STAR-IDAZ
International Research
Consortium on Animal Health

1. **Roadmaps for the development of diagnostic tests and therapeutics for helminths**
2. **Roadmaps for the development of candidate vaccines and control strategies for liver fluke and nematodes**
3. **Roadmaps for the development of candidate vaccines, diagnostic tests and control strategies for FMD**
4. **Roadmap for research to underpin the development of control strategies for ASF**

SIRCAH Deliverable 3.4

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Interactive versions of the roadmaps in this report can be found at https://roadmap.star-idaz.net

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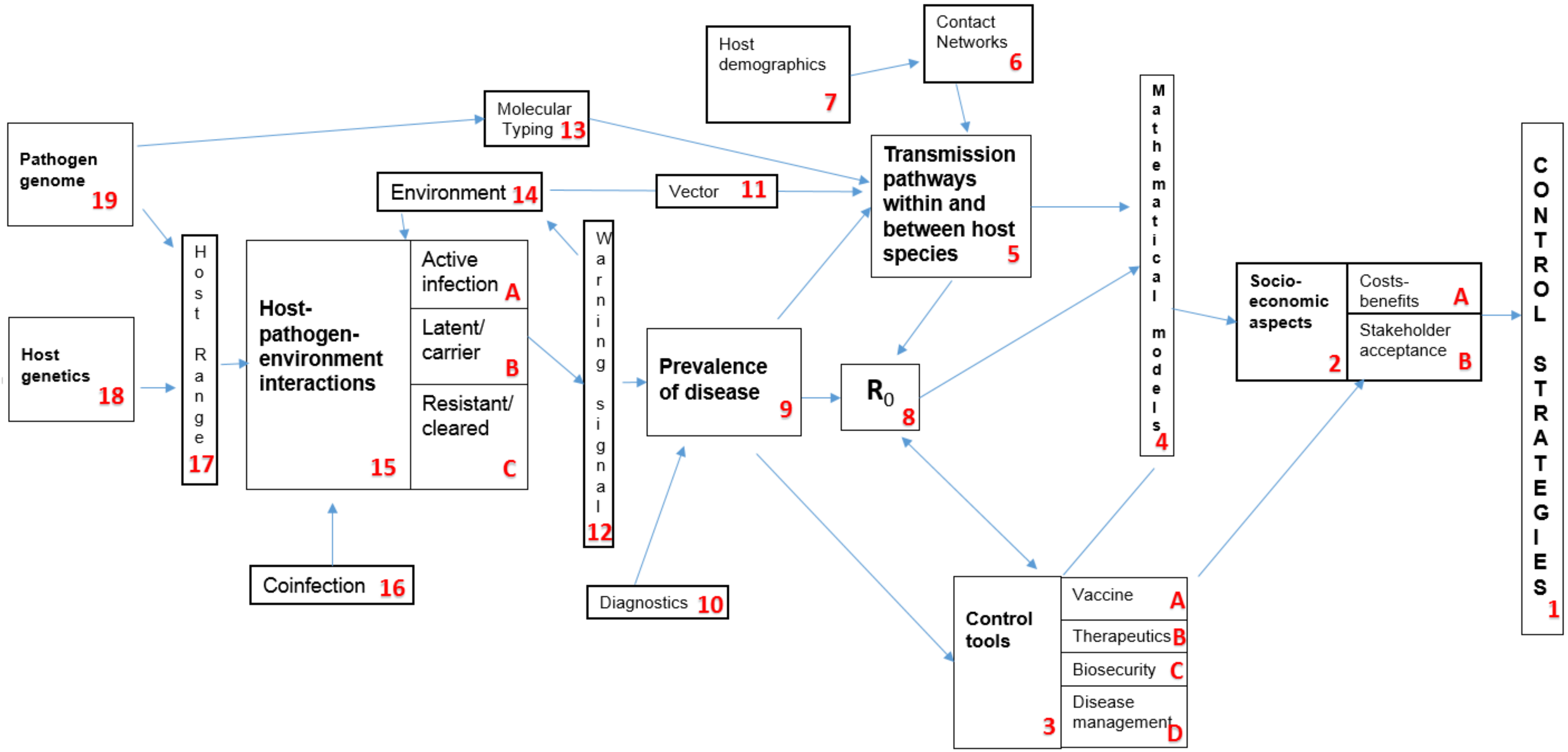
2bii) Roadmap for the development of control strategies for nematodes



The roadmap for development of Nematode control strategies has been developed by the Livestock Helminth Research Alliance (LiHRA; June 2019) with major contributions of Eric Morgan, Felipe Torres Acosta, Pedro Gonzàles-Pech, Theo De Waal, Stig Milan Thamsborg, Hervé Hoste, Smaro Sotiraki, Andy Greer, Jan Van Wijk and Jozef Vercruysse.

Nematode epidemiology - Lead Summary 1 (Overview of control strategies)

Title:	Control strategies for nematode infection in livestock

Research Question

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

Sustainable management of nematode parasites to minimise production loss and welfare implications. Problem is drug resistance so need to simultaneously reduce dependence on conventional anthelmintics and maintain efficacy of current and novel control methods.

Challenge(s)

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

Main industry challenge is failure of current drug-based control methods due to anthelmintic resistance (AR). Headline technical /scientific challenges are consequently:

Measurement of AR. Gap: reliable and affordable tests for field and laboratory use to monitor efficacy and allow early reaction.
Preservation of drug efficacy. Gaps: (a) understanding of how refugia can attenuate AR development and providing adequate evidence base and technical tools to implement refugia in practice in different production systems. (b) Lack of proven tools and/or methods to restore efficacy once lost.
Evaluation of alternative parasite management approaches. Gaps: standardised methods to quantify effects of alternative control methods; optimisation of their use to maximise production / economic impacts; integration of multiple methods in different environments.

Itemised list of priority challenges:
(a) Practical tests with high sensitivity and specificity for detection of AR, to enable routine efficacy monitoring.
(b) Robust and user-friendly means to quantify infection thresholds for intervention in groups and/or individual animals across ages, physiological stages and breeds, in different management conditions.

(c) Quantitative knowledge of the factors acting on nematode stages outside the definitive host in different ecosystems and vegetation types and how they contribute to refugia and can be managed to slow resistance and/or reduce overall nematode exposure.
(d) Mechanisms used by different host species and possibly breeds to avoid, control or expel their infection, including immune resistance, innate responses, repellence and resilience.
(e) Changes caused in micro-biota and host environment in case of infection and when consuming different types of vegetation, and how this could be associated with different levels of host susceptibility.
(f) Identify mechanisms of interaction between nematodes and other parasites and microbes, and how they influence integrated parasite control strategies.
(g) How to identify and produce susceptible nematodes to enhance the reversion of resistance of parasites at local and regional levels.
(h) Identify what level of nutrition can achieve sufficiently high resilience and resistance against nematodes to reduce dependence on anthelmintic treatments.
(i) Dose confirmations for 'minor' host species such as goats, deer, camelids, rabbits, turkeys, pheasants, etc.
(j) Thresholds of consumption of fresh or preserved nutraceutical/ bioactive plants for significant control of nematodes.
(k) Identify the role of wildlife in the epidemiology of nematodes in livestock.

Solution Routes

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

(a) Validation of pen-side field diagnostic tools to measure levels of infection, drug resistance and individual animals needing treatment.
(b) Define thresholds (economic + parasitological) that support decisions for treatment regimens that minimise unnecessary use of drugs, and slow the development of AR.
(c) Identify the mechanisms of defence of different livestock species and breeds.
(d) Identify the genetic basis of host resistance to support targeted treatment and selective breeding.
(e) Design control strategies with a holistic perspective that involve the most relevant nematodes and co-infections for each region.
(f) Evaluate integrated use of bioactive plants in pasture management.
(g) Different global regions must preserve treatment-naïve parasites for future attempts to achieve reversion to susceptibility.
(h) Perform dose confirmation trials for treatment options in those host animal species considered of minor economic relevance.
(i) Implement worldwide production of *Haemonchus contortus* vaccine for all the areas where this parasite may cause problems.
(l) Implement clear harmonization guidelines for the evaluation of plant materials used either as nutraceuticals or in the form of medicinal remedies.

Dependencies

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

Cost benefit analysis of the various treatment options.
Knowledge of stakeholder acceptability.
Generate information on the survival of on-pasture nematode stages in different regions to confirm viability of grazing management strategies.
Develop new vaccines and means for their effective global dissemination.
Develop new therapeutics.

Animal management strategies that minimise disease including using less susceptible breeds of animals and co-grazing strategies.
Guidelines to evaluate nutraceutical materials.

State of the Art

Existing knowledge including successes and failures

(a) Most studies focus on single species infections but multiple parasite species are the norm.
(b) Nutrition is the source of parasites and also a cornerstone solution for integrated parasite control of livestock, but is rarely considered when evaluating control strategies.
(c) Interactions between plants, gut microbiota and parasites have been neglected.
(d) Missing information on feeding behaviour patterns affecting level of infection, and mechanisms affecting plant selection and appetite.
(d) Lack of harmonization guidelines to test the efficacy of plant medicinal remedies or nutraceuticals.
(f) Available tools to identify animals with high worm burdens, and drug efficacy, depend on time-consuming laboratory methods, or indirect methods with very poor sensitivity and specificity, leaving farmers without a practical on-farm diagnostic alternative.
(g) There is sufficient evidence of efficacy against *Haemonchus contortus* for copper oxide wire particles and the Barbervax© vaccine (in sheep) and lungworm vaccine (for cattle in endemic areas) to propose them as viable alternative approaches for the control of nematodes that may reduce the use of conventional drugs.
(h) Nematophagus fungi can also be considered a viable alternative control tool but needs more evidence under hot tropical farming conditions were larvae die naturally in short periods of time.
(i) For other promising alternative control approaches evidence is generally insufficient to underpin strong adoption recommendations.

Projects

What activities are planned or underway?

Harmonization guidelines for nutraceutical materials and medicinal plants in preparation.
A large amount of bioactive compounds/material is continuously screened worldwide for anthelmintic (AH) activity
Several field-based methods for nematode faecal egg count diagnostics under evaluation.
Worldwide evidence based on the small proportion of animals with high worm burdens in different ecosystems, species, breeds, etc. increment the support for targeted treatment methods.
World-wide hunt for anthelmintic susceptible GIN isolates that could be used for reverting resistant strains to susceptible strains under way.

Nematode Epidemiology - Lead Summary 2A (Socio-economics)

Title:	Socio-economic aspects of nematode control: costs and benefits

Research Question

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

Determine the production and economic impacts of nematodes and AR for different species and breeds in different ecosystems.
Develop tools to quantify the economic impact of nematode infections at national, regional and farm levels.
Support decision-making by governments, animal health organisations and farmers, taking into account socio-psychological processes.

Challenge(s)

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

Current systems use average production estimates and thus lack farm-specificity. They are based on partial budgeting and do not reflect the effect on the whole-farm economic performance.
Evaluation of farmer practices currently takes little account of drivers behind their decisions, leading to top-down recommendations for changes in control strategies that have little impact on behaviour.

Solution Routes

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

Surveys of economic impact that consider farm performance holistically and not just the immediate impact of parasite on production.
Evaluations of the relative production impact of nematodes on more or less resistant/resilient animals within a farm.
Systems to capture parasite levels and production impacts easily on-farm and translate information into decision support.
Concentrate data from the latter into data-bases over wider geographical areas that can be updated with mobile phones, tablets or computers, in order to take account of wider comparisons in decision support.
Additional studies to determine the production impact of nematode infections in various geographical settings, with inclusion of less-studied impacts such as fertility, greenhouse gas emissions.
Use development of various economic modelling approaches and adapt them to the over-dispersed nature of nematode infections.

Dependencies

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

Stronger collaboration between parasitologists and field vets or farmers with experience in counting nematode eggs, and with animal production background to be able to develop strong field data.
Linking economic models to real data collected on farm, rather than economic models that estimate impact based on previous knowledge on productivity impact only.
A closer collaboration between the model-makers and model-users and the stimulation to develop concrete business cases may be the critical success-factor for these systems to become self-sustainable in the near future.
Tools to enable accurate information of the level and prevalence of infection to be collected practically by farmers and fed into decisions.

State of the Art

Existing knowledge including successes and failures

Whereas an increasing amount of data are being generated for the direct production impacts of nematode infections, more emphasis should now be given to the production and economic impacts of AR.

Vets, researchers and farmers should be willing to confirm the efficacy of the drugs used against nematodes on a yearly basis.

Over the last decade, some progress has been made in assessing the production economic impacts of nematodes in ruminants, and these have extensively been reviewed in sheep and in cattle highlighting the need for more specialized research, particularly in the definition of the nutritional cost of nematodes.

A remaining gap is to establish the impact on fertility parameters using randomized intervention field studies.

The major challenge is to develop tools that are able to quantify the economic impact of nematodes at national, regional and farm level to support decision-making by various stakeholders and that can be used as management tools.

An efficiency analysis approach was successfully developed for GI nematodes in cattle, but it should be converted into a user-friendly advice tool and to other parasite and livestock species.

Projects

What activities are planned or underway?

Generating an App platform to capture faecal egg counts of GI nematodes from different animals within a farm and collect that information together with production data.

Generating a task force of farmers, vets and statisticians and economists to determine costs of GI nematodes in those farms with or without AR.

Co-ordination of methodologies for investigating farmers' practices and drivers of behaviour (COST Action COMBAR).

Nematode epidemiology - Lead Summary 2B (User acceptance)

Title:	Socio-economic aspects of nematode control: stakeholder acceptance

Research Question *What are we trying to achieve and why? What is the problem we are trying to solve?*
Improve the development and uptake of best practice management of nematode control.

Challenge(s) *What are the scientific and technological challenges (knowledge gaps needing to be addressed)?*
Develop user-friendly tools for farmers to help them identify animals with high nematode burdens or production consequences. Utilise production records that include information on treatments or egg counts to be able to advise farmers when to treat an individual. Demonstrate and quantify the economic benefits of best-practice interventions such as diagnosis of AR and implementation of targeted control. Investigate communication methods to reach farmers in different parts of the world and let them feel secure to share their nematode information and production data.

Solution Routes *What approaches could/should be taken to address the research question?*
Development and extension of decision support tools that can act either alone but can also be integrated in general farm or pasture management software. Development of nematode control decision support systems for beef, sheep, goat and pigs. Demonstration trials showing the feasibility and beneficial outcomes of best practices approaches Propagate information about the importance of nutrition as the corner stone of resistance and resilience against gut nematodes, hence reducing the need for antiparasitic treatments.

Dependencies *What else needs to be done before we can solve this need?*
Develop long-term relationships with farming communities.

Cost-benefit analysis demonstrating the cost of disease and the economics of various treatment options. Develop animal production and nutrition expertise within the parasitological community. Vets need to receive updated training to implement targeted control strategies and increase user acceptance.

State of the Art *Existing knowledge including successes and failures*
Good evidence-based nutritional advice is already available to achieve best possible levels of resilience and resistance to nematodes. Educational courses for vets on implementation targeted control strategies have been performed sporadically.

Projects *What activities are planned or underway?*
Diffusion of extension material proposing the implementation of good nutrition of sheep as the cornerstone of nematode control. Start propagating information on the efficacy of copper oxide wire particles, and make sure farmers have a place to obtain them, with clear knowledge of the possible toxicity problems of this method.

Nematode epidemiology - Lead Summary 3 (Mathematical models)

Title:	Mathematical models for prediction and control

Research Question *What are we trying to achieve and why? What is the problem we are trying to solve?*
Can we improve current mechanistic mathematical models to replace current forecasting systems that are only applicable to certain regions and to evaluate novel control strategies?

Challenge(s) *What are the scientific and technological challenges (knowledge gaps needing to be addressed)?*
Current forecasting systems cannot be extrapolated to other regions without further development and validation. Poor quantitative understanding of acquired immunity mechanisms. Poor understanding of the proportion of animals really showing high quantity of nematodes, i.e. drivers of aggregation. Poor understanding of the importance of nutrition on the onset of production impact or clinical problems. Poor understanding of the pivotal importance of adult animals as carriers of nematode populations from summer to spring or from rainy season to the next rainy season.

Solution Routes *What approaches could/should be taken to address the research question?*
Experiments on effects of environmental conditions on the development and survival of infective stages on pasture in different geographical settings.

Development of transmission models that simulate disease dynamics and host responses, and production consequences. Develop easy methods for farmer input of data on animal density and status, treatments and movements, to calibrate models. Also means of presenting results to farmers for decision support.

Dependencies *What else needs to be done before we can solve this need?*
Field data on levels of infection to validate models. Impact of climate change in all the epidemiological models of infective stage development and survival.

State of the Art *Existing knowledge including successes and failures*
There is information on the paddock infectivity in many temperate areas but need to be re-visited w.r.t. climate change Information in non-temperate ecosystems is limited and points to lower survival of free living stages. Modelling must consider the death of most infective larvae in the dry season of many tropical areas, which means that adult animals become the carrier of susceptible or resistant GI nematodes. Hence, TST schemes are crucial in those conditions.

Projects *What activities are planned or underway?*

Ongoing work to develop forecast models and farm-directed models that utilise additional information from the farmer to provide real-time decision support.

Nematode epidemiology - Lead Summary 4A (Control tools - vaccines) See separate roadmaps for vaccines.

Title:	Epidemiologic requirements of vaccine against nematodes and consequences of vaccine use on the epidemiology of nematodes.

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

How long should a vaccine protect livestock and what levels of protection would be sufficient to prevent disease and production losses?
Do all animals in a group need to be vaccinated?
Is there a benefit to female vaccination for protection of the offspring?
What are the consequences of a mono-valent vaccine on the species composition and structure of worm populations?

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

Levels of efficacy required may vary among nematode species, the class of livestock targeted and between regions, depending on climatic context and local farm management practices.
Vaccine efficacy may vary between breeds depending on mechanisms of defence; also depending on the nutritional status of the vaccinated hosts; and in offspring co-grazing with dams.

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

For logistical, financial and animal welfare reasons, it will be practically impossible to test all possible scenarios by vaccine trials in the field. Evaluating vaccine efficacy requirements through mathematical modelling could be a valuable tool to help define useful levels of protection and to model integrated use of vaccines with other parasite control measures.

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

At present, regulatory authorities are not familiar with registration of nematode vaccines.
Modelling of the required efficacy of a vaccine for any given environment to provide a meaningful epidemiological benefit.

State of the Art
Existing knowledge including successes and failures

A hidden antigen vaccine (Barbervax©) has been developed and tested in different parts of the world against *H. contortus* with excellent levels of protection under natural conditions. This vaccine might not be sufficient where other parasites are more relevant.
A model simulating the effect of vaccines against larval stages or adult *H. contortus* in sheep has been developed, but a threshold

for protection needed to protect animals from acquiring harmful burdens during the entire grazing season has not been determined.
A live attenuated vaccine against lungworm (*Dictyocaulus viviparus*) in cattle has been in use for some decades.

Continue to test the existing *H. contortus* vaccine in different countries. Try to set-up production facilities for this vaccine in different countries to avoid importation restrictions.
Recombinant vaccines are in development for several GIN species and liver fluke but none are yet registered for use.

Projects *What activities are planned or underway?*

Nematode epidemiology - Lead Summary 4B (Control tools - therapeutics)

Title:	Sustainable use of anthelmintics in livestock production.

Research Question

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

What is the prevalence and incidence rate of anthelmintic resistance in nematode populations?
To reduce the use of AH by implementing integrated control with alternative solutions.
Can we use a targeted selective treatment (TST) scheme to slow selection of AH resistant strains at each farm?
Can copper oxide particles (COWP) be used in a sustainable approach for ruminant livestock?

Challenge(s)

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

Gathering information on the availability and use of AH in the different countries worldwide and gathering information on the status of AR and how this varies even within a season.
Establish if rotating anthelmintics delays the development of resistance.
Confirming what is the proportion of TST treated animals that may help to stop further development of AH resistance.

Solution Routes

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

(a) Generate a user-friendly tool to determine FEC of animals to confirm whether a drug was effective or not.
(b) Use indices such as the happy factor®, FAMACHA© or the BCS to identify candidates for treatment and confirm with a pen side egg count tool to immediately implement TST schemes.
(c) Quick and reliable test to detect AR in the field
(d) Quick and reliable test to measure levels of refugia in fields.
(e) Can we obtain local susceptible nematode strains to implement management strategies to reverse the anthelmintic resistance status on a farm?

Dependencies

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

Development of new therapeutics.
Field studies of the integration of therapeutics in disease management strategies.
An effort to educate vets and farmers to obtain a yearly diagnosis of the efficacy of the drug used at the farm in the previous year.

State of the Art

Existing knowledge including successes and failures

Recently, it was found that if the use of multiple active AH is combined with “best practice parasite management,” based on avoiding overuse of anthelmintics, minimizing nematode challenge to susceptible animals, and maintaining a nematode population in refugia, can help delaying development of AR.

It has been confirmed that the use of AH drugs in a TST scheme may help stop further development of AH resistant strains in a farm by maintaining a high proportion GIN in refugia.
The use of COWP against *H. contortus* has been proven in sheep and goats with good levels of efficacy for preventive and curative objectives. However, Cu accumulation is evident and Cu contamination in the paddock needs to be considered.

TST schemes in sheep and goat farms in USA, Mexico, Costa Rica, Brasil, South Africa, Botswana, Malawi, Mozambique and other countries.
Develop an application for mobile phones/tablets that provides information to farmers on the use of AH treatments and, in return, farmers can provide information on when, what, why in regards of AH treatments.

Projects
What activities are planned or underway?

Nematode epidemiology - Lead Summary 4C (Control tools – natural tools)

Title:	Biocontrol tools including nutrition, nutraceuticals and nematophagous fungi for the integrated control of nematodes

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

To evaluate the impact of alternative solutions based on natural tools (such as supplementary feeding, nutraceuticals and nematophagous fungi) on the epidemiology of nematodes in different farming systems and host species, with and without the use of chemical drugs.
Address the question of variability of resources and the practicality of large-scale application in different environmental and farming conditions.

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

Develop and validate harmonization guidelines for the in vitro/in vivo evaluation of different plant resources as nutraceuticals.
Large scale production and easy distribution of spores of nematophagous fungi.
Implement a practical delivery route for nutraceutical materials.

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

Include quantitative data on efficacy from different alternative control measures obtained in different production systems to feed mathematical models that can help to predict the best practices for nematode management.

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

Cost-benefit of these methods in comparison with synthetic anthelmintics, and the resulting reduction in AH use.
Possible interactions between these natural tools and with therapeutic tools, vaccines, grazing management and host genetics.
Deliver information of results to farmers with these methods and explore practical and complimentary ways to use natural alternatives on-farm.

State of the Art
Existing knowledge including successes and failures

Proofs of concept for supplementary feeding, nutraceuticals and for nematophagous fungi have been obtained with different hosts, ages, and physiological status, either against mono specific or mixed nematode infections. Large-scale implementation requires further evaluation under different production systems.

Projects *What activities are planned or underway?*

Provide quantitative data on the control of nematodes with the natural alternatives in different livestock production systems and different nematode life stages.

Identify thresholds concentration and time of distribution to ensure efficacy and impact on nematode epidemiology and cost-benefit.

Data to calibrate and validate models of alternative control.

Nematode epidemiology - Lead Summary 4D (Control tools - biosecurity)

Title:	Preventing the introduction of drug-resistant nematodes onto farms.

Research Question *What are we trying to achieve and why? What is the problem we are trying to solve?*
Prevent the introduction of AR parasites into farms where not already present.

Challenge(s) *What are the scientific and technological challenges (knowledge gaps needing to be addressed)?*
The relative importance of new animal introduction and on-farm management in any change of AR status. Identify seasons when animal introduction can be more dangerous as carriers of AH resistant worms from other farms. Favour the entrance of susceptible worms from farms where the level of susceptibility has been previously confirmed (avoid quarantine AH treatment). Establish and communicate best practice AH quarantine procedure.

Solution Routes *What approaches could/should be taken to address the research question?*
Generate user-friendly tools to determine FEC of animals to confirm whether a drug was effective or not after quarantine treatment. Establish local susceptible nematode strains to implement management strategies to reverse AR status of worms from animals introduced to a farm?

Dependencies *What else needs to be done before we can solve this need?*
Pen-side diagnosis of egg counts will make AR diagnosis possible and verify effective quarantine. Effective communication of best-practice quarantine protocols.

State of the Art *Existing knowledge including successes and failures*
There is evidence suggesting that we can revert AR by substituting worm communities in sheep, and this could be attempted in animals after quarantine treatment. By avoiding quarantine treatment, we can introduce susceptible GIN from those farms where that type of population exists.

Evidence for the effectiveness of quarantine exists but farmer surveys indicate that correct application is rare.

Projects *What activities are planned or underway?*

Continue motivating the use of AR tests on a yearly basis based on egg counts (either with or without control untreated groups). Identifying AH susceptible local populations that can be used for safe reversion to susceptibility.

Nematode epidemiology - Lead Summary 3E (Infection management)

Title:	Infection control through pasture management

Research Question

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

Animals obtain infection from infective elements present in the grass or vegetation. Pasture infectivity will depend on the number of nematode eggs deposited in the paddock, their ability to hatch into larvae and the survival of the latter, which is also limited by the environment. In some areas of the world the infective larvae die in approximately one month but in other places they can survive for several months. We need to confirm under what conditions is possible to use grazing management as a nematode control tool. Such techniques should be based upon the principle that grazing management aims to utilise vegetation when available at its best nutritional quality, and pasture infectivity is a secondary consideration.

Challenge(s)

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

Identify the persistence of survival of infective larvae in many environmental conditions where this has not been investigated.
Methods to evaluate presence of infective larvae in grass and other plant species (i.e. herbs and shrubs).
Confirm what plant species hosts in each ecosystem consume, and whether such materials are contaminated with L3 larvae.

Solution Routes

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

Implement tracer studies with species of host of interest as different animal species displays different feeding behaviour in each type of sward.

Dependencies

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

Confirm that rotation or mixed grazing are realistic options to reduce the presence of infective elements on paddocks.
Sometimes paddocks are communal and farmers cannot avoid other farmers to use the paddocks in any rotational scheme.

State of the Art

Existing knowledge including successes and failures

Plenty of experimental information shows viability of paddock change, rotational or mixed schemes. However, those methods are still not disseminated. Rotation schemes require a high level of management, including fencing, trained staff or motivated farmers. The goal is also to take advantage of the vegetation, allowing re-generation and avoiding over-exploitation.

Projects

What activities are planned or underway?

Research on the feeding behaviour of ruminants and levels of infectivity in tropical paddocks.

Nematode epidemiology - Lead Summary 5 (Transmission pathways within and between host species)

Title:	Identification of transmission pathways of nematodes and anthelmintic resistance.

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

Transmission pathways, i.e. the life cycle, is already well-established for the important nematode species of livestock. Further understanding of the role of host demographics and farm organisation in the transmission of nematodes and AR could assist control, especially more limited and targeted use of drugs and maintenance of their efficacy.

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

To understand the use of pathways and organisation of pasture exploitation e.g. different stocking rate, continuous or rotational use, resting time, types of vegetation, possible mixed grazing in different farm systems (milk or meat production or temperate *vs.* tropical conditions) and different grazing management/residual levels.

To identify situations of interactions between different flocks (i.e. transhumant flocks, communal grazing) or buying animals from another herd/flock.

Confirming for every ecosystem which are the months of the year when eggs and infective larvae die out by themselves, and alert farmers that in those months they should only treat those animals that really need anthelmintic intervention.

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

Perform tracer studies in different ecosystems where the host species are important for the economy.

Develop software to describe the organisation at farm level, to understand the dynamics of infection.

Dependencies

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

Identify the main inputs (environment and also structure of the herd/flock and use of the pasture) to feed mathematical models for describing the farming organisation.
Recording the use of AH treatment in different groups of animals within the flock.
Use mobile phone/tablet/computer application or programmes to help decision-making at farm level with information collected into a large international or national database for future epidemiological work.
Train vets and researchers to produce worm free tracers, identify eggs, infective larvae and adult worms.

State of the Art

Existing knowledge including successes and failures

There are differences between nematodes in terms of host specificity. This has been exploited to control nematodes, especially GIN, at the farm level by using different host species (e.g. mixed or rotational grazing).
Prior exposure to drugs in the host will result in the survival of resistant adult worms that will seed resistant eggs and larvae to the paddock, making the spread of AR more likely.
There are expert groups that can train vets and other researchers to perform those studies.

Projects

What activities are planned or underway?

Train vets and researchers to produce worm free tracers, identify eggs, infective larvae and adult worms.
Generating the large-data base with AH treatments world-wide (who, what, when, how, why).

Nematode epidemiology - Lead Summary 6 (Contact networks) See also Box 13 (host range).

Title:	Role of animal contact patterns in nematode transmission and control.

Research Question

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

Nematodes, like other infectious agents, are transmitted through shared contact with pasture, so contact networks between individual animals are less relevant to transmission than patterns of pasture utilisation, in relation to contamination patterns and climate (hence Host-Parasite-Environment interactions, see box 15).
Contact between host species, including wildlife, can influence transmission but is currently not usually estimated.
Effect of management and animal movement on gene flow between populations might be better understood by applying (group-pasture based) contact network approaches.

Challenge(s)

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

Integrate movement of livestock groups between pastures, including sharing of pastures between different stock classes, species and with wildlife, into epidemiological understanding and modelling.

Solution Routes

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

Match population genetic data with movement / contact networks to validate models and/or to estimate contact rates.
Develop and apply molecular markers of infection and AR to track contact patterns and the role of contact networks in the spread of resistance.

Dependencies

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

Adapt network approaches to pasture-based contact and nematode transmission.
Develop molecular tools to enable network model validation.

State of the Art

Existing knowledge including successes and failures

Contact networks are well-established in disease transmission theory but need to be considerably adapted to the nematode situation and may or may not offer advantages over purely empirical approaches or existing transmission model frameworks.

Projects

What activities are planned or underway?

None known on this topic.

Nematode epidemiology - Lead Summary 7 (Host demographics)

Title:	Role of animal characteristics in nematode epidemiology

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

Evaluate and quantify the impact of various host-related factors (age structure, physiological stage, level of production, species, breed, etc.) of a herd/flock on contamination levels and transmission.
The nutritional coverage of animal requirements is a key aspect modifying the presence and level of GIN infections in particular.
It is important to consider the possible presence of different host species at farm level as a component of host demographics.

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

We need to determine the role of nutritional status, and other animal factors on nematode infection in livestock species under different environmental conditions, and for the various nematode species.

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

What is the nutritional status of animals that help to limit the worm population and their effects?

Use different livestock species in mixed grazing systems to reduce pasture contamination.

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

Evaluate the importance of acquired resistance and resilience in different livestock hosts.

State of the Art
Existing knowledge including successes and failures

Control of nematodes using nutrition, genetics, vaccines and nutraceuticals can affect the immune response of infected hosts, and consequently epidemiology.
Host stocking density is a major determinant of nematode transmission and can be manipulated to aid control.
It is known that some parasites are specific to some hosts, and that can be used to effectively reduce pasture infectivity.

Projects
What activities are planned or underway?

Implementing methods of culling animals not showing sufficient resilience at farm level, to reduce the density of highly susceptible hosts.

Exploring mixed grazing systems in different conditions to evaluate their value in the control of nematodes through reduction in effective host density.

Modelling studies to quantify the impact of grazing intensification on nematode transmission potential.

Nematode epidemiology - Lead Summary 8 (R_0)

Title:	Apply standard epidemiological approaches such as R0 threshold quantities, to nematode infections.

Research Question *What are we trying to achieve and why? What is the problem we are trying to solve?*
The basic reproduction ratio has been a useful tool in the epidemiology and control of infectious disease, to characterise factors leading to high transmission potential and to set aims and priorities to reduce it. Application to nematode infections has been limited so far and might prove similarly useful, especially when communicating with epidemiologists and policy makers already familiar with the R0 concept but less familiar with the complexities of nematode transmission.

Challenge(s) *What are the scientific and technological challenges (knowledge gaps needing to be addressed)?*
Setting immunity aside, conditions of host density, climate and other environmental components, and treatment, influence the inherent tendency towards establishment and population increase in nematodes and can be quantified using R0. This approach must be adapted to the particular context of nematodes, including parasite-based rather than host-based epidemiological unit, variation in within-farm exposure due to grazing patterns, and the importance of burden rather than prevalence in driving disease outcomes.

Solution Routes *What approaches could/should be taken to address the research question?*
Development of population dynamic models for nematodes and extraction of R0 and related metrics for major nematode species. Application of R0 to make broad comparisons of climate-driven and other factors governing nematode transmission spatially and temporally at various scales, to enhance assessments of climate change impacts as well as design appropriately targeted intervention strategies.

Dependencies *What else needs to be done before we can solve this need?*
Compilation of suitable data on nematode distribution and abundance to enable model testing under different environmental conditions.

State of the Art
Existing knowledge including successes and failures
R0 can already be calculated for many nematode species but wider use would rely on education of target audiences on the concept and its uses and limitations.

Projects
What activities are planned or underway?
Ongoing programme(s) of work to develop R0 to nematodes.

Nematode epidemiology - Lead Summary 9 (Prevalence)

Title:	Prevalence of nematodes and anthelmintic resistance

Research Question *What are we trying to achieve and why? What is the problem we are trying to solve?*
Can we set up a monitoring system to detect variation and changes in nematode prevalence and AR over time, to inform decisions at various spatial scales?

Challenge(s) *What are the scientific and technological challenges (knowledge gaps needing to be addressed)?*
Lack of harmonisation of diagnostic tests and systems. No means of collating and analysing data over large scales for unregulated endemic diseases. Surveys of AR tend to be opportunistic and suffer from strong selection bias. Prevalence does not necessarily relate directly to the more relevant metrics of nematode abundance and level of drug efficacy (c.f. proportion of farms with <95% efficacy).

Solution Routes *What approaches could/should be taken to address the research question?*
Use existing epidemiological methods to select representative farms for surveys and robust sample sizes. Use of existing sample collection schemes based on bulk tank milk (BTM) monitoring programmes and veterinary and hunting networks for the collection of faecal samples from non-dairy livestock and wildlife.

Dependencies *What else needs to be done before we can solve this need?*
Harmonize or integrate diagnostic methods and systems across various countries and regions for comparable results. Develop robust methods to determine nematode species especially GIN from eggs in faeces. Use of private data requires informed consent for all parameters in question.

State of the Art *Existing knowledge including successes and failures*
Complementary to predictive systems, it is important to set up surveillance systems that monitor infection status at farm level on a regular basis. Such systems can capture unexpected deviations from mathematical model predictions and indicate whether farmer management is able to cope with altered disease risk or not. Moreover longitudinal monitoring approaches have been shown to be an effective decision support tool.

Projects *What activities are planned or underway?*
Promote the use of pre- and post-treatment faecal egg counts as a means to confirm the AR situation in each farm at least in a yearly basis. Improving the use of BTM-based recordings for herd

diagnostics. Continue with AR surveys in different countries; integrate data regionally using collaborative networks, e.g. EU COST Actions.

Nematode epidemiology - Lead Summary 10 (Diagnostics) N.B. Separate roadmap for diagnostic test development

Title:	Diagnostic tools for the identification of animals in need of control measures.

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

We need to define diagnostic tools and thresholds useful to decide which animals need treatment, and to determine production and epidemiological outcomes in different hosts and settings.

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

Diagnostic tools are needed that can practically measure (i) levels of nematode infections, (ii) pathophysiological effects in the host (resilience), (iii) immune response (resistance level).
Apply those diagnostic methods at herd/flock or individual levels, including evaluating the efficacy of treatments.
Molecular tools to identify nematode species; resistance status.
Robust intervention thresholds for production or parasitological indicators or combinations.
Use new tools such as sensors of animal behaviour to expand phenotypic markers of high nematode impacts or to improve epidemiological information.

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

Pen-side tools for parasitological or other markers of infection.
Wider validation of simple phenotypic markers (e.g. BCS, FAMACHA©) and use to decide treatments.
Robust methods to determine nematode species, especially of GIN from eggs in faeces.
Use mobile phone computer applications to integrate information from diagnostics and help decision-making at farm level, with information collected into a large international or national database for future epidemiological work.

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

Practical and low cost methods to automate markers of nematode infection, e.g. FEC for GIN, and the means to collect data and deliver it in a form useful for farmer decision support and epidemiological analyses.
Understanding of socio-psychological factors influencing adoption of diagnostics in support of improved control.

State of the Art
Existing knowledge including successes and failures

Few methods for detection of nematodes or AR in the field except faecal egg/larval counts. Poor standardisation of laboratory tests for AR. Little use of diagnostics by farmers to determine time or type of intervention/ treatment.

Projects *What activities are planned or underway?*
Several initiatives to develop and improve pen-side FEC for GIN and other markers of infection, e.g. copro-antigen for liver fluke. Extension programs to increase the farmer awareness of the use of diagnostic tools to avoid unnecessary treatments.

Nematode epidemiology - Lead Summary 11 (Vectors)

Title:	Intermediate host factors influencing control measures.

Research Question *What are we trying to achieve and why? What is the problem we are trying to solve?*
How do intermediate hosts ('vectors'), where involved in life cycles, influence epidemiology and approaches to control?

Challenge(s) *What are the scientific and technological challenges (knowledge gaps needing to be addressed)?*
Current knowledge of the population dynamics of intermediate hosts (IH) especially snail IH of trematodes, and how they affect epidemiology, is implicit and not explicit. How does genetic diversity within snail IH species influence their suitability as hosts and asexual amplification of nematodes? In the absence of favoured IH, can nematodes switch to alternative IH species and maintain transmission? Can IH populations be manipulated to decrease transmission and infection risk for livestock?

Solution Routes *What approaches could/should be taken to address the research question?*
Ecological studies of snail and other relevant IH species especially in situ, to include abiotic (e.g. topography, soil type, climate) and biotic (e.g. competitors, predators, co-infectors) factors that could influence spatial distribution and transmission potential. Impacts of farm practices on IH habitat and exposure of livestock. Studies of IH genetics and susceptibility in controlled conditions.

Dependencies *What else needs to be done before we can solve this need?*
Laboratory investigations on snail IH are compounded by difficulties in keeping populations in captivity (for *Galba* spp.). Better ways of quantifying snail IH and infection status at pasture would facilitate field-based population ecology studies. Using fencing and/or drainage depends on legislation on environmental integrity and farm subsidies.

State of the Art *Existing knowledge including successes and failures*
Suitable snail habitats are well characterised and various topographical and botanic indicators and predictive models have been developed to help identify them, and integration of IH factors in control are mainly based on avoiding these areas.

Projects *What activities are planned or underway?*
New detection methods for IH (e.g. eDNA) are in development. Genetic factors affecting *Galba* vectorial capacity under way.

Increasing studies on agro-environmental factors and IH habitat.

Nematode epidemiology - Lead Summary 12 (Warning signal)

Title:	Early warning systems for nematode infections.

Research Question *What are we trying to achieve and why? What is the problem we are trying to solve?*
How can we use environmental and animal data to improve risk prediction for nematode infections at various geographical levels? Can we understand farmers' perspectives and experience to better identify high risk of negative impacts in livestock systems?

Challenge(s) *What are the scientific and technological challenges (knowledge gaps needing to be addressed)?*
We need to better define whether animals with high production and large prolificacy are more at risk of nematode infection and impacts. Explore the use of sentinel animals *vs*. the whole flock monitoring as the best approach to detect and prevent problems.

Solution Routes *What approaches could/should be taken to address the research question?*
Knowledge of impacts of climate on transmission processes can be used to generate risk predictions for key nematode species. Models to predict infection should consider climatic data, stocking rates, nutritional conditions, level of production and physiological stage to make a better early warning system for negative impacts on productivity rather than only for infection hazard.

Dependencies *What else needs to be done before we can solve this need?*
User-friendly tools to non-invasively measure infection and its impacts, for farmer early warning and also to calibrate risk models. Analysis of complex data (e.g. production metrics and animal sensors) in real time depends on big-data approaches, e.g. machine learning.

State of the Art *Existing knowledge including successes and failures*
There are already some areas of the world where weather data are used to predict transmission risks (e.g. *Haemonchus contortus, Nematodirus battus, Fasciola hepatica*); these are usually large scale and generic and not easily translated to farmer decision support. Tools for early warning of health status are in use for some nematodes (e.g. FAMACHA), and behavioural sensors are being widely evaluated.

Projects *What activities are planned or underway?*
Development of climatograms and models to predict levels of transmission potential over time in different parts of the world. Refinement and wider testing of monitoring tools and protocols for early warning at herd/flock level, e.g. FAMACHA, pen-side FEC systems. Decision-making of farmers around nematode risk included in ongoing socio-psychological research.

Nematode epidemiology - Lead Summary 13 (Molecular typing)

Title:	Molecular epidemiology

Research Question *What are we trying to achieve and why? What is the problem we are trying to solve?*
What is the importance of genetic diversity to nematode control and how can molecular typing help to elucidate epidemiology, especially gene flow between populations and the establishment and detection of anthelmintic resistance?

Challenge(s) *What are the scientific and technological challenges (knowledge gaps needing to be addressed)?*
In contrast to their application in viral and bacterial infections, population genetic studies have been a relatively underexploited approach to unravel host-parasite interactions and co-evolution, despite their potential to add insights to epidemiology and control.

Solution Routes *What approaches could/should be taken to address the research question?*
Further develop methods for and studies of population genetic structure for the major nematodes of ruminants and pigs and apply them in local studies and on isolates collected from across the world, including populations from wildlife.

Dependencies *What else needs to be done before we can solve this need?*
Parasite genome sequences will facilitate selection of appropriate genetic markers for population studies.

State of the Art *Existing knowledge including successes and failures*
The population genetic structure of nematode species has important implications for evolutionary processes such as adaptation to host defences and the development of AR. Despite some foundation work, surprisingly little is known about the population genetic structure of most species of parasitic nematodes in livestock. Widespread livestock movement at a range of scales is common and normally undertaken with little or no monitoring or effective quarantine measures against nematode parasites. Wildlife, such as rabbits, hares, deer and others, may act as reservoirs and transporters of certain nematode infections and may conversely contribute to *refugia*. Population genetic studies can help unravel the scale and drivers of parasite movements between farms and their role relative to on-farm factors in selection for AR.
Projects *What activities are planned or underway?*
Development of a worldwide network of laboratories working on common tools and protocols to identify population genetic markers for different nematodes. It may include specimens with phenotypic AH resistance and susceptibility.

Nematode epidemiology - Lead Summary 14 (Environment)

Title:	The role of environmental factors and refugia in sustainable control of nematodes and the prevention of anthelmintic resistance.

Research Question

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

Environment is known to affect pasture infectivity, the distribution of nematode populations, and maintenance of refugia at pasture. To date, however, the pathways to use this knowledge effectively to enhance sustainable control are unclear.

Challenge(s)

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

What is the impact of climate and management especially in unusual years, e.g. prolonged grazing season, hot dry summers and cold winters, on worm transmission and burdens?
How large must environmental *refugia* be and how long should they persist in order to minimize selection for AR?
How can we improve the timing of treatment to not only enhance parasite control in the short term but also slow AR?
What are the main environmental factors affecting parasites in *refugia* under temperate and tropical conditions?
We lack knowledge on the movement and survival of GI nematode infective larvae under tropical conditions, particularly for heterogeneous vegetation (browse).
Can knowledge on environmental determinants of liver and rumen fluke be used to guide grazing to reduce disease risk?
Does AR carry a fitness cost to the parasite and how can this be exploited to develop strategies to lead to a reversion to susceptibility?
Are refugia-based strategies appropriate for all nematodes, e.g. fluke, and how do differing life cycles affect approaches?
Climate change is altering infection patterns, and empirical approaches to designing control strategies are of limited use when dealing with increasingly unpredictable transmission.

Solution Routes

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

Build further on mathematical models of nematode epidemiology, including extension to predict *refugia* under varying environmental conditions and treatment strategies.
Integrate nematode management into grazing management at farm level, e.g. under precision grass management systems.

Dependencies

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

Better quantification of development and survival of nematode stages in the environment and intermediate hosts in different ecosystems and vegetation types.

User-friendly tools to deliver pasture-level risk assessments to the farmer in a form that permits appropriate action.

State of the Art *Existing knowledge including successes and failures*
There is abundant experimental work to support predictive approaches to infection pressure for nematodes and trematodes, and sound model frameworks, but there are still important knowledge gaps. Models also need to be validated using stronger field data sets, applied to realistic farm management contexts, and translated more effectively into practical nematode control practices. Empirical knowledge of the topographical and other environmental determinants of liver fluke risk within farms is sound but practical avoidance strategies are still not fully developed and certainly not widely applied, in favour of routine anthelmintic use.

Current knowledge of the genetic basis of AR limits attempts to generate accurate predictions of the impacts of environmental refugia on rate of development of resistance.

Projects *What activities are planned or underway?*
Model frameworks continue to be refined and applied specifically to the challenges of AR and utilisation of refugia-based approaches. Initiatives under way to enhance targeting of AH treatment through risk forecasts and other online tools. Attempts under way to use of the principle of reversion to susceptibility by importing susceptible larvae to the farm when the infective stages in the farm are eliminated. Evaluations under way of alternative approaches affecting environmental nematode stages, e.g. nematophagous fungi, bioactive swards, alternate grazing, reduction of snail populations.

Nematode epidemiology - Lead Summary 15A (HPE interactions – active infection)

Title:	How do host and environmental factors together determine the establishment of infection and shedding of propagules?

Research Question

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

Can we improve the quantitative understanding of innate and acquired immunity against nematodes in livestock in order to better incorporate this into disease control?
How do parasite communities as a whole respond to human intervention, control methods and environmental changes, as opposed to single genera?
What is the effect of treatment and other control measures, and environment, on immune response of different host species?

Challenge(s)

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

Host-nematode interactions are poorly understood in livestock and largely based on the phenomenology of experimental and natural infections.
Influence of nematode infection (and vaccination) on the immune response to other pathogens is largely unexplored.
Studies of the effect of infection dose, host immune status, environment and nutrition on nematode establishment have been performed largely separate and need to be combined to better understand outcomes in the field and realistic farm-level interventions.
The metabolic and pathological costs of immunity might themselves have negative production impacts and optimised (rather than maximal) responses should be sought during the production cycle and in selective breeding programmes but the theoretical and empirical basis for setting these optima is currently inadequate.

Solution Routes

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

Methodological approaches to study the gut environment, microbiota and different nematode stages under in vivo conditions, ex-vivo and in vitro.
More refined studies of mechanisms of innate and acquired immunity in livestock species, including in the field.
Evaluation of the effects of alternative control methods, e.g. plant-based approaches, on different elements of HPE interactions, including nutrition, parasite establishment, and propagule output.

Dependencies

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

Development and availability of multiplex and NGS technologies to define the whole nema- and pathogenome and also the host immune response (innate and induced). Immunological tools for livestock are far behind those available for rodent models.

State of the Art

Existing knowledge including successes and failures

Control of nematodes with nutrition, genetics, vaccines and nutraceuticals is being investigated, but their effects on the immune response of infected hosts, and consequently epidemiology, much less so.

Assumed that natural immunity to fluke infections is limited but reasons for this and prospects of surmounting this through vaccination are subject to ongoing research.

Projects

What activities are planned or underway?

Studies to explore the immune response against nematodes in different livestock species and breeds are under way, and vaccinology projects, for example, are producing advances in understanding of fundamental processes around establishment of patent nematode infections in livestock.

The production costs of different types of immunity (innate or adaptive) for different livestock and breeds are being explored including through resources allocation model frameworks.

Nematode epidemiology - Lead Summary 15B (HPE Interactions – latent/carrier)

Title:	What factors determine animal resilience to infection and how can resilient animals best be used in nematode control?

Research Question

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

Define the relationship between resilience and resistance in different livestock species/breeds.
To optimize the use of resilience in combination with resistance against nematodes.

Challenge(s)

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

What are the behavioural and pathophysiological mechanisms associated with resilience?
How can continued propagule output from resilient animals be managed so that production is not adversely affected in other animals?

Solution Routes

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

Well-grounded mathematical models that separate the concepts of resistance and resilience and incorporate the resource, immunological and epidemiological trade-offs between them.
Exploration of the environmental (non-genetic) factors that influence resilience, including nutrition.
Pragmatic systems for including resilience in breed improvement schemes in livestock, alongside resistance.
Proof-of-principle studies on using resilient and resistant classes of stock together on farms to maximise effective use of refugia.

Dependencies

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

Better understanding immunity and resource trade-offs is needed before these can be reliably optimised.
Markers of resilience practical for large-scale use, and record-keeping systems to enable evaluation of resilience and resistance in the field to enhance selective ability.

State of the Art

Existing knowledge including successes and failures

There are host species and breeds of livestock that rely considerably on resilience against nematodes and others are more dependent on resistance. Many high-performing animals and breeds are highly susceptible.
Nutrition, genetics and nutraceuticals can be used to improve resilience against nematodes but each has only largely been investigated in isolation to each other.

Projects

What activities are planned or underway?

Implementing methods of culling animals not showing sufficient resilience at farm level. Exploring the decision-making of farmers to cull animals based on signs of lack of resilience.

Nematode epidemiology - Lead Summary 15C (Resistant/cleared)

Title:	How is protective immunity against nematodes maintained?

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

Can we improve the quantitative understanding of the maintenance of innate and acquired immunity against nematodes in sheep, cattle and goats in order to incorporate this more precisely into control strategies?
How do parasite communities as a whole respond to human intervention, control methods and environmental changes rather than single taxa?
What is the effect of treatment and other control measures on immune response of different host species?

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

Poor quantitative understanding of maintaining immunity mechanisms and the factors provoking a breakdown in immunity, e.g. during the peri-parturient rise in nematode faecal egg counts in sheep.

To determine the role of immunity in the process of hypobiosis in different livestock species and environmental conditions.

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

Development and availability of multiplex and NGS technologies to define the whole nema- and pathogenome and also the host immune response (innate and induced).

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

Better understanding of the interactions between nutrition, production and immunity to nematodes in different farm conditions throughout the production cycle.

State of the Art
Existing knowledge including successes and failures

There are differences between livestock species in their ability to maintain immune responses against nematodes.

The more promising vaccines show that resistance against nematodes can be improved, e.g. *Haemonchus contortus* in sheep.
Poor nutrition, parturition and high level of production can break the immune response of adult animals.
Over-protection of replacement young-stock can lead to low immunity in adult animals, e.g. in GIN and lungworms in cattle.

Projects

What activities are planned or underway?

Investigate the duration of the immune response for animals that have no further exposure to GIN and how waning of immunity affects the effectiveness of control.

Nematode epidemiology - Lead Summary 16 (Co-infection)

Title:	Understanding the interactions between parasite species and between parasites and micro-organisms in order to build a holistic approach towards control of parasites in livestock.

Research Question

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

Identify interactions between and within parasite species to build a holistic approach towards parasite control in livestock.

Challenge(s)

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

Which are the factors governing co-infection between (a) different species of nematode, and (b) nematodes and micro-organisms (mainly bacteria or protozoa), within the same organ or through systemic interactions?
What are the consequences of helmint-nematode and nematode-microbe interactions for the outcomes of infection?
Can parasite infection and control methods including anthelmintic therapy have broader consequences for animal health through susceptibility to other diseases or impacts on the microbiome?
Could manipulation of the microbiome (e.g. though pre- or pro-biotics) be used to help control nematodes?

Solution Routes

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

Develop in vitro models measuring co-existence or co-habitation between parasites/microbiota.
In vivo experimental infections with different infections in factorial and multi-factorial designs for different host (livestock) species.
In vitro models testing impacts of excretion/secretion substances from different nematodes and study their interaction with immunity, bacterial pathogens or gut microbiota.

Statistical analysis of large epidemiological datasets to establish population-level interactions, including intervention studies.
Extend advanced methods in community ecology to nematodes.

Dependencies

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

Attempt to evaluate the effect of hosting nematodes on the immune response against other parasites and microbes.
Molecular tools to identify nematode species, to enhance resolution of interaction studies in field populations.

State of the Art

Existing knowledge including successes and failures

There are several descriptive studies but we lack on-farm intervention studies and data across more of the important nematode species.

Projects

What activities are planned or underway?

Studies on microbiome-nematode interactions in livestock species, particularly pigs.
Intervention studies in wild and domestic ruminants to demonstrate effect of nematodes on microbial infections.
Fluke-TB interactions including on bTB immunodiagnosis.

Nematode epidemiology - Lead Summary 17 (Host range)

Title:	Identify the host range involved in the epidemiology and economic impact of nematodes in livestock production.

Research Question

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

Establish the host species involved in the epidemiology of different nematodes under relevant farming systems, including wildlife.
Understand within-species host factors (e.g. age, physiological stages, production levels, nutrition) affecting host susceptibility to nematodes.

Challenge(s)

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

Host range is mostly known but the relative importance of different species for transmission in quantitative terms might vary between systems. Wildlife hosts, e.g. nutria and lagomorphs for liver fluke, deer for GI nematodes, might increase or decrease infection pressure (through addition or removal of infective stages) and resistance development (by spreading resistance genes or providing refugia). Can this be determined for existing systems and predicted for other or future systems?
Parasites might adapt to new hosts. How likely is this to curtail the usefulness of mixed grazing systems?
Trade-offs between fitness and host range in specialist and generalist nematodes are poorly characterised.
Can management effectively utilise less susceptible hosts to remove infective stages and / or to provide refugia without production loss?

Solution Routes

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

Epidemiological studies including relevant alternative and wildlife species associated with different livestock production systems in different parts of the world.
Identify experimental models to explore or confirm host specificity between livestock species or wildlife and the factors that explain the specificity.
Develop predictive approaches to epidemiology that take account of host range and potentially host switching.

Dependencies

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

Develop the epidemiological skills and models to perform the studies in the field and in the evaluation of parasite specificity.
Adapted molecular tools to identify GI nematode species from the faeces of different hosts (livestock and wild animals).
Use "omics" tools to determine the reason behind host specificity.

State of the Art

Existing knowledge including successes and failures

Host range is mostly known but the relative importance of different species for transmission in quantitative terms might vary between systems.

Parasites might adapt to new hosts.

Projects *What activities are planned or underway?*
Implementation of models to evaluate the specificity of nematodes (especially nematodes) to different hosts. Epidemiological field studies for host range of nematode species.

Nematode epidemiology - Lead Summary 18 (Host genetics)

Title:	Genes governing expression of biological key processes of host responses to nematodes in relation to their ability to establish innate and acquired immune responses, and other determinants of resistance and/or resilience.

Research Question *What are we trying to achieve and why? What is the problem we are trying to solve?*
Identify the genetic basis and expression of key biological processes of hosts that influence the ability of nematodes to establish and negatively affect health and productivity.

Challenge(s) *What are the scientific and technological challenges (knowledge gaps needing to be addressed)?*
Heritability has been quantified in a number of parasitological and related production outcomes but the host processes that are involved (e.g. in heritability in faecal egg counts or anaemia scores) are often poorly understood. How gene-environment interactions shape outcomes of nematode infection; how to therefore optimise phenotype (e.g. resistance/resilience) for given farming systems remain unclear. The role of host genetics in determining effects of alternative control, e.g. vaccination, has only started to be explored.

Solution Routes *What approaches could/should be taken to address the research question?*
Evaluate variation in the expression of genes within and between host species and breeds exposed to nematodes, including under different environments and stressors. High throughput genomic, proteomics and metabolomics to identify the impact of nematodes in different hosts and breeds. Relate parasitological to production impacts. Use new data as sources of possible animal selection programmes. A world-wide harmonized effort to collect tissue samples from different hosts displaying different phenotypes in the face of nematode challenge under different known conditions. Identify and prepare a body of research where the bank of specimens can be analysed with the relevant “omics”.

Dependencies *What else needs to be done before we can solve this need?*
Create a consortium of collaboration working within harmonization guidelines in order to generate data. Create the necessary state-of-the-art hardware and software to analyse large databases. Create a network that can share intellectual property of the database and its outcomes. The available “omics” and future developments can be crucial to develop this area of work.

State of the Art

Existing knowledge including successes and failures
Heritability has been quantified in a number of parasitological and related production outcomes but the host processes that are involved

Projects *What activities are planned or underway?*
Star-Idaz can launch the discussion of the work in the protocols of global sampling, sample processing, data analysis and protection of products.

Nematode epidemiology - Lead Summary 19 (Pathogen genome)

Title:	Genes governing expression of biological key processes of nematodes and their adaptation to xenobiotics, alternative hosts and environmental stressors.

Research Question *What are we trying to achieve and why? What is the problem we are trying to solve?*
Identify the genetic background and expression of key biological processes of nematodes, AR and the influence of environmental cues that may influence those mechanisms.

Challenge(s) *What are the scientific and technological challenges (knowledge gaps needing to be addressed)?*
Some knowledge of extent of genetic variation within and between nematode populations but limited knowledge of how these map to expressed traits relevant to control. Genetic basis of resistance to some anthelmintic drug classes, e.g. ivermectin in nematodes, is not currently understood. For trematodes, complex genetics (ploidy) make these relationships even more difficult to determine. Consequence of genetic changes for parasite fitness (e.g. fitness costs of resistance; compensatory mutations) not known.

Solution Routes *What approaches could/should be taken to address the research question?*
Evaluate the expression of genes from parasites exposed to different stressors (i.e. xenobiotics, plant materials, immune response, anthelmintics etc.). High throughput genomics, transcriptomics, proteomics and metabolomics to identify influence of different stressors. Use new data, e.g. on plant-based therapies, as sources of possible xenobiotics to test adaptation and its genetic basis. A world-wide harmonized effort to collect nematodes of interest from different hosts and environments exposed to known conditions (stressors) to biobank a source of reference material for subsequent genomic analysis.

Dependencies *What else needs to be done before we can solve this need?*
Create consortia for collaboration enabling collection, curation and access to characterised nematode isolates for complementary genetic analysis, using new methodologies as they become available. Create the necessary state-of-the-art hardware and software to analyse large databases, dependent on ongoing rapid advances in molecular biology and bioinformatics.

State of the Art *Existing knowledge including successes and failures*
Some knowledge of extent of genetic variation within and between nematode populations but limited knowledge of how these map to expressed traits relevant to control. Some knowledge of the genetic basis of resistance to bencimidazol resistance

Available "omics" and future developments can be crucial to develop this area of work.

Projects *What activities are planned or underway?*
Star-Idaz can become the starting point to launch the discussion of the work in the protocols of global sampling, sample processing, data analysis and protection of products. To approach main funding bodies for the world-wide effort (FAO, OIE, EU, etc.).