Surveillance Guidelines For SARS-CoV-2 In Farmed Mink In Canada

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This document was developed with input from the COVID-19 One Health working group consisting of Canadian public health and animal health experts, with representation from federal and provincial/territorial governments, the Canadian Wildlife Health Cooperative, the Canadian Veterinary Medical Association, and academia.

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1. Scope of the document

This document aims to provide guidance to the provincial animal health and public health authorities on the surveillance approaches to be applied for SARS-CoV-2 in Canada's farmed mink population. It is part of the National Guidance for Managing SARS-CoV-2 Infections in Farmed Mink.

Disclaimer:

- This document does not cover the surveillance approaches for SARS-CoV-2 that may be applied in human and wildlife populations in Canada. Whenever surveillance in human or wildlife populations is considered, there should be discussions among three groups to ensure cohesiveness in these surveillance components and make any necessary adjustment to achieve the desired surveillance objectives.
- This is an evergreen document. It may need to be updated to reflect new knowledge, information or surveillance data.

2. Early detection of the first SARS-CoV-2 incursion in mink farms in Canada

2.1. General principles

- Early detection surveillance is used for various purposes, including the detection of unusual increases of disease frequency if the disease is present and the first occurrence of a disease in a previously free population. This latter purpose is particularly important for SARS-CoV-2 infection in farmed mink due to the high animal health and public health consequences and the cost of delayed detection of a disease moving to new domestic and/or wild populations.

- The expression ''*Early detection''* refers therefore to the first detection and characterization of SARS-CoV-2 virus circulation in a farm or an area that was previously unaffected.

- This section describes therefore the surveillance approaches aiming to early detect the first case of SARS-CoV-2.

- As the surveillance objective is early detection in the context of absence of SARS-CoV-2 infection or disease in the mink population, the quality of surveillance can be assessed in terms of design prevalence (the hypothetical prevalence of disease that, if it were present, our surveillance would be able to detect) and surveillance (system) sensitivity.

- Key scientific conceptual elements to consider when designing an early detection surveillance component or system are: i) defining the unit of interest; ii) time frame for detection; iii) population coverage, and iv) temporal coverage.

2.2. Unit of interest

- The unit of interest in farmed animal disease surveillance may be individual animals, epidemiological units (e.g. farm) or higher-level units (e.g. province, county). It is proposed that the appropriate target unit for early detection is the epidemiological unit.

- In the context of SARS-CoV-2 surveillance in mink, the unit of interest is the farm.

2.3. Timeframe for detection

- The early detection approach implies a target time frame for detection, and this is the most difficult conceptual element. The estimated mean incubation period for an infectious disease may be used as an appropriate measure as we want to detect the disease before spreading from one epidemiological unit to another or to humans on farms..

- A timeframe for detection of <u>one</u> week is recommended. This refers to the periodicity of testing.

2.4. Population coverage

- The population coverage is the probability that a mink farm will be included in the surveillance system. When surveillance is based on representative sampling, this is equal to the number of units (e.g. mink farms) sampled and tested divided by the total number of units in the population (of farms).

- Therefore, it is important to have valid demographic data on farmed mink in order to make a valid estimation of the performance of the surveillance.

- A surveillance method that uses a higher population coverage will lead to higher surveillance sensitivity.

2.5. Temporal coverage

- The temporal coverage is the conditional probability that any mink farm in the population will be tested within the specified time frame of one week given that it is under surveillance.

2.6. Early detection methods

2.6.1. Clinical surveillance – Producer clinical reporting

- Clinical (or passive surveillance) typically takes the form of a disease-reporting system. If a producer or farm worker notices clinical signs suggestive of SARS-CoV-2 infection in mink or an increase in mortality rate (above a normal threshold), this must be reported and recorded in a systematic fashion.
- A producer clinical reporting system has theoretically a coverage of the entire population of farms, as every animal is owned by a farmer, and therefore every animal has a chance of being reported and detected if it becomes infected.
- Clinical surveillance involves a reporting chain that is dependent on several people (e.g. producer, private veterinarian). The weakest link in the reporting chain is usually the producer, who may not recognise the disease, or may fail to report it for other reasons.

- A typical 'detection cascade' in a passive farmer reporting system may look like this:
  - Infected animal shows clinical signs
  - Farmer is able to observe clinical signs
  - Farmer contacts veterinary services
  - Veterinarian examines animal and perform thorough disease investigation
  - Samples taken for diagnostic testing, and
    Samples tested for SARS-Cov-2. The initial testing of samples will occur in laboratories identified by provincial authorities and the confirmatory testing in National Centre for Foreign Animal Diseases (NCFAD), CFIA.

- Clinical surveillance must be applied in all mink farms in Canada. However, the performance of this type of surveillance may vary from one province to another and can be affected by the following factors but not limited to:
  - Under-reporting by producers;
  - Lack of legal requirements for SARS-CoV-2 notifications to authorities
  - Delays in detection– as the detection cascade comprises many steps;
  - Knowledge and awareness among producers on clinical observation of disease

- Annex #1 provides an example of information and data to collect on weekly basis for clinical surveillance.

- Given that it can be difficult to detect early infections in mink, active monitoring has been recommended by both the World Health Organization (WHO) and the World Organization for Animal Health (OIE) (OIE, 2020a, 2020b; WHO, 2020) . If a decision is made to not implement active surveillance on a routine, ongoing basis, the following triggers may be considered to move from clinical surveillance to active surveillance:
  - A confirmed SARS-CoV-2 infection in a farm worker or a producer on-farm.
  - A confirmed SARS-CoV-2 infection in a wild animal in the vicinity of a mink farm.
  - A confirmed SARS-CoV-2 infection in a mink farm surrounding other mink farms.
  - Unexplained clinical signs or mortalities on-farm.

- As the detection of infected mink farms may occur after the detection of SARS-CoV-2 cases in humans on-farm (e.g. Spain (Ministerio De Agricultura, 2020)) there would be a need for active surveillance for SARS-CoV-2 at the farm level in a context where there is an absence of clinical signs in mink (i.e.

asymptomatic animals present on the farm). In other countries such as France and Sweden where active surveillance was initiated in absence of clinical signs at the farm level, led to new detections of SARS-CoV-2 in farmed mink suggesting the need to conduct active surveillance in farms.

Key points– Clinical surveillance

- Clinical surveillance must be applied in all mink farms in Canada.
- Clinical surveillance may not be sufficient to detect the first case of SARS-CoV-2 in farmed mink.
- Active surveillance has been recommended by both the WHO and the OIE.

2.6.2. Active surveillance

- In the field of animal disease surveillance, data collection methods have been classified as 'active' or 'passive' depending on whether the provision of data is investigator-initiated (active) or observer-initiated (passive) (Hoinville et al., 2013). All surveillance activities where an investigator is looking for a disease or an infection (e.g. clinical signs, antibodies or antigens) are referred to as "active surveillance" (Hoinville et al., 2013). Active surveillance is a routine ongoing activity.

2.6.2.1. Risk-based surveillance

- Risk-based surveillance involves looking for disease where it is most likely to be present. We use our understanding of the disease to determine those animals that are most likely to be infected, and concentrate our surveillance effort there.

- The design of risk-based surveillance should be based on a risk assessment and it is a useful approach to optimise the use of surveillance resources.

- The design of a risk-based surveillance system requires prior, epidemiological knowledge on, e.g., the difference in occurrence of disease between population strata or the influence of risk factors.

- In the context of early detection, mink population strata should be defined at the farm or area levels depending on the presence of absence of sampling frame:
  - Applying risk-based surveillance at the farm level, or
  - Applying risk-based surveillance at the area level

- Sample size considerations:

  - Desired surveillance system sensitivity (commonly 95%)
  - Specified design prevalence (among sampling units)
  - Relative risk for sampling units in the high-risk group (relative to low-risk group)
  - Proportion of population in high-risk group
  - Test sensitivity
  - Specificity is assumed to be 100% after follow-up of any positives

2.6.2.1.1. Stratified sampling (Risk-based sampling method #1)

Meaning of ''stratified sampling''

- All mink on farm have a non-zero probability of being selected but sampling intensity is different between high-risk and low-risk strata resulting in a different sample size for each stratum.

Defining a risk factor and population strata

- It is possible to identify high-risk strata of farms where the probability of incursion is higher based on the following factors but not limited to:
  - Status of SARS-CoV-2 infection in humans linked with farms
  - Biosecurity measures on farms
  - Status of SARS-CoV-2 in wild animals surrounding the mink farms
  - Density of the farms

- To use a risk factor in the surveillance design, we need two things:

  - Defining and identifying the high-risk and low-risk farm populations
  - Describing the differences in risk between them. Quantifying the difference in risk is done using the relative risk also called the risk ratio, and abbreviated as RR.

Risk-based selection of population strata

- Random selection of farms should occur in each farm population stratum (High and low-risk farms)

Required sample sizes in high-risk and low-risk groups

- Regardless of the chosen risk factor to use (and associated data) we want to know: *''What should be the minimum required population coverage in each risk-group to be able to achieve a 95% surveillance sensitivity''.* To answer this question a risk-based surveillance model was developed where four scenarios were explored to analyze the impact sample sizes and relative risk on the required population coverages in both risk strata :

  - Scenario 1:
    - 5 samples to be collected and tested per farm
    - Relative risk in the high-risk stratum varied from 2 to 5

- Scenario 2:
  - 10 samples to be collected and tested per farm
  - Relative risk in the high-risk stratum varied from 2 to 5
- Scenario 3:
  - 15 samples to be collected and tested per farm
  - Relative risk in the high-risk stratum varied from 2 to 5
- Scenario 4:
  - 20 samples to be collected and tested per farm
  - Relative risk in the high-risk stratum varied from 2 to 5

- Assuming a time coverage of one, the proportion of farms to be tested in each risk group per week to achieve a detection level of 95% as well as the minimum number of animals to test are calculated and described in the table below:

Table 1. Minimum required population coverage in high and low-risk farms (at a within-farm design prevalence of 0.2) for each scenario

Scenarios	Relative risk	Required population coverage		Combined Surveillance Sensitivity (HR and LR)
		HR	LR	
1	2	1	1	0.65*
	3	1	1	0.65*
	4	1	1	0.65*
	5	1	1	0.65*
2	2	1	1	0.88*
	3	1	1	0.88*
	4	1	1	0.88*
	5	1	1	0.88*
3	2	1	0.96	0.95
	3	1	0.96	0.95
	4	1	0.94	0.95
	5	1	0.93	0.95
4	2	1	0.88	0.95
	3	1	0.85	0.95
	4	1	0.80	0.95
	5	1	0.76	0.95

*HR: high-risk stratum; LR: Low-risk stratum; *Refers to the maximum surveillance sensitivity for scenario 1& 2, therefore a (95% surveillance sensitivity is not achieved for both scenarios). Similar results were seen even with a finite population.*

- To maintain 95% surveillance sensitivity and depending on the relative risk input value to be used:
  - A minimum of 15 animals per farm should be sampled per week from each farm group (HR and LR groups) with a population coverage in the HR and LR strata of 100% and 93% (a minimum) respectively; OR
  - A minimum of 20 animals per farm should be sampled per week from each farm group (HR and LR groups) with a population coverage in the HR and LR strata of 100% and 76% (a minimum) respectively;
  - Oropharyngeal swabs should be collected.[1]
  - As the relative risk input value has an impact on the population coverage, a good justification should be provided to make sure that the population coverage estimates are valid.
- The context of application of stratified risk-based in a given province should depend on the feasibility of the surveillance and most importantly on the availability of risk factor data/information and the number of farms (in the province).

Spatial sampling

- If there is no sampling frame of the farms, geographical locations can be identified and selected.
- All mink farms located in the higher-risk area should be identified and targeted.

Key points– Stratified sampling

- **High-risk stratum:** All high-risk farms should be sampled and tested.
- **Low risk stratum:** A minimum of 93% of low-risk farms should be sampled and tested.
- **Sample size**: Sample a minimum of 15 animals per farm on a weekly basis from each risk stratum.
- **Sample type:** Oropharyngeal swabs.

[1] SARS-CoV-2 virus was found in the majority of throat and rectal swabs collected from dead mink from two farms in the Netherlands (Oreshkova et al., 2020). Data from the Netherlands outbreak showed that viral loads in mink were higher in the throat swabs than in the rectal swabs (Munoz-Fontela et al., 2020). Molenaar et al. recommended the use of oropharyngeal swabs in mink for surveillance purposes (Molenaar et al., 2020). Danish outbreak data demonstrated that oropharyngeal swabs are an effective sample type for detecting SARS-CoV-2 in mink (Hammer AS, 2021).

2.6.2.2.1. Targeted sampling (Risk-based sampling method #2)

Meaning of targeted sampling

- Sampling is focused on a defined sub-population that is expected to have a higher prevalence of the disease which results in a single sample size.

Targeted unit of interest

- This approach should ideally be targeting a farm in a high-risk stratum.
- Targeted sampling could also be applied in a farm (regardless of risk of introduction) where a specific animal type is sampled (dead or sick subpopulation vs apparently healthy animal subpopulation)

Sampling plans

- **Sampling plan #1– Dead & Sick Mink Surveillance (D&SMS)**

  - Required sample size: Sample a minimum of 15 animals per farm on a weekly basis (assuming a within-farm design prevalence of 20%).
    - Sick and dead mink are targeted and sampled.
  - Sample type: Oropharyngeal swabs should be collected on selected animals.
  - If the pooling strategy is applied, annex #2 provides more information on the minimum required number of pooled samples to provide a 95% probability of detection for varying prevalence estimates and pool size.
  - Sampling plan #1 should be applied on a high-risk farm (with a high risk of introduction)
  - Sampling plan #1 can be applied in a farm with unknown risk of introduction or when ongoing testing started for the first time.

- **Sampling plan #2– Dead Mink Surveillance (DMS)**

  - Required sample size: Sample a minimum of five (5) dead animals per farm on a weekly basis (assuming a within-farm design prevalence of 50%).
  - Sample type: Oropharyngeal swabs should be collected on dead mink.
  - If the pooling strategy is applied for DMS, please refer to annex #2 .
  - Sampling plan #2 targets **dead animals** in which SARS-CoV-2 is most likely to be detected if present in the farm. Dead mink surveillance is an efficient and biosecure method for detecting viral infection with SARS-CoV-2 at an early stage of the disease.

- Mortalities should ideally be sampled at the "roadside". The premises are not entered by the sampler (e.g. private veterinarians) reducing therefore unnecessary contacts with animals on site.
- This surveillance is not statistically valid sampling (convenience sampling), but it is cost-effective for case detection and monitoring the health of the farm.
- Sampling plan #2 should be applied on a farm with a low risk of introduction.
- Sampling plan #2 can be converted to sampling plan #1 (see above) if there is a increase of risk of introduction.

Key points– Targeted sampling

- **Sampling plan #1 (Dead & Sick Mink Surveillance)** should be applied on a high-risk farm or a farm with an unknown health status.
- **Sampling plan #2 (Dead Mink Surveillance)** should be applied on a farm with a low risk of introduction.
- **Sampling plan #2 can be converted to sampling plan #1** if there is a increase of risk of introduction.

2.6.2.3. Periodic surveys– Representative sampling

- The design of a structured survey will depend on the knowledge of animal and farm population sizes, structure and distribution of the population, the epidemiology of the infection and the resources available. The followings are key considerations to consider when designing periodic surveys.

Surveillance objective

- Periodic surveys imply recurrent/ongoing testing over time at the farm level with the objective of early detection of SARS-CoV-2 in the population.

Timeframe for early detection

- As stated above, the ideal timeframe for early detection in the context of active surveillance should be one week.

Design prevalences and sampling

- When selecting units from a target population to have a representative sample, probability-based sampling, such as a simple random selection should ideally be used.
- The detection level at the farm level should be low (1% of the farms) to be able to fulfill the surveillance objective. Given the small number of mink farms (approximately 70 farms current stocked farms across Canada) and the detection level of 1% at the farm level, we expect that all farm will be tested. The within-farm prevalence should be 20% of the animals, based on the high level of transmission reported within mink farms.
- The selection of animals must be random. Two options are possible, either selecting a representative number of animals from each barn/building or from the whole farm (without taking into the clustering at the building/barn level). Feasibility, risk of introduction, cost and resources considerations should be taken into account in the final design of the surveillance as this is an ongoing surveillance strategy.

Sensitivity and specificity of the diagnostic testing regime

- The performance of diagnostic tests on individual animals is described by the sensitivity and the specificity. The sensitivity is the probability that the test will give a positive results in an infected animal (the true positive rate). The specificity is the probability that the test will give a negative result in an uninfected animal (the true negative rate).
- When the purpose of surveillance is to early detect SARS-CoV-2 infection, imperfect specificity means that there is a possibility of false positives. A false

positive means that we will conclude that the farm is infected, when it is truly uninfected. This is a major issue as it may result in the implementation of costly emergency control activities and the potential loss of trade opportunities. For these reasons, steps are normally taken to ensure that the specificity of any diagnostic system in such surveillance is as good as possible. Normally there are a series of confirmatory tests, and an animal is only considered positive if it gives a positive result to each of the confirmatory tests. This makes the specificity very high (but decreases the sensitivity).

- Based on this logic, the specificity of the surveillance system to detect SARS-CoV-2 infection is normally assumed to be 100%.
- In the context of SARS-CoV-2 surveillance in mink population, serological and virological tests can be used. Serological testing will aim to confirm past/historical exposure to the virus and whereas virological testing is used to detect the presence of an active SARS-CoV-2 infection.
- Currently, virological testing is more readily available for surveillance in Canada (** confirmation from all provincial labs is needed**).
- In this document, it is assumed that PCR test sensitivity is 0.95. When validation data is available, this test performance assumption should be confirmed with the laboratory for the PCR test that will be used. At the moment, no test validation data is available from NCFAD on the performance of PCR testing.
- Serological testing may be considered in the testing regime if validated serological tests are available.

Specimens to collect and test

- Oropharyngeal swabs should be collected for PCR testing.

Desired surveillance system sensitivity

- In epidemiological descriptive studies, we must specify the probability (usually 95%) that the confidence interval[2] for your estimate will include the true population value. In the context of early detection the confidence is the probability that a surveillance system (or component) will detect infection if the population were infected (at a specified design prevalence or greater). Confidence therefore refers to our confidence in the ability of a surveillance system to detect infection.
- In practice, a confidence level of 95% as a minimum standard should be used assuming a Type I (alpha) error rate of 5%.

Size of the animal population

[2] *Confidence interval: An estimated range of values within which, 95% of the time, the true value would fall.*

- A finite population refers to 1,000 animals or less. An infinite population refers to 1,000 animals or more.

Minimum required sample size

- As the data on the population size of the mink farms were not available yet, different farm sizes were used to calculate the minimum required sample sizes (see Table 2).

  Table 2. Number of samples to test by farm size (assuming a 95% test sensitivity and assuming no clustering within the farm)

Population type	Farm size (range)	No. of animals to test
Infinite population	1,000 and more	15
Finite population	Less than 11	All animals
	11 - 13	9
	14 - 18	10
	19 - 25	11
	26 - 38	12
	39 - 73	13
	74 - 362	14
	≥ 363	15

Pooling of samples

- To reduce the cost of the testing or when individual results are not needed, specimens from a number of animals may be pooled and tested as one sample. It is important to know that many factors affect the sensitivity and specificity of a pooled sample (PlSe and PlSp) such as: the homogeneity of mixing, the effects of dilution of analyte, the increased possibility of having extraneous cross-reacting substances added to the pool because of the inclusion of material from more animals.
- The pool-level test sensitivity and specificity should be estimated by the diagnostic laboratory to allow an appropriate calculation of the number of pools required. It is ***assumed*** to be 0.95 (**this is optimistic. The laboratory should provide a valid point estimate**).
- Annex #2 provides more information on the minimum required number of pooled samples to provide a 95% probability of detection for varying prevalence estimates and pool size.

3. Surveillance When SARS-CoV-2 Is Clinically Suspected

*** This section may be needed depending on the provincial legislative framework where a provincial animal health authority needs to confirm the presence or absence of virus circulation based on clinical signs (see below case definition) once they receive a notification from the producer or a private veterinarian.***

3.1. Baseline surveillance

Surveillance plan objective

- To confirm presence or absence of an active infection of farmed mink.

Case definition

- A suspected case is defined in the ''Guidance for managing SARS-CoV-2 infections in farmed mink in Canada''

- As clinical surveillance is based on the clinical inspection of animals and on the monitoring of mortality rate at the farm level, different scenarios may be seen in practice: 1) presence of clinical signs only (without unusual mortality), 2) presence of clinical signs and unusual mortality, 3) presence of an unusual mortality without the presence of clinical signs.

- No data is available to-date to estimate the ''baseline'' mortality rate at the farm level and what would constitute an alert or an ''unusual mortality'' as stated above on farmed mink sites. For example, Belgium recommended that as soon as more than 5% of the mink on farms present clinical signs or a mortality exceeding 1%, samples should be collected for testing.

- Provincial authorities can recommend to producers to record daily feed consumption, clinical signs and mortality so that unusual trends can be identified quickly.

Sensitivity and specificity of the diagnostic testing regime

- Sensitivity and specificity of tests should be obtained from the laboratory that will perform testing.
- In this document, we assumed the following: a PCR test sensitivity of 0.95 and perfect test specificity.

Within-farm design prevalence and sample type:

- Oropharyngeal swabs will be tested by PCR.
- The required sample size provides 95% confidence in detecting SARS-Cov-2, if the prevalence of infection in the shed is 5% or greater. A surveillance design in the context of demonstrating absence of virus circulation using high design prevalence values of more than 5%, are, in general, less convincing, and must be justified and supported by sound arguments as to why failing to find infection at the specified level may be considered equivalent to complete freedom from infection.

Minimum required sample size

- Number of animals to test per shed within the farm
  - Live animals: Sample **62 animals per shed** (assuming a 5% design prevalence and a large population– i.e. 1,000 animals or more). Table 3 (on page 20) provides the required sample size for a finite population (farm population size less than 1,000 animals).
  - Deadstock (if present): a minimum of 5 dead mink are required for testing (assuming of 50% design prevalence in this subpopulation).

- Pooling of samples: See Annex #2.

Table 3. Number of samples to test by farm size (assuming a 95% test sensitivity, a within-farm design prevalence of 5% and assuming no clustering within the farm)

Population type	Farm size (range)	No. of animals to test
Finite population	< 44	All animals
	44 - 47	35
	48 - 53	37
	54 - 55	38
	56 - 59	39
	60 - 63	40
	64-67	41
	68-71	42
	72-77	43
	78-83	44
	84 - 89	45
	90 - 95	46
	96 - 103	47
	104 - 113	48
	114 - 123	49
	124 - 137	50
	138 - 151	51
	152 - 169	52
	170 - 191	53
	192 - 219	54
	220 - 255	55
	256 - 305	56
	306 - 377	57
	378 - 487	58
	488 - 685	59
	686 - 999	60

4. Outbreak surveillance– Surveillance Following the Index Case

*** The terminology of infected zone or restricted zone for example is avoided as it may have a different meaning at the provincial level, a generic terminology is used instead.***

***It is recognized that provincial disease response plans may use different zoning strategies. The following can be considered during outbreak management depending on the epidemiological context and desired outcomes. ***

4.1. Zone #1: One to three-km radius surrounding the index case

- The delineation of the area may vary depending on physical and geographic boundaries, the apparent progression of the outbreak, the density of farms
- A minimum 1-km radius and up to 3 km surrounding an infected farm is considered Zone #1.
- Quarantine release surveillance for the farm(s) under quarantine. The quarantine release surveillance validates the success of disease control measures, and provides confidence that they have been successful, thus supporting the rationale for releasing the quarantine. Quarantine release surveillance applies to all farms under quarantines and should include two rounds of testing:
  - A first round of testing: conduct baseline surveillance as explained above once the quarantine is put in place.
  - A second round of testing: baseline surveillance to be repeated 14 days after the first round of testing.
- Conduct surveillance as follows for farms in Zone 1 that are still not considered infected:
  - Provide information to the owners on clinical signs of SARS-CoV- and the call-in numbers to report any sick animal;
  - Monitoring clinical and mortality data on the farm (Annex 1)
  - Dead & Sick mink surveillance (D&SMS) or Dead mink surveillance (DMS)
  - Pre-movement surveillance if needed (same as baseline surveillance). Pre-movement surveillance provides information on the active infection status of a premises, to avoid disease spread through movements of animals or products.

4.2. Zone #2: A radius of 10 km from the infected premises

May be established depending on the extent of the outbreak.

- Identify all mink farms in zone #2;
- Provide information to the producers on clinical signs of SARS-CoV-2 and the call-in numbers to report any sick animal;
- Conduct surveillance as follows:
  - Dead mink surveillance **or** Dead & sick mink surveillance (targeted sampling);
  - pre-movement surveillance if needed (same as baseline surveillance)

4.3. Zone #3: Where absence of SARS-CoV-2 circulation is assumed

- In order to build an evidence of absence of virus circulation, ideally testing of farmed mink should start before the detection of the first case.
- The concept of a ''free'' zone may be challenged: 1) given the circulation of the virus in a the human population, and 2) the unknown status of wildlife. Compartmentalisation may be a good approach to apply to confirm negative status.
- If Zone #3 is defined as a zone where there is absence of SARS-CoV-2 circulation in the mink population. The following ongoing surveillance methods can be considered to provide a proof or an evidence of absence of virus circulation.
  - Clinical surveillance (ongoing); and
  - Dead mink surveillance or Dead & sick mink surveillance (targeted sampling) or Stratified-risk based sampling method with HR and LR groups.

5. Post-Outbreak Surveillance

- The objective here is to confirm absence of virus circulation in mink farms. In this context, compartmentalisation is a reasonable and ideal approach to apply.

5.1. Maintaining a ''negative'' disease status at the farm level

- To maintain a 'negative'' disease status of a mink farm, it is critical to take into account the risk of introduction (RI) of SARS-CoV-2 at the farm level and adapt the level of sampling to the RI.
- Two surveillance options can be implemented:
    - Option #1: Dead & sick mink surveillance. Testing a minimum of 15 animals per the farm (and not per shed) on a weekly basis. Sick and dead animals are targeted. Option #1 is recommended when there is a higher risk of introduction of SARS-CoV-2 to the farm.
    - Option #2: Dead mink surveillance as described above.
      Option #2 is recommended when a low risk of introduction of SARS-CoV-2 to the farm is assumed or justified.

5.2. Compartmentalisation

Meaning of a compartment (OIE definition)

- *'' means an animal subpopulation contained in one or more establishments, separated from other susceptible populations by a common biosecurity management system, and with a specific animal health status with respect to one or more infections or infestations for which the necessary surveillance, biosecurity and control measures have been applied for the purposes of international trade or disease prevention and control in a country or zone. ''(OIE, 2019b)*

Principles for defining a compartment

- Please refer to Chapter 4.4 of the Terrestrial animal health code (OIE, 2019a).

Defining the compartment requirements

- Scott et al. (2006) developed criteria and guidelines for the application of the concept of 'compartmentalisation'' that can be applied to the mink sector in Canada (Scott A., 2006). The authors defined the following seven (7) fundamental requirements:
  1. *'' Definition of the compartment;*
  2. *Epidemiological separation of the compartment from potential sources of infection;*
  3. *Documentation of factors critical to the definition of a compartment;*
  4. *Supervision and control of the compartment;*
  5. *Surveillance for the agent or disease;*
  6. *Diagnostic capabilities;*
  7. *Emergency response, control, and notification capability''*

- Testing requirement for farm workers and wildlife in the vicinity of the compartment should be considered.

6. References

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Annex 1. Template For Monitoring Mink Illness and Mortality Data At The Farm

Weekly Mink Illness and Mortality Monitoring Sheet

Farm ID: _____ Herd veterinarian: _____

Shed ID: _____

Respiratory signs: sneezing, coughing, rapid/laboured breathing, eye/nose discharge

Gastrointestinal (GI) signs: vomiting, diarrhea, bloody stool

Week of:	**Mon**	**Tues**	**Wed**	**Thurs**	**Fri**	**Sat**	**Sun**
# found dead							
# respiratory signs							
# GI signs							
# decreased appetite							
# culled							
# medicated (see notes)							
# escaped							
Total # mink at end of day							
NOTES: (Include names of any drugs given to animals on what day, and any notable conditions that may affect the condition of the mink (e.g. extreme weather, intrusions by wildlife, change in feed supply, water issues etc.). Use back of sheet for additional space.)							

Please complete one sheet per shed per week
Submit weekly (every Monday) to XXXX
[enter contact information here]

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Annex 2. Pooled sampling– Sample sizes for varying prevalence and pool size

Assumptions:

- No dilution effect on analyte of interest
- Homogeneous mixing
- Assumed pool sensitivity (PlSe) = 0.95
    - Test validation studies are needed to provide a valid estimate of PlSe
- Confidence level= 0.95

For example: For a pool size of **2** (i.e. combining two samples from two animals), a minimum of **8** pools (thus a total of 16 animals) must be tested to provide 95% probability of detecting a **prevalence of 20%**.

No. of individual samples in one pooled sampled (pool size)	Design prevalence							
	0.01	0.02	0.03	0.04	0.05	0.1	0.2	0.5
1	314	157	104	78	62	31	15	5
2	157	79	52	39	31	16	**8**	3
3	105	53	35	26	21	11	5	2
4	79	40	26	20	16	8	4	2
5	63	32	21	16	13	7	3	2
10	32	16	11	8	7	4	2	2
15	22	11	7	6	5	3	2	2
20	16	8	6	4	4	2	2	2
25	13	7	5	4	3	2	2	2
30	11	6	4	3	3	2	2	2