OFFLU Guidelines for High Pathogenicity Avian Influenza Virus Risk Mitigation in Cattle

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1. Background

High pathogenicity avian influenza viruses (HPAIVs) of the A(H5) Goose/Guangdong (Gs/Gd) lineage[1] continue to pose a major threat to animal and human health worldwide [1–3]. Previously largely restricted to avian hosts, these viruses have recently been involved in numerous interspecies transmission events affecting an expanding range [1–3]. In early 2024, the first confirmed transmission of A(H5N1) virus to dairy cattle in the United States (US) was reported, involving clade 2.3.4.4b, US genotype (as defined by the 'GenoFlu' [4]) B3.13 [5–7]. Since then, cattle have shown their capacity to sustain the circulation of the B3.13 virus lineage, and the detection of at least two additional US genotype D1.1 viruses in dairy herds in early 2025 suggests multiple independent interspecies transmission events [7,8]. Experimental infections further confirm cattle's susceptibility to other A(H5N1) [9–11]. As of September 2025, sustained spread in cattle appears geographically limited to the US. However, the repeated occurrence of these viruses in an atypical host raises urgent concerns about zoonotic risk, animal health, and the potential for similar incursions in other regions and species. Given its animal and public health impact, HPAIV in cattle meets the WOAH Terrestrial Code definition of an "emerging disease," requiring Member Countries to notify its occurrence, and underscores the need for timely, evidence-based risk mitigation strategies.

This **OFFLU Applied Epidemiology Technical Activity** document provides **practical, evidence-based risk mitigation measures** to support countries in making informed decisions to curb the spread of HPAIVs into and within cattle populations, and offers a flexible framework that can be adapted to diverse regional contexts. Using the 2024- onwards A(H5N1) clade 2.3.4.4b outbreak in US dairy cattle as a case study, we first outlined putative risk pathways for virus introduction into farms, transmission within and between herds, and onward spread to other species, including humans. These pathways were then assessed through an extensive literature review to propose intervention strategies, proportionate to the identified risks, and grounded in current scientific evidence. It is evident that high rates of virus transmission have occurred both within and between US dairy farms, likely influenced by local structural characteristics of the production system, including intensive management practices, large herd sizes, spatial clustering of farms, and substantial inter-farm movement of cattle, workers, and vehicles. However, the mechanisms of transmission to and within cattle herds are not fully elucidated, representing a key constraint in the development of risk mitigation measures [5,12–14]. While experimental infections show multiple possible routes, the dominant pathways under field conditions remain unresolved [11,12,15–17].

2. Risk Mitigation Measures

The recommendations presented in this document should be adapted to local contexts, considering the characteristics of the relevant production systems (**Fig. 1, Appendix**). These systems plausibly vary in their likelihood of acquiring and transmitting infection, and they present different opportunities and constraints regarding the feasibility and sustainability of risk mitigation measures. Although current evidence links infection primarily to dairy cattle, limited investigations in beef and non-lactating cattle mean that the susceptibility of these populations, and their potential role in onward

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[1] This term refers to A(H5) viruses genetically associated with, but not necessarily direct descendants of, the A(H5) Goose/Guangdong/1/96 isolate.

transmission remains uncertain [5,12]. For surveillance planning, we refer to the '**FAO Recommendations for the surveillance of influenza A(H5N1) in cattle (2024)**' [2] as a framework for adapting strategies to local capacities, production systems, and epidemiological conditions.

2.1. Pathway 1: Incursion into a cattle farm of an HPAIV lineage not yet circulating in cattle

Risk context: To date, only three independent events of HPAIV transmission into cattle from other host species have been documented, highlighting the apparent rarity of such occurrences. However, cattle in regions where HPAIV is endemic in poultry have not been systematically screened, and infections, particularly subclinical cases, may have remained undetected. Nevertheless, it is unlikely that such infections have resulted in undetected, long-term sustained transmission of a HPAIV lineage among cattle populations outside the US.

Key recommendations:

- Although wild birds are recognised reservoirs of HPAIV, transmission to cattle may also occur indirectly through peri-domestic animals, for example, via contaminated water or feed [5,7,18,19]. However, given the very low likelihood of such events leading to sustained transmission in cattle, and the difficulty of fully preventing contact between cattle and peri-domestic wildlife in most production systems, no additional biosecurity measures are recommended beyond regular/standard, non-pathogen-specific practices (namely pest control, restricting access to feed, water, bedding, and milking equipment; the latter being essential for routine mastitis prevention). Poultry populations in which HPAIV is endemic may also serve as a potential source of infection for cattle, meaning that enhanced infection prevention and control minimising HPAIV prevalence in poultry remains the key strategy to reduce the risk of cattle exposure.
- Emphasis should be placed on surveillance to enable the early detection of viral incursions that are transmitting in a cattle population in previously unaffected countries or territories, allowing for a rapid response to limit onward transmission among cattle. Approaches may include serology, testing of individual cow milk samples, and, where feasible, bulk milk testing. Bulk milk testing may be particularly relevant given its practicality and greater sensitivity for detecting herd-level infection compared to individual animal testing. Surveillance should ideally be risk-based, focusing on high-risk populations identified by HPAIV spatio-temporal patterns in wild birds and poultry, as well as by assessments of the wild bird–dairy cattle interface and, in endemic regions, the cattle–poultry interface.
- HPAIV should be included as a differential diagnosis, prompting testing in cases of unexplained reductions in milk production, mastitis, respiratory signs, or unexplained mortality in cattle, small ruminants, companion animals (especially cats, including those showing neurological signs [20–22]), and peri-domestic animals on or near farms, particularly in areas identified as high-risk and/or where HPAIV is known or suspected to be circulating.

2.2. Pathway 2: Incursion into a cattle farm of an HPAIV lineage circulating in cattle but not in the focal country or territory

Risk context: Although long-distance transmission of HPAIV via wild birds is possible, current genomic evidence does not support their role in sustained transmission of HPAIV between cattle herds in the US [12,23]. Moreover, preventing all contact between cattle and wild birds is not feasible in most production systems [12,24]. As with **Pathway 1**, no additional biosecurity measures are recommended beyond standard practices aimed at reducing access to feed, water, bedding, and milking equipment.

Key recommendations:

- Risk mitigation measures related to trade should be informed by commodity- and context-specific risk. Given that movement of infected dairy cattle have been identified as a major pathway for long distance transmission events, key considerations include:
    - Prohibiting the movement of dairy cattle from affected herds, and requiring pre-movement HPAIV testing, post-arrival quarantine and re-testing, for animals originating from herds in which the infection was not detected. While the quarantine period prior to re-

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[2] https://doi.org/10.4060/cd3422en

    testing should exceed the virus's latent period, it is important to consider that intermittent viral shedding may result in missed subclinical infections [12,16,25]. In the US, a 30-day quarantine period is currently advised for all introduced animals, as this duration encompasses the period beyond which infected cattle are expected to shed the currently circulating viruses [11,15,26].
    - For lactating cows, quarantined animals should ideally be milked using separate equipment. Where separate quarantine milking facilities are not available, an approach is to milk these animals at the end of the milking sequence, followed by strict cleaning and disinfection of milking equipment and the parlour environment until post-arrival testing is completed.
    - Ensuring adequate thermal treatment of milk (e.g. pasteurisation) before trade into the targeted country or territory.
    - Contamination of meat appears to be rare based on current evidence, and specific mitigation measures are not currently recommended [12,18,27]. No data are currently available regarding the presence of HPAIV in bovine reproductive products such as semen or oocytes.
- Sharing of equipment originating from affected areas should be avoided. Where sharing is unavoidable, strict cleaning and disinfection protocols must be followed. In contexts where affected and unaffected countries or territories are neighbouring and cross-border husbandry practices occur – such as transboundary or long-distance movements towards shared grazing areas and watering points – additional measures may be needed to reduce contact between herds. Two complementary approaches may be considered: **(i)** minimising opportunities for inter-herd mixing, for example during grazing, and/or **(ii)** implementing testing and quarantine at re-entry points into the target country or territory.
- In regions where farm workers move between affected and unaffected countries or territories, individuals who have had contact with cattle or poultry in affected areas should be asked to report any clinical signs that they develop. Where possible, their access to cattle premises in the target country or territory should be minimised for a period corresponding to the potential course of infection following their last contact with cattle or poultry in an affected country or territory. If access is unavoidable, entry should be conditional on strict adherence to hygiene and biosecurity protocols to minimise the risk of them acting as fomite.
- Surveillance should aim to enable early detection and may be risk-based and targeted, following the principles outlined under **Pathway 1**.

2.3. Pathway 3: Incursion into a cattle farm of an HPAIV lineage circulating in cattle in the focal country or territory

Risk context: Transmission of HPAIV between cattle farms likely involves multiple direct and indirect routes [12,23,28,29]. The movement of infected cattle is the most clearly documented route [1,7,11,23,30]. However, infections have also been reported on farms without recent cattle movements [12,18]. This suggests the possibility of indirect routes of transmission. Potential routes include the movement of people, vehicles, and equipment between premises, wind-based dispersal, contacts with wild birds and peri-domestic animals that may have become infected or contaminated on an affected premise, as well as shared use of water sources and grazing areas.

Key recommendations:

- When HPAIV is introduced into cattle in a previously unaffected area, the surveillance priority shifts to the detection of newly affected herds to limit the onward transmission of the virus to other herds. Surveillance efforts should target both the detection of infected individual animals, such as by considering HPAIV as a differential diagnosis for unexplained decreases in milk production mastitis or respiratory signs, and the identification of herd-level viral circulation, for example through bulk milk testing or investigations triggered by unexplained mortality in peri-domestic and domestic mammals or birds (see **Pathway 1**). A component of the surveillance system should ideally be risk-based, targeting herds considered at higher risk of infection, either due to **(i)** intrinsic farm characteristics, their spatial location or the production system structure, or **(ii)** epidemiological links to confirmed cases identified through backward and forward contact tracing.
- Where available, surveillance efforts should incorporate wearable sensor technologies to detect early deviations in rumination or body temperature, which may indicate infection prior to the appearance of overt clinical signs [3,25].

- Movements from affected herds should be prohibited until viral clearance is confirmed based on guidance for surveillance for herd-level freedom from disease outlined in '**FAO Recommendations for the surveillance of influenza A(H5N1) in cattle (2024)**'[3]. Exceptions may be made for movements required for animal welfare, provided that strict biosecurity measures are in place to prevent onward transmission to other herds. In pasture-based systems, the feasibility and modalities of implementing quarantine must consider shared grazing and water sources, long-distance herd movements, and the geographic proximity to affected areas.
- For movements from herds not known to be infected, pre-movement HPAIV testing, post-arrival quarantine and re-testing should be implemented according to the local epidemic context, surveillance capacity, and availability of veterinary resources. Depending on these constraints, testing may be prioritised for high-risk animals (e.g. lactating cows from farms found to be epidemiologically linked to infected premises).
- Other biosecurity measures should be reinforced across all farms. Key actions where possible include: restricting farm access of workers and veterinarians associated with external cattle and non-cattle livestock operations; avoiding the sharing of equipment or personnel between cattle farms or between cattle and non-cattle livestock operations; cleaning and disinfecting incoming vehicles and equipment; heat-treating or acidification of waste milk or ensuring its safe disposal to prevent access by peri-domestic or domestic animals [12,31–34]; complying with standard pest control and limitations of access of peri-domestic and domestic animals to feed, water, bedding and potentially contaminated areas – especially milking parlour and waste storage sites.
- The specific surveillance and risk mitigation strategies and their intensity should be adapted to the epidemiological context – particularly whether the virus has been recently introduced and elimination is considered a short-term, achievable goal, or whether the virus is already established and widespread in the cattle population. In the former scenario, where there is potential to contain the outbreak early, efforts should focus on strict enforcement of cattle movement restrictions, especially where infection is suspected or confirmed, and on limiting the sharing of equipment or personnel between farms (as detailed above). In the latter case, efforts may initially focus on reducing viral burden and reducing the risk of interspecies transmission, including zoonotic, (see **Pathway 5**), with elimination potentially considered as a longer-term objective.

2.4. Pathway 4: On-farm transmission among cattle

Risk context: On-farm transmission of HPAIV may occur through multiple pathways, making interruption of viral spread within herds challenging and potentially resource-intensive. While milk and milking procedures are generally considered the primary routes of intra-herd transmission [1,5,12,18,22], other routes may also contribute, including respiratory transmission, mouth-to-teat transmission, contaminated feed, water, and waste, contacts with domestic or peri-domestic animals [5,7,12–14,17,35,36]. However, given the high levels of viral shedding in milk, strict hygiene during milking is recommended, including strict cleaning and disinfection of milking equipment and parlour environments, and segregating the milking of infected and uninfected cows.

Key recommendations:

- Sick animals should be isolated promptly where possible. If the animals are lactating, they should be milked using separate equipment; where this is not possible, the approach recommended under **Pathway 2**, namely milking them at the end of the sequence followed by strict cleaning and disinfection, may be adopted. However, implementation may be constrained by the limited availability of isolation pens. Moreover, because of the likely high proportion of subclinical infections [12,16,25], isolating sick animals may not be sufficient to interrupt transmission. Where feasible, cohort testing - focusing on high-risk groups such as lactating cows or animals housed near confirmed cases - can support the detection of subclinical cases and inform isolation decisions.

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[3] https://doi.org/10.4060/cd3422en

- These risk mitigation measures should be supported by reinforced biosecurity practices, including: restricting animal movements onto the farm; cleaning and disinfecting equipment, especially following contact with infected animals or contaminated environments; heat-treating and disposing of milk and colostrum from infected cows or ensuring their safe disposal to prevent access by peri-domestic or domestic animals; heat-treating milk and colostrum before feeding to calves; heat-treating or acidification of waste milk or ensuring its safe disposal to prevent access by peri-domestic or domestic animals; complying with standard pest control and limitations of access of peri-domestic and domestic animals to feed, water, and bedding and potentially contaminated areas - especially milking parlour and waste storage sites.

2.5. Pathway 5: Inter-species transmission from infected cattle

For transmission to humans:

- Occupational health precautions should be implemented for farm workers, veterinarians, and other individuals handling cattle, milk, or potentially contaminated waste in an affected country or territory. These should include use of personal protective equipment (particularly eye protection) and hand hygiene protocols. It should be noted that the consistent use of PPE, although strongly advised, may be challenging under field conditions, especially in hot weather or when handling distressed animals [37,38]. Moreover, the close and repeated contact with infected animals and contaminated environments required to manage outbreaks, along with potential difficulties in ensuring timely carcass disposal may increase exposure risks for humans [7,12].
- Awareness of HPAIV clinical signs and the zoonotic potential should be enhanced, and systems should enable early, accessible, and non-stigmatising reporting, testing, and treatment for symptomatic individuals. Where capacity allows, testing may also be extended to asymptomatic individuals with known, or likely, exposure to infected cattle. Voluntary vaccination against seasonal human influenza is recommended to miminise the risk of reassortment between avian and human influenza viruses [3], and, where available, A(H5) avian influenza vaccination may be considered for individuals at high risk of exposure.
- Milk intended for human consumption should undergo appropriate heat treatment (e.g. pasteurisation) [12,31–34].

For transmission to non-bovine livestock:

- The interface between infected cattle and other livestock species (including poultry) should be characterised by assessing mixed farming practices and the likelihood of interspecies contact via shared personnel, equipment, or movement of production inputs and outputs.
- As a first step, feasible biosecurity measures should be identified to: **(i)** reduce direct and indirect contacts between species (e.g. segregation of equipment and personnel); and **(ii)** minimise the risk of virus transmission via such contacts (e.g. cleaning and disinfection to reduce fomite-mediated spread).
- Surveillance should be reinforced in non-bovine livestock holdings that are epidemiologically linked to infected cattle herds.

For transmission to wild/peri-domestic and companion animals:

- Given the above-mentioned difficulty of fully preventing contact between cattle and wild/peri-domestic animals in most production systems, no additional biosecurity measures are recommended beyond compliance with standard, non-pathogen-specific practices (namely pest control, and restricting access to feed, water, and bedding, and potentially contaminated areas – especially milking parlours and waste storage sites).
- Waste milk should be heat-treated or subject to acidification and safely disposed of to prevent access by wild/peri-domestic or domestic animals.
- Surveillance for morbidity and mortality in wild/peri-domestic, and domestic mammals (notably cats [22,35,39]) should be reinforced, especially in areas where cattle infections are confirmed. Carcasses of wild/peri-domestic and domestic animals should be promptly removed and disposed of safely to reduce the risk of environmental contamination and onward transmission to other animals or wildlife.

3. Research Priorities

Infection traits:

- Assess in more depth the individual host-level factors that may influence susceptibility to infection and infectiousness, including breed, production type and stage, sex, and age.
- Improve understanding of key infection parameters in cattle, including latent and infectious periods, routes of transmission between individual hosts, transmission rates from clinical and subclinical individuals, duration and effectiveness of infection-induced protective immunity.
- Explore viral persistence under different environmental conditions, with particular focus on free-grazing systems in regions where they are especially common, as these settings may differ from those previously studied in the context of HPAI in poultry.

Risk factors and transmission dynamics:

- Conduct observational studies (e.g. case–control designs) to identify risk factors, biosecurity measures, and transmission routes associated with **(i)** HPAIV incursion into cattle herds, and **(ii)** HPAIV spread within cattle herds. Observational studies should also aim to quantify the effectiveness of specific control measures in preventing viral incursion and limiting intra-herd transmission.
- Carry out phylodynamic and epidemiological studies of viral transmission dynamics using appropriate sampling design in cattle and other species populations. These studies should aim to assess the rates of viral spread across different types of cattle farms, the direction and frequency of interspecies transmission, particularly between cattle and poultry operations (i.e. whether peri-domestic or non-bovine livestock species act as bridge hosts facilitating transmission between cattle herds), and the potential for viral maintenance in the cattle population.
- Undertake further and more expansive serological studies in both symptomatic and asymptomatic individuals exposed to infected cattle (e.g. farm workers, veterinarians) to estimate the incidence of HPAIV infection in humans, and to better identify risk factors for human infection, and detect potential undiagnosed or subclinical cases.
- Conduct serological studies to assess **(i)** temporal changes in immunity levels in previously infected herds, and **(ii)** evidence of HPAIV exposure in cattle and small ruminants in countries where the virus is not known to circulate in these species but is endemic in poultry.

Configuration of production systems and transmission risk:

- Describe the organisation and diversity of cattle production systems, including patterns of cattle movement, herd composition, size, and turnover, personnel management and practices, particularly the sharing of staff across cattle and other livestock premises, environmental conditions and physical infrastructure relevant to viral persistence and transmission; assess how these characteristics may affect transmission risk and the feasibility of risk mitigation measures.
- Characterise the wild bird–livestock interface, focusing on interactions between waterbirds/other birds and cattle, as well as other peri-domestic species, to better understand species-specific exposure risks.
- Examine the poultry–cattle interface by describing farm types and mapping potential points of contact to inform the design of context-specific and feasible biosecurity measures.

Risk mitigation strategies:

- Develop and assess vaccines for cattle against HPAIV (including duration and effectiveness of vaccine-induced immunity), which may become essential in settings where the virus is established in the bovine population.
- Explore the social, economic, political and behavioural drivers and barriers that influence disease reporting, cattle movement decisions, and adherence to risk mitigation measures (e.g. biosecurity). This includes comparing perceived and actual costs of disease and risk mitigation interventions across stakeholder groups, identifying the factors that drive heterogeneity in behavioural responses, and designing effective economic, political, and institutional incentives to enhance compliance and transparency.

4. Method

Risk Pathway Mapping: Via expert opinion and discussions among co-authors, we mapped the most relevant risk pathways for HPAIV transmission involving cattle across multiple scenarios. First, we characterized potential routes of viral incursion into cattle farms (see **Appendix**), including **(i)** introduction of a lineage not yet detected in cattle, **(ii)** introduction of a lineage circulating in cattle outside the target country or territory, and **(iii)** introduction of a lineage already present in cattle within the target country or territory (**Fig. 2-4**). We then identified pathways for within-farm transmission between infected and susceptible cattle (**Fig. 5**). Finally, we assessed the risk of onward transmission from infected cattle to other species, including humans, non-bovine livestock (e.g., poultry, other mammals), wild animals (both avian and mammalian), and companion animals (**Fig. 6**).

Literature Review: To assess the risk associated with each identified transmission pathway and the factors influencing them, we conducted a scoping literature review following PRISMA 2020 guidelines [40]. On March 18, 2025, we searched PubMed[4], bioRxiv[5], and medRxiv[6] using relevant title, abstract, and keyword searches. Boolean operators were used to combine search terms, which focused on avian influenza viruses in bovines, in line with the scope of the document. Eligible sources included peer-reviewed articles, preprints, and conference proceedings. The initial PubMed search yielded 220 unique records, which were screened based on predefined inclusion and exclusion criteria. Studies were excluded if they did not address both influenza and bovine species, mentioned influenza only in the introduction without methodological relevance, focused solely on molecular properties without discussing implications for interspecies transmission, or were exclusively about vaccine design. After screening, 162 PubMed articles were retained. An additional 80 preprints from bioRxiv and medRxiv had been pre-screened using the same criteria. Thirteen relevant literature sources—including technical reports not published in scientific journals, such as risk assessments and FAO reports—were also identified. Finally, key publications released after the original search date, which were found during subsequent ad-hoc searches of published and pre-print literature and through co-author suggestions, were manually added up to July 10, 2025.

We then conducted full-text screening and systematic data extraction. Studies were retained if they met both of the following criteria: **(i)** the content was epidemiologically relevant to viral incursion or spread within bovine populations, and **(ii)** the study provided insights into the risk of cross-species transmission of avian influenza viruses from cattle, including to humans. For all included studies, data were extracted into a structured table capturing information across key epidemiological domains: **(i)** evidence of the emergence of novel HPAI lineages in bovines, **(ii)** the clinical course and pathogenesis of infection in cattle, **(iii)** routes of transmission within and between farms, **(iv)** the potential for onward transmission to other species, and **(v)** risk mitigation measures, including surveillance strategies. Findings were then reviewed to identify areas of agreement or contradiction across studies, with emerging themes and research gaps summarized in full accordingly.

Risk Mitigation Measures: Using both the identified transmission pathways and findings from the extensive literature review, we evaluated and proposed high-level, evidence-based, and implementable risk mitigation measures targeting the highest-risk routes of transmission. These interventions were developed through expert elicitation and incorporated consideration of key contextual factors influencing their effectiveness across different production systems. This document was then subjected to external review by Les Sims (Asia Pacific Veterinary Information Services, Australia), Arjan Stegeman (Utrecht University, Netherlands) and Cristobal Zepeda (USDA, United States).

Disclaimer: **This document provides the point of view of independent OFFLU experts and does not necessarily reflect the position of the parent organisations FAO and WOAH.**

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[4] https://pubmed.ncbi.nlm.nih.gov
[5] https://www.biorxiv.org
[6] https://www.medrxiv.org

Appendix

	Beef	Dual purpose – beef and milk	Dairy - production of milk
Cattle only	→ Low density, grazing-dependant → High density, feedlot	→ Low density, grazing-dependant (Restricted suckling system)	→ Limited or no outdoor access → On pasture for part of the day → On pasture all day
Cattle and other species managed separately	→ Low density, grazing-dependant → High density, feedlot	→ Low density, grazing-dependant (Restricted suckling system)	→ Limited or no outdoor access → On pasture for part of the day → On pasture all day
Cattle and other species managed together	→ Low density, grazing-dependant → High density, feedlot	→ Low density, grazing-dependant (Restricted suckling system)	→ Limited or no outdoor access → On pasture for part of the day → On pasture all day

Figure 1. Summary of different cattle production systems.

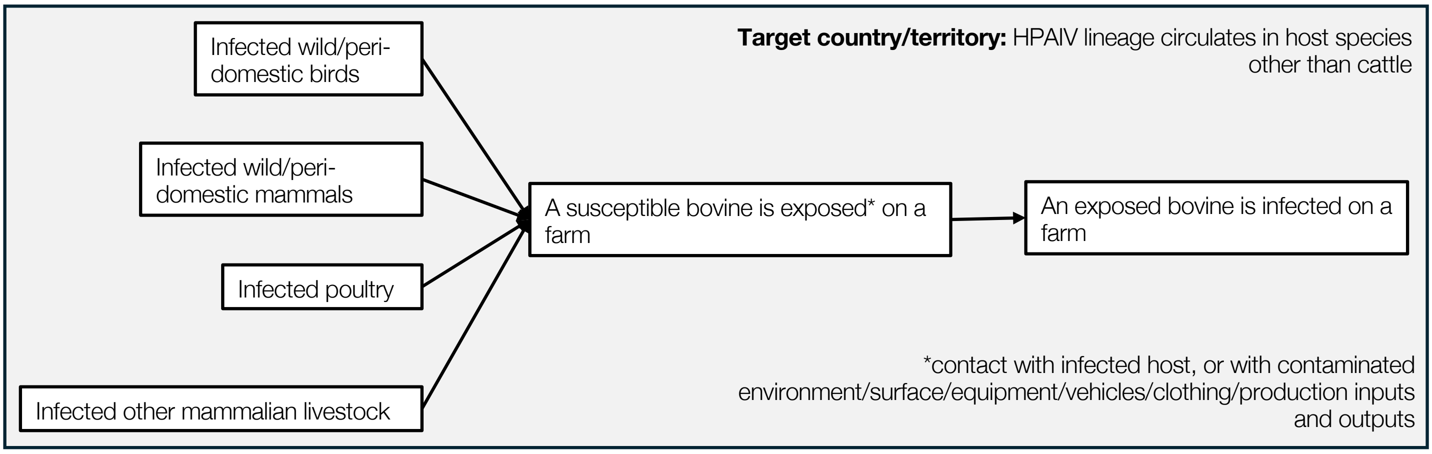

Figure 2. Risk pathways for virus incursion into a cattle farm when no HPAIV lineage is yet circulating in cattle in any location.

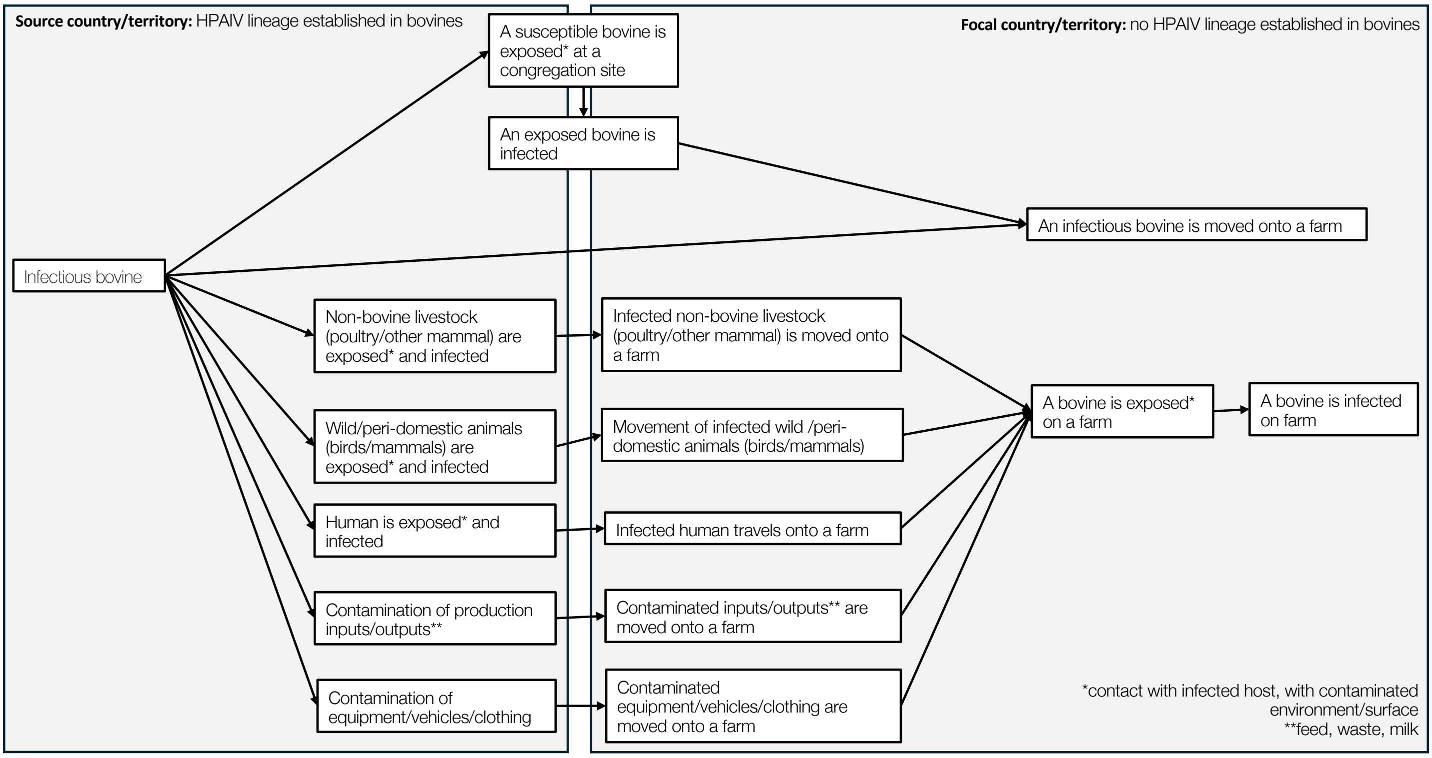

Figure 3. Risk pathways for virus incursion into a cattle farm when an HPAIV lineage is circulating in cattle but not in the focal country/territory.

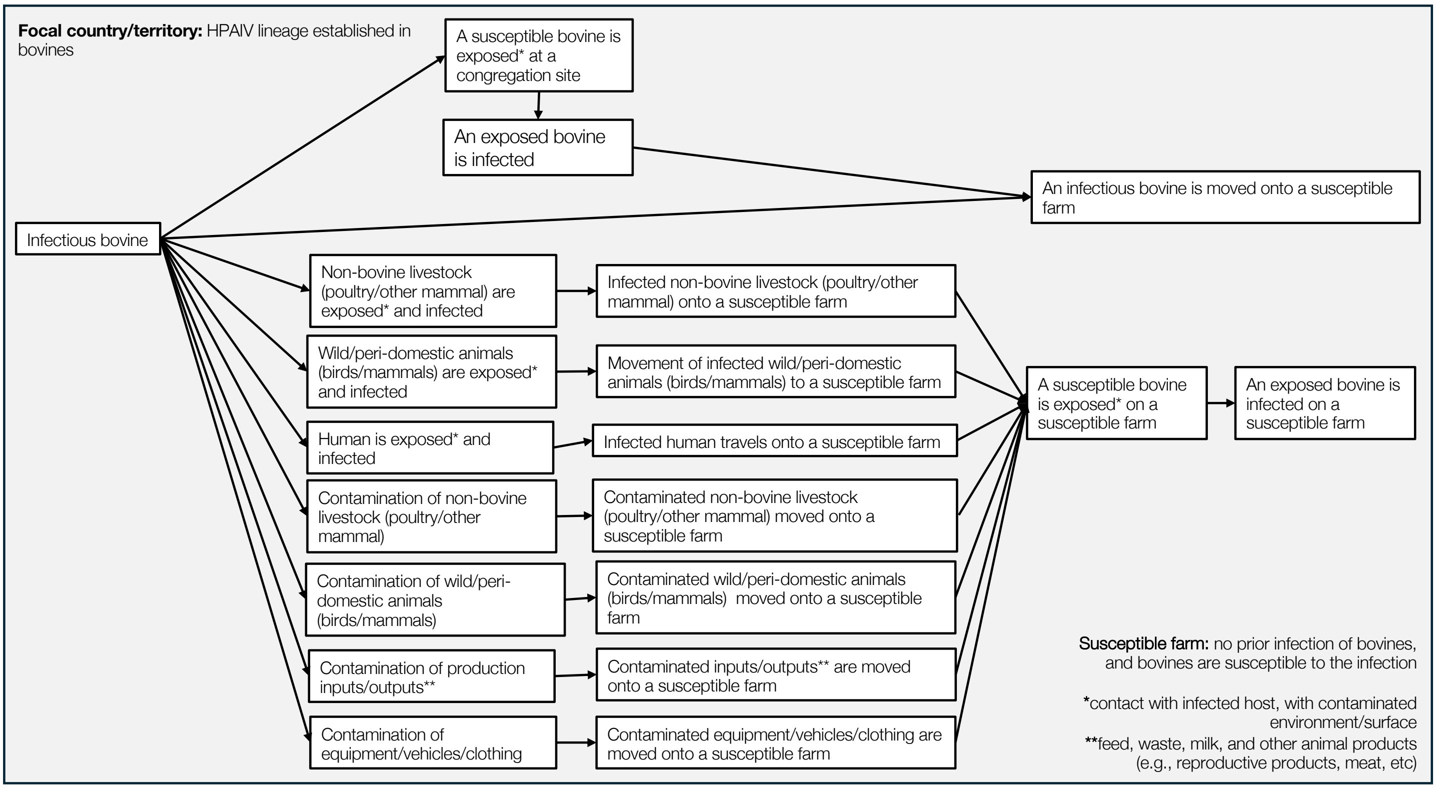

Figure 4. Risk pathways for virus incursion into a cattle farm when an HPAIV lineage is circulating in cattle in the focal country/territory.

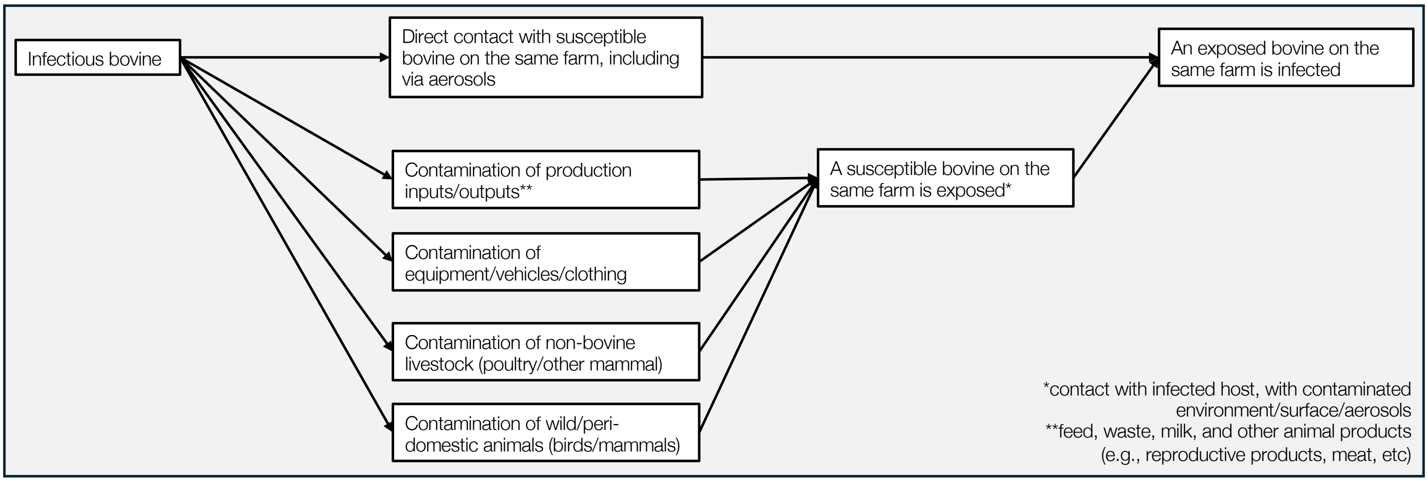

Figure 5. Risk pathways for HPAIV transmission from an infected to susceptible cattle within a farm (within-farm transmission).

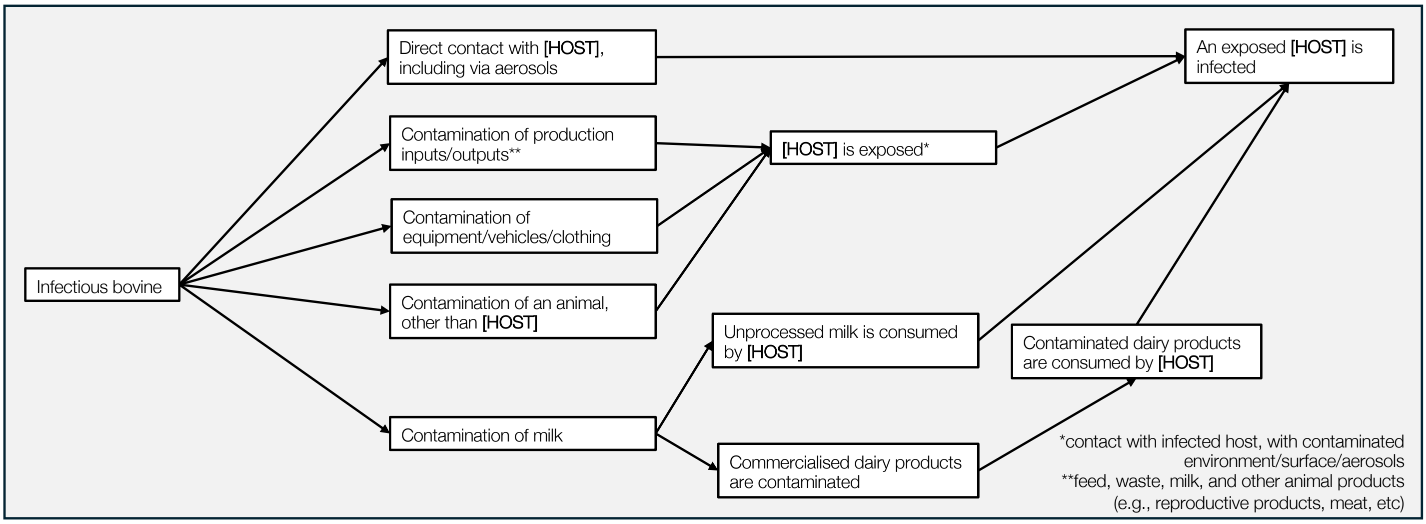

Figure 6. Risk pathways for HPAIV transmission from infected cattle to other species (including humans, non-bovine livestock, wild animals, companion animals).

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