**Mitigation of enteric methane emissions: How can we speed up progress?**

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**Preface**

This synopsis represents a summative interpretation of perspectives provided to Dr. Joseph McFadden (Cornell University) by Dr. Alexander Hristov (Penn State; USA); Dr. Jan Dijkstra (Wageningen University; The Netherlands); Dr. Ermias Kebreab (UC Davis; USA); Dr. Karen Beauchemin (Agriculture and Agri-Food Canada); Dr. Mutian Niu (ETH Zurich; Switzerland); Dr. Tim McAllister (Agriculture and Agri-Food Canada); Dr. Richard Eckard (University of Melbourne; Australia); Dr. Chris Reynolds (University of Reading; UK); Dr. Emilio Ungerfeld (Institute of Agriculture Research; Chile); Dr. David Yáñez-Ruiz (Spanish National Research Council); Dr. Claudia Arndt (International Livestock Research Institute; Kenya); Dr. Peter Lund (Aarhus University; Denmark); Dr. Harry Clark (New Zealand Agriculture Greenhouse Gas Research Centre); Dr. Graeme Attwood (Ag Research; New Zealand); Dr. Paul Kononoff (University of Nebraska-Lincoln; USA); Dr. Andre Brito (University of New Hampshire; USA); Dr. Roger Hegarty (New Zealand Agriculture Greenhouse Gas Research Centre); Dr. Jeffrey Firkins (The Ohio State University; USA), Dr. Daryl Nydam (Cornell University), and Dr. Mike Van Amburgh (Cornell University). The gaps in knowledge are summarized with brevity and objectivity with the intent to be a complete reflection of the shared viewpoints of the aforementioned investigators and his own. For the purpose of this summary, feed additives refer to compounds, that may or may not be defined as a drug, that directly or indirectly reduce ruminal methanogenesis when fed to ruminants.

**Introduction**

Methane is a short-lived climate pollutant that contributes to global warming (IPCC, 2022). The greenhouse gas (GHG) has more than 80 times the warming potential of carbon dioxide over a 20-year period. Current recommendations are to reduce global methane emissions by one-third by 2030 and 45% by 2040. The Global Methane Pledge (2021) set a target to reduce global methane emissions 30% by 2030, relative to 2020 levels, to limit global warming to 1.5°C by 2030, while enhancing public health and agricultural productivity. Methane from livestock agriculture represents ~40% of global methane emissions. Indeed, cattle are part of a natural carbon cycle (McFadden, 2021); however, reducing livestock methane using feed additives is key to lower global methane emissions, enhance the conversion of dietary energy to meat or milk production, and potentially improve animal health. The following document summarizes gaps in knowledge and barriers for the discovery, regulatory approval, and adoption of feed additives that reduce methane. Current feed additives being studied or adopted are referenced to provide a contemporary perspective.

**Gaps in knowledge and barriers to progress**

*Long-duration feeding trials are practically non-existent*

Trials that investigate the effects of long-duration feed additive supplementation on enteric methane emissions, animal health and welfare, milk production and composition, and rumen ecology are urgently needed. These studies are required to demonstrate that technologies, such as 3-nitrooxypropanol (3-NOP) or bromoform, are safe for the animal, to determine whether the percent inhibition of methane production is consistent over time (i.e., does adaptation due to microbial resistance develop), and best understand how changes in life development stages, diet, breed, genetic parameters, and environment impact efficacy over the short- and long-term. For instance, Schilde et al. (2021) investigated the effects of 3-NOP feeding (~50 mg/kg dry matter [DM]) in periparturient Holstein cows fed diets containing high or low α-amylase treated neutral detergent fiber expressed without residual ash (i.e., aNDFom; ~403 versus 340 g/kg DM) from 28 days prepartum until 120 days postpartum. Dietary supplementation with 3-NOP reduced methane emissions (g/d) and intensities (g/kg energy-corrected milk [ECM]) in the short-term but methane emissions and intensities returned to control levels for cows fed diets with higher fiber content. Indeed, Dijkstra and coworkers (2018) demonstrated in a meta-analysis that feeding 3-NOP is negatively related to dietary NDF content, where a high dietary NDF content reduced the ability of 3-NOP to reduce methane yield by 1.52% per 10 g/kg of DM increase in NDF content. Feng and coworkers (2020) suggest that the average net reduction in total GHG emissions from 3-NOP or nitrate feeding are 11.7 and 3.95%, respectively, when these technologies are applied across all dairy growing stages following 1 year of age. Therefore, we must realize that methane-reducing efficacy is unlikely to be constant over time. To overcome this uncertainty, trials need to focus on studying individual cattle over months and potentially years (e.g., calfhood to adulthood; single or multiple lactations). Such studies are also likely to provide an improved understanding of total methane emissions over an animal’s lifetime. For feed additives defined as drugs by the Food and Drug Administration, testing will likely require milk to be dumped.

*Energetic efficiency is poorly understood*

Enteric methane production in cattle represents a loss of 2 to 12% of gross energy intake (Johnson and Johnson, 1995). Therefore, we must diligently ensure that any initial investigation considers the impact of a feed additive on the energetics of growth, pregnancy, and lactation. This requires measuring changes in every energy fraction: gross, digestibility, gaseous, urinary, fecal, metabolizable, maintenance, tissue, and milk. The use of indirect calorimetry is required to estimate heat production. Multiple installation sites across the world provide investigators access to respiration chambers; albeit, severely limited in the United States. However, it is apparent that such equipment is often utilized to measure gas emissions but frequently ignores the opportunity to study energy partitioning. A special focus should be placed on defining energy utilization in cows experiencing negative or positive energy balance as a means to determine whether energy from methane reduction is spared for milk production or tissue deposition, respectively.

The scientific community also lacks a firm understanding of the effects of feed additives on nutrient flow to the lower gut, partly because the use of duodenal and ileal cannulas in scientific research is a lost art and expensive. For instance, studies are needed to study the rumen pool sizes and omasal flows of nutrients to determine digestion parameters including fractional rates of carbohydrate digestion, and microbial growth and yield of microbial biomass, in response to feed additive supplementation and enteric methane reduction. Such information is needed to better understand and model the impacts of feed additives on digestion, especially within the framework of energetics.

*Limited studies have explored diverse cattle production systems*

Research predominantly centers on enteric methane mitigation in confinement dairy systems. This management practice bodes well for the continuous feeding of methanogenesis inhibitors because of the reliance on a total mixed ration. However, cattle production systems are numerous including cow-calf, stocker and pasture fed, pasture or feedlot finishing, subsistence and smallholder, rangeland, mixed livestock, and agropastoral management systems. In these scenarios, contact between farm operators and cattle may be limited and infrequent, especially in the growing phase, and the daily provision of a feed additive that inhibits methane production is likely not feasible. Studies must focus on methane-reducing strategies for these alternative systems, which are unlikely to be the same solutions for confinement dairy. In New Zealand, breeding low-emission cattle (and sheep) is being considered but will take time to develop because of the cost of measuring methane emissions and the extensive number of animals required (Leahy et al., 2019). However, considering data obtained from studying 184 Holstein-Friesian cows, we should be cautious considering a positive genetic correlation between methane production and milk yield (i.e., selecting cows for lower methane production may develop with lower milk yields; Breider et al., 2019). In India, smallholder farmers of milk cooperatives routinely purchase pellet feed at milk collection centers. Such feed could be formulated to contain methane-reducing feed additives; however, the consistency of feeding is a concern. Vaccination against rumen methanogens is a promising path; however, such technology is expected to elicit only moderate reductions in methane emissions (Leahy et al., 2019).

*Alternative modes of delivery and stability for feed additives require attention*

The compound 3-NOP has short-term efficacy to inhibit methane when fed via normal application (Gruninger et al., 2022); therefore, 3-NOP needs to be continually provided in the diet and consumed at a frequent rate for sustained methane-reduction. However, such an approach limits the utility of dietary 3-NOP supplementation to inhibit enteric methane production in non-confinement production systems. Researchers need to explore the use of slow-release boluses, mineral or urea blocks, water, automatic milk systems, or alternative delivery modes to extend the duration of methane inhibition and avoid daily dosing regimens for 3-NOP or alternative feed additives.

One example that is routinely described is monensin controlled-release capsules. Delivery of the polyether ionophore antibiotic to grazing cattle improved the efficiency of milk production but did not modify methane production (Grainger et al., 2008). It is often argued that monensin can reduce methane production by enhancing the propionate to acetate ratio in the rumen (propionate being a hydrogen sink); however, the response is small (<10%) or not detected. If a reduction in methane production is not observed, one potential reason is inadequate sample size of the study population, which is a challenge for detecting nominal changes in methane production (e.g., <10% reduction). Alternatively, the dose of monensin investigated is too low (Ranga Niroshan Appuhamy et al., 2013).

We also need to consider the stability (i.e., shelf-life) of feed additives and any special handling requirements that may preclude farmer adoption. For instance, bromoform in *Asparagopsis taxiformis* has low stability (84% disappearance after 4 months of storage under luminescent light; Stefenoni et al., 2021). Interestingly, oil immersion may extend the shelf-life of bromoform (Magnusson et al., 2020).

*Feed additives are likely not a solution to reduce enteric methane in developing nations*

The efficiency of meat or milk production in developing nations is alarmingly low relative to the developed world. This disparity in efficiency will continue to grow as new technology emerges that only developed countries can adopt. It is also unlikely that feed additive technology that reduces methane production can be adopted in countries that rely on smallholder and subsistence farming practices with few exceptions. The social cost of new technology is also uncertain. Although low-cost early life interventions that require brief human interaction with animals and provide lifelong methane reduction are a possibility, current effort should focus on enhancing the efficiency of meat or milk production in these countries. Efforts centered on improving our understanding of feed chemistry and recommendations on a regional basis, optimizing crossbreeding strategies, and enhancing animal health and management are more likely to reduce methane emissions per unit of milk than focusing on costly feed additive solutions that are unlikely to achieve mainstream adoption. Such an effort will also support the livelihood, nutrition, and health of farmers and their families in these nations.

India is a high-priority country for enteric methane mitigation. It is estimated that India has over 300 million cattle and buffaloes (over 18% and 50% of the world’s total populations, respectively; NDDB, 2022). The vast ruminant population is attributed to Operation Flood, which was a government-sponsored program and a success for Indian agriculture that supported a 400% increase in milk production from 1968-1969 to 2003-2004 (Deka *et al*., 2015). Today, India is the world’s largest producer of milk, producing 195 million metric tons in 2020 or 22% of global production (FAO, 2021). India is also the third largest methane-producing country in the world (Climate Watch, 2021) and it contributes ~7% of global emissions (CO2 equivalent) from agriculture (Pathak, 2015). Unfortunately, milk production efficiency is one of the lowest of any country in the world (Bardhan and Sharma, 2013). The GHG intensity per unit of milk for crossbred cows is low (1.21 kg of CO2e kg-1), relative to indigenous cows (2.96 kg of CO2e kg-1; Patra, 2017). For perspective, the average enteric methane emissions intensity in the United States is ~0.25 kg of CO2e kg-1 milk (Tricarico e*t al*., 2020). Balanced ration formulation is a potential means to increase milk production efficiency in India. Blümmel and coworkers (2009) estimated that milk yield per animal in India can increase from 3.6 to 9 L/d by feeding cows nutrient-balanced diets. This said, increasing milk yield per animal from 3.6 to 12 L/d would increase milk output by over 300%, feed required by 48%, and methane production by 46%; albeit, this is dependent upon increasing the energy density of diets in a country with limited availability of concentrates and poor-quality fodder. The country is ramping up efforts to enhance fodder quality and consistency, utilize in vitro fertilization and sex semen technologies, and expand the use of biogas fermenters, which all may impact methane emissions from their livestock industry.

*Co-supplementation and replacement strategies require more attention*

It is apparent that the use of feed additives to inhibit enteric methane production is likely to be more applicable in developed nations; therefore, the magnitude of inhibition and reduction of methane production should be substantial (e.g., >30%) to compensate for non-adoption of these approaches in developing nations. With the exception of bromoform-containing seaweed, which has human and animal safety concerns, no other additive appears to elicit this effect at the present time. Additionally, the ability of feeding seaweed or 3-NOP (or alternative) to persistently reduce methane production over time is questionable; especially in ruminants fed high forage diets. There is a need to understand the interaction between feed additives that inhibit methanogenesis and the chemical composition of the base diet. Feed additive co-supplementation strategies to examine potential additivity of methane reduction and additive replacement (i.e., alternating) strategies should also be prioritized.

Co-supplementing a methane-reducing feed additive with fatty acids may lower methane production and intensity more than feeding the additive or fatty acids alone (Beauchemin et al., 2008). Dietary fatty acids (medium-chain and polyunsaturated) is an attractive strategy for methane mitigation because 1) they are toxic to methanogens and protozoa, 2) they promote an environment that favors production of propionate (a hydrogen sink), and 3) unsaturated fatty acids sequester metabolic hydrogen via biohydrogenation (Newbold et al., 2015). Moreover, replacement of energy from carbohydrates with lipids may be an effective way to reduce enteric methane. We also cannot ignore the potential of saturated fatty acids to enhance nutrient partitioning to the mammary gland (de Souza et al., 2018) and potentially lower methane intensity.

The combined application of lipids and 3-NOP appears to have an additive effect on methane mitigation. For example, Zhang and colleagues (2021) investigated the effect of dietary co-supplementation of 3-NOP (200 mg/kg DM) and canola oil (50 g/kg DM) for 28 d in the diet of beef heifers. The combined treatment resulted in a 51% reduction in methane yield compared to controls, whereas 3-NOP or canola oil resulted in only a 32% or 27% reduction, respectively. These findings were supported by Gruninger et al. (2022). These researchers suggest that the additive effect of 3-NOP and canola oil on the reduction of methane likely occurred by distinct mechanisms. Feeding 3-NOP reduced methanogens and partly inhibited the hydrogenotrophic methanogenesis pathway, resulting in increased H2 emissions and propionate molar proportion in rumen fluid. Canola oil reduced the abundance of fibrolytic bacteria and protozoa, resulting in altered rumen fermentation. However, we must be cautious not to overfeed fat to avoid negative impacts on dry matter intake, fiber digestibility, or milk fat synthesis. Guyader and colleagues (2015) found that supplementation on non-lactating dairy cows with linseed oil (4% of ration DM) and calcium nitrate (3% of ration DM) decreased methane emissions by 17 and 22%, respectively, when fed alone and had an additive effect when combined (32% reduction).

*Early-life interventions to reduce enteric methane production requires focus*

The effects of early-life interventions (in utero or post-natal) on short- and long-term enteric methane emissions, especially with a focus on microbiome programming, requires consideration. Such efforts would likely be of benefit in non-confinement productions systems, reduce reliance on feed additive feeding later in life, and have broader impact than regimens that require daily feed additive delivery. Studies would also likely improve our understanding of methane emissions over an animal’s lifetime. For example, eighteen Holstein and Montbéliarde calves were assigned to control or 3-NOP feeding daily from birth until three weeks post-weaning (week 14; Meale et al., 2021). The reductive effect on methane production persisted following treatment cessation until up to 1 year of life.

Waiting to alter the rumen microbiome with methanogen-inhibitors until adult life results in more transient effects on methane emissions. For example, while 3-NOP reduced methane emissions by 30% in lactating dairy cows for 12 weeks (assessed using GreenFeed system [C-Lock Inc., Rapid City, SD]; Hristov et al., 2015) and by 59% in beef cattle for 16 weeks (respiration chambers; Romero-Pérez et al., 2014), these effects were diminished back to control levels once treatment ceased. As suggested by Meale and colleagues (2021), applying treatments during crucial periods of development (i.e., microbial establishment and the weaning transition) appears to have the most long-lasting effects on methane production.

*Mode of action for plant secondary compounds and essential oils is undefined*

Unlike 3-NOP, the mode of action for plant secondary compounds and essential oils requires clarity. Numerous feed additives composed of plant-derived compounds that have potential to inhibit ruminal methanogenesis are being considered. These include coriander oil, geranyl acetate, eugenol, cashew nut shell liquid, garlic and citrus extract, grape pomace, tannins, saponins, carvacrol, thymol, and many others (Honan et al., 2022). These compounds are likely to have a nominal but significant effect on methane emissions (perhaps up to 10% reduction). These solutions are worth pursuing considering they are most likely to be adopted in the short-term, will be accepted by the consumer as a safe solution, and potentially provide an additive effect when combined with a potent direct inhibitor of methane production. However, studies investigating plant-derived rumen modifiers are likely to require high sample populations to detect a significant effect on methane production. Moreover, very little information is available that can define their mode of action with confidence. This issue can be complicated by the use of compound blends, which is the common approach for several commercially available products. As described in a meta-analysis, one combination that has received attention is coriander seed oil, eugenol, geranyl acetate, and geraniol, which when fed for a minimum of 8 weeks to dairy cattle can provide a 10% reduction in methane emissions without compromising feed intake or milk composition (Belanche et al., 2020).

*Field trials on commercial farms cannot be adequately controlled*

Field trials on commercial farms lack stringent control of scientific procedures. The majority of farms lack the ability to replicate the experimental unit (i.e., pen), or make impromptu changes to diets based on changing feed supply and cost, are unable to measure individual feed intakes, or maintain high stocking densities, cannot fix cow numbers within pen, and are frequently subjected to deviations in farm management that have the potential to compromise trial integrity. It is generally recognized that the advantage that field trials on commercial farms provide is for end of pipeline studies focused on the effects of additives on fertility and disease outcomes, which can only be achieved on farms that enable a large sample size per treatment. A field trial also provides farmers in the region with a local proof-of-concept case study to demonstrate the effects of a feed additive in a commercial herd setting, which has potential to increase adoption of the approach.

*Manure methane and nitrous oxide emissions are frequently ignored*

The near totality of studies that have focused on the effects of feed additives on enteric methane emissions have grossly ignored their impact on manure methane and nitrous oxide emissions. Any feed additive that impacts nutrient digestion and nitrogen utilization has a strong potential to modify manure nutrient and microbial composition, and thereby influence methane, nitrous oxide, and ammonia emissions. It also recognized that the management of manure capture, storage, treatment, and utilization has potential to influence these outcomes. Dietary 3-NOP supplementation has been shown to decrease fecal nitrogen and total excreta nitrogen in cows, relative to unsupplemented cows (Melgar et al., 2020). Although 3-NOP feeding does not appear to increase GHG emissions during manure storage (Owens et al., 2020), soil nitrous oxide emissions were higher when stockpiled manure derived from cows fed 3-NOP was applied, relative to control manure from cows not fed the additive (Weber et al., 2021). The magnitude of this response was influenced by soil type (i.e., Black Chernozem, Gray Luvisol, or Dark Brown Chernozem).

*Life cycle assessment of technology is missing*

The life cycle assessment of a new feed additive can be overlooked in the early phases of research; however, feed ingredient production has a carbon footprint that cannot be ignored. It is imperative that we consider the net impact of a feed additive on GHG emissions. Manufacturing and supply of a feed additive on a global scale needs to be considered to ensure that impact is broad if the technology is effective. A recent study provided a life cycle assessment for cultivating seaweed (Nilsson and Martin, 2022). Results showed that a high rock salt requirement contributed to 48% the total GHG emissions; however, this could be lowered if sea salt was sourced. The environmental impact from thermal energy was low, contributing 16% of the total GHG emissions. We must consider the global manufacturing (including resource supply), distribution, and handling requirements for a feed additive to ensure that the technology, if proven safe and effective, and has the potential for broad utilization without a net negative environmental impact.

*Weakening global research expertise is a concern*

Scientists with a distinguished career history, that have devoted time to studying dietary solutions to inhibit ruminal methanogenesis, have retired or are transitioning to retirement in the immediate future. Currently, these experts are highly-visible advocates for continued research in this area; but are concerned that the next generation of research positions focused on methane mitigation are not being established. A lack of continuity from one generation to the next weakens the scientific community’s ability to train junior scientists in complex methodology that is required to define methane-inhibiting efficacy using a holistic approach.

*Small and mid-size enterprises lack financial means to adequately study feed additives*

Start-up, and small or mid-size enterprises frequently rely on the use of in vitro ruminal approaches to determine whether a feed additive may impact methane production. However, such findings may not be observed in vivo. Moreover, the cost to perform a robust feeding trial can be cost-prohibitive, especially in a university setting. A researcher may be compelled to study a new product simply due to the lack of other opportunity or utilize a commercial herd testing approach without adequate controls. Alternatively, a researcher may lack relevant expertise to study a compound with a perceived mode of action. Expedited paths to support innovation of solutions with the strongest scientific merit could involve an independent review of new technology solutions by an advisory panel; then the identification of the junior or senior investigator with the most appropriate expertise to complete the work according to a panel-approved protocol with input from the principal investigator. Although not a direct parallel, programs such as the Greener Cattle Initiative, that support academic-industry partnerships, show promise but the limited funding ($5 million over the next 5 years; Tricarico et al., 2022) is inadequate when we consider the breadth of uncertainty described herein.

*Equipment, personnel, and facility infrastructure is potentially a barrier*

**Research labs may lack key equipment, personnel, facility, and animal resources to complete studies with the appropriate scope of work. Examples of defunct or missing equipment include tools to measure methane and other gas emissions (e.g., GreenFeed units and respiration chambers), bomb calorimeters and C/N analyzers to assess energetics, freeze dryers, microbiome sequencing technology, high-throughput in vitro systems, etc. Facilities are subject to the policies of university administration, which means that facility expansion is not always permitted, and consolidation is more routine. Ramping up programmatic efforts require skilled staff including equipment and animal care technicians as well as data managers and analysts. Faculty positions are often not replaced, which can limit momentum and future growth in the discipline and internal collaborations. In the United States, we could benefit from increased research focused on enteric methane mitigation in pasture systems, which would likely require additional faculty and farm facility upgrades. Lastly, few institutions in the world are able to perform large-scale production trials for extended duration with a large sample population (i.e., have 500+ head and ability to study individual intake in 100+ animals at a time). This has resulted in an increased reliance on commercial herds for product testing; however, this approach is rarely acceptable for controlled trials that require individual feed intake and methane measurements.**

*Paths to enhance consumer education of technology is inadequate*

The development of technology that is fed to ruminants with the intent to reduce methane has potential to impact animal health and welfare, the nutritional profile of meat or milk, or promote or increase the presence of compound residues in meat or milk that are of potential human safety concern (i.e., approach a tolerable upper limit). Therefore, consumer education must occur in parallel. We can consider the development of recombinant bovine somatotropin, which was proven safe by the FDA and lowers the carbon footprint of milk production as an example (Capper et al., 2008; FDA, 2022). Misinformation and misunderstanding of the technology by the consumer reduced global use of this technology (Aldrich and Blisard, 1998). We must actively develop transparent communication campaigns to best inform consumers at early stages of development to ensure that scientific progress translates into sustainable practice with consumer acceptance. Of particular concern is seaweed feeding (e.g., *Asparagopsis taxiformis*) in dairy cows, which has been shown to increase milk iodine and bromide concentrations (Stefenoni et al., 2021); however, lower dosing strategies may be able to prevent these outcomes. The presence of arsenic from commercial seaweed feed appears to be less of a concern (Mac Monagail et al., 2018).

*Standard methodology to define the reduction of enteric methane emissions are absent*

At Cornell University in partnership with the Environmental Defense Fund, University of California, Davis, and Global Research Alliance, efforts are underway to define standards for the measurement of efficacy for feed additives that reduce enteric methane production. Historically, researchers have utilized an atomistic approach to measure changes in efficacy for these dietary approaches, which is likely due to resource and skill limitations. However, we cannot ignore measures of energetic efficiency, nutrient digestibility, manure GHG emissions, animal health, and tissue and milk residues within the framework of methane reduction. In addition, methodology is being developed to quantify net reductions in methane emissions on farms to support the development of carbon offsetting or insetting projects. However, our understanding of methane reduction efficacy can be complicated by the lack of standard methodology to quantify changes in methane emissions from an individual cow or methane inventory on individual farms.

Standardized, robust, science-based quantification methodologies for measuring enteric methane emissions from cattle are essential for greater precision and accuracy in both baseline emissions from the livestock sector and evaluation of efficacy of mitigation strategies, including enteric methane inhibiting products such as feed additives. The use of alternative methodologies to measure gas exchange in ruminants requires validation before their use can be accepted. Such validation should involve comparison to the gold-standard respiration chamber system that measures total gas exchange over a 24-h period in a controlled-environment. Any such validation of methodologies requires repeated measurements of gas emissions on the same animal(s) using alternative methane measurement techniques within day and across days under controlled experimental conditions including environment. Correlation coefficients and confidence intervals need to be provided for any such comparison and openly reported in the public domain. Because any potential method may have high within-day and within-animal variance, relative to a pre-established standard, any such validation of methods requires a firm understanding of the experimental parameters including number of animals measured, breed, diet, and performance indicators (e.g., level of intake, milk production, body weight). It is also paramount that we validate emissions based on daily methane production, on a 24-h interval, considering that methane emissions change temporally, and frequency of measurement varies by method. The frequency and type of calibration and gas recovery tests performed also need to be clearly documented and available for public consideration. A database should be developed to include these standardized methodologies and their application for different management scenarios, impact of variables such as breed, life stage, feed composition, management system, etc. on methane emissions, and data demonstrating effectiveness of mitigation strategies using these standardized methodologies.

*Product testing agreements for the sake of regulatory approval lack novelty*

Most research labs in a university setting are led by principal investigators that are interested or encouraged by administration to pursue projects that lead to novel outcomes for peer-review publication as a means to stay competitive and support trainee programs. Few labs provide in vivo testing as a fee-for-service facility to support product testing agreements using established standardized operating procedures. Unfortunately, studies that lack novelty (e.g., dose titration studies at various stages of lactation) have the potential to be avoided by principal investigators that are not positioned with technical staff that can complete product testing agreements in a high-throughput manner.

*Regulatory approval process requires reform*

While enteric methane inhibiting products, of which feed additives are currently the leading solutions, are needed immediately to reduce methane from cattle and minimize global temperature increases over the next couple of decades, the process from concept through product development and regulatory approval to market and adoption of these products is long and resource-intensive. Currently, all products with environmental claims, including enteric methane emissions inhibition, are classified as drugs in the United States. This means that they are submitted to the Food and Drug Administration’s Center for Veterinary Medicine (CVM) for approval through the New Animal Drug Application (NADA) process. The NADA pathway is rigorous and has many components which require the conduct of specific and oftentimes lengthy clinical studies which CVM must then review in detail. The whole process can take many years to complete. While these studies and their review are necessary to ensure the safety and efficacy of these products, the overall timeline is too long given the urgent need. Therefore, the regulatory pathway for enteric methane inhibiting products must be expedited to allow for more timely approval of these products while maintaining safeguards to protect animal health, human health, and the environment. In October 2022, CVM held a public call for input on this topic demonstrating their commitment to re-evaluating the current system.

There are a number of ways that the regulatory process can be reformed including, but not limited to, reducing the requirements within the NADA process such as requiring only a single effectiveness study, providing application support and early agency feedback to sponsors, re-classifying products based on mechanism of action within the gut or other characteristics to leverage existing pathways such as the Food Additive Petition process or other feed ingredient pathways (Generally Recognized as Safe status or Association of American Feed Control Officers-defined ingredients), or creating a new gut modifier pathway which may be similar to the proposed and newly established approaches in Canada (https://inspection.canada.ca/about-cfia/transparency/consultations-and-engagement/share-your-thoughts/proposed-guidance/eng/1658504105578/1658504106063) and the European Union (https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2012.2536), respectively. With each of these options, speed of approval and the rigor of CVM’s safety assessment varies.

Successful implementation of feed additives as a strategy for enteric methane mitigation will require products that are effective without causing negative environmental tradeoffs, are safe for humans and animals, can be widely adopted by the industry, and are accepted by consumers. The regulatory process plays an essential role in meeting these objectives by ensuring confidence in the safety and effectiveness of these products.

**Conclusion**

If we are to achieve the Global Methane Pledge targeted 30% reduction in global methane emissions by 2030, we must ramp up efforts aimed at the discovery, regulatory approval, and adoption of safe and effective enteric methane mitigation strategies for livestock. The gaps in knowledge addressed within this document must be immediately addressed and barriers to progress broken to slow global warming and achieve food security. At the United Nations COP27 Climate Change Conference in Sharm el-Sheikh, United States Deputy Special Envoy for Climate, Rick Duke, said that less than 2% of current climate finance is used to develop methane mitigation solutions. Robust investment must increase if we are to develop practical solutions that reduce enteric methane emissions without compromising animal efficiency or health, the safety of animal-sourced foods, or our environment across different production systems and landscapes that define the global dairy industry. Any solution must also support farmer livelihood and prosperity.

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