

Enteric Fermentation R&D Accelerator Program Strategy

2024 - 2030



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Executive Summary

Decreasing methane (CH₄) emissions is the fastest way to decrease the negative impacts of greenhouse gas emissions on our climate since, in the short term, it is more potent than carbon dioxide in trapping heat in the atmosphere.

The Global Methane Hub (GMH) was established in 2022 in response to the Global Methane Pledge, launched at COP26. GMH aims to coordinate funding for methane (CH₄) mitigation within three principal sectors: Agriculture, Waste, and Energy. With funders and grantees, GMH supports associated action within research, policy, civil society, and the private sector. GMH's Agriculture Program aims to reduce the CH₄ footprint of livestock and rice production systems. Within GMH's Agriculture Program sits the (the Accelerator).

The Accelerator is the largest, globally coordinated public-good investment in breakthrough research tackling livestock CH₄ emissions, the largest single contributor to global food system CH₄ emissions. The Accelerator can fund areas that, to date, have received little support and are potentially crucial to delivering effective mitigation measures that are so urgently required.

The Accelerator aims to fund the development of a holistic and balanced portfolio of research and technologies to decrease the production of CH₄ that will be attractive for farmers to adopt and viable within the diverse nature of livestock production systems globally. The volume of such research has increased in recent decades, but while some solutions exist, scaling their adoption globally has been slow.

A Science Oversight Committee (SOC) was formed to guide the research that the Accelerator will undertake and they have identified seven key research areas as most promising in delivering direct enteric CH₄ mitigation. The Accelerator seeks to deliver answers to priority research questions that address current knowledge gaps within each of the seven areas. Within the key research areas are much-needed underpinning research, such as the development of the tools needed to facilitate research, along with work to understand the fundamental mechanisms behind mitigation.

This strategy identifies current research needs, explains why they are needed, and outlines the priorities for Accelerator funding.

Global Context

There is widespread agreement across the climate science community that reducing CH_4 emissions should be a priority in national climate mitigation strategies. Reducing CH_4 emissions from all sectors is the fastest way to mitigate climate change since in the short term, it is more potent than carbon dioxide at trapping heat in the atmosphere. The global food system is estimated to account for 60% of humaninduced or anthropogenic CH_4 emissions. Enteric CH_4 emissions produced by microbes in the first stomach of ruminants (e.g., sheep, cattle, buffalo, and goats) account for 45% (Figure 1).

Enteric methane is thought to have contributed 95 million metric tonnes CH_4yr-1 in 2010, increasing to 102 million metric tonnes by 2021 (FAOSTAT, 2024). If no action is taken, CH_4 is expected to increase a further 30-40% by 2050. Yet global anthropogenic CH_4 emissions need to be reduced by 50% from 2020 levels by 2050 in order to meet the goal of the Paris Agreement to keep the global temperature rise to a maximum of 1.5 degrees Celsius .

Figure 1 shows the distributed nature of enteric methane globally, with a significant number of countries that represent many livestock production system types contributing more than 0.5%.

Accordingly, tackling CH₄ emissions from global livestock supply chains is a core element of the GMH Agriculture Program and the main focus of the Accelerator. Some promising interventions already exist and are in use on farms in some countries, but adoption is slow, and the need is urgent. Transformative solutions are required and these solutions must create a sustained decrease in CH₄ emissions, adapt to major livestock systems around the world, and be valuable to farmers in meeting national agricultural policy goals.

Recent scientific innovations have the potential to identify new solutions, catalyze the scalability of existing and new interventions, and accelerate their progress to application. The Accelerator will explore these solutions and strive to effect a change in enteric fermentation CH_4 emissions.





Figure 1. Global food system CH₄ emissions by source and major contributors to global enteric methane emissions.



The Accelerator aims to support the rapid identification and development of cost-effective mitigation solutions that directly decrease enteric CH₄. This strategy will evolve dynamically as research advances, taking a comprehensive and iterative approach to developing the best proposals to support the ultimate aim of the Accelerator.

The Accelerator will add to the outputs of other research funders by being catalytic, comprehensive, and collaborative.

Catalytic in that its application to proposal decision-making can be shorter than traditional funding routes (due to shorter governance chains), with the SOC providing the rigor of scientific review.

Comprehensive in that any discipline that complements the CH₄ challenge will be explored, and through its approach, the SOC seeks to attract non-traditional disciplines to enhance research. Also, the Accelerator has no geographical boundaries and a global remit, proactively seeking to identify solutions for livestock systems, which have been underfunded to date.

Collaborative through engaging philanthropist, private sector, and public sector funding across the initial concept, delivery of research outputs to their application in practice.

The Accelerator ultimately seeks to fund research to advance potential CH₄ mitigation solutions that are balanced across a range of development stages. A way to assess the current and evolving developmental stage is crucial. The Accelerator will use Technology Readiness Levels (TRLs) to monitor progress and to help direct support. The TRL classification system is outlined in Figure 2.





Figure 2. Technology readiness level (TRL) classification system (adapted from ISO 16290:2013)

Research Focus

Accelerator funding focuses on seven key research areas. The SOC selected these areas after a thorough assessment of the state of science in enteric fermentation mitigation and several expert convenings. Critical knowledge gaps identified within each area inform priority research questions that Accelerator funding will support to achieve specific research outputs. While these research areas were identified as the starting point for the Accelerator Research Strategy, new areas of research can be added to the strategy as new information becomes available.

The research areas represent a range of TRLs, different modes of deployment, and livestock production system fit. The latter is crucial to ensure geographical applicability as a diverse range of livestock production systems operate around the world, from extensive grazing to intensive feedlot systems. The majority of global livestock production and associated CH₄ emissions are associated with mixed and grazing systems. Different mitigation mechanisms will be appropriate in different systems, and so a range of different solutions will be important to ensure widespread on-farm applicability.

The research areas also encompass underpinning research, ensuring that the individual technologies developed are effective in reducing methane and that co-benefits such as increased animal production are optimized while laying important foundations for future work.

For each research area, a brief synopsis of the "state of science," current priority research questions, and outputs that the Accelerator aims to support in the short (within 3 years) and medium (by 2030) term is provided. Figure 3 provides an overview of the research areas, assigned current and projected TRLs, and anticipated timeframes for outputs. The research areas are presented in order of expected TRL in 2027 from most advanced to least advanced.

Funding will be allocated to ensure that the portfolio includes sufficient work in each research area and a range of technological readiness for potential solutions, balancing lead time and spreading investment risk.





Figure 3. An overview of research areas, their current and expected TRLs and key outputs necessary to reach expected TRLs within the next three years.

Inhibitors

CH₄ is produced by specific microbes (methanogens) within the rumen. The inclusion of inhibitors in the diet can reduce the process of CH₄ production by those microbes. For the purposes of this research strategy, an inhibitor is defined as a biological agent or chemical compound added to the basal diet which disrupts or inhibits methanogenesis. To be effective, an inhibitor needs to be present in the rumen while the animal is digesting its diet. An inhibitor's dosage and inclusion rate is defined by its manufacturer.

One inhibitor is already proven, has regulatory approval and is in use in certain countries. However, current inhibitors require inclusion within each mouthful of feed to be effective and, therefore, are not suitable for use in grazing systems, where animals move and graze freely rather than being confined and fed controlled rations. Developing inhibitors that survive longer in the rumen, therefore facilitating periodic administration, would enable their use in grazing systems.

Additionally, animal trials to date have been relatively short-term and conducted in controlled environments with relatively few animals. Therefore, the longevity of the inhibitory effects (over the animal's lifetime), optimal dosage, and long-term impacts on animal health, reproduction, and production are unclear. Impacts on production will influence on-farm uptake. The metabolic fate of antimethanogenic compounds, such as bromoform in seaweed, also needs testing to ensure food safety requirements are met. The SOC has assigned a current TRL range for inhibitors of 2-6, with an anticipated range of 4-9 expected in three years.

To be effective, an inhibitor needs to be present in the rumen while the animal is digesting its diet.

What are the long-term effects of inhibitors on CH₄ production and animal productivity and health?

Is it possible to deliver inhibitors in slow-release forms and will these be as effective as forms fed within feed rations?

Will the mitigation effect of specific inhibitors be additive or neutral when delivered in combination or in sequence with other inhibitors or CH₄ mitigation measures?

Is the mitigation effect of the inhibitor the same for low-versus high-emitting CH₄ animals?

What is the metabolic fate of active compounds such as bromoform within ruminants, specifically concerning the half-life within the rumen, its absorption, and possible residues in meat or milk?

Anticipated Research Outputs

Short Term

Develop slow-release inhibitors.

Initiate studies that explore CH₄ inhibition on animal health and production.

Understand if residues are present in meat or milk.

Understand the combined effects of inhibitors and other CH₄ mitigation measures.

Understand whether low- and high-CH₄ animals respond to inhibitors in the same manner.

Discover inhibitory compounds not yet known.

By 2030

Determine whether CH₄ reduction is sustained over time using inhibitors.

Understand the long-term effects of inhibiting CH₄ on animal health and production.

Determine whether slow-release forms of inhibitors are as effective as the original compound.

Develop low-cost production methods for the active compounds in seaweeds.

Genetics

Ruminants differing genetically in terms of CH_4 emissions can be identified, and the heritability is sufficiently high (15-25%) to enable breeding programs to develop populations of low-emitting CH_4 animals. Although CH_4 emissions reflect feed intake to a significant extent, research has found that differences in feed intake do not fully account for differences in emissions, indicating the potential to breed for both low-emitting animals and maintained or even higher feed intake (a balanced breeding index), therefore allowing CH_4 mitigation in combination with increased animal production, enhancing the likelihood of adoption. Reductions of at least 1% per year in emissions per animal are available through balanced selection.

Challenges include questions around defining the trait of interest, i.e., whether aiming to reduce CH₄ absolute emissions or relative emissions such as per unit of animal body weight, the measurement of CH₄ production parameters for individual animals (see Measurement Tools), and the period (life-stage, duration) to measure. In addition, current research efforts are globally small, and usually with only limited interaction with industry and commercial breeders.

The core opportunity is to build genomic reference populations – animals measured for CH_4 production and with a genotype, enabling wide-scale selection and screening to identify genetically low emitters. A current TRL range for breeding low CH_4 animals of 2-7 has been assigned, with an expected range of 4-9 in three years.

Reductions of at least 1% per year in emissions per animal are available through balanced selection.

Are there ways to measure individual CH₄ emissions cost-effectively in extensive situations (see Measurement Tools)?

How will other enteric CH₄ mitigation measures perform when applied to low-emitting animals?

To what extent will a reference population developed for one breed or within a country support useful genomic selection in another breed or country?

How best can a reference population and associated dissemination systems be established in developing countries?

Anticipated Research Outputs

Short Term

Determine the traits and the period of measurement to act as a standard for international research.

Develop publicly-available genomic CH₄ prediction models for the major ruminant species to support selection processes based on a significant increase in the numbers of animals recorded for CH₄ output.

Establish a global network or database to facilitate cooperation and encourage the sharing of ideas and data between researchers.

By 2030

Establish multiple co-investment agreements between genotyping companies and researchers.

Establish reference populations (record and genotype 20-50,000 animals within each population) that represent major breeds associated with the main ruminant production systems worldwide.

Measurement Tools

There are several approaches to measuring CH₄ production at an animal level, but continuous measurement over a 24-hour period is expensive and requires restraint of the animals (e.g., calorimeters/ respiration chambers). Cheaper and less restrictive tools for measuring CH₄ do not allow for 24-hour continuous measurement and, therefore rely on assumptions about CH₄ production during rest periods.

There is an urgent need to develop cost-effective, accurate, and standardized measurement tools to measure CH₄. Without such tools, research on individual mitigation measures will be greatly restricted. In addition, there is a need to improve how we measure/ estimate intake in grazing systems in terms of animal behavior during the day and over 24-hour periods, as these parameters govern the pattern of feed intake and potential emissions. A current TRL range for measurement tools of 1-8 has been assigned, with an expected range of 7-9 in three years.

There is an urgent need to develop costeffective, accurate, and standardized measurement tools to measure CH₄.

How can existing sensors be adapted to measure how rumen parameters (e.g. rumen volume, motility, rate of passage) are influenced by specific inhibitors and vaccines and, do these parameters differ between high and low-yielding CH₄ animals?

Can standardized procedures be developed to ensure correct use of existing CH₄ measurement tools for different systems?

Can tools be developed to continuously (24/7) measure CH₄ emissions in grazing animals?

Can tools be developed to measure grazing intake accurately?

Anticipated Research Outputs

Short Term

Improve measurements of CH₄ in grazing animals,.

Measure grazing behavior in low and high-yielding animals.

By 2030

Understand how grazing behavior impacts on CH₄ production.

Make availabile low-cost, standardized tools for measuring grazing intake and CH₄ production suitable for deployment in a range of production systems across the world.

Vaccines

There is evidence that vaccines can be developed that induce an immune response and an associated production of antibodies that bind to methanogens. However, no reliable vaccine that reduces methane production in an animal has been produced to date. Vaccines could potentially be administered by once-off or periodic doses, therefore requiring minimal animal handling. This would be highly advantageous in grazing systems, where access to animals is often limited. As grazing systems dominate global livestock production, the applicability of vaccines and the associated mitigation potential is enormous.

Administering vaccines is a generally accepted and routine farm practice. Multiple knowledge gaps exist, for example, concerning how an animal's immune system recognizes methanogens. This is associated with processes during colonization of the rumen in the early stages of the animal's life. It is also unclear what mechanisms are behind antibodies suppressing methanogens, while the greatest technical challenge is to produce a long-lived response by a vaccine that results in a sustained high concentration of antibodies in the saliva. Fundamental research is required to induce high concentration (titer), high binding power (affinity) specific antibodies that aggregate methanogens, block their function, and /or reduce their numbers. A current TRL range of 1-2 has been assigned for vaccines, with an expected range of 3-7 in three years.

The applicability of vaccines and the associated mitigation potential is enormous.

What role do processes during early-life colonization of the rumen have in the animal's immune response to methanogens?

Vaccination program, doses, timing, etc.

What mechanisms are involved in the suppression of methanogens?

What class of antibody is most effective?

How can long-lived antibody responses be induced?

What are the key methanogen antigens to include in an effective vaccine?

Anticipated Research Outputs

Short Term

Identify the mechanism of immunity for a vaccine.

Identify the key antigens to include in a vaccine.

Determine if there is any natural immune response to methanogens,

Demonstrate proof of concept for the efficacy of a vaccine against methanogens.

By 2030

Identify the key isotype of antibody response for an effective vaccine,

Understand the mechanism through which a vaccine would reduce methane emissions.

Determine how early in the development of the rumen that methanogens are recognized by the immune system.

Determine candidate proteins for inclusion in a vaccine formulation.

Antimethanogenic Feedstuffs

Certain forages and feeds could contain compounds that reduce CH₄ production either directly or through modifying the microbial ecosystem. Compounds such as tannins, saponins, flavonoids, and essential oils occur naturally in some forages, and their utilization offers a potential mitigation option suited to grazing systems. Their introduction into pastures may also help improve animal production and food security. For the purposes of this research strategy, antimethanogenic feedstuffs are defined as forage sources (i.e., grasses, corn silage) representing a large proportion of the animal's basal diet. The remaining portion of the diet could include grains, concentrates, and by-product feeds.

Knowledge gaps and challenges include determining the impacts of the compound or associated forages on intake, digestibility, and animal performance, the vast screening of gene banks necessary to identify useful cultivars, identifying the genes behind antimethanogenic compounds, and the availability of CH₄ and feed intake measurement tools to conduct in-vivo studies. A current TRL range for novel feeds of 2-3 has been assigned, with an expected range of 4-5 in three years

Compounds such as tannins, saponins, flavonoids, and essential oils occur naturally in some forages, and their utilization offers a potential mitigation option suited to grazing systems.



Is it possible to identify anti-methanogenic compounds in forages, and if so, characterize their genes and synthesis pathways?

How can in vitro assays be scaled up to quantify CH₄ inhibition from large numbers of plants?

When fed to animals, what impact do antimethanogenic forages have on dry matter intake, digestibility, CH₄ emissions and animal production?

Can widely used forage crops be enhanced (by gene editing or conventional breeding) to contain anti-methanogenic compounds?

Anticipated Research Outputs

Short Term

Identify anti-methanogenic compounds and determine their mitigation potential via in vitro studies.

Preliminarily validate the mitigation potential of forages via in vivo studies.

By 2030

Isolate forage genes behind antimethanogenic compounds,

Validate mitigation potential via in vivo studies and the establishment of breeding Programs to develop forages known to contain antimethanogenic compounds, and

Introduce genes into widely used forages that may not contain such compounds.

Rumen Microbiome Underpinning Research

Methanogens are part of a much larger microbial ecosystem within the rumen, whose main function is to digest fiber and other components to make them available as nutrients for the animal. Both measures to inhibit growth of the methanogens (via specific drugs, antibodies, lysins, or phages) or promote growth of competing non-methanogens (via directly fed microbes or early life intervention) can modify the balance of microbial species in the rumen and can reduce CH₄ production. However, the rumen microbiome, its development and various interactions, and its links to the animal's physiology, immune system, and behavior (see section below) are poorly understood, a major reason being that genetic systems for the strictly anaerobic rumen microbes have not yet been developed. A better understanding will help explain the mechanisms or mode of action behind mitigation, which is fundamental to identifying new mitigation opportunities and optimizing co-benefits.

Developing mitigation approaches with co-benefits, such as enhanced production, will likely play a key role in driving mitigation at scale. Although the production of CH_4 is a loss of energy to the animal, there is currently no consistent evidence for energy gains or increased production with CH_4 mitigation. However, in some limited studies, there is evidence of changes in, e.g., milk composition, which suggests a potential for increased economic returns, should this be consistently shown.

Hydrogen is produced during the digestion process, on which methanogens act, producing CH₄. There is a major gap in knowledge around differences between the hydrogen produced and then consumed by the methanogens and potential links with the flow of electrons and energy loss, and therefore, animal productivity. The culturing and conservation of rumen microbes is limited and will be crucial to understanding interactions between microbes. The SOC has assigned a current TRL range for modifiers of the rumen microbial ecosystem of 1-2, with a range of 4-9 anticipated in three years.

Can we develop methods (tools, methodologies, and experimental designs) that make working with rumen microbes easier which will facilitate an increased understanding of rumen microbial processes?

How can a comprehensive understanding of electron flow in CH₄ mitigation be achieved?

Can we completely characterize all key rumen methanogens and generate crystal structures for key methanogen proteins required to produce rumen methanogen-specific antibodies?

Can we compile a 'most wanted list' and characterize those key microbes, including developing their genetic systems?

To support vaccine work, can we determine the processes during early-life rumen colonization and how and when the host's immune system identifies the methanogen as a non-threat (commensal)?

Does the rumen microbial community adapt in the long term to anti-methanogen measures?

Anticipated Research Outputs

Short Term

Double the rumen microorganisms successfully isolated, cultured, and genetic and physiological properties studied.

Understand better the CH₄ formed from hydrogen and other substrates.

Understand the role that specific rumen bacteria play in fermentation, as well as hydrogen flows.

Understand the regulation of hydrogen forming and consuming microbes.

By 2030

Understand the reasons behind variation in energy loss via CH₄.

Understand how hydrogen can be redirected by inhibiting CH₄ production to benefit animal production.



Animal Physiology and Behavior Underpinning Research

To predict how ruminant productivity will be affected by methane mitigation efforts on various diets and to understand the combined and long-term impact of such strategies, we must understand the influences of animal behavior and physiology on the rumen microbial ecosystem. Addressing knowledge gaps, such as the relationship between rumen characteristics (volume, surface area) and lowemitting methane animals or the impact of interventions such as methane inhibitors on saliva flow and rates of passage of digesta out of the rumen, is crucial. A current TRL range for underpinning science of 1-3 has been assigned, with a potential range of 3-9 in three years.

We must understand the influences of animal behavior and physiology on the rumen microbial ecosystem.

What is the impact of different inhibitors on the rate of passage out of the rumen on different diets?

Can observations on lower rumen volumes in low CH₄ yielding animals on a range of diets, particularly in low-income countries, be confirmed?

What are the impacts (short-and long-term) of inhibitors on poor-quality diets that are not consistent from day to day?

How do different breeds, particularly indigenous breeds, respond to mitigation measures?

Anticipated Research Outputs

Short Term

Understand the impact that different interventions (inhibitors, genetics, and vaccines) have on rumen parameters beyond the microbiome and what this means for production.

By 2030

Understand better which interventions are most appropriate for different diets, particularly for grazing and mixed systems.



Final Remarks

As outlined, this strategy is not static but a dynamic, living document. An invitation-only, cross-disciplinary meeting of grantees and other relevant experts will be held annually to ensure that relevant research outputs are being factored into the ongoing, updating of the strategy. This will ensure that the Accelerator remains holistic, as developments in one research area can inform work in other areas, allowing priority research questions to evolve in real-time, while also helping to direct funding and fund-raising.

Recent transformative advances in multiple science disciplines provide an opportunity to pursue parallel approaches to reducing enteric CH₄. The Accelerator has been set up in such a way that avoids many of the barriers of existing funding mechanisms. Research teams can be globally inclusive and engage multiple disciplines in solving the enteric CH₄ challenge. This will be a dynamic program evolving in response to scientific findings under the oversight of the SOC and through co-design with scientists and engagement with both the public and private sectors.

The Accelerator has been designed to overcome many of the barriers of existing funding mechanisms.



Additional Resources

The following resources have been prepared by the Enteric Fermentation R&D Accelerator Science Oversight Committee.

Principles of enteric methane reduction in ruminants

<u>Rumen microbiology</u>

Enteric Methane Measurement

3-Nitrooxypropanol, Methane Inhibitor

Asparagopsis Seaweed for Methane Mitigation

Balance of H₂-forming and H₂-consuming fermentations differs by 25%

Genetic and Genomic Approaches to Reducing Methane Emissions

Long-term additive studies

Methane Vaccines

