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To the Director-General of Public Health
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To the Director-General of Agriculture
Ministry of Agriculture, Nature and Food Quality
Ms M. Sonnema, MSc
Postbus 20401
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Date 03 June 2020

Subject Advice regarding OMT-Z on minks and SARS-CoV-2

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Appendix
List of participants

Dear Ms Berg, dear Ms Sonnema,

As announced, I convened an Outbreak Management Team on Zoonosis (OMT-Z) on 3 June 2020 to address the transmission of SARS-CoV-2 from minks and the potential consequences for public health. A summary of the situation and the recommendations of the OMT-Z are provided below.

The OMT-Z consists of experts on veterinary and human infectious diseases. Representatives of both human and veterinary organisations and knowledge institutes were present at the consultation. The list of participants is appended to this letter.

Summary of the situation

SARS-CoV-2 infections were detected in the animals on eight mink farms. The severity of COVID-19 in minks at mink farms ranges from asymptomatic or mild to severe (pneumonia, death).

At the first four farms, infection was detected in late April and early May 2020. Three of those farms had minks that showed symptoms of illness, while the fourth did not have any animals that were ill. Infection at the fourth farm was discovered following intensified surveillance due to a link to another farm. The first two farms had been infected for some time, and the infection appears to be diminishing. At the other two farms, the virus is still in circulation amongst the minks. The expectation is that it could take another one or two months for this outbreak amongst the minks to die out completely. It is not yet known whether a second wave could emerge among the pups, since the young minks only receive temporary protection as a result of the maternal antibodies. At three farms, the virus appears to have been introduced by people, followed by mink-mink transmission. There have been two employees who were infected with a SARS-CoV-2 sequence that was also found in the minks; based on the sequencing, it can plausibly be assumed that humans were infected by minks. One of those people then probably spread it to two other people in their household.

Based on these infections, an Early Warning System has been set up for all mink farms. As part of this system, dead animals at all mink farms are tested for SARS-CoV-2 infection on a weekly basis, and antibody screening is taking place. It was recently revealed that four of the 53 mink farms subsequently investigated also had SARS-CoV-2 infections. It is unclear whether the virus was introduced by employees at these farms, but it seems plausible. We do not yet know how long the infection has been circulating in these farms, nor how long it will persist. The expectation is that all of the nearly 125 mink farms will have had their initial testing done by the end of the week.

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Request for advice

The objective of the OMT-Z is to assess the available research results and arrive at a veterinary assessment of the extent to which circulation of SARS-CoV-2 poses a risk to public health.

The OMT-Z will advise whether any adjustments and/or new measures related to veterinary care are necessary for public health purposes. The following questions from the Ministry of Agriculture, Nature and Food Quality and the Ministry of Health, Welfare and Sport were the guiding parameters in the OMT-Z discussion.

- What does it mean to public health if SARS-CoV-2 at mink farms does not die out quickly, or if it were to continue circulating at these farms for an extended period?
- What does it mean to public health if other animal species, such as cats, are infected with SARS-CoV-2 from these persistently infected mink farms and these species form reservoirs of the virus?
- How likely are these scenarios?
- What measures could be used to mitigate or prevent these risks to public health?
- Do the results of the investigation justify taking measures to prevent the formation of reservoirs of SARS-CoV-2 amongst (minks,) dogs and cats, from a public health perspective, and in what way would that be possible?

What does it mean to public health if SARS-CoV-2 at mink farms does not die out quickly, or if it were to continue circulating at these farms for an extended period?

Infected mink farms have been shown to pose a risk of spreading the virus to humans. This is primarily a risk to people who are exposed to the virus in the sheds at the mink farms. The people at risk are the owner and the owner's employees. It has been shown by now that the virus can in fact be transmitted to employees at the farm. People who contract the virus from the minks can in turn spread the infection to others via their social contacts (onward transmission), as was probably the case in the household mentioned above.

It is possible that more farms will turn out to be infected in the coming time, and/or that more farms will become infected because the virus is circulating amongst people. It is difficult to prevent humans from introducing the virus to minks, since people can be contagious even at a pre-symptomatic stage of infection. It may also be difficult to prevent people who only have mild symptoms from entering the sheds where the minks are housed. As a result, it is not possible to prevent minks from contracting the virus from an infected person in all situations. An additional problem is that the minks do not all display deviations and that the infected animals could be asymptomatic. In other words, an infection

could circulate for some time before being detected. And as long as the virus is circulating amongst the minks at a mink farm, it poses a potential risk for introduction (or reintroduction) to humans. There are still many aspects that remain unclear with regard to the chain of transmission from animal to human, making it difficult to estimate the exact risk to public health. Moreover, it is impossible to exclude the risk of new mutations in the event of ongoing transmission of this virus in the mink farms, followed by selection for specific variants that may pose an additional risk for the further spread of the virus amongst minks or humans. The OMT-Z notes that there are currently no indications of this at this time, and that the observed variations in virus sequence have been limited.

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As the infection pressure in the human population continues to drop in the longer term, and human-to-human transmission occurs relatively less often, it will become increasingly important to prevent mink-to-human infection. Minks could inadvertently become a reservoir for the virus, and thus present a persistent source of human infection, reintroducing the virus into the population from mink farms.

What does it mean to public health if other animal species, such as cats, are infected with SARS-CoV-2 from these persistently infected mink farms and these species form reservoirs of the virus?

If reservoirs of the virus were to form in other animal species than minks, that would also be undesirable. It is known that cats can become infected with SARS-CoV-2. In the Expert Consultation on Zoonosis (DB-Z) on 9 April 2020, the experts estimated that there would be a negligible risk of transmission from cats to humans. Rats and mice are not susceptible to SARS-CoV-2 infection. Dogs can become infected, but are less susceptible than cats.

It does not seem plausible that the undomesticated cats present at the investigated mink farms would form reservoirs, since these cats live solitary lives. These animals have now been chipped, and an initial check showed that they do not travel to other mink farms. Moreover, not all the undomesticated cats present at a mink farm have had an infection; results show that only one-third of them have had an infection. The population of undomesticated cats does not change in terms of structure, and will therefore not form a large reservoir. Although some things are still unknown with regard to the role of the undomesticated cats in the transmission between the mink farms, the expert opinion is that the virus is not expected to persist in this cat population. Similarly, this is not expected to pose a risk to domesticated cats.

Based on current data, this means that there is no threat to public health from animals other than the minks. However, it is advised with regard to the undomesticated cat populations at the infected farms to ensure that they are included in a risk management plan, and to prevent them from running off to other mink farms as long as they are potentially contagious.

How likely are these scenarios?

It has been shown that people pose a risk of introducing infection to minks, and that the virus has, in a few cases, been transmitted from the minks to humans. It is possible that even more infected mink farms will be discovered, since further investigation has only taken place at a total of 57 farms as of this OMT-Z.

Although the infections occurred in the region that has the highest incidence of COVID-19 in the human population in the Netherlands, it is plausible that infections may also have occurred elsewhere. It was also shown that mink farms could test positive for the virus without prior indication, since the animals show little to no symptoms.

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It also became apparent that it is difficult for employees in this sector to avoid entering the sheds when they have mild symptoms. Moreover, the expectation is that it would be a major undertaking to use personal protective equipment (PPE) correctly and consistently if people or animals are infected, since such use requires intensive training and supervision.

The scenario of human-to-mink and mink-to-human transmission can be considered realistic.

The risk of transmission from minks to the cats has also been shown. The risk of transmission from undomesticated cats to humans is considered negligible.

In an international context, only Spain has reported infections of employees at a mink farm. It is not known if the virus was introduced to the minks; further (serological) research is being conducted.

At two of the first mink farms identified, it is likely, based on virological and serological research (>90% of the mink bitches were seropositive), that the infection will die out within a few weeks. Long-term infection is unlikely here, but longitudinal surveillance of the pups will be needed to continue monitoring absence of the infection in this population of young animals.

Two of the mink farms identified later still have an active infection that is expected to persist for longer than a month (based on knowledge gained from the course of the infection at the first two infected farms). However, the infection could last much longer if the pups become actively involved in spreading the virus within the farms. Due to the lack of knowledge about the effects and course of maternal immunity, it is uncertain how the infection will progress in the pups; in the most unfavourable projections, the infection will not die out until the animals are killed around November for pelting purposes. Moreover, the peak viral load at the mink farms could increase above the current level in the event of active viral spread amongst the pups, since that would cause a significant spike in the number of animals involved in the infection (by a factor of 5-6). If that were to happen, it is uncertain whether the absence of the virus outside the shed/cage, as currently measured for adult animals, would still be a good indicator of viral load. The available information on the infected mink farms that were identified recently is not yet sufficient to estimate how the infection will progress on those farms. However, since these farms currently have an active infection (detected in the Early Warning System), and all mink farms are more or less in sync and were birthing pups between about 20 April and 10 May, it is likely that these recently detected infected farms will follow the unfavourable course of infections for the latter two farms, rather than the course of infections for the first two farms.

For other animal species: see the previous question.

What measures could be used to mitigate or prevent these risks to public health?

The following types of measures were discussed to prevent the risk of the continued spread of SARS-CoV-2 within and from mink farms; these measures could be applied separately or in combination.

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For infected mink farms:

1. Very strict isolation of the infected farms (with the measures in place) and longitudinal surveillance of the infection at those farms. This measure would have to take into account the assumption of the presence the virus over a long period of time (measures must not be relaxed). If the virus were to spread between the pups, there is a possibility of a major increase in the total viral load from an infected farm. There are doubts about compliance with the proposed measures, such as PPE use. Detailed protocols for employee protection would have to be developed, from a job safety perspective. Moreover, training courses would have to be organised, and an enforcement place would have to be drawn up. It would also be important to minimise the number of new employees who are allowed access to the farm. This is a challenge in periods involving busy work activity, such as will happen shortly when the young animals are being vaccinated. Moreover, there should be an explicit focus on working conditions and protections for migrant workers who operate in the sector during peak loads.
2. Culling and clearing the minks from the infected farms. This will prevent any mink farm from providing a persistent source of infection for humans, and will also prevent the infection from spreading amongst the pups, possibly accompanied by a major increase in the total viral load from an infected farm.

For non-infected mink farms:

It is essential for these farms to prevent introduction of the virus to the minks and to recognise infection at an early stage. This requires a combination of some of the afore-mentioned measures as well as intensive monitoring.

The OMT-Z discussed the possibility that the measures for these farms could range from good prevention of virus introduction combined with effective hygiene recommendations and intensive monitoring (Early Warning System and serological surveillance) to preventive culling.

Strict compliance with job safety and hygiene protocols is essential, and must be accompanied by symptom-based triage of employees and easy access to testing. Special attention will also be required for instructions to and implementation by migrant workers if they are working on the farms, e.g. taking into account the language barrier. Finally, monitoring cannot be limited to clinical manifestation, since infected minks could be asymptomatic. The OMT-Z realises that the feasibility of implementing strict hygiene measures in a farm setting is problematic, and dependent on appropriate action on the part of the owners/employers of the mink farms. For that reason, the OMT-Z can imagine that it could be a realistic option to come to that an arrangement to assist farmers of non-infected mink farms to end mink farming before 2024. With regard to preventive culling and clearing of non-infected farms, opinions in the OMT-Z were divided.

Do the results of the investigation justify taking measures to prevent the formation of reservoirs of SARS-CoV-2 amongst (minks,) dogs and cats, from a public health perspective, and in what way would that be possible?

For minks: see previous question.

For dogs and cats (and for hamsters and rabbits), it is not yet clear whether reservoirs could be formed. It is clear that cats can transmit the infection to other cats. This has not been shown in dogs. A research study will be starting shortly to

determine the proportion of infected cats belonging to COVID-19 patients and to quantify transmission between cats. Cat-to-cat transmission can be used to model whether cats could form a reservoir of the virus, or possibly maintain circulation along with humans. If that is a risk, then the results of the study can be used to take measures to limit infections in cats.

Mink farms that are cleared must take measures to prevent cats from moving to other mink farms. This could be achieved by feeding the cats for some time, or by placing them in quarantine.

I am available to provide additional verbal explanation of the recommendations.

Yours sincerely,

A handwritten signature in black ink, appearing to read 'J.T. van Dissel', with a horizontal line underneath.

Professor J.T. van Dissel, PhD
Director of the Centre for Infectious Disease
Control (CIb)

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