STAR IDAZ | International Research Consortium on Animal Health

Roadmap Lead Summaries

Disease/pathogen	Coronavirus
Roadmap type	Control Strategies

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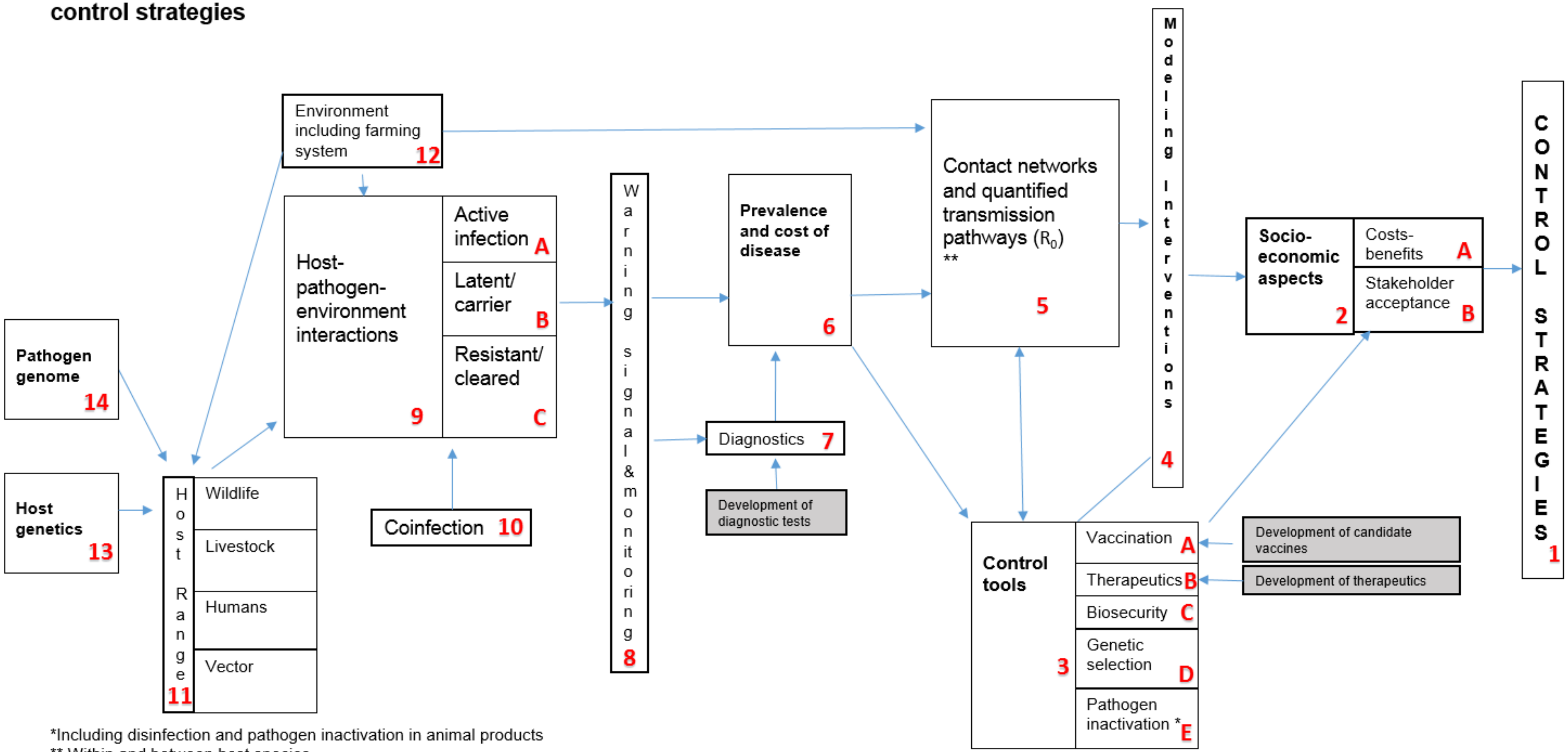
Research roadmap for development of disease control strategies



*Including disinfection and pathogen inactivation in animal products
** Within and between host species

Please note: Lead summaries are not required for the grey boxes above as they have their own dedicated roadmaps

Lead Summary [1] - Control strategies

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

How can we establish effective and affordable disease control (and prevention) strategies for emerging coronaviruses with spillover/spillback (between wildlife, livestock, pets and humans) and pandemic potential?

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

A lack of resources (financial and human) to apply existing technologies for surveillance. Coupled with a lack of sensitive and specific pen-side or rapid diagnostic tests (e.g. lateral flow devices) means we lack the capacity for accessibly global surveillance.

In turn, this leads to an incomplete understanding of coronavirus population dynamics in animal hosts and the transmission risks. If pets or companion animals are involved, reporting is poor, often because of the concerns of protecting the pet against government action.

An incomplete understanding of the drivers for spillover (e.g. land-use changes or viral recombination) means we can't identify risk areas of transmission. Political will and international co-operation are required to change socio-economic drivers of land-use changes that create conditions for pathogen emergence from wildlife reservoirs.

Reforming/movement strategies of animals due to ongoing resistance from the agricultural sector. Alternative control strategies are required which will involve lobbying policy decision-makers and establishing a co-ordinated effort globally.

This is a barrier to coordination of disease control efforts due to local policies.

Acceptability and feasibility of culling as a control strategy within the agricultural sector sometimes lacking, particularly in low-resource settings where compensation is not available for economic recovery

A lack of pan-CoV vaccine that is effective across host-species and CoV strains for control.

Addressing spillback from agricultural animals to wildlife – currently ongoing issues in Chile and South America

Solution Routes

What approaches could/should be taken to address the research question?

Conducting cost-benefit studies to support buy-in from government. This could be supported by social studies to improve the acceptance of the research needs associated with developing control strategies.

Advocating for animal health management of outbreaks to avoid zoonotic disease and communicating these effectively to policy makers by developing policy briefs to ensure that strategies are understandable and accepted by policy decision-makers.

Rapid development of vaccines through improved links between industry and academia for direct knowledge transfer.
Collaborating with industry partners to affect regulatory framework blockers.
Improving data sharing, especially for coronaviruses in wildlife, to support the development of epidemiological modelling to identify risk factors and AI-based prediction models.
Establishment of global surveillance capacity for early warning systems/virus discovery and to establish an understanding of population dynamics across as many host species as possible.
Studying the human-animal-environment interfaces and linking these with known drivers of spillover and spillback

Dependencies

What else needs to be done before we can solve this need?

A commitment to long-term surveillance work, including the development of tools for early detection e.g. standardized sequencing protocols or pen-side LFD.
The introduction of compensation schemes for losses due to culling in low- and middle-income regions agricultural workers who may be disproportionately affected by existing control strategies.
Maintaining a population of appropriately trained and employed veterinarians and researchers in government services, veterinary schools, clinical pathology laboratories to conduct the work needed. This also includes the need for BSL3/CL3 facilities and expertise.

Establishing effective mRNA vaccines to reduce the reliance on live attenuated vaccines (LIAV) that are prone to recombination and the emergence of new variants/mutants with an expanded host range.

State of the Art

Existing knowledge including successes and failures

Avian species are known to be reservoirs of Delta- and Gamma-coronaviruses with low risk of zoonotic potential. Birds (in particular poultry) are effective *in vivo* models for infection to study coronaviruses.
Bats are a known reservoir species for Alpha- and Beta-coronaviruses with a higher risk of zoonosis. There is currently a lack of accessible and appropriate bat *in vivo* model of infection.
In general, we lack reagents and resources for many wildlife species making it challenging to study the natural history of these infections.

Projects

What activities are planned or underway?

Lead Summary [2]- Socio-economic aspects

Research Question
What are we trying to achieve and why? What is the problem we are trying to solve?

We want to achieve socially accepted and proportional control strategies avoiding unnecessary negative economic impacts in both the short- and long-term context. This is needed to convince decision-makers that control strategies are important and deserve attention.

Challenge(s)
What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Counteracting the misinformation available in the public space and influencing public perception of the importance of disease control strategies. We need to identify methods to increase stakeholder acceptance for the control strategies proposed.
Trade of wildlife that is unrelated to animal-product consumption.
Differences in management approaches between different animal species; domestic pets, livestock and wildlife.
Influencing decision-makers to work with the scientific data to establish a space to nurture the development of control strategies.

Solution Routes
What approaches could/should be taken to address the research question?

Social science studies to better understand levels of acceptability and engagement stakeholders in an effective way. Awareness campaigns to increase acceptability and engagement for interventions deemed as necessary
Quantify social and economic losses by follow up of outbreaks and modelling
Advocacy and training of citizens for participatory surveillance

Dependencies
What else needs to be done before we can solve this need?

Quantifying the economic losses from halting wildlife trade
Quantifying the economic loss and impact to human health from spillover events
Understanding the social, cultural and economic drivers of wildlife trade that is unrelated to food-sustainability.
Understanding the differences in management approaches between different animal species; domestic pets, livestock and wildlife and the tolerance levels in each scenario, how these decisions will affect future control strategies.
Understanding the behaviours of decision-makers, their autonomy within the space they work and their aversion to risk.

Projects *What activities are planned or underway?*

State of the Art *Existing knowledge including successes and failures*

Lead Summary [2A] - Costs-benefits

Research Question
What are we trying to achieve and why? What is the problem we are trying to solve?

An understanding of the unintended consequences and indirect costs of a control strategy, both economic and environmental costs.

What approaches could/should be taken to address the research question?

Assessments of socioeconomic effects (including environmental impact) of current control strategies
Developing models to evaluate the socioeconomic effects of alternative strategies.

Challenge(s)
What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

A poor understanding cost-benefits in the context of wildlife control.
Acquiring resources to conduct long-term outbreak management exercises.
Standardizing and benchmarking surveillance methods to establish comparability across labs/regions/host species.
Demonstrating the benefit of control measures when often wildlife and agricultural control is far removed from members of the public.

Dependencies
What else needs to be done before we can solve this need?

Standard methodology for economic assessment on a global scale
Consideration for the ecological impacts of control (e.g. use of disinfectants) and the health impacts of spillback itself

State of the Art
Existing knowledge including successes and failures

Solution Routes

Projects
What activities are planned or underway?

Global burden of animal diseases (GBAD) at University of Liverpool is working to quantify economic costs associated with animal diseases however this does not currently address coronaviruses directly. Human study: https://pmc.ncbi.nlm.nih.gov/articles/PMC10619092/

Lead Summary [2B] - Stakeholder acceptance

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

New ways to engage with stakeholders (public and policy decision-makers) to improve social acceptance of control strategies.

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Identifying relevant key stakeholders and finding ways to engage effectively to communicate the benefits of introducing control measures.
Influencing decision-makers by successfully communicating the future savings (in financial terms) made from the implementation of control measures in the present

Solution Routes

What approaches could/should be taken to address the research question?

Mapping stakeholders and amplifiers in peace time, including social media usage.
Experiences of recently declared global emergencies should be considered (e.g. Monkeypox).
Social studies to meliorate communication campaign.
Increasing stakeholder acceptance within the agricultural sector by lobbying politicians to introduce compensation for farmers.
Comms tools – getting the correct message to the correct people has huge impacts for success. In the case of vaccination, some studies show that communicating the potential harm of the disease influences human behaviour more than communicating the benefit of the vaccine. Nevertheless, animal owners tend to be receptive to vaccination.

Dependencies

What else needs to be done before we can solve this need?

Funder buy-in to conduct studies to assess tolerance of various control measures.
Cost-benefit analysis to be complete, at least partially, to enable economic quantification of financial savings.

State of the Art

Existing knowledge including successes and failures

Projects

What activities are planned or underway?

Lead Summary [3] - Control tools

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

The development and validation of an effective control toolbox, including standardized surveillance and rapid diagnostics (LFD) for environmental samples, disinfection protocols and effective vaccines.

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Developing effective vaccines against the current most pathogenic animal health coronaviruses and future viral emergences.
Biosecurity protocols are variable depending on context.
Epidemiological modelling that is accurate for predicting outcomes, specifically for animal diseases. Included in this is the lack of population data needed e.g. susceptibility of different host species to CoVs
Development of novel diagnostic strategies, including sampling water or air-based technologies for wildlife testing, supported by LFD technologies.
Designing processes to validate disinfection practices without relying on BSL3/CL3 containment facilities.

Solution Routes

What approaches could/should be taken to address the research question?

Investment into networking and knowledge transfer to accelerate the development of technology and prototypes into the market (vaccines and diagnostics tests)
New technologies including artificial intelligence and machine learning for epidemiological modelling.

Dependencies

What else needs to be done before we can solve this need?

Basic science to understand genotype to phenotype mutations.
Establishing safe processes to sample and test environmental and veterinary samples in the field.
Global surveillance to gather population data in animal hosts, and the development of appropriate methods to predict the emergence of variants of concern using surveillance data.
Good communication strategy: addressing misinformation, adapting approach based on audience (pet owners vs livestock).

State of the Art

Existing knowledge including successes and failures

In the case of vaccination, some studies show that communicating the potential harm of the disease influences human behaviour more than communicating the benefit of the vaccine. Nevertheless, animal owners tend to be receptive to vaccination.

Projects *What activities are planned or underway?*
Sampling wastewater for surveillance (various research institutes)

Lead Summary [3A] – Vaccine

Research Question *What are we trying to achieve and why? What is the problem we are trying to solve?*
See related research roadmap

Challenge(s) *What are the scientific and technological challenges (knowledge gaps needing to be addressed)?*

Solution Routes *What approaches could/should be taken to address the research question?*

Dependencies *What else needs to be done before we can solve this need?*

State of the Art *Existing knowledge including successes and failures*

Projects *What activities are planned or underway?*

Lead Summary [3B] – Therapeutics

Research Question
What are we trying to achieve and why? What is the problem we are trying to solve?

Developing affordable antiviral therapeutics for a wide range of animals effective in wildlife, pets and livestock.

Challenge(s)
What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Administering antiviral therapeutics to wildlife populations is challenging due to the unknown infection status of animals. Moreover, regulations/protections for certain species can restrict access.
Cost of therapeutics for livestock systems inhibits widespread use, especially for those in low- and middle-income regions.
A societal behaviour of preserving therapeutics for human, companion animal or high value animal use in an effort to reduce antiviral resistance development could restrict its use in wildlife populations.
Inappropriate use of therapeutics could result in antiviral drug resistance as well as a risk of environmentally acquired antiviral drug resistance

Solution Routes
What approaches could/should be taken to address the research question?

Increase the efforts toward basic science to develop affordable antivirals or evaluate the re-purposing of existing therapeutics, that are then validated against wildtype coronaviruses.
Define therapeutics strategies for different host species, and conduct social studies for acceptability of the interventions.
Basic science to study novel drug combinations that may enhance antiviral activities and mitigate the risk of antiviral drug resistance.

Dependencies
What else needs to be done before we can solve this need?

Conducting basic science in models of wildlife animals will require the development of appropriate tools (e.g. novel cell lines or 3D cultures) for wildlife species. This is currently a limiting factor that hinders our progress.
Residues of several drugs may pose high ecotoxicological risk in receiving waters – studies into the long-term ecological impacts of therapeutic control tools are needed.

State of the Art
Existing knowledge including successes and failures

Projects
What activities are planned or underway?

AGILE - Coronavirus Drug testing Initiative- Different trials can be found on their platform here: https://www.agiletrial.net/agile-trials/ SARS2BlockEntry (INRAE)- Construction of nano-ligands for blocking the entrance of SARS-CoV-2 COVID-19 Drug Interactions Research Programme (University of Liverpool, Saye Khoo)	Evaluation of Paxlovid, Molnupiravir and Remdesivir in small animal models (University of Liverpool).

Lead Summary [3C] - Biosecurity

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

Acceptable and effective biosecurity protocols adapted to a range of specific contexts.
Consideration needs to be given that biosecurity is for agricultural to wildlife AND vice-versa as a two-way route and the management approaches could differ widely.

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

In South East Asia, farming practices are integrated and limiting for bio-security. Economic costs also factors in this region and it's challenging convince farmers to utilise biosecurity measures due to costs. Integrated (mixed animal) farming systems support inter-species mingling and potential disease spread between species.
Cost of implementation, and willingness/ability to invest in the sector generally if there is no quantifiable benefit or empirical evidence of its efficacy.
Applicability of biosecurity in certain field settings where resources may be limited.
Evaluation of biosecurity measures (e.g., efficacy and benefits) in different contexts. Disinfectants are often not suitable for all pathogens, and there may also be off-target consequences of misuse e.g. increases resistance and/or driving mutations. We have a poor understanding of the host-animal-environment interface where transmission occurs.
Daily engagement in biosecurity from workers/animal owners
Consideration to the long-term unknown consequences to the environment

Solution Routes

What approaches could/should be taken to address the research question?

Conducting cost-benefits of accessible biosecurity measures to identify areas where most impact could be achieved economically. Empirically demonstrating the benefits of biosecurity across different scenarios.
Adapting biosecurity measures to local settings, especially in low- and middle-income regions where resources are constrained.
Social science approaches (e.g. focus groups with end-users) to co-design solutions to increase acceptability.

Dependencies

What else needs to be done before we can solve this need?

Need to better understand interactions where transmission may occur between wildlife and domestic animals for example, so that sufficient biosecurity measures can be identified (e.g. physical barriers).

Identifying and quantifying the value/benefit of biosecurity measures especially where measures do not yield cost-savings. This needs to be communicated to end-users, policy decision-makers and other external stakeholders to allow for evidence-based decision-making.
Defining biosecurity and creating a narrative of context – biosecurity currently doesn't mean anything to some sectors.
Understanding the risks of using biosecurity tools – this requires study of the measures themselves.

State of the Art *Existing knowledge including successes and failures*
Some countries link disease compensation to participation in surveillance systems and adoption of biosecurity standards

Projects *What activities are planned or underway?*

Lead Summary [3D] - Genetic selection

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

Breed livestock, wildlife and pets that are resistant to infections and less susceptible to disease. This section is designed around the discussion of host genetics.

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Disease resistance is a complex and polygenic trait, often with varying host-responses across species.
Consequences of genetic improvement for health on other physiological traits. For the agricultural sector, we also need to consider the impact of changes in physiology on economic, animal welfare, ethical concerns and social acceptance of gene selection.
Consequences of introducing genetic mutations on the subsequent food safety and regulation of animal-derived products.
Availability and adaptability of the new breeds to extreme climates and/or LMICs.
Lacking resources e.g. high-quality full genome sequences (including metagenomics data and getting access to that), that would allow us to perform the genome manipulation.

Solution Routes

What approaches could/should be taken to address the research question?

Creation and exchange of open databases, improving the access to genomics data for host species.
Identification and characterization of suitable genes that confer resistance to infection.
Genetic selection and gene editing (e.g. CRISPR) of production animals (including testing native breeds rather than existing commonly used breeds in production)
Development and validation of diagnostic tools to confirm the presence/absence of inserted/modified genes and resistance to infection by standardized diagnostic pen-side approaches.

Dependencies

What else needs to be done before we can solve this need?

Basic science to understand the intricacies of early-stage infection across a range of host animal species.
Genome-sequencing of many animal species, including native breeds and wildlife that may typically be underrepresented compared to animal species commonly handled in laboratories for infection studies.
Ethical and legal framework that allows for genetic modification to be performed and socially accepted.

State of the Art

Existing knowledge including successes and failures

Genome editing technology, especially CRISPR/Cas mediated gene knock-out/knock-in and precise modification, improved the efficiency of disease resistance animal breeding. Zhiguo et al 2022 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9266401/ CRISPR has been used to produce Coronavirus resistant pigs, by editing a presumed receptor of the transmissible gastroenteritis virus Whitworth et al 2019 https://link.springer.com/article/10.1007/s11248-018-0100-3?utm_source=getftr&utm_medium=getftr&utm_campaign=getftr_pilot

Projects *What activities are planned or underway?*

Lead Summary [3E] - Pathogen Inactivation

Research Question
What are we trying to achieve and why? What is the problem we are trying to solve?

Develop and validate standardised and accessible methods to inactivate virus in farming, domestic and wildlife settings.

Challenge(s)
What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Understanding the persistence of different viruses on different surfaces and how much log reduction is needed to prevent transmission. This feeds into the challenge of identifying standards for declaring pathogen free status in the environment and on farms.
Identifying the most effective methods for inactivating different strains in the field to ensure safe handling protocols and procedures for sample collection.
We currently have incomplete data on the comparative effectiveness of inactivation methods (e.g., heat, chemicals, UV light) across different coronavirus strains, host species and contexts. Further study into the applicability in farm and wildlife settings is needed.
Current approaches to validate inactivation may rely on molecular diagnostics to detect viral nucleic acids, however this is flawed due to the lack of differentiation between the presence of infectious and historic viruses. Improvement to diagnostics testing should introduce diagnostics of active replication and these tests need to be implemented widely.
Due to the limitations of molecular testing, current approaches also require viral isolation to prove a presence/absence of infectious virus. Therefore, achieving regulation and approvals for pathogen inactivation methods requires access to- and expertise in BSL3/CL3/SAPO for safe handling and process validation.
Local policies, external stakeholder perceptions and in-country legislation will affect the acceptability of the proposed methods leading to variability. A global co-ordinated effort is needed to standardise methods for wider implementation.
Moving away from using animals in experimental work due to a lack of species-specific resources, cost, animal welfare/ethical considerations, the requirement for relevant expertise and facilities. We need new cell systems for investigations of this sort; however, consideration should be given to the emergence of lab adaptions in viral isolates which may affect viral kinetics and response to inactivation and therapeutics.

Solution Routes
What approaches could/should be taken to address the research question?

Developing new tools e.g. pseudoviruses, that bypass the need to work under SAPO/BSL3/CL3 containment.
Developing and optimising tools to inactivate virus by air system (i.e. UV power per different airflow).
Study the influence of environmental factors e.g. temperature, humidity, and surface type, on the efficacy of inactivation.
Modelling of inactivation methods in real setting.

Study environmental impact and safety of inactivation methods.
Develop standardized protocols to ensure consistent inactivation rates and safety across different settings.
Exploring alternative methods of pathogen-inactivation e.g. composting, which occurs in low- and middle-resource settings.

Dependencies

What else needs to be done before we can solve this need?

The establishment and validation of standardised methods to measure virus inactivation and clarification on which gold-standard test to use to demonstrate negative result given that molecular testing can give positive results but do not infer live viruses. This is particularly important for farming practices following outbreak where access to laboratory testing may be constrained. Consideration could be given the expanding on the use of sentinel animals more widely.

State of the Art

Existing knowledge including successes and failures

Single pass UVC air treatment (1254 L/min) can effectively inactivate bovine coronavirus (2.4-log reduction). (Snelling, W. J., Afkhami, A., Turkington, H. L., Carlisle, C., Cosby, S. L., Hamilton, J. W. J., Ternan, N. G., & Dunlop, P. S. M. (2022). Efficacy of single pass UVC air treatment for the inactivation of coronavirus, MS2 coliphage and Staphylococcus aureus bioaerosols. Journal of Aerosol Science, 164, Article 106003). https://pure.ulster.ac.uk/ws/portalfiles/portal/101170681/1_s2.0_S0021850222000477_main_1_.pdf

Projects

What activities are planned or underway?

UVC air treatment for the inactivation of coronavirus in Bioaerosol- Ulster University

Lead Summary [4] - Modelling interventions

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

The development of accurate mathematical models to study viral epidemiology and establish the capacity to assess control strategies across contexts and interfaces.

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

A need for disease dynamic models (including testing of interventions) as well as epidemiological modelling.
A poor understanding and knowledge on coronavirus infection in wildlife. This lack of data limits our ability to populate existing models with wildlife data to accurately model outcomes and to assess the risk species or populations of becoming reservoir host(s).
Identifying ways to improving the use of molecular epidemiological data, especially when data is fragmented.

Solution Routes

What approaches could/should be taken to address the research question?

Computational risk modelling based on epidemiological and surveillance data.

Using genotypes to model outbreaks.

Syndromic surveillance to provide data for modelling.

Dependencies

What else needs to be done before we can solve this need?

Increase the capacity to perform modelling as we are currently underpowered. This includes ensuring that we train and maintain a population of trained experts.
Improved diagnostic programmes in wildlife to gather the required data to populate the models.

State of the Art

Existing knowledge including successes and failures

A framework to predict zoonotic reservoirs under data uncertainty: a case study on beta coronaviruses (2024 - preprint)
https://www.researchsquare.com/article/rs-4304994/v1

Wardeh, M., Baylis, M. & Blagrove, M. S. C. (2021) Predicting mammalian hosts in which novel coronaviruses can be generated. *Nat Commun.* 12 (1): 780. doi: 10.1038/s41467-021-21034-5.

Projects

What activities are planned or underway?

COVRIN: One Health research integration on SARS-CoV-2 emergence, risk assessment and preparedness. Van Der Poel W et al. EC funding (2021-2023) https://onehealthejp.eu/projects/integrative/jip-covrin

PANDASIA: Pandemic literacy and viral zoonotic spillover risk at the frontline of disease emergence in Southeast Asia to improve pandemic preparedness. Norges et al. NVI- EC funding https://cordis.europa.eu/project/id/101095444

EU Partnership for Animal Health and Welfare About Us (eupahw.eu)

Lead Summary [5] - Contact networks and quantified transmission pathways (R_0)

Research Question
What are we trying to achieve and why? What is the problem we are trying to solve?

Understanding and quantifying the contact networks and transmission pathways of coronaviruses, particularly how they contribute to the spread of the virus within populations.

Challenge(s)
What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Lack of knowledge on host susceptibility, virus circulation and general wildlife disease occurrence making it difficult to spot deviations from transmission trends and identify the cause of any unusual disease outbreaks.
Asymptomatic and pre-symptomatic transmission can introduce challenges in identifying infectious animals.
Differences in susceptibility and transmission between host species makes understanding and predicting transmission networks challenging.
Understanding the role of intermediate “hosts” which act as fomites, such as rodents or wild birds, for onward transmission.
The population structures/densities and social behaviour of wildlife animals is not well understood therefore it’s difficult to develop accurate contact networks that reflect in situ transmission.
Existence of undocumented/informal or illegal wildlife trade means that a proportion of transmission will also be unaccounted.

Solution Routes
What approaches could/should be taken to address the research question?

Investing resources to study transmission pathways, particularly at the human/wildlife/domestic interphase.
Continuous improvement of current models available, feeding in new data as it emerges.
Developing better understanding of animal social behaviours, especially in wildlife animals and learn how to use this data to parameterise models.
Identify wildlife strains of coronaviruses, sequence them and measure the importance of circulating strains in wildlife to infer potential impacts for transmission of emerging viruses/VOCs

Dependencies
What else needs to be done before we can solve this need?

The creation of efficient surveillance systems for coronaviruses, which includes establishing access to technologies in local settings.
Creating and sharing a dataset of viruses and their corresponding susceptible host species.

State of the Art
Existing knowledge including successes and failures

Reservoir-People (RP) transmission network model for CoV-2 to calculate Ro and assess transmissibility Chen et al. 2020.

https://idpjournal.biomedcentral.com/articles/10.1186/s40249-020-00640-3?report=reader; median incubation period is approximately 4–6 days for SARS, MERS, and COVID-19 Kane et al. https://www.annualreviews.org/doi/full/10.1146/annurev-animal-020420-025011#_i7

Projects
What activities are planned or underway?

One Health EJP response to COVID-19: COVRIN: One Health research integration on SARS-CoV-2 emergence, risk assessment and preparedness. Van Der Poel W et al. EC funding (2021-2023) https://onehealthejp.eu/projects/integrative/jip-covrin

CORUVA: Surveillance of coronaviruses in cattle and pigs with emphasis on the zoonotic risk. Kristien Van Reeth et al (2021-2024) UGhent https://research.ugent.be/web/result/project/68f25c6d-055e-480c-b29c-8fffddd35393/details/en

Lead Summary [6] - Prevalence and cost of disease

Research Question *What are we trying to achieve and why? What is the problem we are trying to solve?*
Collecting data on coronavirus prevalence in animals and quantifying the cost of diseases (including social costs) to justify intervention

Challenge(s) *What are the scientific and technological challenges (knowledge gaps needing to be addressed)?*
Extensive worldwide surveillance, particularly in wildlife and for the detection of new and emerging coronaviruses. Limitations to this include costs, sampling restrictions and the need to align surveillance strategies globally which requires resources and tools that are currently lacking. Assessing the short- and long-term cost of diseases, including a focus on determining the value in the contexts of wildlife or and/or biodiversity. Developing a method to address the different values of livestock in a range of contexts e.g. breeding versus production, backyard vs commercial. We have a partial understanding of pathogen survival in the environment and different species. This data feeds into our understanding of prevalence and the drivers of transmission.

Solution Routes

What approaches could/should be taken to address the research question?
Risk analysis for surveillance in hot-spots and at the human-animal interface Standardization of livestock/pet/wildlife surveillance and improvements to accessibility of technologies required to conduct this. Standardization of methods to quantify short term and long-term burden of coronavirus infections, potentially with stratification into country-specific contexts.

Dependencies *What else needs to be done before we can solve this need?*
Creating a method to quantify value created from prevention of disease, and characterize the cost of disease accurately (social AND economic) Investment into the effective surveillance infrastructure and standardisation across reporting.

State of the Art *Existing knowledge including successes and failures*

Projects *What activities are planned or underway?*

GBADs is currently creating a methodology for assessing the burden of animal diseases (see our Approach – GBADS – Global Burden of Animal Diseases (animalhealthmetrics.org)

Lead Summary [7] - Diagnostics

Research Question *What are we trying to achieve and why? What is the problem we are trying to solve?*
See specific research roadmap

Challenge(s) *What are the scientific and technological challenges (knowledge gaps needing to be addressed)?*
See specific research roadmap

Solution Routes *What approaches could/should be taken to address the research question?*
See specific research roadmap

Dependencies *What else needs to be done before we can solve this need?*
Effective diagnostic algorithm

State of the Art *Existing knowledge including successes and failures*

Projects *What activities are planned or underway?*

Lead Summary [8] - Warning Signal & monitoring

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

Development of effective early warning systems to detect and monitor coronaviruses.

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Poor, costly surveillance systems (particularly among wildlife) and a lack of sufficiently reliable diagnostics.
Limited trust among stakeholders and transparency in information sharing among and between countries.
Limited resources (including capacity and financial support) – requires effective targeting to likely sources of transmission (prioritisation).
Interoperability and linkage with public health data.
Consideration for seasonality of different pathogens in different geographical regions is required.

Solution Routes

What approaches could/should be taken to address the research question?

Study factors which contribute to novel pathogen emergence or spillover to better understand where and when to intervene.
Define and identify 'hot-spot' areas for risk-based surveillance and targeted sequencing of isolates.
Conduct a cost-effectiveness modelling study to assess monitoring systems across different scenarios.
Utilise sensors and artificial intelligence (predictive analytics) to identify early warning signs of coronaviruses in 'digital farms'.
Utilise 'citizen science' to support for wildlife surveillance.
Integrated surveillance of farms, domestic and wild animals (in high-risk areas).

Dependencies

What else needs to be done before we can solve this need?

Acceptability of reporting (citizen science and agricultural industry self-reporting) needs to increase.
Cost-effective and continuous surveillance systems need to be developed/utilised.
Availability of accurate cost models and prevalence estimates.
Continuous training and professional development on disease preparedness. This includes provision of tools and knowledge to local communities, particularly in high-risk, remote areas, to support early monitoring.
Consistent consideration of wildlife and ecology in peacetime is required.
Collaboration among different countries to develop shared surveillance and early warning protocols, and prompt data reporting to WAIHS. Standardised surveillance strategies should include who, what, where and when to collect samples, and for what pathogens.

Development of a One Health systems approach using innovative technologies.

State of the Art *Existing knowledge including successes and failures*

Projects *What activities are planned or underway?*
USDA Animal and Plant Health Inspection Service (APHIS) developing field tests for wildlife and domestic animals https://www.usda.gov/media/press-releases/2022/12/21/usda-developing-new-tools-identify-covid-virus-wild-and-domestic

Lead Summary [9] - Host-pathogen-environment interactions

Research Question *What are we trying to achieve and why? What is the problem we are trying to solve?*
Improve understanding of host-pathogen-environment interactions in order to implement effective control.

Challenge(s) *What are the scientific and technological challenges (knowledge gaps needing to be addressed)?*
There is a need to understand the role and impact different environmental factors play in disease development and emergence. This should consider how different land uses and animal husbandry practices influence the emergence and spread of infections. There is a need to understand different transmission pathways and the circumstances that may led to emergence of infections in wildlife and livestock. It is difficult to identify and prevent interaction [of coronaviruses] with wildlife.

Solution Routes *What approaches could/should be taken to address the research question?*
Modelling studies and transmission studies *in vitro*, *ex vivo* and *vivo*. Modelling future land-use and agricultural practises scenarios. Targeted field research to better understand potential pathways of transmission amongst wildlife, livestock and humans.

Dependencies *What else needs to be done before we can solve this need?*
Identification of appropriate wildlife hosts. Collecting of data as a resource to facilitate modelling. Citizen education on how to avoid/manage potential high-risk wildlife-humans interactions. Increase understanding of host differences in infectivity, immune responses, and pathogenesis. In particular, in bats and other animal species that are known to host CoVs.

State of the Art *Existing knowledge including successes and failures*

In CoV infections is usually the S protein component that binds host cell receptors. SARS-CoV, HCoV-NL63, and SARS-CoV-2 seems to use ACE2 for cell entry, while MERS-CoV seems to use DPP4 as the receptor for host cell infection. Petrosillo et al. 2020. https://www.sciencedirect.com/science/article/pii/S1198743X20301713?via%3Dihub	
Projects *What activities are planned or underway?*	SARS-Cov-2 infection at the animal-human interface: longevity and re-infection dynamics with virus evolution.(UKRI)

Lead Summary [9A] - Active Infection

Research Question *What are we trying to achieve and why? What is the problem we are trying to solve?*
Identifying active infection for a risk of onward infection.

Challenge(s) *What are the scientific and technological challenges (knowledge gaps needing to be addressed)?*
PCR is used for identification but does not indicate whether the host is infectious or not. The link between viral presence, levels, and infectivity needs to be better understood. Sero-surveillance is flawed – there is an inability to distinguish between historic and active infection. There is a strong reliance on virus isolation to determine the presence of active and/or live virus. This often requires availability of BSL3/CL3 facilities and relevant expertise.

Solution Routes

What approaches could/should be taken to address the research question?

Dependencies *What else needs to be done before we can solve this need?*
Developing appropriate model systems for study e.g., organoids or cell culture systems. Improved access to appropriate research facilities (including BSL3/CL3 laboratories).

State of the Art *Existing knowledge including successes and failures*

Projects *What activities are planned or underway?*

Lead Summary [9B] - Latent/carrier

Research Question *What are we trying to achieve and why? What is the problem we are trying to solve?*
Identification of latent/carrier hosts, with a particular focus on wildlife and pets.

Challenge(s) *What are the scientific and technological challenges (knowledge gaps needing to be addressed)?*
Resistant and persistently-infected animals can influence coronavirus containment. Understanding and addressing this will require longitudinal and lifetime studies which are expensive to conduct. Emergence of drug-resistant isolates makes it difficult to identify infectious strains.

Solution Routes *What approaches could/should be taken to address the research question?*
Long-term studies, especially in wildlife and pets.

Dependencies *What else needs to be done before we can solve this need?*
Availability of funding and appropriate resource to conduct long-term studies.

State of the Art *Existing knowledge including successes and failures*

Projects *What activities are planned or underway?*

Lead Summary [9C] - Resistant/cleared

Research Question *What are we trying to achieve and why? What is the problem we are trying to solve?*
Identifying resistance and recovered/cleared animals i.e., understanding patterns of infection.

Challenge(s) *What are the scientific and technological challenges (knowledge gaps needing to be addressed)?*
Variable response to pathogens across different species.

Solution Routes *What approaches could/should be taken to address the research question?*

Dependencies *What else needs to be done before we can solve this need?*

State of the Art *Existing knowledge including successes and failures*

Projects *What activities are planned or underway?*

Lead Summary [10] – Coinfection

Research Question *What are we trying to achieve and why? What is the problem we are trying to solve?*

Challenge(s) *What are the scientific and technological challenges (knowledge gaps needing to be addressed)?*
Co-infection with similar/multiple pathogens and/or viral recombination can influence transmission dynamics and confound diagnostics. It is possible for an organism to become reinfected with the same isolate or strain. Treatment and recovery in multi-pathogen infection can be challenging due to contraindications or emergence of AMR bacteria – super infections.

Solution Routes *What approaches could/should be taken to address the research question?*
Whole genome sequencing (metagenomics/virome sequencing) - balancing short and long read sequencing techniques depending on the question being asked.
Use of alternative antibiotics or immunopotentiation agents e.g. probiotics, phage viruses, nanoparticles for treatment.

Dependencies *What else needs to be done before we can solve this need?*
There is a need to understand what the normal host virome/ microbiome is. Availability of effective alternatives to antibiotics.

State of the Art *Existing knowledge including successes and failures*

Projects *What activities are planned or underway?*

Lead Summary [11] - Host range

Research Question *What are we trying to achieve and why? What is the problem we are trying to solve?*
Understand the host range of coronaviruses to determine the factors that allow these viruses to infect different species, including humans.

Challenge(s) *What are the scientific and technological challenges (knowledge gaps needing to be addressed)?*
Understanding which species are susceptible to which coronaviruses. Cell culture work relies on materials not currently available for wildlife animals, including surveillance, laboratory capacity, sequences, and cells. Identifying molecular markers to identify spillover. Identifying factors that will address whether viral-cell binding leads to infection and onward transmission. There is a general lack of understanding of basic science and transmission. Ethical, economic, and practical concerns, particularly among animal studies. Exchange of material among laboratories (Nagoya). Lacking a basic understanding of the species susceptibility and how it can vary across families or breeds even of animals. Differentiating between evidence of viral presence and determining the role of any specific host species as a reservoir for onward transmission. Matching CoV vaccines – are vaccines available seroconverting and protecting against the virus present. A lack of availability of species-matched vaccines – separate workshop.

Solution Routes *What approaches could/should be taken to address the research question?*
Collaborative surveillance programmes. Phylogenetic studies to trace the evolution of coronaviruses and their interactions with various host species. Identify and characterize viral receptors across different host species. Study cross-species transmission and identify molecular markers of spillover.

Dependencies

What else needs to be done before we can solve this need?
Availability of funding, especially for studies to identify reservoirs of transmission and to identify host range. Addressing ethical and economic concerns for animal experiments that could otherwise be a solution. Training of pathologists. Availability of cell culture systems (and other reagents) for different animals (especially wildlife) – addressing surveillance and (BSL3) laboratory capacity.

State of the Art *Existing knowledge including successes and failures*
Differential susceptibility of SARS-CoV-2 in animals: Evidence of ACE2 host receptor distribution in companion animals, livestock and wildlife by immunohistochemical characterisation - PubMed (nih.gov) SARS-CoV, MERS-CoV and SARS-CoV-2 had involved domestic or wildlife animal as reservoir or as intermediate host.

Projects *What activities are planned or underway?*
CORUVA (UGent)- Surveillance of coronaviruses in cattle and pigs with emphasis on the zoonotic risk. ConVErgence project: ERAnet ICRAD project 1ste call- Assessing swine as potential hosts for emerging Coronaviruses (IZS VE Paola De Benededictis). MUSECoV: ERAnet ICRAD project 1ste call - Multi-scale Eco-evolution of Coronaviruses: from surveillance toward emergence prediction (ANSES). Acquisition of scientific and epidemiological field evidence on the susceptibility of animals to SARS-CoV-2 and other coronaviruses from a One Health perspective (IZSLT-Italy Marcello Sala). Susceptibility of mammals to SARS-COV-2: risks of reverse zoonosis and possibilities in translational medicine. (Network project) (IZSLER- Calogero Terregino).

Lead Summary [11A] – Wildlife

Research Question
What are we trying to achieve and why? What is the problem we are trying to solve?

Prevent spill-over from and to wildlife.

Challenge(s)
What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Current research effort is heavily biased towards describing known diseases rather than considering the 'pre-emergent' diversity in bats.
Complexity of evolutionary routes and biogeography in bats.
There is a need to increase understanding of the mechanisms of macroevolution.
Better understanding of the high-risk interfaces between wildlife and humans and our domestic animals.
Surveillance and availability of data is poor.
Understanding long-term drivers of spill-over events e.g. biodiversity loss, changing land-use, mining and extraction industries.
Understanding viral shedding into the environment and impacts on wildlife.
Effect of climate change and how they are driving changes in wildlife population behaviours and migration patterns, including efforts to achieve 'net zero'
Understanding how backyard poultry contributes to wildlife disease.

Solution Routes
What approaches could/should be taken to address the research question?

Study mechanism(s) of cross-species transmission.
Targeted (at high-risk species and interfaces) studies of wildlife host ecology.
Study on the genetic evolution of coronaviruses.
Modelling future landscape changes.
Better understanding of the industries driving spillover events.

Dependencies
What else needs to be done before we can solve this need?

Surveillance in regions where risk of spill over is high (high viral biodiversity)
In rural and backyard poultry systems birds may not be vaccinated.
Raise the profile of the link between biodiversity loss and disease.

State of the Art

Existing knowledge including successes and failures
CoVs largest diversity has been isolated from bats, particularly alpha-CoVs and beta-CoVs have been detected in mammals. A survey of CoV diversity carried out on approximately 20,000 animals in Latin America, Africa, and Asia, found host ecology to be the primary driving factor of bat-CoVs . Anthony et al. 2017 https://academic.oup.com/ve/article/3/1/vex012/3866407?login=true

Projects *What activities are planned or underway?*
PREDICT Project Sars-CoV-2 and other coronaviruses in Wildlife (UK)

Lead Summary [11B]- Livestock

Research Question *What are we trying to achieve and why? What is the problem we are trying to solve?*
Mitigate the risk of the occurrence of new and existing coronaviruses causing severe diseases in livestock and/or potential zoonotic severe impact and/or spillover to wildlife.

Challenge(s) *What are the scientific and technological challenges (knowledge gaps needing to be addressed)?*
It is difficult to predict what the next coronavirus capable of causing severe disease in livestock will be. Limited knowledge on cross-species transmissions (especially at the wildlife-livestock interface). Data on several CoV in livestock are not monitored. Vaccination strategy and approach varies between backyard and commercial poultry industries. This has an impact on viral shedding. Animal management and housing strategies – co-habitation of livestock and handlers in low- or middle-resource regions means that there is risk of spillover/spillback.

Solution Routes

What approaches could/should be taken to address the research question?
Surveillance programme for CoV genetic evolution. Integration of one health approach into the surveillance of coronaviruses.

Dependencies *What else needs to be done before we can solve this need?*

State of the Art *Existing knowledge including successes and failures*
Expression of DPP4 from various livestock species on BHK cells suggested a broad range of livestock animal groups as potential amplifying hosts of MERS-CoV. Kane et al. https://www.annualreviews.org/doi/full/10.1146/annurev-animal-020420-025011#_i7 List of the main coronaviruses infecting farm animals https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7537542/

Projects *What activities are planned or underway?*

Coronavirus in domestic ruminants in southern Italy; description of cases of inverse zoonotic infections.(IZS ME/Italy Giovanna Fusco)

Lead Summary [11C] – Humans

Research Question
What are we trying to achieve and why? What is the problem we are trying to solve?

Mitigate potential spill-over from (and to) animals, including pets, wildlife, and livestock.

Challenge(s)
What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Predicting the next 'jump' of species.
Pets are a risk as well as wildlife and livestock.
Socio-economic challenges.
Environmental degradation, increased housing and disruption can lead to human disease.
Consideration of dual-use activities and intentional release which threatens safe research.
Methods to differentiate between intentional/deliberate and natural spill over.

Solution Routes
What approaches could/should be taken to address the research question?

Quantify risk of animal product consumption for emergence of variants of public health concerns.
Identify high-risk interfaces between humans and wildlife.
Identifying changes in the virus in crossover to humans.

Dependencies
What else needs to be done before we can solve this need?

Cross-sector working across environment, health, housing, etc.

Ensure laboratory biosecurity standards are maintained.

Trade of live animals of high-risk species should be avoided and/or highly controlled.

State of the Art
Existing knowledge including successes and failures

SARS-CoV, MERS-CoV and SARS-CoV-2 had involved domestic or wildlife animal as reservoir or as intermediate host.

Projects
What activities are planned or underway?

Surveillance of immune responses to SARS-CoV2 and vaccination using serology. Anna Lacasta et al. ILRI (2020-2021)
Animal coronaviruses in humans: knowing them to prepare for new pandemics.(IZS LER/Italy Maria Beatrice Boniotti)
OneCoV: Emerging animal coronaviruses and their impact on public health (IZS AM, Italy Alessio Lorusso)

Lead Summary [11D] – Vectors

Research Question *What are we trying to achieve and why? What is the problem we are trying to solve?*
Identification of potential vectors.

Challenge(s) *What are the scientific and technological challenges (knowledge gaps needing to be addressed)?*
Unknown role of mechanical vectors in transmission. Better understanding of role of vectors in transmission of coronaviruses is required.

Solution Routes *What approaches could/should be taken to address the research question?*

Dependencies *What else needs to be done before we can solve this need?*

State of the Art *Existing knowledge including successes and failures*
Not relevant route of infection for coronavirus.

Projects *What activities are planned or underway?*

Lead Summary [12] - Environment including farming systems

Research Question
What are we trying to achieve and why? What is the problem we are trying to solve?

Role of different environments, including farming systems, in virus patterns transmission.

Challenge(s)
What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

High capacity of CoV to mutate and adapt in different settings.
Farming/trade of highly susceptible species e.g., mink, racoon dogs.
Humans keep a variety of species as pets.
Lack of legal framework (e.g. proximity law in agriculture) in some regions which introduces disease risk.

Solution Routes
What approaches could/should be taken to address the research question?

Assess critical environment at interface.
Evaluate exposure risks associated with density in farming systems, agricultural intensification and environmental changes, trade of domestic and wild animals, changing distribution of invasive species.
Understand how current trends in land-use change (e.g. to achieve net zero targets) may influence pathogen emergence risks.
Increase biosecurity requirements for breeding and trade of possible high-risk products, including eg mink/mink skins.

Dependencies
What else needs to be done before we can solve this need?

Improved monitoring and data accessibility.

State of the Art
Existing knowledge including successes and failures

Projects
What activities are planned or underway?

Lead Summary [13] - Host genetics

Research Question *What are we trying to achieve and why? What is the problem we are trying to solve?*
Understand how host genetics influence susceptibility to coronavirus infections.

Challenge(s) *What are the scientific and technological challenges (knowledge gaps needing to be addressed)?*
Identifying specific genetic variants linked to immune response and understanding their mechanisms. Interdisciplinary collaboration to bridge existing knowledge gaps. Lack of SNP CHiP data reporting guidelines and online repository so sharing and using this data is very challenging.

Solution Routes *What approaches could/should be taken to address the research question?*
Large scale Genome Wide Association Studies (GWAS). CRISPR-Cas9, and other gene-editing technologies, for functional genomics to study genetic variants and their role in immune response. Population genetic studies focusing in identifying protective alleles. Multi-omics approaches. Models to integrate genetic, transcriptomic, and clinical data, to understand interactions between genetic variants and immune responses.

Dependencies *What else needs to be done before we can solve this need?*
Advanced genomic techniques. Bioinformatics systems. Establishment of infrastructure for data management and interpretation. Farms cannot manage the recording necessary for phenotypes and genotypes. Public acceptance.

State of the Art *Existing knowledge including successes and failures*

Projects *What activities are planned or underway?*

Lead Summary [14] - Pathogen genome

Research Question
What are we trying to achieve and why? What is the problem we are trying to solve?

Understanding which genome changes increase pathogenicity and cross-species jump.

Challenge(s)
What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Little is known on pathogenesis of bat viruses.
Unknown genomic changes that can increase pathogenicity and cross-species jump.

Solution Routes
What approaches could/should be taken to address the research question?

Identify genomic targets that are highly conserved and specific to the pathogenic strains.
Reverse genetic studies in-vivo and in vitro infection assays.

Dependencies
What else needs to be done before we can solve this need?

Facilitating data sharing and interoperability.
Surveillance strategies.
New technologies for multiplex detection and sequencing strategies.
Continued improvement of whole genome sequencing.
technologies (e.g. high-throughput sequencing technologies) for genomic surveillance.

State of the Art
Existing knowledge including successes and failures

Projects
What activities are planned or underway?

CORUVA (UGent)- Surveillance of coronaviruses in cattle and pigs with emphasis on the zoonotic risk.
Study of endogenous viral elements integrated into the genome (EVE) of domestic and wild species and their significance in the course of Coronavirus infection. Epidemiological investigations on domestic and wild animals for the search for specific antibodies. (IZSME-Italy Marita Georgia Riccardi)