS-CoV-2 was diagnosed on April 25<sup>th</sup>.  
 194 Retrospective analysis showed that one employee from NB2 had been hospitalized with SARS-  
 195 CoV-2 on March 31<sup>st</sup>. All samples from the 8 employees taken on April 30<sup>th</sup> were negative by  
 196 RT-PCR but tested positive for SARS-CoV-2 antibodies. The virus sequence obtained from  
 197 animals was distinct from that of farm NB1, indicating a separate introduction (**Figure 2 and**  
 198 **3**, cluster B).

199



200

201

**Figure 1: Zoom of the phylogenetic analysis of NB1.** A maximum likelihood analysis was performed

202

using all available SARS-CoV-2 Dutch sequences. Sequences from mink on NB1 are depicted in red and

203

from the employee on NB1 in blue. The two sequences in black at the root of the cluster are the closest

204

matching human genome sequences from the national SARS-CoV-2 sequence database. Scale bar

205

represents units of substitutions per site.

206

207

### **Zoonotic transmission of SARS-CoV-2**

208

On mink farm NB3 SARS-CoV-2 infection was diagnosed on May 7<sup>th</sup>. Initially all seven

209

employees tested negative for SARS-CoV-2, but when retested between May 19<sup>th</sup> and May

210

26<sup>th</sup> after developing COVID-19 related symptoms, 5 out of 7 individuals working or living on

211

the farm tested positive for SARS-CoV-2 RNA. WGS were obtained from these five individuals

212

and the clustering of these sequences with the sequences derived from mink from NB3,

213

together with initial negative test result and the start of the symptoms, indicate that the

214

employees were infected with SARS-CoV-2 after the mink on the farm got infected. Also, an

215

additional infection was observed based on contact-tracing: a close contact of one of the

216

employees – who did not visit the farm – got infected with the SARS-CoV-2 strain found on

217 NB3. Animal and human sequences from farm NB3 were related to those from farm NB1, but  
218 were both part of cluster A.

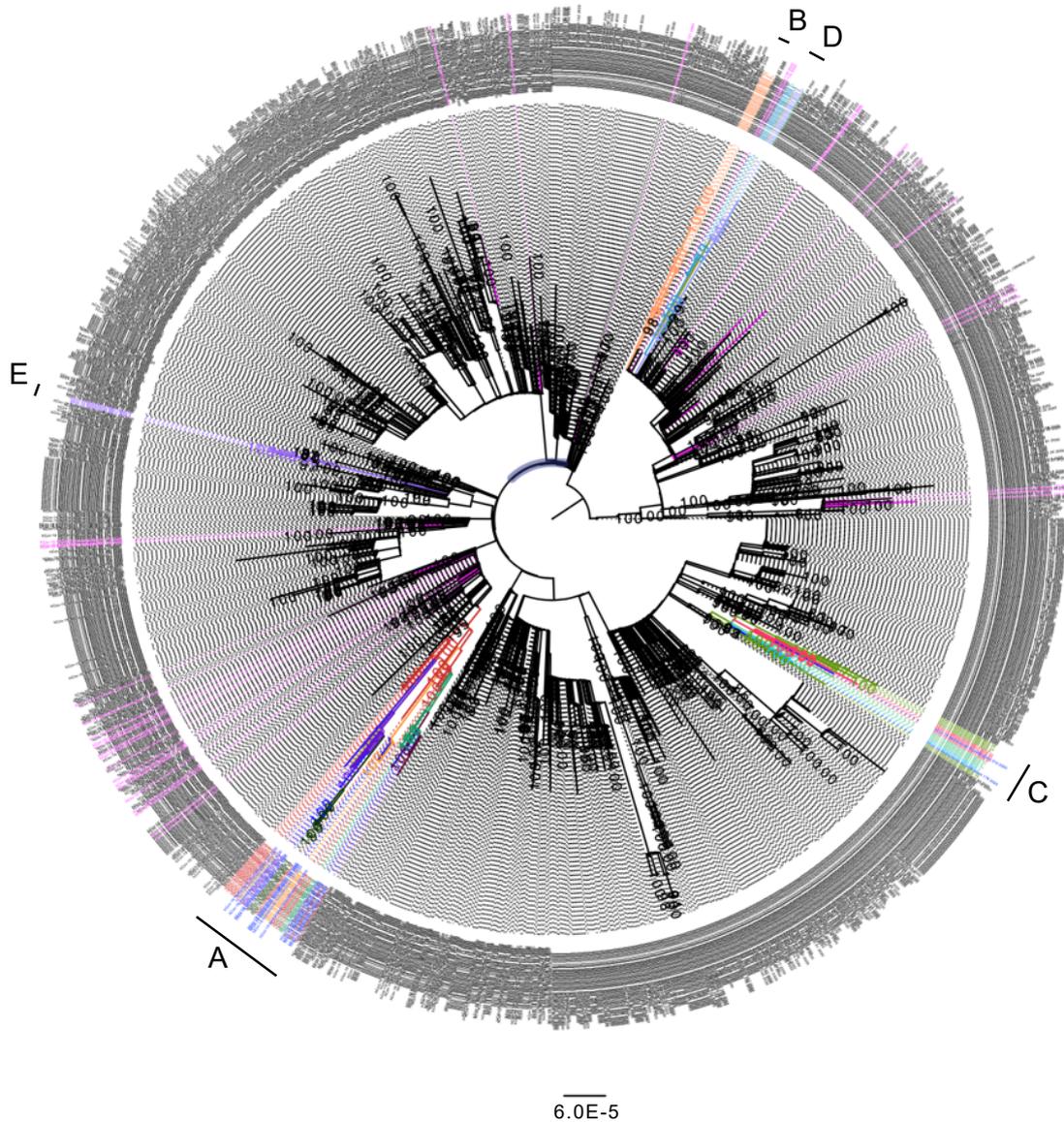
219 Similarly, on mink farm NB7 zoonotic transmission from mink to human most likely  
220 occurred. On this farm, SARS-CoV-2 infection in mink was diagnosed on May 31<sup>st</sup> and  
221 employees initially tested negative for SARS-CoV-2 but started to develop symptoms at a later  
222 stage. Samples were taken between June 10<sup>th</sup> and July 1<sup>st</sup> from 10 employees of which 8 tested  
223 positive for SARS-CoV-2 RNA. From 2 samples WGS could be generated from the employees  
224 which clustered together with the sequences from the animals from this farm.

225

#### 226 **Comparison with national reference database and enhanced regional sampling**

227 The sequences generated from mink farms and from mink farm employees were compared  
228 with the national database consisting of around 1,775 WGS. In addition, to discriminate  
229 between locally acquired infections and mink farm related SARS-CoV-2 infection, and to  
230 determine the potential risk for people living close to mink farms, WGS was also performed  
231 on 34 SARS-CoV-2 positive samples from individuals who live in the same four-digit postal  
232 code area compared to the first four mink farms. These local sequences reflected the general  
233 diversity seen in the Netherlands and were not related to the clusters of mink sequences  
234 found on the mink farms, thereby also giving no indication of spill-over to people living in close  
235 proximity to mink farms (sequences shown in magenta, **Figure 2**). The sequences from the  
236 mink farm investigation were also compared to sequences from Poland (n=65), since many of  
237 the mink farm workers were seasonal migrants from Poland, but these were not related.

238



239

240 **Figure 2: Maximum likelihood analysis of all SARS-CoV-2 Dutch sequences.** The sequences derived

241 from minks from different farms are indicated with different colors, human sequences related to the

242 mink farms in blue and samples from similar 4-digit postal code are indicated in magenta. Scale bar

243 represents units of substitutions per site.

244

245 **Mink farm related sequence clusters**

246 Phylogenetic analysis of the mink SARS-CoV-2 genomes showed that mink sequences of 16

247 farms grouped into 5 different clusters (**Figure 2 and 3**). Viruses from farms NB1, NB3, NB4,

248 NB8, NB12, NB13 and NB16 belonged to cluster A, sequences from NB2 were a separate  
 249 cluster (B), those from farms NB6, NB7, NB9 and NB14 grouped together in cluster C, NB5,  
 250 NB8, NB10 and NB15 grouped to cluster D, and NB11 had sequences designated as cluster E.  
 251 On farm NB8, SARS-CoV-2 viruses could be found from both cluster A and cluster D. A detailed  
 252 inventory of possible common characteristics, like farm owner, shared personnel, feed  
 253 supplier and veterinary service provider, was made. In some cases, a link was observed with  
 254 the same owners of several farms, for instance for cluster A for NB1 and NB4, and for NB8 and  
 255 NB12. Although NB7, NB11 and NB15 were also linked to the same owner, viruses from these  
 256 farms belonged to cluster C, D and E respectively. No common factor could be identified for  
 257 most farms and clustering could also not be explained by geographic distances as multiple  
 258 clusters were detected in different farms located close to each other (**Table 2 and figure 4**).

259

260 **Table 2.** Overview of the clusters detected on the different farms.

Farm:	Date of diagnosis:	Sequence cluster:	Same owner:	Feed supplier:	Vet**:	Number of sequences (human):	Sequence diversity (average):	Mink population size:	Detection***:
NB1	24-04-20	A	NB1, NB4	1	I	17 (1)	0-9 (3.9)	75,711	Notification
NB2	25-04-20	B		1	II	8	0-8 (3.6)	50,473	Notification
NB3	07-05-20	A		2	III	5 (5)	0-2 (0.6)	12,400	Notification
NB4	07-05-20	A	NB1, NB4	1	I	1	NA	67,945	Contact tracing NB1
NB5	31-05-20	D		1	IV	1	NA	38,936	EWS-Ser+PM-1st
NB6	31-05-20	C		3	V	9	0-12 (6.8)	54,515	EWS-Ser+PM-1st
NB7	31-05-20	C	NB7, NB11, NB15	3	II	6 (2)	0-4 (1.4)	79,355	EWS-PM-1st
NB8	02-06-20	A/D	NB8, NB12*	3	V	6 (5)	0-6 (2.6)	39,144	EWS-Ser+PM-1st
NB9	04-06-20	C		2	V	2 (1)	0-3 (1.5)	32,557	EWS-Ser+PM-2nd
NB10	08-06-20	D		3	II	4	0-3 (1.1)	26,824	EWS-Ser+PM-2nd

<b>NB11</b>	08-06-20	E	NB7, NB11, NB15	3	II	4	0-4 (2.2)	38,745	EWS-PM-2nd
<b>NB12</b>	09-06-20	A	NB8, NB12*	3	II	5	0-3 (1.2)	55,352	Notification
<b>NB13</b>	14-06-20	A		3	V	5 (3)	0-5 (3.2)	20,366	EWS-PM-5th
<b>NB14</b>	14-06-20	C		3	II	5 (1)	0-7 (3.7)	28,375	EWS-PM-5th
<b>NB15</b>	21-06-20	D	NB7, NB11, NB15	3	II	5	0-2 (0.6)	35,928	EWS-PM-6th
<b>NB16</b>	21-06-20	A		3	II	5	0-4 (1.6)	66,920	EWS-PM-6th

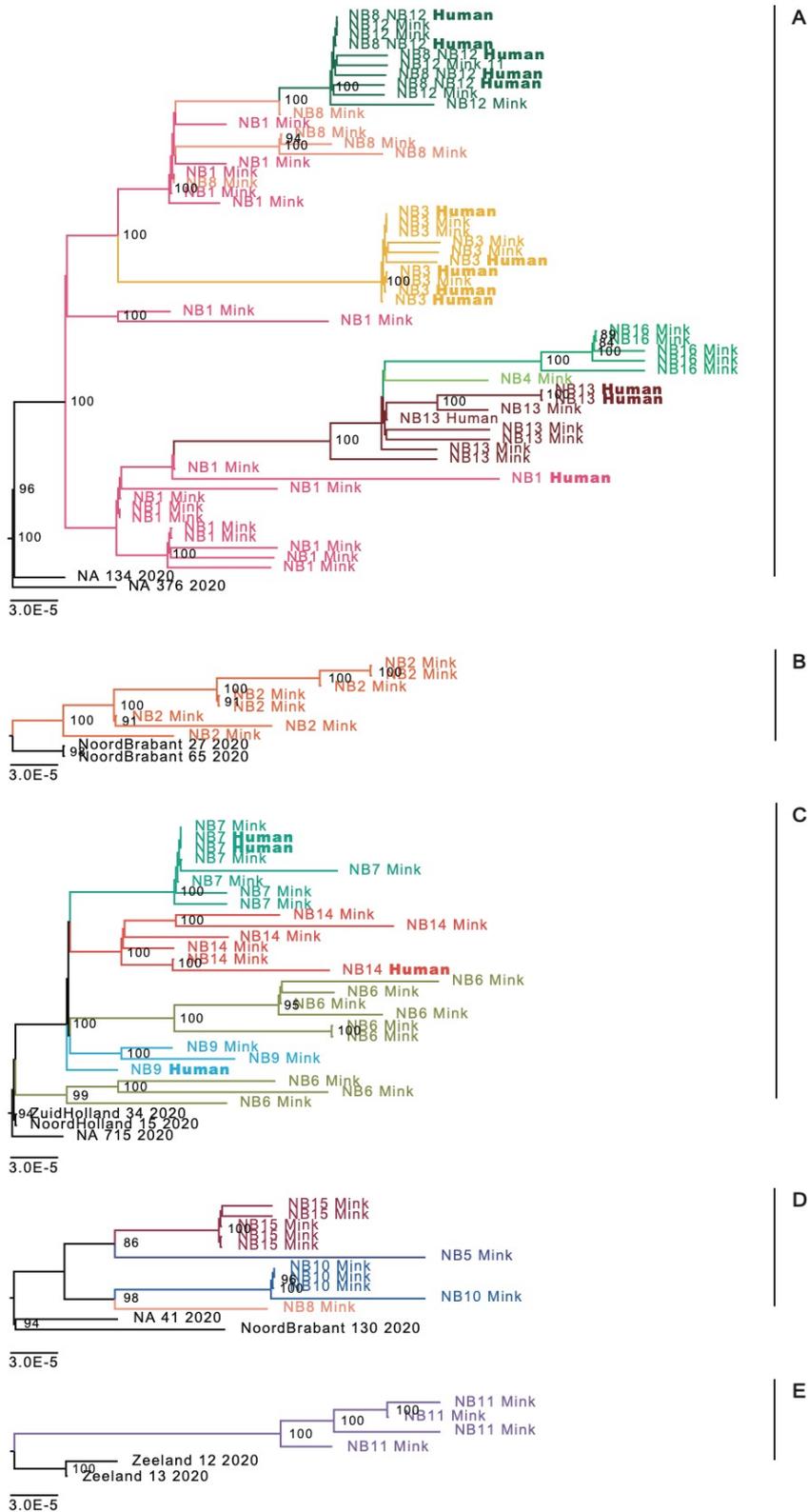
261 \* There was exchange of personnel in these two locations.

262 \*\* Veterinarian II and V were both from the same veterinary practice.

263 \*\*\* Notification: based on reporting of clinical signs which was obligated from 26 April onwards; EWS-Ser-  
 264 Detection based on a one-off nation-wide compulsory serological screening of all mink farms at the end of  
 265 May/early June by GD Animal Health; EWS-PM-Detection based on the early warning monitoring system  
 266 for which carcasses of animals that died of natural causes were submitted weekly for PCR testing by GD  
 267 Animal Health from the end of May onwards in a weekly cycle (EWS-PM 1<sup>st</sup> to 6<sup>th</sup> post mortem screening).

268

269 In total 18 sequences from mink farm employees or close contacts were generated from seven  
 270 different farms. In most cases, these human sequences were near-identical to the mink  
 271 sequences from the same farm. For NB1 the situation was different and the human sequence  
 272 clusters deeply within the sequences derived from mink (Figure 1), with 7 nucleotides  
 273 difference with the closest related mink sequence. This was also the case on farm NB14, with  
 274 4 nucleotides difference with the closest related mink sequence. Employees sampled at mink  
 275 farm NB8 clustered with animals from NB12 which can be explained by the exchange of  
 276 personnel between these two farms.



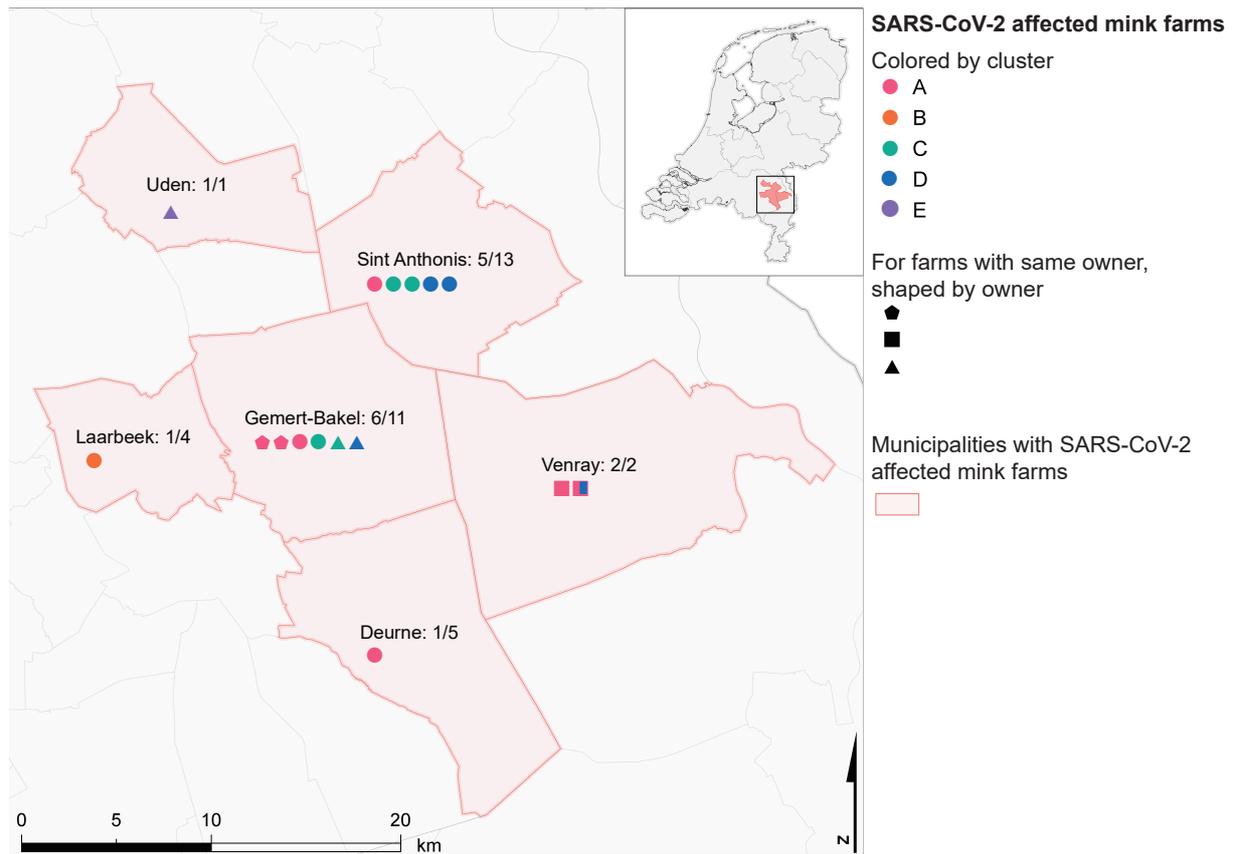
277

278

279

280

**Figure 3: Phylogenetic analysis of SARS-CoV-2 strains detected in the 5 mink farm clusters.** The sequences derived from different farms are depicted in different colors. Scale bar represents units of substitutions per site.



281

282 **Figure 4. Geographical overview of SARS-CoV-2 positive mink farms per municipality affected.** The

283 proportion of SARS-CoV-2 positive mink farms over the total number of mink farms (CBS, 2019) is

284 indicated. Symbols for positive farms are colored by cluster and shapes indicate farms with a same

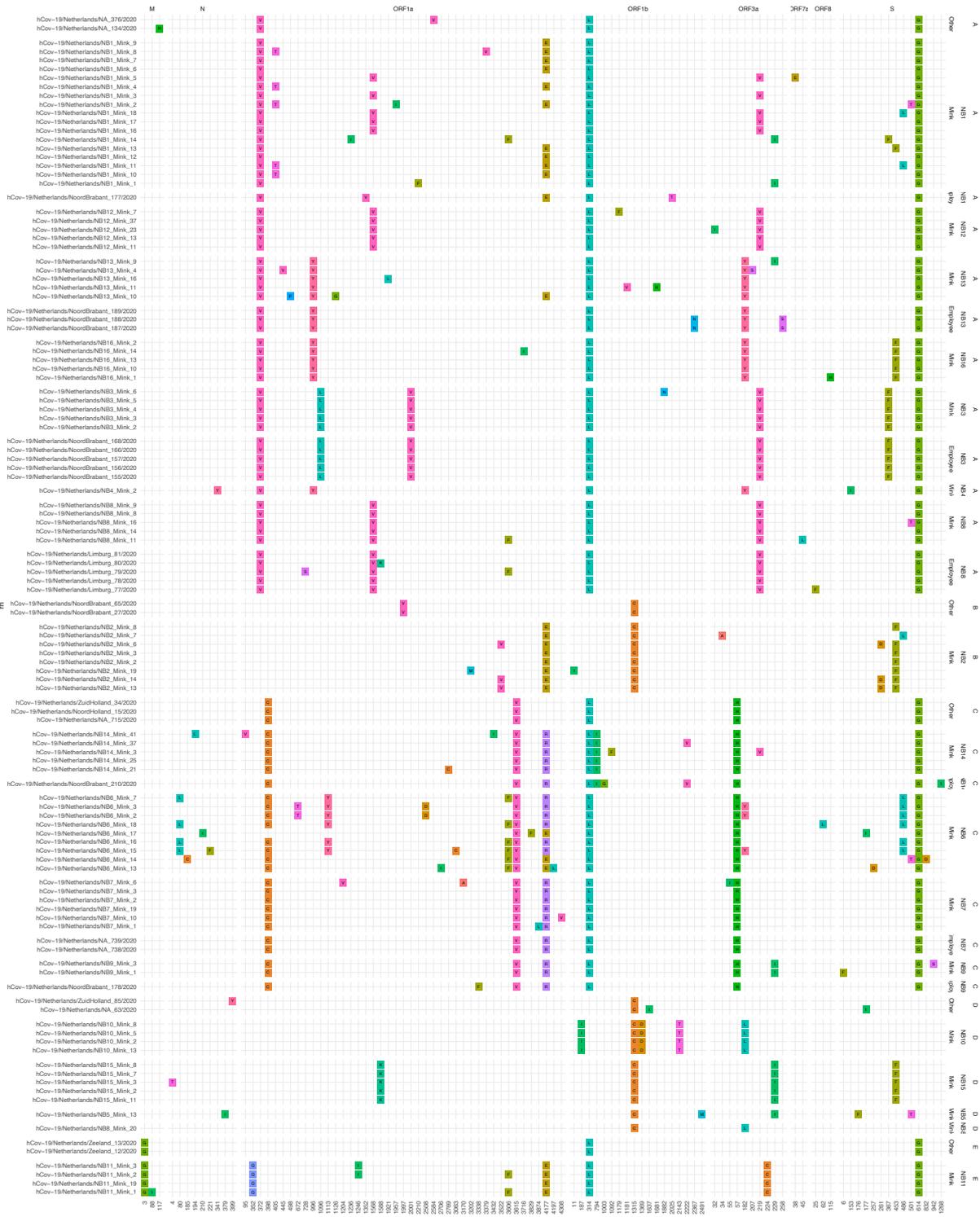
285 owner.

286

287 **Within farm diversity**

288 SARS-CoV-2 was detected on mink farm NB1-NB4 after reports of respiratory symptoms and  
289 increased mortality in mink. The sequences from farm NB1 had between 0 and 9 nucleotides  
290 differences (average 3.9 nucleotides) and from NB2 between 0 and 8 nucleotides differences  
291 (average of 3.6), which is much more than what has been observed in outbreaks in human  
292 settings. The sequences from NB3 had 0 to 2 nucleotides difference suggesting that the virus  
293 was recently introduced, in line with the observed disease in humans, which occurred in the  
294 weeks post diagnosis of the infection in mink. After the initial detection of SARS-CoV-2 on  
295 mink farms, farms were screened weekly. The first, second, fifth and sixth weekly screening  
296 yielded new positives. The sequences of mink at NB6 had between 0 and 12 nucleotides  
297 differences, whereas diversity was lower for the subsequent farm sequences (Table 2).

298 Several non-synonymous mutations were identified among the mink sequences  
299 compared to the Wuhan reference sequence NC\_045512.2. However, no particular amino  
300 acid substitutions were found in all mink samples (**Figure 5**). Of note, three of the clusters had  
301 the position 614G variant (clusters A, C and E), and 2 had the original variant. There were no  
302 obvious differences in the presentation of disease in animals or humans between clusters  
303 based on the data available at this stage, but further data collection and analysis, also for cases  
304 after NB16, are ongoing to investigate this further. The observed mutations can also be found  
305 in the general population and the same mutations also were found in human cases which were  
306 related to the mink farms.



307

308

309

310

**Figure 5. Overview of the specific amino acid mutations found in mink farms.** Above the x-axis the open reading frames (ORF) are indicated and on the x-axis the amino acid position within each ORF is indicated. On the y-axis the sequence names are indicated and on the right side of the

311 graph the cluster numbers and specific farm identifiers and the type of host are used to group  
312 the samples.

313

## 314 **Discussion**

315 Here we show ongoing SARS-CoV-2 transmission in mink farms and spill-over events to  
316 humans. To the best of our knowledge, these are the first animal to human SARS-CoV-2  
317 transmission events documented. More research in minks and other mustelid species, to  
318 demonstrate if these species can be a true reservoir of SARS-CoV-2 although from our  
319 observations we consider this likely. After the detection of SARS-CoV-2 on mink farms, 68% of  
320 the tested farm workers and/or relatives or contacts were shown to be infected with SARS-  
321 CoV-2, indicating that contact with SARS-CoV-2 infected mink is a risk factor for contracting  
322 COVID-19.

323         A high diversity in the sequences from some mink farms was observed which most  
324 likely can be explained by many generations of infected animals before an increase in  
325 mortality was observed. The current estimates are that the substitution rate of SARS-CoV-2 is  
326 around  $1.16 \times 10^{-3}$  substitutions/site/year (53), which corresponds to around one mutation  
327 per two weeks. This could mean that the virus was already circulating in mink farms for some  
328 time. However, there was also a relatively high sequence diversity observed in farms which  
329 still tested negative one week prior, hinting towards a faster evolution of the virus in the mink  
330 population. This can indicate that the virus might replicate more efficiently in mink or might  
331 have acquired mutations which makes the virus more virulent. However, no specific mutations  
332 were found in all mink samples, making increased virulence less likely. In addition, mink farms  
333 have large populations of animals which could lead to very efficient virus transmission.  
334 Generation intervals for SARS-CoV-2 in humans have been estimated to be around 4-5

335 days(54), but with high dose exposure in a high-density farm could potentially be shorter.  
336 Recently, a specific mutation in the spike protein (D614G) was shown to result in an increased  
337 virulence *in vitro* (55), while it was not associated an increased growth rate for cluster nor an  
338 increased mortality (56). This mutation was present in farm clusters A, C and E, but no obvious  
339 differences in clinical presentation, disease severity, or rate of transmission to humans was  
340 observed.

341         While we found sequences matching with the animal sequences on several farms, not  
342 all of these can be considered direct zoonotic transmissions. For instance, the two employees  
343 from mink farm NB3 were most likely infected while working at the mink farm given the  
344 specific clustering in the phylogenetic tree and the timing of infection. Subsequent human  
345 infections may have originated from additional zoonotic infections, or from human to human  
346 transmission within their household. Further proof that animals were the most likely source  
347 of infection was provided by the clear phylogenetic separation between farm related human  
348 cases and animal cases, from sequences from cases within the same 4-digit postal code area.  
349 Spill-back into the community living in the same 4-digit postal code area was not observed  
350 using sequence data, but cannot be entirely ruled out as the testing strategy during April and  
351 May was focusing on health care workers, persons with more severe symptoms, and persons  
352 at risk for complications, rather than monitoring community transmission and milder cases.

353         While the number of SARS-CoV-2 infected individuals was decreasing in the  
354 Netherlands in May and June, an increase in detection of SARS-CoV-2 in mink farms was  
355 observed. Based on WGS these sequences are part of multiple individual transmission chains  
356 linked to the mink farms and are not a reflection of the situation in the human population  
357 during this time. In some cases, the farms had the same owner but in other cases no  
358 epidemiological link could be established. People coming to the different farms might be a

359 source but also semi-wild cats roaming around the farms or wildlife might play a role (27). So  
360 far, the investigation failed to identify common factors that might explain farm to farm spread.  
361 During interviews, it became clear that farms had occasionally hired temporary workers that  
362 had not been included in the testing and were lost to follow-up, stressing the need for vigorous  
363 biosecurity and occupational health guidance. Since our observation, SARS-CoV-2 infections  
364 have also been described in mink farms in Denmark, Spain and the USA (57–59), and mink  
365 farming is common in other regions of the world as well, also in China where around 26 million  
366 mink pelts are produced on a yearly basis (60). The population size and the structure of mink  
367 farms is such that it is conceivable that SARS-CoV-2 – once introduced – could continue to  
368 circulate. Therefore, continued monitoring and cooperation between human and animal  
369 health services is crucial to prevent the animals serving as a reservoir for continued infection  
370 in humans.

371

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### 636 **Authors contributions**

637 Conceptualization: B.B.O.M, R.S.S, A.S., M.P.G.K; investigation: B.B.O.M, D.F.N., R.S.S, A.S.,  
638 M.P.G.K, L.A.M.S, W.H.N.v.d.P, R.J.M, R.J.B, E.M, R.M, A.v.d.S, P.T, A.R, M.B, N.B-V, F.H,  
639 R.H.v.d.H, M.C.A.W-B, R.J.B, C.G, A.A.v.d.E, F.C.V, L.A.M.S; supervision: M.P.G.M; writing  
640 original draft: B.B.O.M, R.S.S, M.P.G.K; writing review and editing, all authors

641

### 642 **Competing interests:**

643 Authors declare no competing interests.

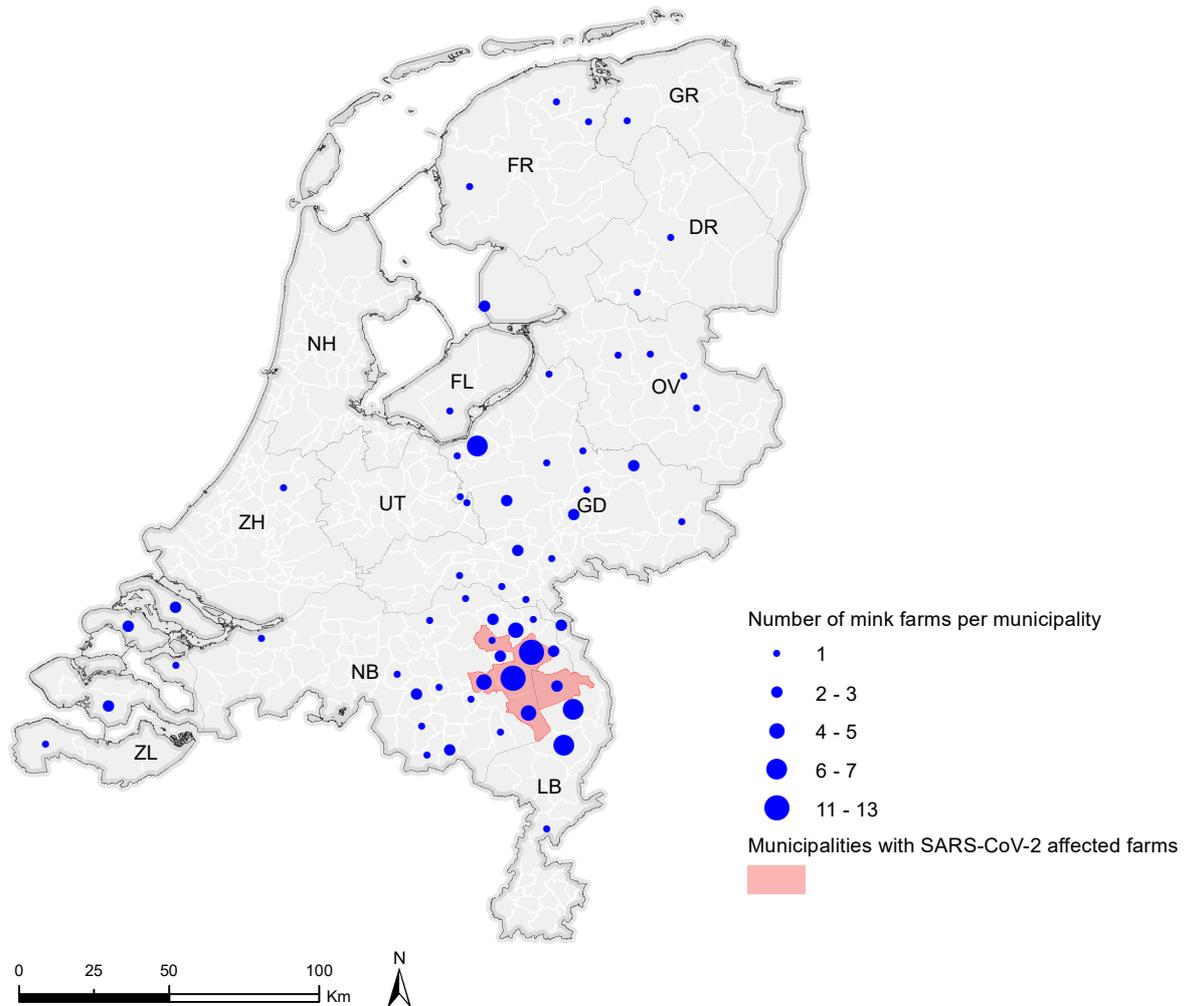
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### 645 **Data and material availability:**

646 All data, code and materials used described in this manuscript are publicly available.

647

## 648 **Supplements**



649

### 650 **Supplementary Figure 1: Number of mink farms per municipality in the Netherlands.**

651 Overview of the total number of mink farms per municipality (CBS, 2019). Municipalities

652 with SARS-CoV-2 affected farms by June 21<sup>st</sup> 2020 are shown in red.

653

654 **Supplementary table 1:** GISAID acknowledgement table.

# **Exhibit CC**

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# Transmission of SARS-CoV-2 on mink farms between humans and mink and back to humans

**Bas B. Oude Munnink<sup>1\*</sup>, Reina S. Sikkema<sup>1</sup>, David F. Nieuwenhuijse<sup>1</sup>, Robert Jan Molenaar<sup>2</sup>, Emmanuelle Munger<sup>1</sup>, Richard Molenkamp<sup>1</sup>, Arco van der Spek<sup>3</sup>, Paulien Tolsma<sup>4</sup>, Ariene Rietveld<sup>5</sup>, Miranda Brouwer<sup>5</sup>, Noortje Bouwmeester-Vincken<sup>6</sup>, Frank Harders<sup>7</sup>, Renate Hakze-van der Honing<sup>7</sup>, Marjolein C. A. Wegdam-Blans<sup>8</sup>, Ruth J. Bouwstra<sup>2</sup>, Corine GeurtsvanKessel<sup>1</sup>, Annemiek A. van der Eijk<sup>1</sup>, Francisca C. Velkers<sup>9</sup>, Lidwien A. M. Smit<sup>10</sup>, Arjan Stegeman<sup>9</sup>, Wim H. M. van der Poel<sup>7</sup>, Marion P. G. Koopmans<sup>1</sup>**

<sup>1</sup>Erasmus MC, Department of Viroscience, WHO collaborating centre for arbovirus and viral hemorrhagic fever Reference and Research, Rotterdam, Netherlands. <sup>2</sup>Royal GD, Deventer, Netherlands. <sup>3</sup>Netherlands Food and Consumer Product Safety Authority (NVWA), Utrecht, Netherlands. <sup>4</sup>Municipal health Services GGD Brabant-Zuidoost, Eindhoven, Netherlands. <sup>5</sup>Municipal health Services GGD Hart voor Brabant, 's-Hertogenbosch, Netherlands. <sup>6</sup>Municipal health Services GGD Limburg-Noord, Venlo, Netherlands. <sup>7</sup>Wageningen Bioveterinary Research, Lelystad, Netherlands. <sup>8</sup>Stichting PAMM, Veldhoven, Netherlands. <sup>9</sup>Farm Animal Health, Utrecht University, Utrecht, Netherlands. <sup>10</sup>Institute for Risk Assessment Sciences (IRAS), Utrecht University, Utrecht, Netherlands.

\*Corresponding author: Email: b.oudemunnink@erasmusmc.nl

Animal experiments have shown that non-human primates, cats, ferrets, hamsters, rabbits and bats can be infected by SARS-CoV-2. In addition, SARS-CoV-2 RNA has been detected in felids, mink and dogs in the field. Here, we describe an in-depth investigation using whole genome sequencing of outbreaks on 16 mink farms and the humans living or working on these farms. We conclude that the virus was initially introduced from humans and has since evolved, most likely reflecting widespread circulation among mink in the beginning of the infection period several weeks prior to detection. Despite enhanced biosecurity, early warning surveillance and immediate culling of infected farms, transmission occurred between mink farms in three big transmission clusters with unknown modes of transmission. Sixty-eight percent (68%) of the tested mink farm residents, employees and/or contacts had evidence of SARS-CoV-2 infection. Where whole genomes were available, these persons were infected with strains with an animal sequence signature, providing evidence of animal to human transmission of SARS-CoV-2 within mink farms.

Late December 2019, SARS-CoV-2 was identified as causing a viral pneumonia outbreak, possibly related to a seafood and a live animal market in Wuhan, China (1). Since then, SARS-CoV-2 spread across the world and by October 8 2020, over 36,100,000 people had been infected with SARS-CoV-2 resulting in over 1,000,000 deaths (2). In the Netherlands, over 155,000 infections have been confirmed, over 6,500 SARS-CoV-2 related deaths have been reported, and non-pharmaceutical interventions have been put into place to prevent further spread of SARS-CoV-2 (3).

In view of the similarities of the new virus with SARS-CoV-1, a zoonotic origin of the outbreak was suspected linked to the Wuhan fresh market where various animals were sold including fish, shellfish, poultry, wild birds and exotic animals. The finding of cases with onset of illness well before the period observed in the Wuhan market-associated cluster suggests the possibility of other sources (4). Although closely related coronaviruses found in bats (5, 6) and pangolins (7, 8) have greatest sequence identity to SARS-CoV-2, the most likely divergence of SARS-CoV-2 from the most closely related bat sequence is estimated somewhere between 1948-1982 (9). Therefore, the animal reservoir(s) of SARS-CoV-2 is (are) yet to be identified.

Similar to SARS-CoV-1, SARS-CoV-2 binds to the host angiotensin-converting enzyme 2 (ACE2) receptor. Based on ACE2 similarities, a range of different animals have been used as models. Experimental infections in dogs (10), cats (10-13), ferrets (10, 14), hamsters (15, 16), rhesus macaques (17), tree shrew (18), cynomolgus macaques (19), African green monkey (20), common marmosets (21), rabbits (22), and fruit bats (23) have shown that these species are susceptible to SARS-CoV-2, and experimentally infected cats, tree shrews, hamsters and ferrets could also transmit the virus. In contrast, experimental infection of pigs and several poultry species with SARS-CoV-2 proved to be unsuccessful (10, 23, 24). SARS-CoV-2 has also sporadically been identified in naturally infected animals. In the USA and in Hong Kong, SARS-CoV-2 RNA has been detected in dogs (25). In the Netherlands, France, Hong Kong, Belgium, Spain and the USA, cats have tested positive by RT-PCR for SARS-CoV-2 (26-30). Furthermore, SARS-CoV-2 has been detected in four tigers and three lions in a zoo in New York (31). In Italy, the Netherlands and in Wuhan, antibodies to SARS-CoV-2 have been detected in cats (29, 32, 33). Recently, SARS-CoV-2 was detected in farmed mink (*Neovison vison*) resulting in signs of respiratory disease and increased mortality (29, 34).

In response to the outbreaks in mink farms, the Dutch national response system for zoonotic diseases was activated, and it was concluded that the public health risk of exposure to animals with SARS-CoV-2 was low, but that there was a need for increased awareness of possible involvement of animals in the COVID-19 epidemic. Therefore, from May 20th 2020 onwards, mink farmers, veterinarians and laboratories were obliged to report symptoms in mink (family *Mustelidae*) to the Netherlands Food and Consumer Product Safety Authority (NFCPSA) and an extensive surveillance system was set up (35).

Whole genome sequencing (WGS) can be used to monitor the emergence and spread of pathogens (36–39). As part of the surveillance effort in the Netherlands over 1,750 SARS-CoV-2 viruses have been sequenced to date from patients from different parts of the Netherlands (40). Here, we describe an in-depth investigation into the SARS-CoV-2 outbreak in mink farms and mink farm employees in the Netherlands, combining epidemiological information, surveillance data and WGS on the human-animal interface.

SARS-CoV-2 was first diagnosed on two mink farms in the Netherlands on April 23rd (NB1) and April 25th (NB2), respectively. After the initial detection of SARS-CoV-2 on these farms an in-depth investigation was initiated to identify potential transmission routes and to perform an environmental and occupational risk assessment. Here, we describe the results of the outbreak investigation of the first 16 SARS-CoV-2 infected mink farms by combining SARS-CoV-2 diagnostics, WGS and in-depth interviews.

Owners and employees of the 16 SARS-CoV-2 positive mink farms were included in the contact tracing investigation of the municipal health services and tested according to national protocol. In total, 97 individuals were tested by either serological assays and/or RT-PCR. In total, 43 out of 88 (49%) upper-respiratory tract samples tested positive by RT-PCR while 38 out of 75 (51%) serum samples tested positive for SARS-CoV-2 specific antibodies. In total, 66 of 97 (68%) of the persons tested had evidence for SARS-CoV-2 infection (Table 1).

During the interview on April 28th, four of five employees from NB1 reported that they had experienced respiratory symptoms before the outbreak was detected in minks, but none of them had been tested for SARS-CoV-2. The first dates of their symptoms ranged from April 1st to May 9th. For 16 of the mink, sampled on April 28th, and one farm employee, sampled on May 4th, a WGS was obtained (hCov-19/Netherlands/NoordBrabant\_177/2020). The human sequence clusters within the mink sequences although it displayed 7 nucleotides difference with the closest mink sequence (Fig. 1 and cluster A in Figs. 2 and 3). On farm NB2, SARS-CoV-2 was diagnosed on April 25th. Retrospective analysis showed that one employee from NB2 had been hospitalized with

SARS-CoV-2 on March 31st. All samples from the eight employees taken on April 30th were negative by RT-PCR but tested positive for SARS-CoV-2 antibodies. The virus sequence obtained from animals was distinct from that of farm NB1, indicating a separate introduction (Figs. 2 and 3, cluster B).

On mink farm NB3 SARS-CoV-2 infection was diagnosed on May 7th. Initially all seven employees tested negative for SARS-CoV-2, but when retested between May 19th and May 26th after developing COVID-19 related symptoms, five of seven individuals working or living on the farm tested positive for SARS-CoV-2 RNA. WGS were obtained from these five individuals and the clustering of these sequences with the sequences derived from mink from NB3, together with initial negative test result and the start of the symptoms, indicate that the employees were infected with SARS-CoV-2 after mink on the farm became infected. An additional infection was identified from contact-tracing: a close contact of one of the employees who did not visit the farm, became infected with the SARS-CoV-2 strain found in farm NB3. Animal and human sequences from farm NB3 were close to those from farm NB1, and both fell in cluster A.

Similarly, on mink farm NB7 zoonotic transmission from mink to human likely occurred. On this farm, SARS-CoV-2 infection in mink was diagnosed on May 31st and employees initially tested negative for SARS-CoV-2 however, subsequently several NB7 employees began to show symptoms. Samples were taken between June 10th and July 1st from 10 employees of which eight tested positive for SARS-CoV-2 RNA. From two NB7 employee samples, WGS showed their virus sequences clustered with the sequences from the mink at this farm.

The sequences generated from mink farms and from mink farm employees were compared with the national database consisting of around 1,775 WGS. To discriminate between community acquired infections and mink farm related SARS-CoV-2 infection, and to determine the potential risk for people living close to mink farms, WGS was also performed on 34 SARS-CoV-2 positive samples, sampled from 04-03-2020 until 29-04-2020, from individuals who live in the same four-digit postal code area as the first four mink farms. These local sequences, sampled in a proxy of around 19 km<sup>2</sup>, reflected the general diversity of SARS-CoV-2 seen in the Netherlands and were not related to the clusters of mink sequences found on the mink farms, thereby indicating no spill-over to people living in close proximity to mink farms had occurred and that the sequences from SARS-CoV-2 infected animals and farm workers clustered by farm (sequences from community shown in magenta, Fig. 2). The sequences from the mink farm investigation were also compared to sequences from Poland (n = 65), since many of the mink farm workers were seasonal migrants from Poland, but these sequences were more divergent.

Phylogenetic analysis of the mink SARS-CoV-2 genomes showed that mink sequences of 16 farms grouped into 5 different clusters (Figs. 2 and 3). Viruses from farms NB1, NB3, NB4, NB8, NB12, NB13 and NB16 belonged to cluster A, sequences from NB2 formed a distinct cluster (B), those from farms NB6, NB7, NB9 and NB14 formed cluster C, NB5, NB8, NB10 and NB15 formed cluster D, and NB11 had sequences designated as cluster E. On farm NB8, SARS-CoV-2 viruses were found from cluster A and cluster D. A detailed inventory of possible common characteristics, including farm owner, shared personnel, feed supplier and veterinary service provider, was made. Multiple farms within a cluster shared the same owner; however, in most cases no common factor could be identified for most farms and clustering could not be explained by geographic distance (Table 2 and Fig. 4).

In total 18 sequences from mink farm employees or close contacts were generated from seven different farms. In most cases, these human sequences were near-identical to the mink sequences from the same farm. For NB1 the situation was different and the human sequence clusters deeply within the sequences derived from mink (Fig. 1), with seven nucleotides difference from the closest related mink sequence. This was also the case on farm NB14, with four nucleotides difference from the closest related mink sequence. Employees sampled at mink farm NB8 clustered with animals from NB12, likely because personnel were exchanged between these two farms.

SARS-CoV-2 was detected on mink farm NB1-NB4 after reports of respiratory symptoms and increased mortality in mink. The sequences from farm NB1 showed between 0 and 9 single nucleotide polymorphisms (SNPs) difference (average 3.9 nucleotides) and sequences from NB2 had between 0 and 8 SNPs difference (average of 3.6), which is more than generally observed in outbreaks in human settings. In addition, two deletions, one of 12 and one of 134 nucleotides were observed in single sequence from NB1. The sequences of mink at NB6 had between 0 and 12 SNPs differences and in one sequence a deletion of 9 nucleotides was observed, whereas diversity was lower for the subsequent farm sequences (Table 2). After the initial detection of SARS-CoV-2, farms were screened weekly. The first, second, fifth and sixth weekly screening yielded new positives.

Several non-synonymous mutations were identified among the mink sequences compared to the Wuhan reference sequence NC\_045512.2. However, no particular amino acid substitutions were found in all mink samples (fig. S1). Of note, three of the clusters had the position 614G variant (clusters A, C and E), and two had the original variant. There were no obvious differences in the presentation of disease in animals or humans between clusters based on the data available at this stage, but further data collection and analysis also for cases after NB16, are ongoing to investigate this further. The

mutations we observed can also be found in the general human population and the same mutations also were found in human cases which were related to the mink farms.

Here we show ongoing SARS-CoV-2 transmission in mink farms and spill-over events to humans. More research in minks and other mustelid species is important to understand if these species are at risk of becoming a reservoir of SARS-CoV-2. After the detection of SARS-CoV-2 on mink farms, 68% of the tested farm workers and/or relatives or contacts were to be or have been infected with SARS-CoV-2, indicating that contact with SARS-CoV-2 infected mink is a risk factor for contracting COVID-19. Recently, a 8-fold increase in cytidine-to-uridine (C->U) compared to U->C substitutions were described, suggestive of host adaptation (41). In the mink sequences we observed a 3.5-fold increase in C->U compared to U->C substitutions but the number of substitutions was limited (185).

A high diversity in the sequences from some mink farms was observed which is likely explained by multiple generations of viral infections in animals before the increase in mortality was detected. The current estimates are that the substitution rate of SARS-CoV-2 is around  $1.16 \times 10^{-3}$  substitutions/site/year in the human population (42), which corresponds to around one mutation per two weeks. This could mean that the virus was already circulating in mink farms for some time. However, there was also a relatively high sequence diversity observed in farms which still tested negative one week prior, hinting toward a faster evolutionary rate of the virus in the mink population. Mink farms have large populations of animals, living at high density, which could promote virus transmission. However, the moment of introduction was not known, making it difficult to draw definite conclusions on the substitution rate in mink farms. Our sequencing did not reveal any systematic mutations that would need to be assessed for potential phenotypic effects. Generation intervals for SARS-CoV-2 in humans have been estimated to be around 4-5 days (43), but with high dose exposure in a farm with a high number and density of animals, this could potentially be shorter.

Further evidence that animals were the most likely source of human infection was provided by the clear phylogenetic separation between mink farm related human and animal sequences and sequences from human cases within the same 4-digit postal code area. However, some of the farm related humans may have been infected within their household, and not directly from mink. Spill-back into the community living in the same 4-digit postal code area was not observed in our sequence data.

So far, the investigation failed to identify common factors that might explain farm-to-farm spread: possibly via temporary workers who were not included in testing. Since our observations, SARS-CoV-2 infections have also been described

in mink farms elsewhere (44–46). It is imperative that fur production and trading sector should not become a reservoir for future spillover of SARS-CoV-2 to humans.

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## ACKNOWLEDGMENTS

We would like to acknowledge Robin van Houdt, Janke Schinkel, Jelle Koopsen and Rens Zonneveld (Amsterdam UMC), Bas Wintermans (ARDZ), Eva Schmid (GGD Goes), Babette Rump (GGD Zeeland), Jacky Filipse and Claudy Oliveira dos Santos (Isala Hospital, Laboratory of Clinical Microbiology and Infectious Diseases), Theo Schuur (Izore), Roel Nijhuis (Meander Medisch Centrum), Suzan Pas (Microvida), Bertie de Leeuw (RLM Microbiologie) and Ruud Jansen, Jayant Kalpoe and Wil van der Reijden (Streeklab Haarlem) for sample provision and Anne van der Linden, Marjan Boter and Irina Chestakova from the ErasmusMC for technical assistance. **Funding:** This work has received funding from the European Union's Horizon 2020 research and innovation program under grant agreement No. 874735 (VEO), No. 848096 (SHARP JA) and No. 101003589 (RECoVER), from ZonMW (grant agreement No. 10150062010005), and from the Netherlands Ministry of Agriculture, Nature and Foods. **Author contributions:** Conceptualization: B.B.O.M, R.S.S, A.S., M.P.G.K; investigation:

B.B.O.M, D.F.N., R.S.S, A.S., M.P.G.K, L.A.M.S, W.H.N.v.d.P, R.J.M, R.J.B, E.M, R.M, A.v.d.S, P.T, A.R, M.B, N.B-V, F.H, R.H.v.d.H, M.C.A.W-B, R.J.B, C.G, A.A.v.d.E, F.C.V, L.A.M.S; supervision: M.P.G.M; writing original draft: B.B.O.M, R.S.S, M.P.G.K; writing review and editing, all authors. **Competing interests:** Authors declare no competing interests. **Data and material availability:** All data, code and materials used described in this manuscript are publicly available. All sequences are publicly available in the GISAID database under the accessions: EPI\_ISL\_461190 – EPI\_ISL\_461192, EPI\_ISL\_461200, EPI\_ISL\_461202, EPI\_ISL\_461203, EPI\_ISL\_522987 – EPI\_ISL\_523034, EPI\_ISL\_523040, EPI\_ISL\_523046, EPI\_ISL\_523068, EPI\_ISL\_523070, EPI\_ISL\_523072, EPI\_ISL\_523073, EPI\_ISL\_523075, EPI\_ISL\_523085, EPI\_ISL\_523089 – EPI\_ISL\_523120, EPI\_ISL\_523282 – EPI\_ISL\_523286, EPI\_ISL\_523301, EPI\_ISL\_523310 – EPI\_ISL\_523312, EPI\_ISL\_523333, EPI\_ISL\_523493 and EPI\_ISL\_523494. Ethical approval was not required for this study as anonymous aggregated data were used, and no medical interventions were made on animal or human subjects. This work is licensed under a Creative Commons Attribution 4.0 International (CC BY 4.0) license, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. To view a copy of this license, visit <https://creativecommons.org/licenses/by/4.0/>. This license does not apply to figures/photos/artwork or other content included in the article that is credited to a third party; obtain authorization from the rights holder before using such material.

## SUPPLEMENTARY MATERIALS

[science.sciencemag.org/cgi/content/full/science.abe5901/DC1](https://science.sciencemag.org/cgi/content/full/science.abe5901/DC1)

Materials and Methods

Fig. S1

Table S1

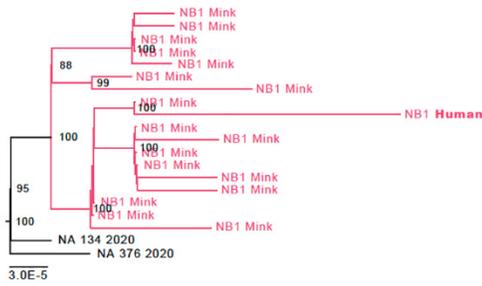
References (47–63)

MDAR Reproducibility Checklist

1 September 2020; accepted 5 November 2020

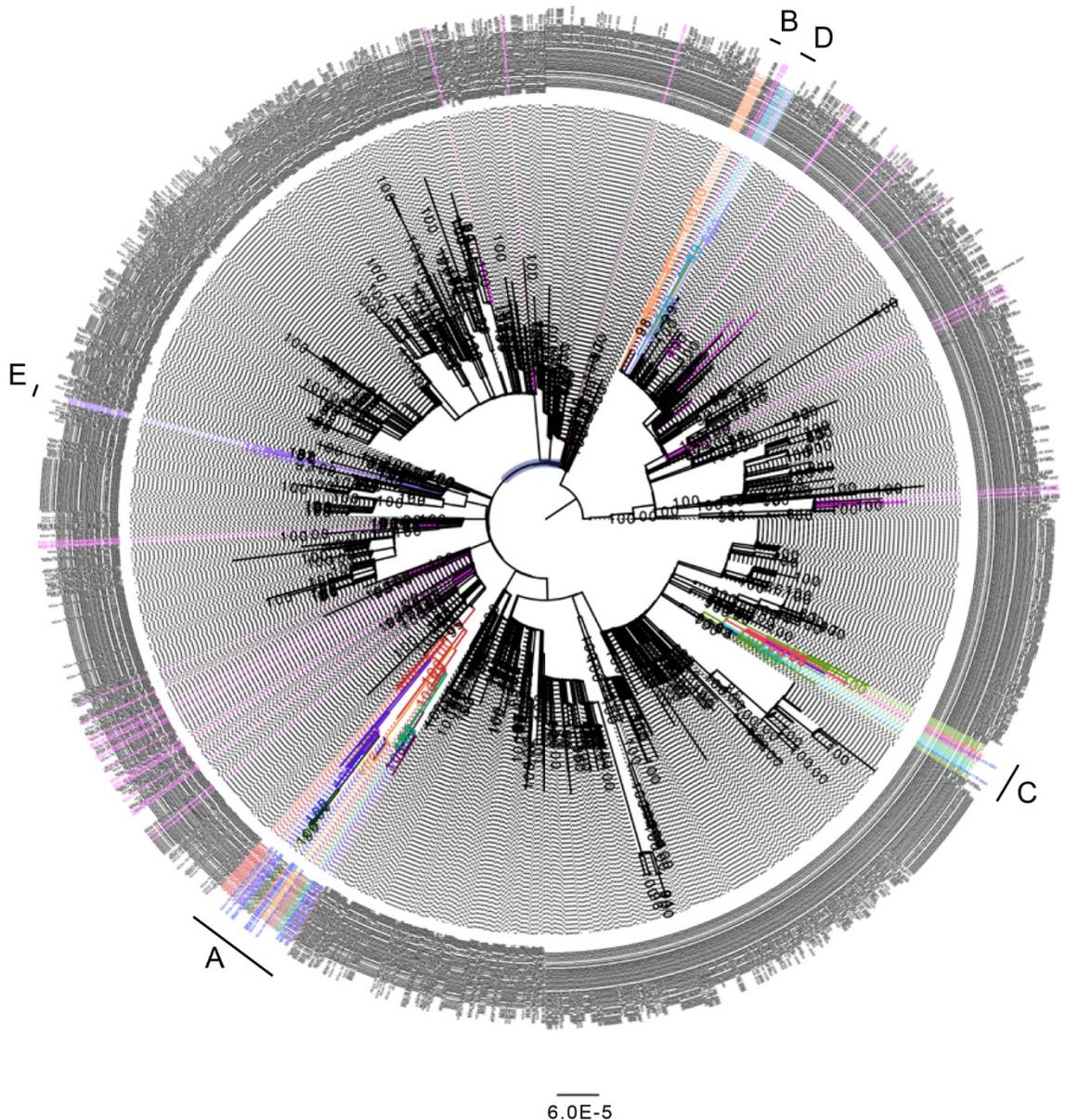
Published online 10 November 2020

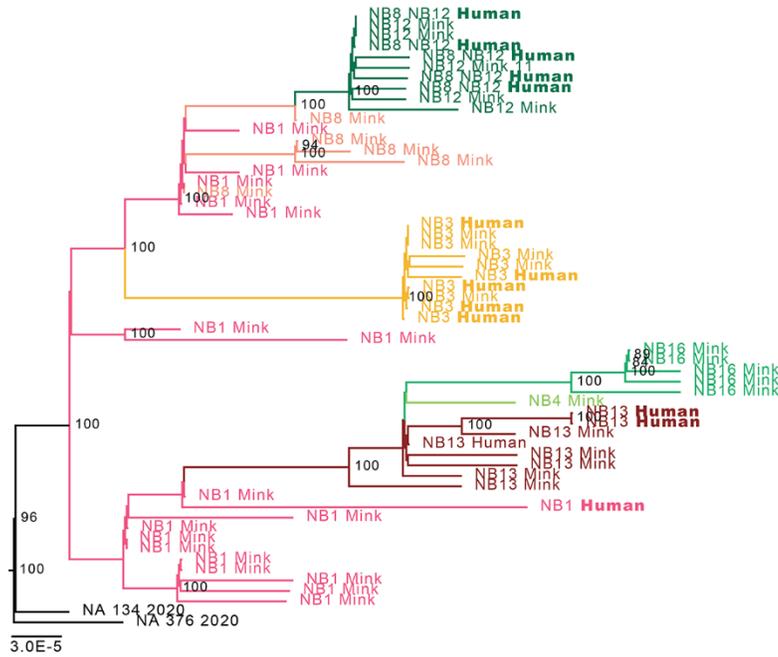
10.1126/science.abe5901



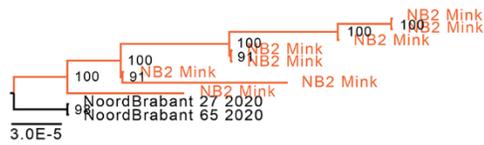
**Fig. 1. Phylogenetic analysis of mink farm NB1.** A maximum likelihood analysis was performed using all available SARS-CoV-2 Dutch sequences. Sequences from NB1 are depicted in red and the employee on NB1 is depicted in bold. The two sequences in black at the root of the cluster are the closest matching human genome sequences from the national SARS-CoV-2 sequence database. Scale bar units represent numbers of substitutions per site.

**Fig. 2. Maximum likelihood analysis of all SARS-CoV-2 Dutch sequences.** The sequences derived from minks from different farms are indicated with different colors, human sequences related to the mink farms are shown in blue and samples from similar 4-digit postal code are shown in magenta. The sequences derived from different farms are depicted in different colors. Scale bar represents units of substitutions per site.

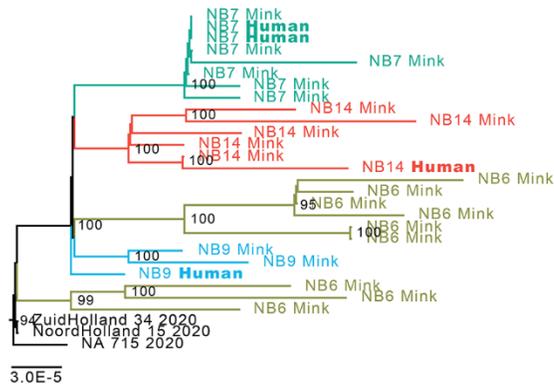




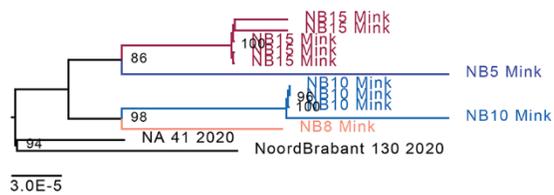
A Fig. 3. Phylogenetic analysis of 88 mink and 18 mink-related human SARS-CoV-2 sequences detected in the 5 mink farm clusters. The sequences derived from different farms are depicted in different colors. Scale bar represents units of substitutions per site.



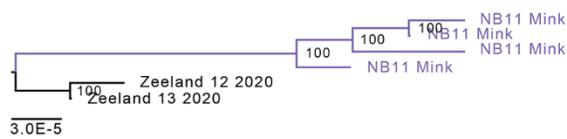
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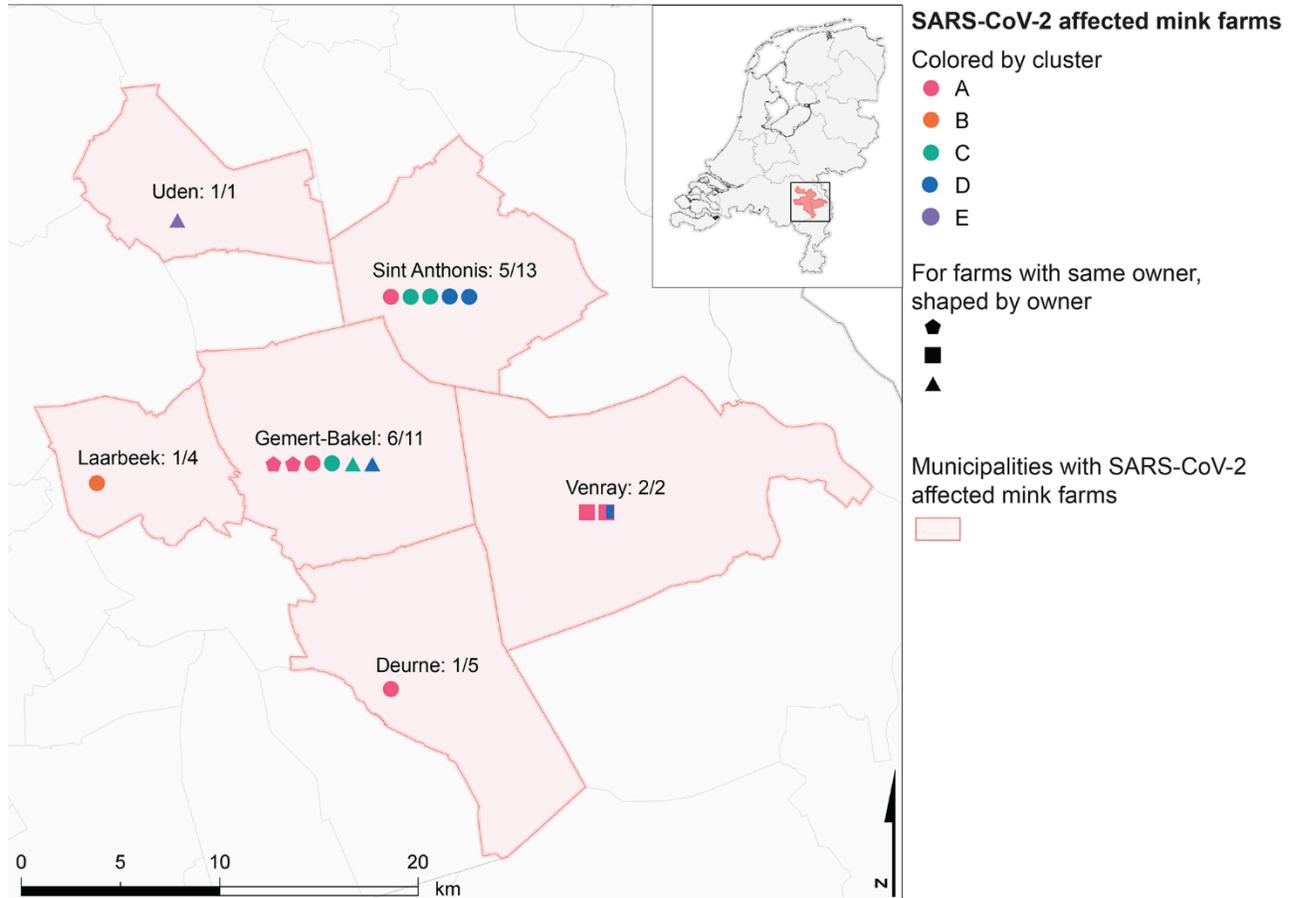
C



D



E



**Fig. 4. Geographical overview of SARS-CoV-2 positive mink farms per municipality affected.** The proportion of SARS-CoV-2 positive mink farms over the total number of mink farms (CBS, 2019) is indicated. Symbols for positive farms are colored by cluster and shapes indicate farms with a single owner.

**Table 1. Overview of human sampling on SARS-CoV-2 positive mink farms.**

Farm	First diagnosis in animals	Date(s) of sampling employees and family members	PCR positive (%)	Serology positive (%)	Employees and family members tested positive (PCR and/or serology)
NB1	23-04-2020	28-04-2020 – 11-05-2020	5/6 (83%)	5/5 (100%)	6/6 (100%)
NB2	25-04-2020	31-03-2020 – 30-04-2020	1/2 (50%)	7/8 (88%)	7/8 (88%)
NB3	07-05-2020	11-05-2020 – 26-05-2020	5/7 (71%)	0/6 (0%)*	5/7 (71%)
NB4	07-05-2020	08-05-2020	1/3 (33%)	2/2 (100%)	2/3 (66%)
NB5	31-05-2020	01-06-2020	2/7 (29%)	3/6 (50%)	3/7 (43%)
NB6	31-05-2020	01-06-2020	1/6 (17%)	4/6 (66%)	4/6 (66%)
NB7	31-05-2020	10-06-2020 – 01-07-2020	8/10 (80%)	NA**	8/10 (80%)
NB8	02-06-2020	03-06-2020	5/10 (50%)	5/9 (56%)	8/10 (80%)
NB9	04-06-2020	07-06-2020	1/7 (14%)	1/7 (14%)	2/7 (29%)
NB10	08-06-2020	11-06-2020	1/8 (13%)	3/8 (38%)	4/8 (50%)
NB11	08-06-2020	11-06-2020	1/3 (33%)	0/2 (0%)	1/3 (33%)
NB12	09-06-2020	11-06-2020	6/9 (66%)	2/8 (25%)	7/9 (78%)
NB13	14-06-2020	11-06-2020 – 18-06-2020	3/3 (100%)	0/2 (0%)	3/3 (100%)
NB14	14-06-2020	14-06-2020	1/3 (33%)	5/6 (83%)	5/6 (83%)
NB15	21-06-2020	10-06-2020 – 30-06-2020	2/2 (100%)	NA**	2/2 (100%)
NB16	21-06-2020	23-06-2020	0/2 (0%)	NA**	0/2 (0%)
Total			43/88 (49%)	37/75 (49%)	66/97 (68%)

\*Serology was done approximately one week before the positive PCR test.

\*\*No serology was performed.

**Table 2. Overview of the clusters detected on the different farms.**

Farm	Date of diagnosis	Sequence cluster	Same owner	Feed supplier	Vet**	Number of sequences (+human)	SNPs differences (average)	Mink population size	Detection***
NB1	24-04-20	A	NB1, NB4	1	I	17 (+1)	0-9 (3.9)	75,711	Notification
NB2	25-04-20	B		1	II	8	0-8 (3.6)	50,473	Notification
NB3	07-05-20	A		2	III	5 (+5)	0-2 (0.6)	12,400	Notification
NB4	07-05-20	A	NB1, NB4	1	I	1	NA	67,945	Contact tracing NB1
NB5	31-05-20	D		1	IV	1	NA	38,936	EWS-Ser+PM-1st
NB6	31-05-20	C		3	V	9	0-12 (6.8)	54,515	EWS-Ser+PM-1st
NB7	31-05-20	C	NB7, NB11, NB15, NB8, NB12*	3	II	6 (+2)	0-4 (1.4)	79,355	EWS-PM-1st
NB8	02-06-20	A/D		3	V	6 (+5)	0-6 (2.6)	39,144	EWS-Ser+PM-1st
NB9	04-06-20	C		2	V	2 (+1)	0-3 (1.5)	32,557	EWS-Ser+PM-2nd
NB10	08-06-20	D		3	II	4	0-3 (1.1)	26,824	EWS-Ser+PM-2nd
NB11	08-06-20	E	NB7, NB11, NB15, NB8, NB12*	3	II	4	0-4 (2.2)	38,745	EWS-PM-2nd
NB12	09-06-20	A		3	II	5	0-3 (1.2)	55,352	Notification
NB13	14-06-20	A		3	V	5 (+3)	0-5 (3.2)	20,366	EWS-PM-5th
NB14	14-06-20	C		3	II	5 (+1)	0-7 (3.7)	28,375	EWS-PM-5th
NB15	21-06-20	D	NB7, NB11, NB15	3	II	5	0-2 (0.6)	35,928	EWS-PM-6th
NB16	21-06-20	A		3	II	5	0-4 (1.6)	66,920	EWS-PM-6th

\*There was exchange of personnel in these two locations.

\*\*Veterinarian II and V were both from the same veterinary practice.

\*\*\*Notification: based on reporting of clinical signs which was obligated from 26 April onwards; EWS-Ser-Detection based on a one-off nationwide compulsory serological screening of all mink farms at the end of May/early June by GD Animal Health; EWS-PM-Detection based on the early warning monitoring system for which carcasses of animals that died of natural causes were submitted weekly for PCR testing by GD Animal Health from the end of May onwards in a weekly cycle (EWS-PM 1st to 6th post mortem screening).

# **Exhibit DD**

# COVID-19 likely spreading from people to animals—and vice versa

[cidrap.umn.edu/news-perspective/2020/09/covid-19-likely-spreading-people-animals-and-vice-versa](https://cidrap.umn.edu/news-perspective/2020/09/covid-19-likely-spreading-people-animals-and-vice-versa)

Mary Van Beusekom | News Writer | CIDRAP News | Sep 18, 2020



Three new studies suggest that high proportions of cats and dogs may have acquired COVID-19 from their owners and that the virus jumped back and forth between humans and minks on farms in the Netherlands.

## **SARS-CoV-2 antibodies in dogs, cats**

The first, a small, unpublished study from the University of Guelph in Ontario, Canada, suggests that a large proportion of pet cats and dogs may have gotten COVID-19 from their owners, as evidenced by antibodies against the coronavirus in their blood.

The study, which will be presented at the Sep 23 to 25 virtual European Society of Clinical Microbiology and Infectious Diseases (ESCMID) Conference on Coronavirus Disease, involved collecting nose, throat, and rectal swabs from 17 cats, 18 dogs, and 1 ferret owned by people diagnosed as having COVID-19 or reporting symptoms consistent with the coronavirus in the previous 2 weeks.

If more than 2 weeks had passed, the pets were tested for antibodies. The results were compared with those of stored blood samples collected from animals before December 2019.

All animals tested negative for SARS-CoV-2, the virus that causes COVID-19, on reverse transcription polymerase chain reaction (RT-PCR), except for one cat, which had ambiguous results but tested positive for coronavirus antibodies, indicating previous infection. Overall, seven of eight cats with blood samples (88%) had coronavirus antibodies. The owners of all cats with inconclusive COVID-19 tests or positive antibody results said they and their pets had displayed coronavirus-like respiratory symptoms at the same time.

Two of 10 dogs with blood samples (20%) had coronavirus antibodies. One dog had previously had displayed respiratory symptoms.

The authors noted previous reports of SARS-CoV-2 infections in different animal species, but none have identified risk factors for or clinical characteristics of infection.

Lead author Dorothee Bienzle, DVM, PhD, of the University of Guelph, said in an ESCMID [news release](#) that blood testing the animal after the owner recovers is the best way to assess human-to-animal transmission because the window of time to identify current infections in pets is narrow.

In the meantime, Bienzle said, pet owners infected with COVID-19 should isolate themselves. "There is sufficient evidence from multiple studies, including ours, to recommend that SARS-CoV-2 infected persons should isolate from people and animals," she said.

## **Virus RNA, identical genomes in cats**

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In the second [study](#), a research letter published yesterday in *Emerging Infectious Diseases*, researchers in Hong Kong tested the respiratory and fecal samples of 50 cats from COVID-19–infected households or their close contacts for coronavirus RNA from Feb 11 to Aug 11.

Six of the 50 cats (12%) tested positive for SARS-CoV-2 RNA on RT-PCR, and virus genomes from one owner-and-cat pair were identical. All cats were asymptomatic but had lung abnormalities similar to those of infected humans. The researchers were unable to grow the virus on cell culture.

"Although feline-to-human transmission is theoretically possible, we did not find any evidence of this transmission," the authors said. "The timeline of infection in cat 1 and the finding of an identical SARS-CoV-2 genome sequence in a human from the same household is consistent with human-to-animal transmission. In support of these findings, the cat had no outdoor access."

The researchers called for broader serologic surveillance of cats connected to COVID-19 patients to determine the prevalence of human-to-cat spread.

The Agriculture, Fisheries and Conservation Department of Hong Kong quarantines and tests pets from infected households or their close contacts in a holding facility if other care is not available. The pets are isolated until they test negative on RT-PCR on two occasions. COVID-19 infections identified in dogs as part of this testing were reported in a study published on May 14 in *Nature*—the first published evidence of the disease in dogs.

### **Likely zoonotic transmission from mink**

---

The third study, which will also be presented at the ESCMID conference, involved monitoring COVID-19 infections at 16 mink farms with more than 720,000 animals in the Netherlands. The findings suggest that the coronavirus jumped back and forth between people and mink, in the first known published case of animal-to-human, or zoonotic, transmission, according to the authors.

Of course, SARS-CoV-2 likely first jumped from animals to humans in late 2019, sparking the pandemic in Wuhan, China.

In the study, posted Sep 1 on the preprint server bioRxiv, Dutch researchers investigating outbreaks of coronavirus in both animals and humans on mink farms conducted testing and whole-genome sequencing to trace the sources of infection. Sixty-six of 97 people (67%) living or working on the farms were diagnosed as having COVID-19 on PCR or antibody testing.

The authors said in an ESCMID news release that they believe at least two people on the farms were infected by mink. "Unfortunately, based on our research we cannot make definite conclusions on the direction of most of the infections, so we do not know the total number of people that were infected by minks," they said.

"We conclude that initially the virus was introduced from humans and has evolved on mink farms, most likely reflecting widespread circulation among mink in the first SARS-CoV-2 mink farms, several weeks prior to detection."

The coronavirus was first detected on two mink farms in late April. Some farms involved in the outbreaks were owned by the same person, but no epidemiologic link could be identified for the others.

Genome sequencing showed that the SARS-CoV-2 virus was the same as those found in the mink and not identical to those found in COVID-19 patients living near the farms. The sequences from all infected mink farms were part of one of five distinct disease clusters, demonstrating spread among the farms.

Currently, COVID-19 is still spreading on the farms, despite efforts to combat it, the authors said, and three large clusters with unknown modes of transmission have been identified.

"The population size and the structure of mink farms is such that it is conceivable that SARS-CoV-2—once introduced—could continue to circulate," the authors wrote.

"Therefore, continued monitoring and cooperation between human and animal health services is crucial to prevent the animals serving as a reservoir for continued infection in humans.

They add in the news release, "Close collaboration between human and animal health departments is essential for early identification and control of SARS-CoV-2 infections."

# **Exhibit EE**

# Global COVID-19 total clears 49 million, experts weigh in on mink variant

[cidrap.umn.edu/news-perspective/2020/11/global-covid-19-total-clears-49-million-experts-weigh-mink-variant](https://cidrap.umn.edu/news-perspective/2020/11/global-covid-19-total-clears-49-million-experts-weigh-mink-variant)

Lisa Schnirring | News Editor | CIDRAP News | Nov 06, 2020



With COVID-19 levels surging in Europe and the United States, the world was on track today to record its highest single-day case total as the pandemic total sped past 49 million cases and health officials weighed in on a mink variant of the virus.

## **WHO urges country self-assessments, appeals for polio, measles vaccination support**

The World Health Organization (WHO) online dashboard showed that nearly 582,000 cases have been recorded today so far, with more to be reported.

At a WHO media telebriefing today, Director-General Tedros Adhanom Ghebreyesus, PhD, said 21 countries so far have conducted intra-action reviews to learn lessons from and strengthen their COVID-19 response, as suggested by the World Health Assembly back in May. He noted that reviews by other countries are in progress.

Tedros urged more countries to do the same and said the best time to conduct a review of emergency response capacity is during an emergency. "There's hope, and now is the time to double down on efforts to tackle this virus," he said. "Wherever a country is in terms of the outbreak, countries can turn it around by driving a whole-of-government and whole-of-society response."

In other WHO developments, the group and UNICEF today launched a \$655 million emergency appeal to boost measles and polio vaccination, which have been suspended or slowed due to the pandemic. Tedros said health officials are starting to see outbreaks of diseases like polio, measles, and pneumonia in children, especially those in high-risk areas.

## Europe cases rise more steeply

---

European countries continue to report record-high single-day case totals, including France, with 60,486 new cases. Others include Russia, where daily cases topped 20,000 for the first time, and Sweden, which reported 4,697 new cases today.

In the United Kingdom, which just entered a 1-month lockdown, government officials said cases have leveled off some to about 50,000 a day, Reuters reported.

In other global developments:

- The United Kingdom's Recovery Trial, a large randomized controlled clinical study of potential COVID-19 treatments, announced today that researchers will investigate aspirin as a possible therapy. It noted that aspirin, an antiplatelet agent, may reduce the risk of blood clots in patients with COVID-19.
- Malaysia reported a record daily high of 1,755 cases, most of them from local transmission, CNN
- The global pandemic total today climbed to 49,129,021 cases, with 1,239,896 deaths, according to the Johns Hopkins online dashboard.

## More mink SARS-CoV-2 variant details

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The European Center for Disease Prevention and Control (ECDC) said today that it will assess the human implications of extensive spread of SARS-CoV-2, the virus that causes COVID-19, at Danish mink farms. In a statement, it said as of Nov 3, 197 farms have been affected, and Denmark has taken strong control measures, which include culling the entire mink population, restricting movements of people in the farm areas, and conducting enhanced testing in the population.

When the virus is introduced to mink farms from humans, it can spread quickly, and possibly due to biological differences between minks and people, can accumulate mutations, which result in variants with the potential to jump back into humans.

The statement said that Denmark's Statens Serum Institute (SSI) found seven unique mutations on the variant virus' spike protein in mink, with the variant also found in humans. It said the possibility of an antigenic mutation could have implications for immunity, reinfections, and vaccine effectiveness, but currently, there's a high level of uncertainty.

Further analyses are needed, and the ECDC said it is in close contact with Danish officials and will publish a risk assessment by Nov 12.

In its weekly communicable disease threat report today, the ECDC said five different clusters of mink variants have been found in Denmark and that a variant from one cluster showed less sensitivity to neutralizing antibodies from people with previous COVID-19 infection.

Tyra Krause, MD, PhD, of SSI, said so far the variant has been detected in 12 people and that more such cases are likely to be identified in the weeks ahead, NBC News reported.

At today's WHO media briefing, Maria Van Kerkhove, PhD, the WHO's technical lead for COVID-19, said mutations are normal, and each change needs to be evaluated to see if the affected viruses behave differently. And Mike Ryan, MD, who directs the WHO's health emergencies program, said currently, evidence doesn't suggest there are any differences in the way the variant virus behaves and that it might have a slightly different signature but is still the same virus. However, he added that further evidence is needed.

WHO officials also added that the organization is working with its global health partners on a risk assessment of the variant virus.

Peter Ben Embarek, PhD, a food safety and animal disease expert with the WHO, said minks are raised in a range of conditions in different countries, some with farm environments that are easier to control. He added that the risk of the virus passing from other livestock such as cattle and poultry may be much less, because they're not as susceptible as mink and can't sustain and spread SARS-CoV-2 in the same way.

# **Exhibit FF**



Amanda Price &lt;amandaprice@utah.gov&gt;

## Fwd: Mink farm update?

Dean Taylor <djtaylor@utah.gov>  
To: Amanda Price <amandaprice@utah.gov>

Thu, Oct 15, 2020 at 9:20 AM

----- Forwarded message -----

From: **Dean Taylor** <djtaylor@utah.gov>  
Date: Wed, Oct 14, 2020 at 4:03 PM  
Subject: Re: Mink farm update?  
To: Taylor Stevens <tstevens@sltrib.com>

Yes that is what that means. The guidance is publicly available at this point, the link follows.

Thanks

Dean

[https://www.aphis.usda.gov/publications/animal\\_health/sars-cov-2-mink-guidance.pdf](https://www.aphis.usda.gov/publications/animal_health/sars-cov-2-mink-guidance.pdf)

On Wed, Oct 14, 2020 at 2:16 PM Taylor Stevens <tstevens@sltrib.com> wrote:

Sorry, it can be difficult to be sure of meaning in emails sometimes. When you say "Breeding has occurred for the year at this point" does that mean the breeding season is over for the calendar year?



**Taylor Stevens**

Government reporter

O: 801.257.8754

C: 801.205.5919



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On Wed, Oct 14, 2020 at 1:27 PM Dean Taylor <djtaylor@utah.gov> wrote:

ALL testing refers just to what we have done here in Utah. I will ask USDA if sharing that document would be appropriate and if they feel it is I will share it. I was passing on some of that information to the farms before the document was finalized but it is now final, so I will see if I can share it with you. I see no value in what the UARC is asking for. Breeding has occurred for the year at this point and with regards to the health of the industry as a whole I don't have enough information to comment on that. Mandating testing on thousands of mink would cripple the labs currently, similar to delays seen in human test labs. The results we are waiting on will help us determine the need and scope of screening we will need to do. I will send you the information from USDA if they approve it.

Dean

On Wed, Oct 14, 2020 at 1:09 PM Taylor Stevens <tstevens@sltrib.com> wrote:

Hey, Dean: I really appreciate you getting back to me. (And thanks Caroline for coordinating.)

To be clear, when you say "ALL studies so far indicated that the spread was from humans to mink," do you mean all studies of the Utah outbreaks? Or was your statement meant to be more universal than that?

Would it be possible to share the document with USDA recommendations for mink farms?

Do you see any value in implementing the requests the Utah Animal Rights Coalition has included in its letter, or have those already been implemented? (Immediately suspending all breeding operations on mink farms and mandating COVID-19 testing protocols for both animals and workers.)

Finally, the Utah Animal Rights Coalition says the state's mink farming industry has been shrinking over the last several years. Is that accurate, based on what you've seen?

**Taylor Stevens**

Government reporter

O: 801.257.8754

C: 801.205.5919

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On Wed, Oct 14, 2020 at 12:59 PM Dean Taylor <[djtaylor@utah.gov](mailto:djtaylor@utah.gov)> wrote:

Taylor,

I am in between meetings at a conference. I will try to help with a response to the questions that you have. Certainly a strong focus of research with the ongoing SARS-CoV-2 cases in mink would be to determine if there was any spread from the mink back to the people on the farms. The CDC, several agencies from the USDA and the health department have all been very actively involved with UDAF in the response to the outbreak here in Utah with 2 goals in mind: contain the outbreak as much as possible and understand the route of transmission. They responded within a couple days of the first confirmation and were on the ground sampling to see if a reservoir existed. We still had some active cases dying at that time so not surprisingly we found live mink with virus. CDC is just finishing up a convalescent study to see if these mink retained the virus. These results are not yet available.

ALL studies so far indicated that the spread was from humans to mink and none indicate the reverse, as has been reported in the Netherlands. The mink industry has been provided with a document from USDA on response and containment and many are employing those recommendations currently.

Total losses in Utah are just over 10,000 at this time. These are across 9 facilities in 3 counties and all farms seem to have run their course at this time. All farms are still under a quarantine restricting any movement of mink, products or waste as well as human traffic on or off the facilities.

We are hoping to gain more information in the next few weeks that will direct our response going forward and the way these farms are managed.

Regards

Dean J Taylor, DVM

State Veterinarian

On Wed, Oct 14, 2020 at 10:56 AM Caroline Hargraves <[carolinehargraves@utah.gov](mailto:carolinehargraves@utah.gov)> wrote:

Hello Dr. Taylor,

Rather than respond to this request with the information in the statement we prepared, considering the details of this request it seemed best to connect her directly to you. Is there a time you'd like to suggest so that I can arrange a call with her or would you like to call this reporter at your convenience?

If you prefer I respond with the information in the statement and that material is still up to date and accurate as far as what you'd like to share, please let me know. (<https://docs.google.com/document/d/1wi1Tskb6pkvd8XF8eronhXsBcwTVrDpQGK5lqKZheY/edit?usp=sharing>)

I'll forward the UARC document to Commissioner Wilde and Deputy Commissioner Pehrson in a separate email so they're aware of the situation.

Thank you,  
-Caroline Hargraves

----- Forwarded message -----

From: **Taylor Stevens** <[tstevens@sltrib.com](mailto:tstevens@sltrib.com)>

Date: Wed, Oct 14, 2020 at 10:46 AM

Subject: Mink farm update?

To: <[carolinehargraves@utah.gov](mailto:carolinehargraves@utah.gov)>

Hey, Caroline:

My name is Taylor Stevens and I'm a reporter at The Salt Lake Tribune. I hope you're doing well!

I'm looking into some claims made in a letter the Utah Animal Rights Coalition sent to the governor yesterday in which they push back on claims by the state veterinarian about the danger COVID-19 outbreaks in mink farms pose to humans. I was wondering if it would be possible to set up a follow up interview with the Dr.

Taylor on that point, as well as on what, if anything, he thinks the governor should do to address these outbreaks?

Additionally, I'm wondering if the department can provide more information about the outbreaks, including how many mink have been affected and died and how many facilities have outbreaks in the state.

Thanks!



**Taylor Stevens**  
Government reporter  
O: 801.257.8754  
C: 801.205.5919



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**CAROLINE HARGRAVES** | Communications Specialist  
[carolinehargraves@utah.gov](mailto:carolinehargraves@utah.gov) | 801.982.2353 office  
[Website](#) | [Twitter](#) | [Facebook](#) | [Instagram](#)

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**Dean J Taylor, DVM** | State Veterinarian  
Office 801-982-2243 Cell 385-290-9462  
[djtaylor@utah.gov](mailto:djtaylor@utah.gov)  
[Website](#) | [Twitter](#) | [Facebook](#) | [Instagram](#)

--



**Dean J Taylor, DVM** | State Veterinarian  
Office 801-982-2243 Cell 385-290-9462  
[djtaylor@utah.gov](mailto:djtaylor@utah.gov)  
[Website](#) | [Twitter](#) | [Facebook](#) | [Instagram](#)

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**Dean J Taylor, DVM** | State Veterinarian  
Office 801-982-2243 Cell 385-290-9462

# **Exhibit GG**



## State of Utah

GARY R. HERBERT  
Governor

SPENCER J. COX  
Lieutenant Governor

## Department of Agriculture and Food

R. LOGAN WILDE  
Commissioner

KELLY PEHRSON  
Deputy Commissioner

LEANN HUNTING  
Director, Animal Industry

October 19, 2020

Jeremy Beckham, MPA, MPH  
Executive Director  
Utah Animal Rights Coalition  
PO Box 3451  
Salt Lake City, UT 84110  
[jeremy@uarc.io](mailto:jeremy@uarc.io)

Re: GRAMA Request for the Utah Animal Rights Coalition

Dear Mr. Beckham,

The Utah Department of Agriculture and Food (Department) Division of Animal Industry received your request for:

- *Email communications between Dr. Dean Taylor and The Salt Lake Tribune (Oct 1, 2020-Oct 14, 2020)*
- *Records regarding the "studies in Utah" referenced in this excerpt, including any research protocols, design descriptions/narratives, diagnostic reports, abstracts, and any published manuscripts.*

The Department has conducted a thorough search of its records based on your GRAMA request and has attached two responsive records. These records are the email communications between Dr. Dean Taylor and Taylor Stevens of the Salt Lake Tribune and the "statement" referred to in the email from Caroline Hargraves to Dr. Taylor.

The Department must partially deny your request for the following reasons:

1. The records you have requested regarding the "studies in Utah" are not prepared, owned, or maintained by the Department. The studies referenced in your request were developed and conducted by the USDA National Veterinary Services Laboratory and the Centers for Disease Control and Prevention, and therefore they are the owners of those records. Pursuant to Utah Code, 63G-2-204 (2), *a person making a request for a record shall submit the request to the governmental entity that prepares, owns, or retains the record*; and Subsection (2)(c) *"if a governmental entity is prohibited from providing a record it shall, deny the records request and inform the person making the request that records requests must be submitted to the governmental entity that prepares, owns, or retains the record."*

The Department is granting your request for a fee waiver for this information.

If you believe that the attached response is incomplete or deficient, you may appeal the GRAMA Officer's decision to the Chief Administrative Officer for the Department: Kelly Pehrson, 350 N Redwood Rd, Salt Lake City, UT 84116, (801) 982-2200. Any appeal must be within thirty (30) days of the above date of determination and must be by filing a

“notice of appeal” compliant with Utah Code 63G-2-401; Appeal to Head of Governmental Entity. Thank you for your cooperation, and if you have any questions, please feel free to contact our counsel Melissa Ure at 801-982-2200.

Sincerely yours,

A handwritten signature in blue ink that reads "Amanda Price". The signature is written in a cursive, flowing style.

Amanda Price, DVM, MS  
GRAMA Officer, Division of Animal Industry

# **Exhibit HH**

HEALTHCARE  
SECTORNOVEMBER 10, 2020 / 1:17 PM /  
UPDATED 22 DAYS AGO

# Coronavirus kills 15,000 U.S. mink, as Denmark prepares for nationwide cull

By Tom  
Polansek

4 MIN READ



CHICAGO, Nov 10 (Reuters) - More than 15,000 mink in the United States have died of the coronavirus since August, and authorities are keeping about a

dozen farms under quarantine while they investigate the cases, state agriculture officials said.

Global health officials are eyeing the animals as a potential risk for people after Denmark last week embarked on a plan to eliminate all of its 17 million mink, saying a mutated coronavirus strain could move to humans and evade future COVID-19 vaccines.

The U.S. states of Utah, Wisconsin and Michigan - where the coronavirus has killed mink - said they do not plan to cull animals and are monitoring the situation in Denmark.

“We believe that quarantining affected mink farms in addition to implementing stringent biosecurity measures will succeed in controlling SARS-CoV-2 at these locations,” the U.S. Department of Agriculture told Reuters on Tuesday.

The USDA said it is working with

the U.S. Centers for Disease Control and Prevention, state officials and the mink industry to test and monitor infected farms.

The United States has 359,850 mink bred to produce babies, known as kits, and produced 2.7 million pelts last year. Wisconsin is the largest mink-producing state, followed by Utah.

Sick mink in Wisconsin and Utah were exposed to people with probable or confirmed COVID-19 cases, the USDA said. In Michigan it is still unknown if the mink were infected by humans, according to the agency.

#### TRENDING STORIES

U.S. prosecutors investigating potential White House 'bribery-for-pardon' scheme

Israel receives its most advanced warship as Iran tensions rise

Biden to carry Georgia after second recount: state election official

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U.S. Senate leader McConnell urges new COVID-19 aid in broad funding bill

In Utah, the first U.S. state to confirm mink infections in August, about 10,700 mink have died on nine farms, said Dean Taylor, state veterinarian.

“On all nine, everything is still suggesting a one-way travel from people to the minks,” he said. Coronavirus testing has been done on mink that die and randomly on the affected farms, Taylor said. Like people, some mink are asymptomatic or mildly affected, he said.

The CDC said it was supporting states' investigations into sick mink, including testing of animals and people.

“These investigations will help us to learn more about the transmission dynamics between mink, other animals around the farms and people,” the CDC said. “Currently, there is no evidence that animals play a significant role in the spread of SARS-CoV-2 to people.”

Coronavirus is thought to have first jumped from animals to humans in China, possibly via bats or another animal at a food market in Wuhan, although many outstanding questions remain.

In Wisconsin, about 5,000 mink have died on two farms, State Veterinarian Darlene Konkle said.

One farm is composting the dead mink to dispose of the carcasses without spreading the virus, Konkle said. Authorities are

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working with the second farm to determine how to dispose of the mink, and dead animals are being kept in a metal container in the meantime, she said.

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“They are basically in a metal container, a roll-off type container, that is sealed off at this point,” Konkle said.

Michigan declined to disclose how many mink have died, citing privacy rules.

U.S. authorities are urging farmers to wear protective gear like masks and gloves when handling mink to avoid infecting the animals.

State officials said they are working

with the USDA to determine whether farmers can sell the pelts of infected mink. The pelts are used to make fur coats and other items.

“It’s our desire and certainly the owners’ desire to be able to use those pelts,” Konkle said.

The coronavirus has also infected cats, dogs, a lion and a tiger, according to the USDA. Experts say mink appear to be the most susceptible animal so far.

“Whatever we learn about mink is going to help understand the virus across species,” Taylor said. “It’s going to give us a better response to people to stop this pandemic.”

Reporting by Tom Polansek in Chicago;  
Additional reporting by Carl O’Donnell in  
New York; Editing by Cynthia Osterman

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# **Exhibit II**



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## About UDAF



With roots dating to 1921, the Utah Department of Agriculture and Food is one of the State's oldest agencies. It oversees dozens of legislatively mandated programs that promote the healthy growth of Utah agriculture, the conservation of our natural resources and the protection of our food supply. Two important programs are the Utah Grazing Improvement Program and the Invasive Weeds Mitigation Program. Both work to improve the health of our rangelands and watersheds.

In the area of food safety, the Department inspects the state's 4,000 retail stores and the many food processing plants for food quality and safety and correct item pricing.

The Department's Utah's Own Program works to reconnect consumers with their food supply and promotes the benefits of Utah's locally grown and processed foods which represent 15 percent of Utah's economy. The Department also protects animal health and the state's \$1 billion livestock industry, as well as guards against invasive insects.

**+ Divisions & Programs**

**- UDAF Mission, Values, and**

### LOCATION AND CONTACT

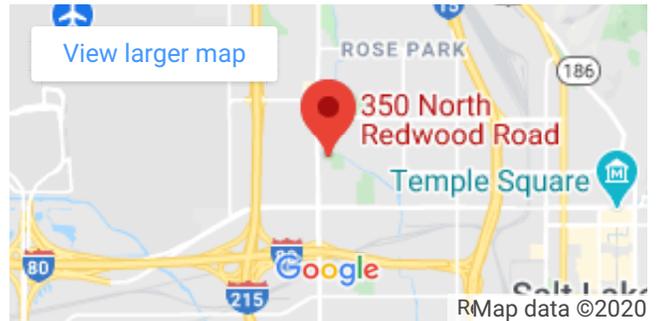
#### Utah Department of Agriculture and Food

350 North Redwood Road  
PO Box 146500  
Salt Lake City, UT 84114-6500  
(801) 982-2200  
(801) 982-2200 TDD/Hearing Impaired  
(385) 465-6022 Fax  
[agriculture@utah.gov](mailto:agriculture@utah.gov)

#### Business Hours

8 AM – 5 PM, Monday – Friday (MST)

#### Map



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# Priorities

## Our Mission

Promote the healthy growth of Utah agriculture, conserve our natural resources and protect our food supply

## Our Values

Integrity and respect; Stewardship and accountability; Growth and achievement; People and partnerships; Heritage and culture

## Our Priorities

Improve communication and awareness of agriculture; Conserve and enhance Utah's lands and natural resources; Ensure food safety and consumer protection; Build partnerships, advocates and develop agricultural leaders

## + UDAF Powers and Functions

## + Ag Affiliates, Committees, and Boards

## + UDAF Annual Report and USDA Statistics

## + UDAF Policies and Procedures Handbook

## + GRAMA Request Form

## [Plant Industry](#)

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## RECENT NEWS



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Utah Department of Agriculture and Food Issues Warning About Fraudulent Sanitizer and Disinfectant Claims Against Coronavirus



Department of the Interior Returns Management and Protection of Wolves to State, Tribes Following Successful Recovery Efforts



Just Released: UDAF's 2020 Annual Report



UDAF Migrating Information to New Software