

Comparison of Regulatory Management of Authorized Ingredients, Approval Processes, and Risk-Assessment Procedures for Feed Ingredients

Jurisdictions Covered:

Brazil, Canada, China, European Union, Japan, South Africa, and United States

July, 2013

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Report Objective: To address similarities and differences among 7 regulatory jurisdictions on the regulatory management of authorized (existing) feed ingredients, the approval process, and risk management assessment for feed ingredients. The tool can assist in global marketing as well as supporting in the harmonization/convergence efforts in identifying areas of dissimilarity.

The report is organized such that a number of the regulatory attributes of interest for the feed ingredients (new and existing) are compared in a series of tables in a side-by-side comparison for each jurisdiction. A summary table of the nuances of this information on sentinel examples of ingredients is provided. In addition, a description of the specific data requirements for two example feed ingredients, an inorganic mineral source and a pelleting aid, is provided. A summary is included that outlines some commonalities as well as underscores differences that may affect global trade as well as harmonization of requirements across jurisdictions. Appendices to the report provide specific jurisdictional requirements for the authorization of new ingredients and definitions of the regulatory terms covering feed ingredients.

EXECUTIVE SUMMARY:

This report builds on the 2011 IFIF report, “Comparison of Approval Process and Risk-Assessment Procedures for Feed Ingredients: Canada, European Union, and United States.” The current report is based on a questionnaire formulated by the IFIF Feed Additive Comparison Project Task Force and covers both the regulatory management of authorized ingredients, as well as the approval process and risk-assessment procedures for feed ingredients. The questionnaires were provided to National Feed Associations within the 7 jurisdictions. Each jurisdiction completed the questionnaire, using input it deemed appropriate. Some jurisdictions included assistance from governmental authorities. The report was then circulated for review and concurrence with the National Feed Associations and governmental authorities.

A series of 15 tables are laid out to provide immediate comparisons on the policy and procedures of each jurisdiction as related to the regulation of animal feed ingredients. The report highlights the array of terminology used by each jurisdiction to cover feed ingredients. The report has adopted Joint FAO/WHO Expert Committee on Food Additives language for feed ingredient (a component part or constituent of any combination or mixture making up a feed, whether or not it has a nutritional value in the animal's diet, including feed additives. Ingredients are of plant, animal or aquatic origin, or other organic or inorganic substances.). This is the broadest definition and covers all ingredients used in animal feeds.

Of primary interest is the fact that all 7 jurisdictions require pre-market authorization for most new feed ingredients for use in animal feed. The authorization procedures cover the basic tenets of safety (target animal and human food/consumer safety); data to support intended use, and manufacturing information (that includes specifications, stability, and analytical methodology). Each jurisdiction may have its own specific studies or requirements for these assessments, but the issues must be addressed. Some of the jurisdictions have requirements beyond those provided above; for example environmental safety assessment is required by Canada, China, EU, Japan, South Africa and U.S. (for some submissions). Worker safety assessment is required by Canada and the EU; China and South Africa require submission of OSHA or MSDS determination. The information to support the manufacturing chemistry assessment can be significantly different in each jurisdiction. In every jurisdiction the submission requirements may vary as related to composition of the new additive, intended use, species, and the method of manufacture.

Four of the jurisdictions (Canada, China, U.S. and South Africa) are currently revising their feed ingredient regulation, so the report was correct at the time it was written but changes (some significant) will likely ensue.

The use of a positive list in which includes all permitted ingredients, also varies by jurisdiction. Canada, Brazil, China, and South Africa (under development) use a positive list. The EU has a list of authorized feed additives and a non-exhaustive catalogue of feed materials. Japan has a complete list of feed additives, but not feed ingredients. The U.S. has a near-complete list of ingredients in the American Association of Feed Control

Officials Official Publication, but it does not include common feed ingredients and all GRAS substances.

A point of interest is whether the authorizations granted by the jurisdictions are specific to the requester (or proprietary). In the U.S., Japan, some ingredients in the EU (category 1, 2, and 3 food additives and feed materials) and some Canadian ingredients (those on part 1 of the schedules) are non-holder specific; that is, ingredients once authorized can be marketed by any person.. Ingredients in Brazil, some ingredients in China (newly authorized feed additive within the first 5 years), South Africa, Canada (Part 2 of the schedule) and the EU (category 4, 5, and 6 feed additives) are proprietary or holder-specific listings, such that only persons receiving the authorization can market under that authorization.

Authorization periods may be unlimited or limited. China, Japan, U.S., and Canada (for part 1 ingredients of Schedule IV & V) have an unlimited authorization period. Once authorized, unless safety or other issues would retract the authorization period, the feed ingredients are permanently authorized. Brazil authorization period is 5 years. Canada's authorization period (for part 2 ingredients in schedule IV and V) and South Africa's authorization are 3 years. The EU feed additive authorization period is 10 years, and the feed material is unlimited.

The regulations or laws of Brazil, China, EU, Japan, and South Africa have specific requirements for the regulation and/or labeling of feed ingredient manufactured using genetically modified organisms or plants. Canada and the U.S. have no specific laws or regulations for these products. They rely on laws/regulations that cover all feed ingredients.

The regulation of companion animal versus livestock (animals intended for use as human food) also varies among jurisdictions. The definition of companion versus livestock also varies (for example, the FDA in the United States considers horses to be companion animals, and not raised for food, while horses are considered livestock in Canada). China, EU, South Africa, and the U.S. do not have separate regulations that are specific for feed intended for companion animals and the regulation of companion animal and livestock ingredients are similar (some obvious data differences such as human/consumer safety are the exception). Brazil and Japan have a separate law that covers the regulation of companion animal feed. Canada does not authorize ingredients for companion animals (as their Feeds Act only covers specific livestock species).

All jurisdictions reported that the claim or function of a feed ingredient can alter the regulatory category of the ingredient. South Africa and U.S. have the most dramatic examples, as all products that are intended to increase animal production are regulated as drugs. All jurisdictions reported that ingredients intended to diagnose, prevent, mitigate or treat a disease were regulated as animal (veterinary) health products. However, the EU has special categories of feed additives for coccidiostats and histomonistats; Brazil also includes coccidiostats feed additives. Brazil, South Africa, and the U.S. permit animal feed authorization for ingredients with claims on maintaining feeds salmonella-negative.

The report also provided information on foreign establishment requirements. Brazil requires the Brazilian importer to be authorized, requires products to have a certificate of free sale and a declaration of compliance with GMPS by competent authority. In Canada all imported mixed feeds must be registered, ingredients must meet all Canadian regulations. In China products must be registered via registration agent in China, the operator must be authorized by competent authority in the country of origin, and products must be registered with the Ministry of Agriculture. In the European Union operators must be registered with their location and must be represented within the EU. Other requirements are the same for an EU or foreign operator. In Japan, importers must notify the MAFF two weeks prior to the start of business operations. Ingredients new to Japan that have undergone significant manufacturing processes or are from a new facility must register their ingredients (the same as domestic production). In South Africa ingredients marketed must be authorized, and manufacturers must have proof of compliance by competent authorities in the country of origin. In the U.S. all establishments must be registered as food facilities; States also require registration of establishments and distributed products (same as domestic firms).

The 15 tables within the report provide a comparison of the requirements in each covered jurisdiction. The appendices of the report provide the legal definitions of feed terms for that jurisdiction as well as a summary of the requirements for obtaining authorization for feed ingredients. The reference section of the report provides, when available, the linkable references to available laws, regulations, and guidances that cover the animal feed ingredients.

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A. Common Definitions Used in the Report

To ensure that the report uses a common language the report has adopted the CODEX definition of terms:

Feed Ingredient: A component part or constituent of any combination or mixture making up a feed, whether or not it has a nutritional value in the animal's diet, including feed additives. Ingredients are of plant, animal or aquatic origin, or other organic or inorganic substances. (CODEX code of practice on good animal feeding CAC/RAP 54-2004)

Feed: A feed ingredient or a mixture of at least two feed ingredients.

Feed business operator: A natural or legal person that "places" product on the market (manufacture, store, distribute, sell, import/export, fractionate).

Establishment: Defined here as a unit/facility of the feed business operator. This facility could be a manufacturing site, a storage facility, a trading organization, etc.

In sections that are specific to a jurisdiction, the terms defined by that jurisdiction are used in keeping with the jurisdictional definitions. Some tables list a Q number, which is in reference to the questionnaire each jurisdiction answered as the basis of this report.

B. Jurisdictions' Legal Definitions of Ingredients and Their Mixtures

Each jurisdiction defines feed terms in its own legal language, and in some instances similar terms have different meanings. The specific feed terms are all covered under the general term "feed ingredient" -- that is, a component of feed -- as defined by CODEX and as used in this report. When feed terms are in the general sections of the report, the CODEX terms will be used; however in sections of the report specific to that jurisdiction, the jurisdictional language will be used. The legal definition of the feed terms for each jurisdiction is provided in the jurisdiction-specific appendix (see Appendices A-G).

Table 1. Terminologies and Legal Citation for Feed Ingredients and Feed Mixtures for Each Regulatory Jurisdiction

Jurisdiction	Feed Ingredient Terms	Feed Mixtures
BRAZIL	Feed Additive (IN 13/2004) Ingredient or raw materials (Decree 6296/2007, X, art 5)	Food (pet) (IN 30/2009) Concentrate Nucleus Premixtures Complete Feed Supplement(IN 15/2009) Medicated Feed (IN 65/2006)
CANADA	Feed (Feeds Act, 1985, c.F-9) Single-Ingredient Feed (Feed	Complete feed Trace Mineral Salt

Jurisdiction	Feed Ingredient Terms	Feed Mixtures
	Regulations, 1983,) Medicating ingredient (Feed Regulations, 1983,) Drug (Food and Drugs Act, 1985, c.F-27)	Macro-premix Micro-premix Mineral Feed Mixed Feed Novel Feed Supplement Medicated feed Veterinary Prescription Feed Specialty Feeds (e.g. Enzyme supplements, Flavoring agents, pelleting agents, mould inhibitors, etc)
CHINA	Feed material (State Council Decree No.609, Feed and Feed Additive Administrative Regulation, articles 2 and 49). Single feed (SCD No. 609, article 2 and 49). Feed additive (SCD No. 609, article 2). Nutritional feed additive (SCD No.609, article 49) General feed additive (SCD No.609, article 49)	Premix (Complex premix, Mineral premix, Vitamin premix) Concentrated feed Complete feed Supplemental feed Feed additive blender (SCD.609, article 49, MOA Decree No.3, 2012, and MOA Notification No. 1849)
EUROPEAN UNION	Feed (Reg.178/2002) Feed material (Reg. 767/2009) Feed additive (Reg. 1831/2003) Processing aids (Reg. 1831/2003) Daily ration (Reg. 1831/2003) Veterinary medicinal product	Premixtures Reg. 1831/2003 Compound Feed , complete feed, complementary feed, mineral feed, milk replacer , particular nutritional purpose (for so called "dietetic feed") (Reg. 767/2009)
JAPAN	Feed (Law No. 35, 1953 article 2) Feed Additive (Law No. 35, 1953 article 2)	
SOUTH AFRICA	Farm feed (FFFARSCA 36(a)(i)) Unmixed farm feed of plant and animal origin (FFR) Feed Additive (FFR) Technological additive (FFR) Sensory additive (FFR) Nutritional additive (FFR)	Complete Animal Feed (FFR) Complementary, supplementary & concentrated animal feed Complete Pet Food (FFR) Complementary pet food

Jurisdiction	Feed Ingredient Terms	Feed Mixtures
	Zootechnical additive (FFR)	
UNITED STATES	Food (FFDCA 201(f); 21 CFR 570.3(m)) Food Additive (FFDCA 201(s); 21 CFR 570.3(e)) Animal Feed (FFDCA 201(x)) Generally Recognized as Safe Substances(FFDCA 201(2); 21 CFR 570.30) Feed Ingredients (AAFCO Official Publication) Animal Drugs (Medicated feeds) (FFDCA 201(w)) Medicated Type A Article (21 CFR 558.3)	Animal Feed and Food (FFDCA 201(f); 21 CFR 570.3(m)) Type C Medicated Feed (21 CFR 558.3)

There are jurisdictional differences when regulatory authority may be altered by the mixture of feed ingredients. Most jurisdictional authorities cover single-ingredient feeds; however, when approved ingredients are combined, most jurisdictions do not have additional pre-marketing registration or authorization requirements. In addition, some jurisdictions can consider a mixture of feed ingredients to be a “sole ingredient,” hence the combination can be covered under a specific pre-market registration or authorization. “Q” numbers in the table headers, are a direct reference to the questionnaire developed by the IFIF Feed Additive Comparison Project Task Force.

Table 2. Jurisdictional Considerations on Whether Mixtures May Be Considered Sole Ingredients

Jurisdiction	Can Mixtures be Considered Sole Ingredients? Q5
BRAZIL	No, mixtures of ingredients are not considered an ingredient.
CANADA	Yes. These would fall under a single-ingredient feed in Canada which is “any substance or mixture of substances that is assessed or evaluated as being acceptable for use in feeds and that is described in an item of Schedule IV or V” (reference: <i>Feeds Regulations, 1983</i>)
CHINA	No, only the feed additive once mixed with a carrier or diluent is considered as feed additive.
EUROPEAN UNION	No, mixtures of feed additives or of feed materials are not subject to specific further authorization and are not considered a sole ingredient, in general. (Reg.1831/2003). Only a few additives, i.e. some holder-

Jurisdiction	Can Mixtures be Considered Sole Ingredients? Q5
	specific authorizations for coccidiostats and a few other additives, are preparations containing the additive substance plus carrier excipients, etc. and are authorized under those specifications.
JAPAN	Yes, when a feed additive is mixed with a vehicle it can be a considered a single-ingredient feed. When a feed additive is combined with one or more feed ingredients the mixture is considered a feed.
SOUTH AFRICA	Yes, when a feed additive is mixed with a carrier it can be considered a single-feed ingredient.
UNITED STATES	No, a mixture of more than one ingredient must be considered a mixture and all ingredients listed in the ingredient statement (including processing aids).

C. Jurisdictions' Legal Requirements of Operators

This section considers the legal requirements of business operators located within the jurisdiction (domestic) and outside of that country (foreign). These issues are related to the required authorization/license to place feed on the market (Example: for import, for manufacturing, for fractionating, for storing, for trading, authorization is per establishment, per product). In addition this section provides information as to whether the requirements vary depending on the type of feed.

Table 3. Business Operations Requirements for Feed Import, Manufacturing, and Distribution

Jurisdiction	Business within Country/Jurisdiction Q6	Foreign Business (Outside of the Country/Jurisdiction) Q7
BRAZIL	Establishments that manufacture, fractionate or import feed require authorization (exception for establishments that only do the marketing of feed). The requirements vary depending on the type of product (e.g. medicated feed). (Decree 6296/2007, IN15/2009, and IN 65/2006).	Foreign establishments exporting to Brazil do not need authorizations. However, the Brazilian importing company requires authorization. There are specific requirements for imported products registration, including a declaration issued by the operator enabling the Brazilian importer to report to the Ministry of Agriculture on any regulatory requirement; a product certificate of official authorization of the country of origin or official certificate of free sale or official certificate of

Jurisdiction	Business within Country/Jurisdiction Q6	Foreign Business (Outside of the Country/Jurisdiction) Q7
		exclusive manufacturing for export; and declaration of Good Manufacturing Practices issued by the competent authority. (Decree 6296/2007, IN15/2009)
CANADA	Feed business operators do not need a license or authorization to place feed on the market. It is the product itself that might require product authorization/approval registration. The exception is for rendering facilities that require a permit to manufacture rendered animal by-products.	No specific license is required for importers. All imported mixed feeds must be registered. They must follow all Canadian acts and regulations.
CHINA	<p>All the feed and feed additive manufacturers require an establishment (production) license. In addition, feed additive, feed additive blender, and premix authorizations pertain to both, establishment and product.</p> <p>The establishment licenses of feed additive, feed additive blender and premix are authorized by the Ministry of Agriculture (MOA); the licenses of single feed, concentrated feed, supplemental feed and complete feed are authorized by animal feed authority at provincial level.</p> <p>The requirements vary depending on the type of feed.</p> <p>A business operator for importing, storing and distribution does not require specific authorization, but their businesses should be in compliance with relevant regulations.</p>	<p>1) The operator should apply for product registration in MOA via a registration agent in China. It is forbidden to import any feed or feed additive without an import registration certificate.</p> <p>2) The operator should be authorized by the competent authority of country of origin, including establishment and product.</p> <p>3) Products which need to be registered are as follows: single feed, feed additive, feed additive blender, premix, concentrated feed, complete feed, and supplemental feed</p> <p>4) There are some document requirements for the MOA registration, including information about the main ingredient and its physiochemical property, manufacture process, specifications, testing method, efficacy and safety reports of the product, stability report, method of use, risk assessment report, etc.</p>
EUROPEAN	All "feed business operators" regulated under Regulation	Same requirements for EU operators. However, a

Jurisdiction	Business within Country/Jurisdiction Q6	Foreign Business (Outside of the Country/Jurisdiction) Q7
UNION	<p>183/2005 on feed hygiene (producers, traders, storage, transport, etc.) need either approval or registration as operators in the member state where they are located. This is in general a notification process. Obligations are different depending on products and type of feed businesses. Approval is required for most additives producers/traders, for the premixers using some zootechnical (coccidiostats and histomonostats, and growth promoters) and nutritional additives (vitamin A, D, Cu and Se) additives, and for compound feed manufacturer/traders using some additives (coccidiostats and histomonostats, and growth promoters).</p>	<p>representation within the EU is necessary. Also a prerequisite to import into the Community must be in a register (third country list).</p>
JAPAN	<p>Manufacturers must notify the Minister of Agriculture, Forestry and Fisheries, and distributors must notify the prefectural governor 2 weeks before the start of business operations. (Safety Assurance and Quality Improvement of Feeds, article 51). The submissions must include the “Safety Evaluation criteria and Evaluation Procedure for Feeds” in following 3 cases: 1) feeds that have not been used in target animals in Japan; 2) feeds that have undergone major changes in the manufacturing process; or 3) feeds that contain enzymes, microbe and/or adjuster which has no experience in process of manufacturing of feed and food.</p>	<p>Foreign businesses who import to Japan have no legal requirement to notify. However, the Japanese businesses that are importing feeds must notify the Minister of Agriculture, Forestry and Fisheries 2 weeks before the start of business operations. The “Safety Evaluation criteria and Evaluation Procedure for Feeds” are the same as described in the previous column.</p>

Jurisdiction	Business within Country/Jurisdiction Q6	Foreign Business (Outside of the Country/Jurisdiction) Q7
SOUTH AFRICA	Business operator requires a premarketing authorization per product. This requirement is the same for all types of products. A registration number is allocated to each product after the Registrar of Farm Feeds has established that the manufacturing establishment meets the legal requirements as per Act 36 of 1947 Regulations.	Products imported into South Africa also require pre-marketing authorization and it is the same as the one given to local business operators. Also required is proof of compliance with competent authority in the country of origin. This information may include a hard copy of a Free Sale Certificate; a hard copy of a Good Manufacturing Practice (GMP) Certificate; and any other form of proof that product complies with legal requirements in country of origin. In addition animal by-products have to comply with the Animal Diseases Act, 1984 (Act 35 of 1984)
UNITED STATES	All business that manufacture, transport, store, or distribute feed must be registered with the FDA Food Facility Registration program. Manufacturers of medicated feed have additional yearly registration and reporting requirements. Most states also require either a license or permit to manufacture and distribute feed. Most states require registration of products marketed in their state, as well as collect fees associated with the product or quantity marketed within the state.	The requirements for foreign establishments importing to the U.S. are the same as domestic establishments.

D. Jurisdictional Management of Authorized Ingredients

Table 4 specifies for each feed ingredient terminology/classification/definition if the marketing authorization is holder-specific (proprietary approval) or non-holder-specific (non-proprietary approval). In addition the table highlights who is permitted to hold the marketing authorization. For Japan and the United States all feed ingredients are non-proprietary, and others may market based on the definitions or terms of the feed ingredients. Other jurisdictions have a mix of holder-specific and non-proprietary ingredients. In the EU there are some specific cases in which non-holder specific

ingredients are considered proprietary (for example where a strain number is provided in the authorization).

Table 4. The Legal Nature (Holder-Specificity (Proprietary)) of Feed Authorizations

Jurisdiction	Feed Categories	Authorization
BRAZIL	<ul style="list-style-type: none"> a. Additives, ingredients, supplements (except for ruminants) and coadjuvant pet food b. All other feeds 	<ul style="list-style-type: none"> a. Holder-specific (authorizations are held by Brazilian establishment or authorized importer) b. Exempt from authorization
CANADA	<ul style="list-style-type: none"> a. Single-Ingredient Feed <ul style="list-style-type: none"> 1. Schedule IV 2. Schedule V b. Veterinary Drug (not a feed, regulated under the Food and Drugs Act) 	<ul style="list-style-type: none"> a. Schedule IV and V listing of feeds have two parts each. Single-ingredient feeds listed in Part 2 are proprietary approvals b. Drugs placed on the market require a drug identification number (DIN). DINs are specific to each product produced by each company.
CHINA	<ul style="list-style-type: none"> a. New single feed and feed additives during supervision period (the first 5 years) b. Feed materials and feed additives after supervision period 	<ul style="list-style-type: none"> a. Proprietary b. Non-holder specific
EUROPEAN UNION	<ul style="list-style-type: none"> a. Feed material b. Feed additive <ul style="list-style-type: none"> 1. technological additives 2. sensory additives 3. nutritional additives 4. Zootechnical 5. Coccidiostats and Histomonostats 6. Feed materials and feed additives consisting, containing or produced from a GMO c. Veterinary animal product 	<ul style="list-style-type: none"> a. Non-holder specific b. Non-holder specific <ul style="list-style-type: none"> 1. Non-holder specific 2. Non-holder specific 3. Non-holder specific 4. Holder specific 5. Holder specific 6. Holder specific (including if falling under the categories a, b, 1, 2, or 3) c. Holder Specific (applicant or a representative of applicant must be 'established' in the community)

Jurisdiction	Feed Categories	Authorization
JAPAN	<ul style="list-style-type: none"> a. Feed Additive b. Feed 	<ul style="list-style-type: none"> a. Non-holder specific b. Non-holder specific
SOUTH AFRICA	<ul style="list-style-type: none"> a. Farm feed b. Unmixed farm feed of plant and animal origin c. Feed Additive <ul style="list-style-type: none"> Technological additive Sensory additive Nutritional additive Zootechnical additive d. Complete Animal Feed e. Complementary, supplementary and concentrated animal feed f. Complete Pet Food g. Complementary pet food 	All registration numbers are holder specific; a person residing in the Republic of South Africa or a juristic person who has a registered office in the republic can be the registration holder of a product.
UNITED STATES	<ul style="list-style-type: none"> a. Food b. Food Additive c. Animal Feed d. Generally Recognized as Safe Substances e. Animal Drugs (Medicated feeds) f. Feed Ingredients (AAFCO) 	<ul style="list-style-type: none"> a. Non-holder specific b. Non-holder specific c. Non-holder specific d. Non-holder specific e. Proprietary sponsor approvals f. Non-holder specific (sponsors are not restricted to US businesses)

Some jurisdictions (Brazil, Canada, and China) have a positive list that provides all feed ingredients that may be used in animal feeds. Other jurisdictions have a near-inclusive list, and South Africa is working toward completing a positive list. Authorizations in China, Japan, and the U.S. are in effect indefinitely; however, all other jurisdictions have a set time that ingredients must be reauthorized.

Table 5. Jurisdictional Comparison of Listing of Authorized Ingredients for Use in Animal Feed

Jurisdiction	Positive List Used	Citation for the Positive List	Length of time of authorization
BRAZIL	YES	www.agricultura.gov.br However the listing is restricted for use by business operators only (user ID and password required)	5 years

Jurisdiction	Positive List Used	Citation for the Positive List	Length of time of authorization
CANADA	YES	The positive list (Schedule IV and V) is available in the Feeds Regulations. However, this positive list can only be updated in the regulations by regulatory amendment, which is not done often. Therefore, a consolidated version is prepared with updates from time to time and is available now on the website, or a request may be made directly to the Canadian Food Inspection Agency (CFIA).	Unlimited for Part 1 ingredients; 3 years for those requiring registration (i.e., Part 2)
CHINA	YES	Feed materials catalogue (MOA announcement No.1773) (Chinese only) Feed additives listing (MOA announcement No.1126) These positive lists are updated periodically, all the latest versions may be obtained from http://www.moa.gov.cn	Unlimited
EUROPEAN UNION	There is a positive list of feed additives No, there is not a positive listing of all permitted feed materials.	Feed additive listing Feed Material Listing (There is a catalogue of feed materials which is a non-exhaustive list, i.e. products not on the list can also be marketed as feed materials in the EU.)	Feed Additive, 10 years

Jurisdiction	Positive List Used	Citation for the Positive List	Length of time of authorization
JAPAN	There is not a positive list for feed ingredients; however, a listing of nutritional values for feed ingredients is available. A full listing of Feed Additives are listed by name	Nutritive value listing for raw materials (Japanese, only) Feed Additive Listing	Unlimited
SOUTH AFRICA	YES, but it is not an exhaustive list	<u>Farm Feeds Guidelines</u>	All products used in farm feeds require pre-marketing approval, valid for 3 years
UNITED STATES	Partial, most acceptable ingredients are listed in the AAFCO OP, which included Food Additive authorizations; but common feed ingredients and non-affirmed GRAS substances are not listed	The Official Publication of the American Association of Feed Control Officials is available for purchase at www.aafco.org . In the near future an electronic copy of the ingredient listing will be available for purchase. 21 CFR 558 provides the positive listing of all drugs permitted to be used in animal feeds	Unlimited

Specific information provided in the feed ingredient authorizations (list of acceptable feed ingredients) for each jurisdiction is provided below.

TABLE 6. Jurisdiction-Specific Information Describing the Authorized Feed Ingredients

Jurisdiction	Information on the Feed Ingredient within the Public Description of the Authorization. Q12
BRAZIL	I – Name of the product and trademark, if any. II – Physical form of presentation. III – Description and form of packaging. IV - Composition. V – Levels of guarantee. VI – Description of the manufacturing process and of the raw material and finished product control. VII – Indication of its use and of the animal species for which the product is to be fed. VIII – Manner of using. IX – Net content expressed in the decimal and metric system. X – Validity period. XI – Conservation conditions. XII – Name, address, and CNPJ registration number of the establishment owning the product. XIII – Name, address, and CNPJ registration number of the importing establishment in the case of and imported product. XIV – Restrictions and other recommendations. XV – Layout of the label.
CANADA	Schedule IV -- Ingredient name, definition and specifications, manufacturing information (some), labeling requirements (including warnings, cautions and guarantees), maximum residue levels (if any), conditions of use for species, or inclusion rates (if any) Schedule V (non-nutritive flavoring agents) -- International feed name and common name, maximum limit, CAS number
CHINA	For Feed Material: product name (common name), product code, characteristic description (including source, process description, key technical parameters, important specification requirement and hygiene requirement etc.), mandatory labeling provisions For Feed Additive: category, product name (common name), chemical formula or description (including source, process description), source, specifications (purity, active part), conditions of use (including target animal,

Jurisdiction	Information on the Feed Ingredient within the Public Description of the Authorization. Q12
	recommended use level and maximum limit in complete feed or total mixed ration, where applicable), other precautions in usage
EUROPEAN UNION	Feed Additives: Name, identity, identification number, category/functional group, specification, purity criteria, method of analysis, minimum/maximum use in complete feeds, conditions of use (animal species for which the additive is to be used, dosage, types of feeds, route of administration), specific labeling conditions, if necessary.
JAPAN	Feeds: nutritional values Feed Additives: concentrations, properties, purities, other component specifications, standards for manufacturing and storage methods. (Info in the Gazette, not on website. The website only provides the names of the accepted feed additives, as such any imported product.)
SOUTH AFRICA	Trade name, class of animal species, category of additive, registration number, nutritional composition of the product, quantity of product in container, ingredient statement using collective terms, warning statements, feeding recommendations, name and address registered person, batch number, and shelf life.
UNITED STATES	Common name, definition, conditions of use, specifications (some), manufacturing information (some), and labeling provisions

Some jurisdictions have special requirements for feed ingredients that have been manufactured using genetic modification through bioengineering (for example plants, enzymes, or ingredients). Regulatory definitions, which may be jurisdiction-specific, for genetic engineering will further blur the lines of acceptability. Table 7 outlines the differences or provides the legal citation for the differences.

Table 7. Regulatory Considerations for Feed Ingredients Manufactured Using Genetic Engineering

Jurisdiction	Special Consideration for Genetically Modified Feed Ingredients Q13
BRAZIL	Any GM ingredient shall be approved according to Law 11.105/2005 and Decree 5591/2005, which establish safety rules and inspection mechanisms on activities with GMO. Products that contain more than 1% of genetically modified ingredients should indicate such on the label in accordance with Decree 4680/2003.
CANADA	The CFIA evaluates and regulates all feed ingredients, including

Jurisdiction	Special Consideration for Genetically Modified Feed Ingredients Q13
	<p>novel feeds, in the same manner. Any feed ingredient that is new (i.e., not already listed in the Feeds Regulations), or has been modified such that it differs significantly from a conventional ingredient, is required to undergo a pre-market assessment and approval. The purpose of all feed assessments is the same: to ensure via a pre-market assessment, that the feed ingredient is safe (in terms of animal health, human health via food residues and worker/by-stander exposure, and the environment) and effective for its intended purpose. The evaluation also ensures that the feed is accurately defined in the Feeds Regulations and is labeled appropriately for its safe, effective use and for consumer protection.</p> <p>Specific guidance, outlining data requirements, is available for the application for the authorization of the release of a novel feed (e.g., plants and microbes); including those derived from genetic engineering, (RG1; Section 2.6).</p> <p>The Canadian regulatory system for novel products is product-rather than process-based. As a result, Canada has adopted a very broad definition of biotechnology and has focused regulations on novel traits or “new” organisms rather than “genetic engineering” itself.</p>
CHINA	<p>A feed ingredient genetically modified or produced/derived from a genetically modified organism should get approval under Regulations on Agricultural Genetically Modified Organisms Safety Administration (<i>State Council Decree No. 304, 2001</i>) before applying for authorization as a feed or feed additive. The safety assessment of GMOs intended to be used as feed shall be carried out under Administrative Measures on Agricultural Genetically Modified Organisms Safety Assessment (MOA Decree No.8, 2002). In addition, GMOs have some specific identification requirements for labeling according to Administrative Measures on Agricultural Genetically Modified Organisms identification labeling (MOA Decree No. 10, 2002).</p>
EUROPEAN UNION	<p>Specific regulations that cover ingredients manufactured through genetic modification, include labeling ((EC) No 1829/2003 and 1830/2003). In addition the EU has both identification labeling and post-marketing plans required for these products.</p>
JAPAN	<p>For feeds containing genetically modified material(s), safety verification is required by law in accordance with the Ordinance Concerning the Ingredient Specifications for Feed and Feed Additives. In addition, safety verification procedures for feeds and</p>

Jurisdiction	Special Consideration for Genetically Modified Feed Ingredients Q13
	feed additives using recombinant DNA technologies, allowable residue levels of the modified live organism obtained through recombinant DNA technologies, and manufacturing standards for feeds and feed additives using recombinant DNA technologies are specified in accordance with the ordinance.
SOUTH AFRICA	<p>Genetically Modified Organisms Act, 1997 (Act No. 15 of 1997) provides for an authorization procedure for using genetically modified food and feed. Genetically modified products shall only be registered after undergoing an authorization procedure provided for under the GMO Act.</p> <p>Products that contain more than 5% genetically modified ingredients should indicate on the label in accordance with the Consumer Protection Act, 2008 (Act No. 68 of 2008)</p>
UNITED STATES	<p>Producers of animal food from genetically modified plants are encouraged to use the voluntary Consultation Procedures in which the FDA evaluates the food/feed produced using bioengineering. USDA/APHIS requires certain notifications and permits for production of these plants.</p> <p>If requesting authorization from FDA/AAFCO for a new food additive, GRAS substance, or feed ingredient definition that includes a bioengineered plant or micro-organism, the manufacturing information must be described in detail for review by the regulatory officials. This is not different from a conventionally manufactured new food additive, GRAS substance, or feed ingredient definition.</p> <p>Animal food products derived from plant varieties or other organisms developed by new methods of genetic modification are regulated within the existing United States regulatory framework. The assessment scheme for these products focuses on characteristics of the new animal food substance, based on characteristics of the host and donor species, the nature of the genetic change, the identity and function of newly introduced substances, and unexpected or unintended effects that accompany the specific genetic change. Thus, these animal food products, like new plant varieties, are evaluated on a case-by-case basis. Also, enzymes that are produced by GMO micro-organisms must be previously cleared by FDA/AAFCO, even if listed in the OP. The Enzyme Marketing Coordination Document in the AAFCO OP describes the process for enzymes using genetically engineered microorganisms.</p>

Some regulatory jurisdictions provide tolerances for certain feed ingredients and contaminants. In addition, some provide a listing of prohibited feed ingredients in certain cases. A summary of those are provided in Table 8.

Table 8. Feed Ingredient Contaminant Tolerances and Prohibited Feed Ingredients

Jurisdiction	Tolerances for Contaminants Q13	Prohibited Feed Ingredients Q14
BRAZIL	Companies have to exert self-control for the substances that can cause adverse effects to animal and human health according to IN 04/2007 (items 6.1.2; 6.1.3 and 7.1.a), Decree 6296/2007 Art 60, item 6; Art 47 and 48. For dioxins there are limits established in IN 09/2001.	List of prohibited additives published in the Agriculture Minister webpage . In this list the legal basis is also provided. (<i>This information is only available in Portuguese</i>). Animal proteins prohibited in ruminant feed, IN 08/2004
CANADA	Canada lists action levels and tolerances for certain contaminants and undesirable substances. Section 19.(1) of the Feeds Regulations also lists substances that feeds shall not contain and a general requirement that feeds must be safe for humans and animals. Other tolerances are found within the ingredient descriptions in schedules IV and V and in Regulatory Guidance documents available on the website.	Section 4 of the Feeds Regulations contains a deleterious substance list that is not exhaustive and has not been updated. Otherwise, only approved substances as listed in Schedule IV or V, or those medicinal products with a Drug Identification Number (DIN), may be used in feeds in Canada. There are restrictions on feeding prohibited material and Specified Rendered Materials due to the BSE controls. These are in the Health of Animal Regulations.
CHINA	The limits of undesirable substances/contaminants of the feed ingredients material, feed additive and feed product shall meet the requirements of the mandatory Feed Hygiene Standard (GB 13078-2001).	Feed ingredients are only restricted to the positive list. However, there are three forbidden-substance lists: - Drug List Prohibited To Be Used In Animal Feed and Drinking Water (MOA Announcement No. 176) - Veterinary Drugs and Compound Substances Prohibited To Be Used in Food-Producing Animals (MOA Announcement No. 193) - Substances Prohibited To Be

Jurisdiction	Tolerances for Contaminants Q13	Prohibited Feed Ingredients Q14
		Used In Animal Feed and Drinking Water (MOA Announcement No 1519)
EUROPEAN UNION	<p>All products marketed in the EU must be safe.</p> <p>Undesirable substances are provided in Dir. 2002/32, as amended</p> <p>In addition MRLs on pesticides in feeds of vegetable and animal origin are also defined (Regulation (EC) No 1107/2009 concerning the placing of plant protection products on the market and Regulation No 396/2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin)</p>	List of prohibited materials for placing on the market or use for animal nutrition purpose. (Annex III of Reg. 767/2009) such as feces, urine, solid urban waste, wood treated with wood preservatives, etc...)
JAPAN	<p>-Allowable residue levels of pesticide in feeds and feed additives are set in accordance with the Ordinance.</p> <p>-In addition, maximum residue limits of pesticide in unhulled rice, rice straws, and fermented rice roughage as well as maximum residue limits of heavy metals, mycotoxins, and melamine in formula feed, hay, fishmeal, and meat-and-bone meal are specified in the Administrative Guidelines for Hazardous Substances in Feeds</p>	There is no list, but the Ordinance specifies that 1) feeds must not contain antimicrobial substances (except for those listed as feed additives), and 2) raw materials that are confirmed or suspected of containing hazardous substances or those with confirmed or suspected contamination with pathogenic microorganisms must not be used for manufacture.
SOUTH AFRICA	<p>- There is a list of undesirable substances (Table 2) with maximum permissible levels in the Farm Feeds Regulations.</p> <p>- Animal diseases Act 1984 (Act 35 of 1984)</p>	<p>A product shall not be registered as an animal feed if</p> <ul style="list-style-type: none"> - It contains any feedstuffs of such nature or in such quantities that it could cause an interaction leading to the loss of one or more of the nutrients in that product such as to be below the intended nutritional requirement for that product. - It consists of or contains any substance of animal origin, including excreta or other

Jurisdiction	Tolerances for Contaminants Q13	Prohibited Feed Ingredients Q14
		<p>byproducts, and which has not been sterilized beforehand to such extent that the infection or contamination of such product with <i>Bacillus anthracis</i>, organisms of the gas-gangrene type, other pathogenic or putrefactive organisms of viable micro-organisms or substances has been reduced to the level where such organisms or substances will be injurious to or endanger the health or detrimentally affect the productive capacity of animals to which such product is fed.</p> <ul style="list-style-type: none"> - The weed seed content or foreign material thereof exceed the maximum determined in the grading regulations of the product as determined under the Agricultural Product Standards Act, 1990 (Act No. 119 of 1990), for the product concerned; and - It contains ingredients which are prohibited for use as products intended for animal feeding as listed in Table 3 of the Farm Feeds Regulations. - Animal Diseases Act 1984 (Act 35 of 1984): Animal proteins of mammalian origin are not allowed in feed for ruminant species.
UNITED STATES	All products marketed in the U.S. must be safe. FDA lists action levels and tolerances for certain contaminants and undesirable substances (CPGM 7371.003). In addition, EPA publishes tolerances for pesticides approved for use in animal feed. AAFCO OP provides a prohibited heavy metal contaminant	<p>Gentian Violet (21 CFR 589.1000)</p> <p>Propylene glycol in cat food (21 CFR 589.1001)</p> <p>Animal proteins prohibited in ruminant feed (21 CFR 589.2000)</p> <p>Cattle materials prohibited in animal food (21 CFR.589.2001)</p>

Jurisdiction	Tolerances for Contaminants Q13	Prohibited Feed Ingredients Q14
	levels for mineral feed ingredients. None of the lists are all-inclusive for potential contaminants.	

Some regulatory jurisdictions provide specific requirements for labeling hazardous chemicals that may be associated with feed.

Table 9. Special Labeling Provisions for Hazardous Chemicals

Jurisdiction	Special Labeling Provisions for Hazardous Chemicals Q13
BRAZIL	Chap V, Art 29 to 33 Decree 6296/2007, General Rule for Labeling IN 22/2009, and IN 30/2009 (specific for pet food).
CANADA	Labeling requirements for Canada are found within the individual ingredient descriptions in schedules IV and V and under the labeling section of the Regulations (s. 26).
CHINA	There are no specific labeling requirements for hazardous chemicals associated with feed, but if a feed additive or feed material needs special handling, the authorization will note.
EUROPEAN UNION	GHS/CLP (Reg. 1272/2008), Undesirable substances (Dir. 2002/32), Hygiene (HACCP) (Reg. 183/2005), animal by-products (Reg. 1069/2009),
JAPAN	The law provides for no specific labeling for dangerous chemicals.
SOUTH AFRICA	The use of dangerous chemicals is regulated by the Department of Health under the Hazardous Substances Act 1973 (Act No. 15 of 1973). The transportation of dangerous substances is regulated by the Department of Transport under the National Road Traffic Act, 1996 (Act No. 93 of 1996).
UNITED STATES	There are no specific FDA labeling requirements for hazardous chemicals. In the review process, if special handling of a food additive or feed ingredient is noted, the regulation/definition will require special labeling (for examples see formaldehyde or formic acid food additive regulations).

E. Jurisdictional Management of New Ingredients

A “new” feed ingredient describes an ingredient that requires a pre-marketing authorization before being placed on the market. Therefore the concept of new is specific to the jurisdiction. For non-holder specific (non-proprietary) ingredients it is the initial authorization for that ingredient. In jurisdictions that have holder-specific (proprietary) feed ingredients, it is the authorization for that holder. The report describes many of the specific issues related to submissions requesting authoritative bodies for permission to market a new feed ingredient (See Tables 10-15). However, detailed jurisdiction-specific information on the requirements for authorizations is provided in the appendices (A-G).

Table 10.a Jurisdictions’ Administrative Issues for New Ingredients

Jurisdiction	Process Legal Reference	Applicant	Review Authorities
BRAZIL	Application for authorization for new feed ingredients and additives (IN13/2004 item 7.2.)	Authorized manufacturers and importers	Ministry of Agriculture, Livestock and Food Supply - Department of Livestock Inputs Inspection
CANADA	Premarket approval or registration required by the Director of the Animal Feed Division, CFIA. (Regulatory Guidance, RG.1, Chapter 1)	Any person; if a non-resident, the application must be signed by an agent of the applicant who is permanently a resident of Canada	Canadian Food Inspection Agency (for livestock feed). Health Canada reviews and authorizes veterinary drugs.
CHINA	Administrative measures on New Feed and New Feed Additives(MOA Decree No.4, 2012)	Legal person (researcher or producer) located in China.	National Feed Assessment Committee carries out the scientific assessment; Ministry of Agriculture makes the final review for the authorization.
EUROPEAN UNION	Feed Additive Applications for ingredients falling under the definition of feed additive (procedure to follow as described in Regulation (EC) No 429/2008	Any interested party located in the EU	The European Commission (EC) handles the application and requests risk assessment of the technical dossier by EFSA. The EFSA opinion is used by the EC to make risk-

Jurisdiction	Process Legal Reference	Applicant	Review Authorities
	Feed Materials: nothing except listing in the online Register of Feed Materials.		management decisions (i.e. authorize or not the product and define the authorization conditions).
JAPAN	Safety Evaluation Criteria and Evaluation Procedure for Feeds and a review by the Agricultural Materials Council of the Ministry of Agriculture, Forestry and Fisheries of Japan (JMAFF). (Law No. 35 of 1953)	Not restricted, but submission must be in Japanese	Notifications to the Minister of Agriculture, Forestry and Fisheries of Japan. Distributors must notify the prefectural governor. For rDNA technologies, the Ministry of Health, Labor and Welfare and the Food Safety Commission of the Cabinet Office of Japan is also involved.
SOUTH AFRICA	Application forms	Person residing in the Republic of South Africa or a juristic person	Registrar of Farm Feeds
UNITED STATES	-Food Additive Petition 21 CFR 571 -GRAS Notification Proposed 21 CFR 570.36 -AAFCO Ingredient Definition Process AAFCO OP	Not restricted, typically manufacturers (foreign or domestic).	FAPs and GRASN reviewed by Center for Veterinary Medicine/FDA . For AAFCO definition submissions, joint review by AAFCO and CVM/FDA

Table 10.b Additional Administrative Issues for New Ingredients

Jurisdiction	Is Applicant Notified?	Public Notice of Authorization	Review/Authorization Time Frames
BRAZIL	The applicant is notified	Included on positive list (access to list is restricted to business establishments)	3 to 9 months.
CANADA	The applicant is informed directly through a letter from CFIA.	Not published except when regulatory amendment is made to the Schedule IV/V on the consolidated list. Labels are public information. Exceptions for Novel Feeds from Plant sources where a decision document is published.	Average 7 months. Service standard is 90 days for 90% (excluding novel feeds applications) of files and includes a one-time go-around with applicant. Files may be closed if all information is not submitted after the 2nd request.
CHINA	Certificate issued for new feed or feed additive.	Announcement that approves the new feed or new feed additive is published on MOA website.	9 to 12 months
EUROPEAN UNION	Product included in positive list, published in the EU Official Journal; also through the minutes of the meetings of the Standing Committee on the Food Chain and Animal Health and publication of the EC decision in the EU official journal. EFSA review is also publicly available.	Authorization in the form of a regulation in the official journal. Approved Feed Additives added to the Community Register for Feed Additives.	9 months-5 years
JAPAN	Publication in the official gazette by the JMAFF	Publication in the official gazette by the JMAFF	3 to 9 months, if complete submission (except GM feed)

SOUTH AFRICA	Certificate issued (firm initially contacted by phone or email)	No listing, but registration number must be included on all labels	4 months
UNITED STATES	Petitioners and GRAS notifiers receive an FDA letter; AAFCO Definition-FDA will copy submitter. AAFCO Vote is Public (website)	-Food Additives published in Federal Register and codified in 21 CFR 573 - GRAS Notification responses are found on CVM website -New AAFCO Definitions are published in AAFCO OP as tentative definition	6 months-4 years

F. Jurisdictional Assessment of New Ingredients

The details of each region's requirements for the review of a new feed ingredient are provided in Appendices A-G. As a means of comparison of the covered jurisdictions, following are three tables that cover some specific issues, as well as a summary table that provides the listing of a number of examples of feed ingredients, and how they would be considered in each covered jurisdiction.

Table 11: Specific Issues Related to Authorization of New Ingredients

Jurisdiction	Are The Submission Requirements for a National Company Different than a Foreign Company? Q24	Are Requirements for Food Producing vs. Companion Animals Different? Q26	Are Requirements for Major vs. Minor species Different? Q27
BRAZIL	NO	NO	NO
CANADA	NO	Yes, only ingredients for livestock (including horses) are regulated as feeds in Canada. Companion animals are not defined in the Feeds Act as livestock. Pet food (other than drugs) – not regulated in Canada	The pre-market approval of ingredients are required by the CFIA only for livestock species as defined in the Feeds Act and Regulations.

Jurisdiction	Are The Submission Requirements for a National Company Different than a Foreign Company? Q24	Are Requirements for Food Producing vs. Companion Animals Different? Q26	Are Requirements for Major vs. Minor species Different? Q27
CHINA	NO	NO	Yes, sometimes data may be extrapolated from major species to a minor species.
EUROPEAN UNION	NO	NO, similar except no human health safety assessment for pets	YES, Major species and minor species defined
JAPAN	NO	YES, different governing laws	NO, see clarification in Appendix E
SOUTH AFRICA	YES, proof of compliance with competent authority in COO	NO, except no mammalian origin products can be used in ruminant feed	NO
UNITED STATES	NO	NO, similar except no human food safety assessment for companion animals (including horses)	Yes, if approved for a major species, data may be extrapolated to minor species as appropriate.

G. Other Specific Questions That May Highlight Differences Among Jurisdictions

Table 12a: Specific Issues Related to Authorization of New Ingredients: Claims or Intended Use

Jurisdiction	Can the Claim or Function Change the Regulatory Category? Q28	How are substances to diagnose, prevent, mitigate or treat diseased regulated? Q29	Can Feed Ingredients prevent Coccidiosis or Histiomonosis ? Q29	Can Feed Ingredients include production claims (feed efficiency, growth)
BRAZIL	YES	Veterinary Products	Coccidiostats- Yes Histiomonosis- No	YES
CANADA	YES	Veterinary drugs	NO	YES*
CHINA	YES	Veterinary drug	NO	YES

Jurisdiction	Can the Claim or Function Change the Regulatory Category? Q28	How are substances to diagnose, prevent, mitigate or treat diseased regulated?	Can Feed Ingredients prevent Coccidiosis or Histiomonosis ? Q29	Can Feed Ingredients include production claims (feed efficiency, growth)
EUROPEAN UNION	YES, In the European Union claims are defined in Reg 767/1831.	Veterinary Medicinal Product	Yes, (category 5, feed additives)	YES**
JAPAN	YES, Feed Additives	Veterinary Medical Product	NO	YES
SOUTH AFRICA	YES	Controlled by Medicine and Related Substances Control Act	NO	NO
UNITED STATES	YES	Animal Drug	NO	NO

* Improvement of appetite, weight gain, feed efficiency and other production parameters within normal ranges as defined in current National Research Council (NRC) for viable microbial and yeast cell wall products.

** Only feed additives belonging to the category zootechnical additives receive an assessment as examined by EFSA.

Table 12b: Specific Issues Related to Authorization of New Ingredients: Claims or Intended Use

Jurisdiction	Can Feed Ingredients be used to maintain feed Salmonella Negative?Q31	Can Feed Ingredients be Prebiotics or Probiotics? Q32
BRAZIL	YES, as technological feed additives	YES, as zootechnical feed additives.
CANADA	Regulated as a veterinary drug by Health Canada	NO with that function they are considered drugs. Viable Microbial products and yeast cell wall products can be approved as a feed with data in support of other feed production claims as above.
CHINA	No clear legal status	YES, Feed Additive
EUROPEAN UNION	No clear legal status	There is no mention of the terms "prebiotics" and "probiotics" in EU legislation concerning feed. There are the following explicit defined functions within the zootechnical additives: "digestibility enhancers", "gut flora stabilizer", and "other zootechnical additives" (see clarification in Appendix D)
JAPAN	Some feed additives are used in practice, but have not been approved in the feed additive process.	YES, Feed Additive
SOUTH AFRICA	YES, Technological	YES, Zootechnical
UNITED STATES	YES	Yes

In an attempt to summarize how specific products will be evaluated in each of the regulatory jurisdictions, Table 13 provides a comparison of processes for a selection of feed ingredients selected to demonstrate differences among regulatory jurisdiction. Table 13 is in landscape format.

Table 13. Comparison of Jurisdictions' Regulatory Processes For Example New Ingredients For Specific Intended Use

	Brazil	Canada	China	EU	Japan	South Africa	U.S.
Non-traditionally fed plant	New Ingredient	Premarket authorization as a Novel Feed from Plant Sources, Feeds Regulations	Feed material	Feed Material	Feed	Farm Feed: unmixed animal feed of plant origin	Food Additive or AAFCO Ingredient Process when intended for nutritional purposes
Genetically engineered corn	Approval under Law 11.105/2005 and Decree 5591/2005	Pre-market authorization as a Novel Feed from Plant Sources, Feeds Regulations	Feed Material with special GMO approval (SCD No. 304, 2001)	Feed included in regulations for genetically modified food and feed (Reg. 1829/2003)	Feed Additive	Requires Authorization under GMO Act	Premarket biotechnology notification (see 6FR4706)
New inorganic required mineral (nutritional)	Nutritional Feed Additive	Single-Ingredient Feed	Nutritional Feed Additive	Nutritional Additive	Feed Additive	Farm Feed: Unmixed nutritional feed additive	Food Additive or AAFCO Definition
New vitamin-derivative	Nutritional Feed Additive	Single-Ingredient Feed	Nutritional Feed Additive	Nutritional Additive	Feed Additive	Farm Feed: Unmixed nutritional	Food Additive or AAFCO Definition

	Brazil	Canada	China	EU	Japan	South Africa	U.S.
						feed additive	
Enzyme (feed effect)	Zootechnical Feed Additive	The fermentation product is approved as a Single- Ingredient Feed, or Novel Feed (if new or has a novel trait)*	Nutritional Feed Additive	Zootechnical Additive or Technological Additive	Feed Additive	Farm Feed: Feed Additive	Food Additive GRASN or AAFCO Definition*
Enzyme (feed effect) manufacture d by GE	Zootechnical Feed Additive	see above - enzyme	Nutritional Feed Additive with special GMO approval (SCD No. 304, 2001)	Zootechnical Feed Additives for genetically modified food and feed (1829/2003)	Feed Additive	Farm feed Zootechnical feed additive	Food Additive GRASN or AAFCO Definition
Enzyme (animal production)	Zootechnical Additive	see above - enzyme	Nutritional Feed Additive	Zootechnical Additive	Feed Additive	Farm Feed Zootechnical feed additive	Animal Drug
Herb Extract (flavor)	Feed Additive	Single- Ingredient Feed, Listed in Schedule V	General Feed Additive	Feed Material	Feed	Farm Feed Sensory feed additive	Food Additive GRASN or AAFCO Definition

	Brazil	Canada	China	EU	Japan	South Africa	U.S.
Synthetic Flavor	Feed Additive	Single-Ingredient Feed, Listed in Schedule V	General Feed Additive	Feed Additive	Feed Additive	Farm Feed Sensory feed additive	Food Additive GRASN or AAFCO Definition
Antioxidant (feed)	Technological Feed Additive	Single-Ingredient Feed or a registered mixed feed (Specialty)	General Feed Additive	Technological Additive	Feed Additive	Farm Feed Technological feed additive	Food Additive GRASN or AAFCO Definition
Pelleting Agent	Technological Feed Additive	Single-Ingredient Feed or a registered mixed feed (specialty)	General Feed Additive	Technological Additive	Feed Additive	Farm Feed Technological feed additive	Food Additive GRASN or AAFCO Definition
Anti-Salmonella (feed effect)	Technological Feed Additive	Drug	Not Clear	Not Clear	Not Clear, use without claims	Farm Feed Zootechnical feed additive	Food Additive
Feed Ingredient with Feed Production Claims	Feed Ingredient	Single-Ingredient Feed or a registered mixed feed (specialty). Company will need to	Feed Additive	Zootechnical Additive	Feed Additive	Stock Remedy	Animal Drug

	Brazil	Canada	China	EU	Japan	South Africa	U.S.
		register and provide data to substantiate the feed claim.					
Coccidiostat	Feed Additive	Veterinary Drug	Veterinary Drug	Zootechnical Additive	Veterinary Medical Product	Stock Remedy	Animal Drug
Histomono-stat	Veterinary Drug	Veterinary Drug	Veterinary Drug	Zootechnical Additive	Veterinary Medical Product	Stock Remedy	Animal Drug

*Canada Note: Note that enzyme supplements per se are not approved as single-ingredient feeds (i.e., single-ingredient on a carrier). The enzyme supplements are registered with a fermentation product in the formula and enzyme activity highlighted on the label. If a company wants to put a claim on the label (e.g., feed effect), they will need to supply data as part of the registration process.

U.S. Note: The enzyme supplements are registered with a fermentation product in the formula and enzyme activity highlighted on the label. If a company wants to put a claim on the label (e.g. feed effect), it will need to supply data as part of the registration process.

H. Jurisdictional Comparison of Two Feed Ingredients' Authorization Requirements

In order to better compare the requirements for a new feed ingredient authorization, the report will compare two relatively simple ingredients: 1) a new inorganic mineral (e.g. iron sulfate) for use as source of minerals in swine and poultry feed and 2) a processing aid/technological aid (for example a pelleting aid such as sodium hydroxide lignin) to be used in all animal feeds. Tables 14 and 15 will provide a description of the information needed for each section of the application (when required by authorization).

Table 14. Authorization for New Inorganic Mineral in Swine and Poultry Diets
Table 14a: Identity, Manufacturing, Chemistry, Stability, Mixability, and Analytical Methods

Jurisdiction	Identity, Manufacturing, Chemistry, and Analytical Methods
Brazil	<p>Name of the raw material; source of ingredient, flow chart (with details) of the processing steps, including identification of chemical agents and temperatures used.</p> <p>Description of the physical state</p> <p>Purity</p> <p>Presence of contaminants</p> <p>Intended levels of guarantee (based on 3 batches)</p>
Canada	<p>A description of the production and formulation processes, identifying raw materials, chemical reactions, techniques, and any other parameters that may influence the specifications, quality, or safety of a product. A flow-chart diagram accompanying the description is recommended.</p> <p>Description of Additive:</p> <ul style="list-style-type: none"> -- Clear identification of the ingredient -- Physicochemical data -- Composition of the ingredient -- Consideration of contaminants <p>SPECIFICATIONS: The exact formulation including contaminants. An acceptable test method for the analysis of the product must be provided. Suitable methodology needed for the detection of significant amounts of any ingredient, compound or that occurs as a contaminant of the feed.</p> <p>Certificates of analysis are required in support of the label guarantee using the proposed methodology. Also for safety, may require analytical methods for inherent contaminants or ingredient in final feed</p> <p>STABILITY: This includes storage times under ideal conditions, a description of the factors affecting shelf life, what happens when the product degrades or decays, how one can tell if degradation has occurred, whether this creates a particular hazard, and how the manufacturer has substantiated its estimation of shelf life. Shelf life should be determined based upon sensory/quality assessment, nutrient</p>

Jurisdiction	Identity, Manufacturing, Chemistry, and Analytical Methods
	<p>loss profiles, and perishability time.</p> <p>Certificates of analysis and analytical methodology substantiating the guarantee in the ingredient as well as in a mixed feed matrix may be required.</p>
China	<p>Product composition and identification report, physical and chemical properties.</p> <p>Production process and manufacturing method, including process flow chart with text description, focus on key technical parameters (time, temperature and pressure, etc.)</p> <p>Stability Test report</p> <p>Quality standards (specifications and analytical methods), complied with the Guidance on the Rule and Standards for the Structure and Drafting of Standards (GB/T 1.1)</p> <p>When there is a maximum level indicated, the analytical method for the substance in the complete feed, concentrated feed, supplemental feed, or premix is needed.</p>
EU	<p>Identification of the additive</p> <p>Qualitative and quantitative composition (active substance, other components, impurities, batch to batch variation)</p> <p>Purity</p> <p>Physical state of each form of the product</p> <p>Characterization of the active substance(s)</p> <p>Manufacturing process, including any specific processing procedures -- a detailed description of the manufacturing process of the additive shall be submitted.</p> <p>Physical-chemical and technological properties of the additive</p> <p>Stability-Shelf-life of the additive</p> <p>Stability of the additive used in premixtures and feedingstuffs</p> <p>Homogeneity</p> <p>Physico-chemical incompatibilities in feed</p> <p>Analytical methods to be used for the analysis for the official controls of the additive as such, in premixtures, and in feedingstuffs</p>
Japan	<p>Details of origin or discovery and status of approval, usage, etc. in foreign countries</p> <p>Specifications</p> <p>Name</p> <p>Chemical structure</p> <p>Manufacturing process</p> <p>Physicochemical properties</p> <p>Identification test</p> <p>Purity test</p> <p>Content and assay procedure</p> <p>Method of quantitative analysis in feed</p> <p>Change with time</p>

Jurisdiction	Identity, Manufacturing, Chemistry, and Analytical Methods
S. Africa	<p>Qualitative and quantitative composition (active substance, other components, impurities)</p> <p>Physical state, particle size</p> <p>Manufacturing process including any specific processing process</p> <p>Purity</p> <p>Stability on exposure to environmental conditions such as light, temperature, pH, moisture, and oxygen. Expiry date</p> <p>Stability during the preparation of premixtures and feedingstuff, in particular stability to heat, pressure and moisture. Possible decomposition product</p> <p>Stability during the storage of premixtures under defined conditions (Storage time under defined condition) Shelf life</p> <p>Other appropriate physico-chemical, technological or biological properties such as stability to obtain homogenous mixtures in premixtures and feedingstuffs, dust-forming properties, assessment of resistance to degradation or loss of biological activity in the digestive tract or by system of stimulation in vitro</p> <p>Physico-chemical or biological incompatibilities or interactions (e.g. with feedingstuffs, other approved additives or medicinal products)</p> <p>Description of the methods used for the determination of the criteria listed under items for composition, purity, and stability (see above).</p> <p>Description of the qualitative and quantitative analytical methods for routine control of the additive in premixtures and feedingstuffs</p>
U.S.	<p>Full Description of Manufacturing, including critical control points</p> <p>Specifications for starting materials</p> <p>Specifications of final product based on 3-5 batches</p> <p>Stability of final product (as intended to be packaged)</p> <p>Stability of product once incorporated in feed</p> <p>Demonstration of mixability (homogeneity) when mixing in complete feed</p> <p>Validated Analytical Method for final ingredient</p> <p>Validated Analytical Method for ingredient in complete feed</p> <p>Validated Analytical Methods of all pivotal measurements to support safety and utility</p>

Table 14b: Intended Use/Utility

Jurisdiction	Requirements to Support Intended Use/Utility
Brazil	Justify use objectives by scientific evidence.
Canada	<p>New unfamiliar mineral nutrient: Three scientific studies in each species (swine and poultry) to support a nutritional purpose carried out by qualified research personnel, using suitable methods, designed to facilitate statistical analysis, analyzed by appropriate statistical methods, and conducted under conditions similar to those that may be expected to occur in Canada.</p> <p>Familiar mineral nutrient: Bioavailability study in each species (swine and</p>

Jurisdiction	Requirements to Support Intended Use/Utility
	poultry) with comparison with established source of mineral
China	Feeding studies (in vivo) should be conducted for both swine and poultry, except in cases where extrapolation can be used. They shall be conducted by the institutions designated by the MOA and according to the technical guidance for efficacy studies in livestock target animal.
EU	Short-term Bioavailability tests or Digestion Balance studies are adequate. Studies must be replicated three times. DIGESTION TESTS DURATION: Swine: weaned piglet: 42-days; growing/fattening pig at least 70 days; sows: from insemination to the end of second weaning period (two cycles) Poultry: chickens for fattening: 35 days; laying hens: 178 days
Japan	Basic studies proving effectiveness Field trial studies proving effectiveness
S. Africa	Scientific trials performed on target species
U.S.	Bioavailability study in each species (swine and poultry) with comparison with established source of mineral

Table 14c: Target Animal Safety

Jurisdiction	Requirements to Support Target Animal Safety
Brazil	Scientific evidences that support the safe use of the material.
Canada	Mammalian toxicological data and pertinent livestock toxicity data are referenced for both target animal and human safety. Study duration is not specified per se but should be representative of the intended feeding regime. The needs for mammalian toxicology data are generally flexible and are specific to the feed ingredient and any inherent or introduced contaminants and should be discussed with CFIA.
China	Target animal tolerance study report should be provided for both swine and poultry pre-marketing authorization of new feed additive, except in cases where extrapolation can be used. They shall be conducted by the institutions designated by the MOA and according to the technical guidance for tolerance studies in livestock target animal.
EU	Tolerance studies are only required for novel authorizations of compounds of trace elements. Typically tolerance studies are multiples of the intended dose for visual evidence of clinical effects, performance characteristics, product quality where relevant, hematology and routine blood chemistry and for other parameters likely to be related to the biological properties of the additive. Pathology and histopathology is required on animals that die during the study. If a 100X dose tolerance test can be shown to be tolerated, no hematology or routine blood chemistry would be required. TESTS DURATION: It is possible that if a tolerance study is required only the more sensitive species will be studied. Swine: weaned piglet: 42-day; growing/fattening

Jurisdiction	Requirements to Support Target Animal Safety
	pig: 42-days; sows: from insemination to the end of weaning period (one cycle) Poultry: Chickens for fattening: 35 days; laying hens: 56 days
Japan	Feeding studies using target animals
S. Africa	Scientific trials performed on target species
U.S.	<p>If there is enough understanding of the mineral compound (physical, chemical, and biological properties and similarity to currently approved ingredients) and how it would disassociate in the gastro-intestinal tract, FDA may accept a white paper to base the safety assessment.</p> <p>If there is not enough published information to base a safety assessment, FDA may require a target animal safety study in each species, which are GLP studies covering treatment levels of 1X, 5X, and 10X (or 1X, 3X, 5X). Studies should be designed to collect hematology, blood chemistry, gross pathology, and histopathology. Traditional EU 100X tolerance studies are not accepted as pivotal to support target animal safety.</p> <p>Poultry studies are 42-49 days in length (lifetime) and swine studies would be 45 days-3 months depending on FDA's concern. These studies are required to be conducted under Good Laboratory Practice regulations (21 CFR 58).</p>

Table 14d: Human Food Safety/Consumer Safety

Jurisdiction	Requirements to Support Human Food Safety
Brazil	Safety must be demonstrated by studies or published literature, or by national and international bodies' determination.
Canada	<p>Mammalian toxicological data and pertinent livestock toxicity data are referenced for both target animal and human safety.</p> <p>RATE AND DEGREE OF ABSORPTION Distribution, Metabolism and Elimination Data:</p> <ul style="list-style-type: none"> -- Acute toxicity -- Acute median lethality -- Skin/eye irritation -- Skin sensitization -- Mutagenicity -- Short-term toxicity -- Teratogenicity -- Developmental toxicity -- Reproductive toxicity -- Carcinogenicity -- Epidemiological studies -- Chemical interaction <p>In particular for food safety, the following studies are required in the event that a residue may be present in the food produced -- i.e., meat, milk, eggs, fish.</p>

Jurisdiction	Requirements to Support Human Food Safety
	<ul style="list-style-type: none"> -- Suggested Maximum Residue Limit (MRL) or Tolerance -- Livestock Metabolic Fate and Residue Studies -- Metabolic Fate and Elimination Studies -- Residue Studies for the Parent Compound and Its Possible Metabolites <p>Should it be determined that the use for the ingredient may result in residues, CFIA will consult with Health Canada for support of the safety determination.</p> <p>- Microbial contaminants if applicable</p>
China	<ul style="list-style-type: none"> • Toxicology safety evaluation report: Toxicology data published by international authorities (such as JECFA, OECD) or data published by GLP laboratory is acceptable. • Metabolism and residue evaluation report: chemical synthesized product shall carry out metabolism and residue evaluation, except the several exemption provisions. • The impact on human health analysis report: to evaluate and analyze the impact of the additive on human health based on the results from the efficacy and safety evaluations and the consultation of relevant data, by making reference to the methods of risk assessment
EU	<p>The evaluation process takes into account if the product is also authorized in food. If not, studies in support would include:</p> <ul style="list-style-type: none"> Metabolic and residue studies Metabolic Studies Metabolic profiling, identification of the metabolite(s) in excreta and tissues and distribution in tissues and products shall be established following repeated dose administration of the labeled compound to animals to the steady state (metabolic equilibrium) identified by plasma levels. Residue Studies Toxicological studies Proposal of a Tolerable Upper Level (usually based on evaluation for consumers) Comparison of the ADI or the UL with consumer exposure considering all possible sources of the additive.
Japan	<p>Residue studies using target animals toxicity test</p> <p>General toxicity test</p> <ul style="list-style-type: none"> Single-dose toxicity Repeated-dose toxicity (short-term) Repeated-dose toxicity (long-term) Special toxicity test <ul style="list-style-type: none"> Multi-generation reproduction Teratogenicity Carcinogenicity

Jurisdiction	Requirements to Support Human Food Safety
	Mutagenicity Other toxicity test (local toxicity, inhalation toxicity) Pharmacology Metabolism Feeding studies using target animals Studies regarding development of resistant bacteria
S. Africa	Acute Toxicity Acute Inhalation Toxicity Skin and Eye Irritancy Mutagenicity Ames/Salmonella Test Chromosomal Aberration Test Pharmacokinetics Aspects Subchronic Toxicity Chronic Toxicity/Carcinogenicity Reproductive Toxicity Metabolism and Toxicokinetics Residue Studies
U.S.	<p>If there is enough understanding of the mineral compound (physical, chemical, and biological properties and similarity to currently approved ingredients) and how it would disassociate in the gastro-intestinal tract, FDA may accept a white paper to base the safety assessment.</p> <p>If there is not enough published information to base a safety assessment, FDA will require residue studies to demonstrate that potential residues are safe (both swine and poultry). There will need to be sufficient data to demonstrate a safe residue level based on traditional toxicology data, unless an Acceptable Daily Intake level has been set for another use of the compound or like compound. All safety studies must be conducted under Good Laboratory Practice regulations (21 CFR 58)</p>

Table 14e: Worker User Safety

Jurisdiction	Requirements to Support Worker/User Safety
Brazil	None. Under the competence of the Labor Ministry and not the Agricultural Ministry.
Canada	Human Exposure Data And Exposure Estimation <ul style="list-style-type: none"> -- Major routes of exposure -- Amount of product handled by workers and consumers -- Frequency and duration of exposure -- Exposure concentrations -- Exposure studies Material Safety Data Sheet (MSDS) required Labeling requirements when needed
China	Product safety protection information, such as MSDS is required.
EU	Assessment of user safety will be based on the available specific studies, the MSDS, and the nature of the active substance(s)/agent(s). Additives with a high dusting potential or those used under circumstances which could generate aerosols are of particular concern. Any data on dusting potential will be used for exposure assessment. Toxicological risk assessment for user/worker safety (inhalation, dermal, mucosal, allergenicity, optic, and toxicity (from consumer safety data). <ul style="list-style-type: none"> -- Exposure assessment -- Mitigating measures MSDS required Labeling requirements when needed
Japan	none
S. Africa	Material Safety Data Sheet (MSDS) required
U.S.	There is no FDA requirement for information to support worker or user safety. Label may include warnings, if warranted.

Table 14f: Environmental Safety

Jurisdiction	Requirements to Support Environmental Assessment
Brazil	None. Under the competence of the Environmental Ministry and not the Agricultural Ministry.
Canada	DETERMINATION OF ENVIRONMENTAL FATE AND EFFECTS (studies required as appropriate) <ul style="list-style-type: none"> -- Vapor pressure and volatilization -- Hydrolysis -- Photodegradation -- Adsorption-Desorption -- Biotransformation in soil -- Biotransformation in aquatic systems -- Biochemical oxygen demand -- Toxicity to aquatic organisms

Jurisdiction	Requirements to Support Environmental Assessment
	<ul style="list-style-type: none"> -- Toxicity to soil organisms -- Toxicity to birds -- Toxicity to wildlife
China	Report of discharges (gas, liquid and solid discharges) treatment: assessing the impact of production on the environment
EU	Predicted Environmental Concentration (PEC) may be required to be calculated. Phase I serves to identify those additives that do not need further testing (natural or physiological substance with no increase in the environment, substance intended for nonfood-producing animals, or when the PEC is very low). For the other situations a second phase (Phase II) assessment is needed to provide additional information, based upon which further studies may be considered necessary.
Japan	Studies on environmental impact (plant toxicity, fish toxicity, and environmental pollution)
S. Africa	Environmental studies
U.S.	If the submission for evaluation is a Food Additive Petition (not a GRAS notification) an environmental assessment must be provided, unless it fits a waiver as provided in 21 CFR 25.32. Generally environmental assessments are very straight-forward documents and the requirements are waived for most food additives that qualify for an exclusion. For an AAFCO definition a statement of environmental safety is needed.

Table 14g. Additional Administrative information

Jurisdiction	Administrative Information to Support Application
Brazil	Identification of the species that will be fed, as well as restrictions for use Classification of Feed Additive category (if feed additive)
Canada	Administrative information to support application, as per the RG 1, Chapter 1. Typically, requests sample for a new ingredient.
China	Application form Summary of Application materials Name of product and naming basis Proposed use of the product Label format, packaging requirements, storage conditions, Samples from three consecutive batches of each product are provided, and four samples for each batch Products manufactured in China must apply for a production license prior to marketing the new product.
EU	Common name of the product and nomenclature basis 3 samples of the product are to be provided Scientific summary of the dossier Application Form Public summary of the dossier Annex entry proposals
Japan	Samples may be requested

Jurisdiction	Administrative Information to Support Application
S. Africa	Certificate of analysis of the product within the last year 2 samples (100 g or 100 ml) – when requested by the Registrar Product label Inspections required for new facilities for the production of animal feed or re-inspection for facilities that have changed hands Name according to main active ingredient as described by IUB/IUPAC, EINECS and CAS Number. Regulatory status in other countries
U.S.	Name and contact information of the requester (petitioner/notifier) Purpose statement Draft definition (or regulation) Label

Table 14h: Post-Marketing Requirements

Jurisdiction	Post marketing Requirements
Brazil	Renewal of registration required for registered products every five years. For additives, the registrant must notify the Ministry with new information in respect to any changes or new information impacting the safety of the additive, IN 13/2004.
Canada	None required in most cases. Re-registration required for registered products. For Novel feeds, the registrant must notify the Minister with new information respecting any changes or new information impacting the safety of the ingredient.
China	New Products are under supervision for the first 5 years. The enterprise should report the relevant information on the product quality, target animal safety, and quality and safety of breeding animal products to MOA.
EU	None required for a mineral product
Japan	None
S. Africa	None
U.S.	None

Table 15: Authorization for New Pelleting Aid Hydroxy Lignosulfonate

Table 15a: Identity, Manufacturing, Chemistry, Stability, Mixability, and Analytical Methods-Pelleting Aid

Jurisdiction	Identity, Manufacturing, Chemistry, and Analytical Methods
Brazil	See Table 14a
Canada	See Table 14a
China	See Table 14a
EU	See Table 14a
Japan	See Table 14a
S. Africa	See Table 14a
U.S.	See Table 14a

Table 15b: Intended Use/Utility-Pelleting Aid

Jurisdiction	Requirements to Support Intended Use/Utility
Brazil	Studies demonstrating the use of the additive as a pelleting aid are required.
Canada	Studies demonstrating the utility of the additive as a pelleting aid are required.
China	Studies demonstrating the utility of the additive as a pelleting aid are required. The test should use representative product applicable to the feed type for the applied product. The test report should be provided by the University, Research Institute and Inspection center at/above provincial level.
EU	Studies demonstrating pellet durability or performance of pellet formation
Japan	Studies demonstrating the utility of the additive as a pelleting aid are required.
S. Africa	Studies demonstrating the utility of the additive as a pelleting aid are required.
U.S.	Data demonstrating the use in forming pellets on a selection of livestock feedstuffs (e.g. nursery swine and poultry) will provide satisfactory data for livestock. For aquaculture, specific testing that demonstrates pellet durability in aquatic environments is required. For use in companion animal diets, testing would be specific to typical formulation of those diets.

Table 15c: Target Animal Safety-Pelleting Aid

Jurisdiction	Requirements to Support Target Animal Safety
Brazil	See table 14c
Canada	See table 14c
China	See table 14c
EU	Generally one tolerance study is required in one target species (or laboratory animal, if it is determined to be the most sensitive species). (See 14c, or Appendix D, for more specific information).
Japan	See table 14c
S. Africa	See table 14c
U.S.	If there is enough understanding of the additive (physical, chemical, and biological properties and similarity to currently approved ingredients), FDA may accept a white paper to base the safety assessment. If there is not enough published information to base a safety assessment, FDA may require one target animal safety study in the identified most susceptible species. These safety studies covering treatment levels of 1X, 5X, and 10X (or 1X, 3X, 5X). Studies should be designed to collect hematology, blood chemistry, gross pathology, and histopathology. These studies are required to be conducted under Good Laboratory Practice regulations (21 CFR 58).

Table 15d: Human Food Safety/Consumer Safety-Pelleting Aid

Jurisdiction	Requirements to Support Human Food Safety
Brazil	See Table 14d
Canada	See Table 14d
China	See Table 14d
EU	See Table 14d
Japan	See Table 14d
S. Africa	See Table 14d
U.S.	See Table 14d

Table 15e: Worker/User Safety-Pelleting Aid

Jurisdiction	Requirements to Support User Safety
Brazil	See Table 14e
Canada	See Table 14e
China	See Table 14e
EU	See Table 14e
Japan	See Table 14e
S. Africa	See Table 14.
U.S.	See Table 14e

Table 15f: Environmental Safety-Pelleting Aid

Jurisdiction	Requirements to Support Environmental Assessment
Brazil	See Table 14f
Canada	See Table 14f
China	See Table 14f
EU	See Table 14f
Japan	See Table 14f
S. Africa	See Table 14f
U.S.	See Table 14f

Table 15g: Administrative Information-Pelleting Aid

Jurisdiction	Administrative Information to Support Application
Brazil	See Table 14g
Canada	See Table 14g– especially if for use in a fish feed
China	See Table 14g
EU	See Table 14g
Japan	See Table 14g
S. Africa	See Table 14g
U.S.	See Table 14g

SECTION I. SUMMARY OF COMPARISON JURISDICTIONAL REQUIREMENTS

TERMINOLOGY: Whenever discussing the feed sector internationally, each jurisdiction has specific definitions for commonly used feed terms. Hence immediate misunderstanding can occur when a common definition used is assumed to have a different meaning. For this report the term “feed ingredient” was used to cover the widest spectrum of all substances that are used in the formulation and manufacture of animal feed. Jurisdiction definitions of terms covering feed ingredients are in the appendices.

AUTHORIZED FEED INGREDIENTS: Canada, Brazil and China have positive lists of feed ingredients that may be used in their jurisdictions. South Africa’s list is under development. Canada’s public list is not routinely updated; but an updated list can be requested from CFIA. Brazil’s list is password protected on its website; as such it is not immediately available. The Chinese catalogue of feed additives is posted in English on the Ministry of Agriculture website, but there is no English version for feed materials catalogue.

The United States has a near positive list of ingredients that can be used in animal feed in the American Association of Feed Control Officials Official Publication, but only available by purchase from that organization. The publication includes the listing of accepted AAFCO defined ingredients, FDA-regulated food additives, and affirmed Generally Recognized As Safe substances. The listing does not include “common feed ingredients” or ingredients that have been determined to be GRAS but that have not been affirmed by the FDA.

The EU has a positive list of all authorized feed additives and a catalogue of feed materials. However the Catalogue of Feed Material list is not comprehensive, and provides a baseline of feed materials. A third list, the EU Feeds Material Register, is an online listing (no authority involvement) where operators are requested to list all feed materials that are “newly” placed on the market (meaning: after the entry into force of the 767 Regulation.)

PROPRIETARY NATURE OF FEED INGREDIENTS: There are more differences in the proprietary nature of feed ingredients than any other area that was reviewed (see Table 4). In most cases certain categories of feed ingredients were considered to be holder-specific listings (proprietary). In China there is a 5-year proprietary period for newly authorized ingredients (during the supervision period). In Canada ingredients that require additional safety or efficacy review are added to Part 2 of their schedules, and these products are proprietary; however, ingredients in Part 1 are non-holder specific. In the U.S. and Japan all feed ingredients are non-holder specific (non-proprietary). In the EU the category of feed additive determines whether the authorization is proprietary. In South Africa all registrations are holder-specific. In Brazil, additives, supplements and dietetic pet food are holder-specific; however feed materials are not.

AUTHORIZATION PERIOD: The U.S., China, and Japan have unlimited time periods for authorized feed ingredients. Canada has separated its list into Part 1 and Part 2 ingredients. Part 1 ingredients have an unlimited authorization period. In Brazil, the authorization period is 5 years; Canada, for those ingredients requiring registration only (i.e., Part 2), 3 years; EU, 10 years; and South Africa, 3 years.

ESTABLISHMENT REQUIREMENTS FOR FOREIGN BUSINESSES for the manufacture and distribution of feed (feed ingredients) are not consistent across jurisdictions (see Table 3). China requires import registration certificates for all imported feed or feed additives. In South Africa, a juristic person must hold the authorization for each feed ingredient. In Brazil, authorizations are held by a Brazilian importer establishment, and the foreign business must comply with Good Manufacturing Practices, confirmed by the competent authority. In Japan the importer must be a Japanese business and must notify the authorities two weeks prior to the start of the importation business. In Canada, all imported mixed feeds must be registered and foreign applicants must have a Canadian agent; there may be import requirements under other government programs (e.g. animal and plant health regulations). Requirements for domicile holders of a registration or establishment are a ready barrier to global marketing.

FEED INGREDIENTS PRODUCED THROUGH BIOTECHNOLOGY OR GMOs: This is the area in which there is widespread discourse, and it has resulted in specific laws governing bioengineered products (see Table 7) in some jurisdictions. Brazil, China, EU, Japan, and South Africa have specific laws or regulations that describe the regulation and/or labeling of feed ingredient manufactured using genetically modified organisms or plants. China, the EU, and South Africa have laws specific to labeling requirements. Canada and the U.S. have no specific laws or regulations covering feed manufactured using genetic engineering, but rely on the laws and regulations that cover the safe manufacture and use of all feed ingredients generically.

SAFETY ASSESSMENT: All jurisdictions compared have similar overall requirements when addressing the safety of a newly authorized feed ingredient with respect to animal health and human health. However, the real differences with convergence are in the details of what is required. The EU has very strict criteria for safety assessment; whereas the criteria in the U.S. and Canada have flexibility in the assessment processes. The U.S. and Canada expect that applicants have a clear characterization of their ingredient and provide enough information to demonstrate its safety. Canada has a list of requirements for safety; the applicant may provide scientific rationale to exempt some data requirements. The U.S. permits the applicant to build a safety assessment based on known information about the feed ingredient and may require a full complement of safety testing. Although each jurisdiction includes a safety assessment, the level of detail offered by respondents' answers to the questionnaires is not able to support a detailed comparison.

PERMITTED INTENDED USE/UTILITY CLAIMS: All jurisdictions indicated that an applicant must provide an intended use for a new ingredient; however, the claim or function of an ingredient can change the regulatory category of the ingredient. Specific issues are addressed below:

Animal Production: Another area of dissimilarity is specific intended uses permitted for feed ingredients. In all cases the regulatory terms associated with feed ingredients in each jurisdiction cover sources of nutrition and technological aids for feed manufacture. However, certain claims are permitted in some jurisdictions that are not in others (see Table 12). The U.S. and South Africa have a strong prohibition on claims associated with animal production for feed ingredients; these claims are restricted to animal drugs. Canada permits claims -- including improvement of appetite, weight gain, feed efficiency and other production parameters -- to within normal ranges as defined in current National Research Council (NRC) or equivalent published literature, under normal conditions of animal husbandry; products with such label claims must be registered. Other jurisdictions have less concern with the claims of animal production for feed ingredients. Claims above and beyond the NRC parameters may be considered drugs by Health Canada.

Coccidiostats: Brazil and the EU permit coccidiostat claims for feed ingredients. The other evaluated jurisdictions consider coccidiostats a drug product. The EU is the only evaluated jurisdiction that allows histomonostats to be regulated as feed additives.

Salmonella Control in Feeds: Brazil, South Africa, and the U.S. permit these specific claims for feed ingredients. In Canada, salmonella control is considered a drug by Health Canada. The EU, China and Japan have a less-clear position on these claims.

Probiotics/Prebiotic Claims: Brazil, China, Japan, South Africa, and the U.S. permit the use of ingredients as a probiotic or prebiotic (in the U.S. this requires carefully worded claims). The EU permits live cultures used as digestibility enhancers or other zoonotic claims; but not specifically prebiotic or probiotic terms. Canada considers ingredients with prebiotic and probiotics claims to be regulated as drugs.

INTENDED USE/UTILITY REQUIREMENTS FOR AUTHORIZATION OF NEW FEED INGREDIENTS:

The level of detail in the questionnaires does not provide a true picture of what exactly is required to demonstrate utility. For example, for most zootechnical claims the EU requires multiple studies in each species/class, and in the U.S. one or more studies are required in each species (class only in unusual circumstances). Canada is similar to the U.S. It is not clear what the other evaluated jurisdictions would require for categories of new feed ingredients.

AUTHORIZATION OF NEW FEED INGREDIENTS FOR COMPANION ANIMALS:

Brazil, China, South Africa, the U.S. and EU regulate feed ingredients intended for use for all animal feed, using the same regulations and law for companion animals and

livestock. The Canadian feed ingredient evaluation process is specific to livestock, defined as horses, cattle, sheep, goats, swine, foxes, fish, mink, rabbits and poultry (chickens, turkeys, ducks and geese). There are no approval requirements for feeds or single-ingredient feed for non-livestock species (which include companion animals). Japan has a separate law governing the approval of feed additives for companion animals. Since the melamine contamination issue, the U.S. has increased the concern over companion animal feed ingredients, such that target animal safety studies are a significant undertaking, including a full generation of testing. This long-term testing is also more desirable to many companies, as it does not require terminal studies.

GLOBAL HARMONIZATION/CONVERGENCE AS A GOAL:

Generally harmonization is considered a laudable goal, as it eases marketing, allows for studies required for new authorizations to be acceptable in multiple jurisdictions and eases commerce. However, in the era of global food supplies, food safety is the primary concern. Global agreement of defined acceptable feed ingredients, manufacturing controls, and authorization requirements is one step toward the safe food supply. Understanding jurisdictional differences and working toward harmonization will assist in the goal of the global safe food supply.

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All legal documents can be found in

<http://sistemasweb.agricultura.gov.br/sislegis/action/detalhaAto.do?method=abreLegislacaoFederal&chave=50674&tipoLegis=A>

In this web site, the documents are found in Portuguese only. English Translations of specific Decrees and Normative Instruction can be requested from the Brazilian authorities. See list below:

Law No 6198, dated December 26, 1974

Decree No. 6296, dated December 11, 2007

Minister Cabinet-Normative Instruction No 09, dated September 11, 2001

Minister Cabinet-Normative Instruction No 13, dated November 30, 2004

Minister Cabinet-Normative Instruction No 4, dated February 23, 2007

Minister Cabinet-Normative Instruction No. 15, dated May 26, 2009.

Minister Cabinet-Normative Instruction No. 22, dated June 2, 2009.

Minister Cabinet-Normative Instruction No. 30, dated August 5, 2009.

Law 11.105, dated March 24, 2005

Decree 5591, dated November 22, 2005

Decree 4680, dated April 24, 2003.

CANADA

Feeds Act: <http://laws-lois.justice.gc.ca/eng/acts/F-9/>

Feeds Regulations: <http://laws-lois.justice.gc.ca/eng/regulations/SOR-83-593/index.html>

Health of Animals Act: <http://laws-lois.justice.gc.ca/eng/acts/H-3.3/index.html>

Health of Animals Regulations:

http://laws-lois.justice.gc.ca/eng/regulations/C.R.C.,_c._296/index.html

RG-1 Regulatory Guidance: Feed Registration Procedures and Labeling Standards

<http://www.inspection.gc.ca/animals/feeds/regulatory-guidance/rg-1/eng/1329109265932/1329109385432>

RG-8 Regulatory Guidance: Contaminants in Feed

<http://www.inspection.gc.ca/animals/feeds/regulatory-guidance/rg-8/eng/1347383943203/1347384015909>

Foods and Drugs Act (Health Canada)

<http://laws-lois.justice.gc.ca/eng/acts/F-27/index.html>

General Regulatory Guidance:

<http://www.inspection.gc.ca/animals/feeds/regulatory-guidance/eng/1299871623634/1320602307623>

Application for Feed Registration or Renewal:

<http://www.inspection.gc.ca/english/for/pdf/c0009e.pdf>

CHINA

Feed and Feed Additive Administrative Regulation, State Council Decree No. 609, 2011 <http://www.moa.gov.cn>. English: <http://english.agri.gov.cn/>

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Administrative measures on Approval Number of Feed Additive and Feed Additive Premix. MOA Decree No. 5, 2012, <http://www.moa.gov.cn>.

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Feed Additive Catalogue. MOA announcement No. 1126. <http://www.moa.gov.cn>.

Feed Material Catalogue. MOA announcement No. 1773. <http://www.moa.gov.cn>.

The list of drug-feed additive. MOA announcement No. 168. <http://www.moa.gov.cn>.

Practice for Safety Usage of Feed Additive. MOA announcement No. 1224. <http://www.moa.gov.cn>.

Drug List Prohibited To Be Used in Animal Feed and Drinking Water. MOA announcement No. 176. <http://www.moa.gov.cn>.

Veterinary Drugs and Compound Substances Prohibited To Be Used in Food-Producing Animals. MOA announcement No. 193. <http://www.moa.gov.cn>.

Substances Prohibited To Be Used in Animal Feed and Drinking Water. MOA announcement No. 1519. <http://www.moa.gov.cn>.

Requirement for Feed and Feed Additive Official Authorization. MOA announcement No. 611, <http://www.moa.gov.cn> (to be revised,).

The procedure of Feed Administrative License. MOA announcement No. 517. <http://www.moa.gov.cn>. (to be revised)

The guidance of the stability test of feed additive (try out). Document of general office of MOA No. [2008] 82. <http://www.moa.gov.cn>.

The guidance of the efficacy studies in livestock target animal (try out) and the tolerance studies in livestock target animal (try out). Document of general office of MOA No. [2011] 21. <http://www.moa.gov.cn>.

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18. Feed Label (GB 10648-1999). <http://www.sac.gov.cn>. English: http://www.sac.gov.cn/sac_en/

Feed Hygiene Standard (GB13078-2001). <http://www.sac.gov.cn>.

Regulations on Agricultural Genetically Modified Organisms Safety Administration. State Council No. 304. <http://www.moa.gov.cn>.

Administrative measures on Agricultural Genetically Modified Organisms Safety Assessment. MOA Decree No. 8, 2002, <http://www.moa.gov.cn>.

Administrative measures on Agricultural Genetically Modified Organisms identification labeling. MOA Decree No. 10, 2002, <http://www.moa.gov.cn>.

Administrative measures on import feed and feed additives, MOA Decree No.38, which is under revision. <http://www.moa.gov.cn>.

EUROPEAN UNION

Council Directive Feed Materials 96/25 (Current (EC) No. 767/2009)

<http://eurlex.europa.eu/LexUriServ/LexUriServ.do?uri=CONSLEG:1996L0025:20030605:en:pdf>

Food Law Regulation (EC) No. 178/2002

<http://eurlex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2002:031:0001:0024:EN:PDF>

Additives for Use in Animal Nutrition Regulation (EC) No. 1831/2003

<http://eurlex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2003:268:0029:0043:EN:PDF>

Community Register of Feed Additives Pursuant to Regulation (EC) No. 1831/2003, Appendix 3 and 4

http://ec.europa.eu/food/food/animalnutrition/feedadditives/comm_register_feed_additives_1831-03.pdf

Feed Additive Applications Regulation (EC) No. 429/2008

<http://eurlex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:133:0001:0065:EN:PDF>

Market and Use of Feed Regulation (EC) No. 767/2009

<http://eurlex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2009:229:0001:0028:EN:PDF>

Commission Decision on Prohibited Substances 2004/217/EC

<http://eurlex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2004:067:0031:0033:EN:PDF>

Directive 2001/82/EC Veterinary Medicinal Products

http://www.echamp.eu/fileadmin/user_upload/Regulation/Directive_2001-82-EC-Consolidated_Version_.pdf

Regulation (EC) No. 1829/2003 Genetically Modified Food and Feed

<http://eurlex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2003:268:0001:0023:EN:PDF>

Regulation (EC) No. 1830/2003 Traceability and Labeling of Genetically Modified Organisms

http://eurlex.europa.eu/LexUriServ/site/en/oj/2003/l_268/l_26820031018en00240028.pdf

Regulation (EC) No. 1831/2003 Feed Hygiene

http://eurlex.europa.eu/LexUriServ/site/en/oj/2005/l_035/l_03520050208en00010022.pdf

Commission Recommendation: Establishing Guidelines for the Distinction Between Feed Materials, Feed Additives, Biocidal Products and Veterinary Medicinal Products. January 14, 2011

<http://eurlex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2011:011:0075:0079:EN:PDF>

FEFANA classification tool: A practical tool implementing the Commission recommendation to distinguish between feed additives and feed materials:
<http://www.fefana.org/ClassTool/>

Technical Guidance-Tolerance and Efficacy Studies in Target Animals
<http://www.efsa.europa.eu/en/efsajournal/doc/2175.pdf>

Guidance for the Preparation of Dossiers for Technological Additives:
<http://www.efsa.europa.eu/en/efsajournal/doc/2528.pdf>

Guidance for the Preparation of Dossiers for Nutritional Additives:
<http://www.efsa.europa.eu/en/efsajournal/doc/2535.pdf>

Regulation on MRL for pesticides in food and feed (Reg. xxx)

JAPAN

Japanese Feed Law

Act on Safety Assurance and Quality Improvement of Feeds

http://www.famic.go.jp/ffis/feed/obj/sianhou_eng.pdf

Safety Evaluation Criteria and Evaluation Procedure for Feeds

http://www.famic.go.jp/ffis/feed/tuti/20_597.html

Japanese List of Feed Additives

http://www.famic.go.jp/ffis/feed/sub3_feedadditives_en.html

Nutritional values for raw materials

<http://www.famic.go.jp/ffis/feed/kokuji/k51n756-2.html>

Administrative Guidelines for Hazardous Substances in Feeds

http://www.famic.go.jp/ffis/feed/r_safety/r_feeds_safety.html

For hazardous substances, allowable residue levels of pesticide

http://www.famic.go.jp/ffis/feed/hourei/sub1_seibunkikaku.html

http://www.famic.go.jp/ffis/feed/r_safety/r_feeds_safety21.html

JAPAN Feed Ordinances

Pet Food Ordinance

http://www.famic.go.jp/ffis/pet/obj/sub1e_sekourei.pdf

http://www.famic.go.jp/ffis/pet/obj/sub1e_kisoku.pdf

Establishment of the Standards for Evaluation of Feed Additives

<http://www.mhlw.go.jp/english/topics/foodsafety/residue/dl/02.pdf>

For feeds using recombinant DNA technologies, the Ministry of Health, Labor and Welfare and the Food Safety Commission of the Cabinet Office of Japan are involved in addition to JMAFF. Detailed procedures are available at:

http://www.famic.go.jp/ffis/feed/r_safety/r_feeds_safety.html

SOUTH AFRICA

Fertilizers, Farm Feeds, Agricultural Remedies and Stock Remedies Act (FFFARSCA) 1947, (Act No. 36 of 1947)

http://www.nda.agric.za/doaDev/sideMenu/ActNo.36_1947/Act%2036%20of%201947.pdf

Animal Diseases Act, 1984 (Act No. 35 of 1984)

<http://www.nda.agric.za/vetweb/Legislation/Animal%20Diseases%20Act%20MAIN.htm>

Genetically Modified Organisms Act, 1997 (Act No.15 of 1997)

<http://www.nda.agric.za/doaDev/sideMenu/APIS/legislationActs.htm>

Animal Product Standards Act, 1990 (Act No. 119 of 1990)

<http://www.nda.agric.za/doaDev/sideMenu/APIS/legislationActs.htm>

Consumer Protection Act, 2008 (Act No. 68 of 2008)

www.info.gov.za/view/DownloadFileAction?id=99961

Farm Feeds Regulations

http://www.nda.agric.za/doaDev/sideMenu/ActNo.36_1947/FF/FarmFeedsRegulations.pdf

Farm Feeds Guidelines

http://www.nda.agric.za/doaDev/sideMenu/ActNo.36_1947/farmFeeds.htm

Application forms for Registration of Farm Feeds

http://www.nda.agric.za/doaDev/sideMenu/ActNo.36_1947/farmFeeds.htm

UNITED STATES:

Federal Food Drug and Cosmetic Act (FFDCA):

<http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCA/default.htm>

Code of Federal Regulations (electronic copy)

<http://ecfr.gpoaccess.gov/>

GRAS Notification Proposed Rule 75 FR 31800; June 4, 2010

<http://edocket.access.gpo.gov/2010/pdf/2010-13464.pdf>

AAFCO A Guide to Submitting New Ingredient Definitions to AAFCO

http://www.aafco.org/Portals/0/AAFCO/idc/definition_request_guidelines_020112.pdf

66 FR 4706, January 18, 2001 Premarket Notice Concerning Bioengineered Foods

<http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/Biotechnology/ucm096149.htm>

State Registration Requirements

http://aafco.org/Portals/0/AAFCO/state_regulatory_requirement_summary_2011-2012.pdf

FDA Policy and Procedures Guide 1240.3605. Regulating Animal Foods with Drug Claims

<http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/PoliciesProceduresManual/UCM046883.pdf>

GFI 3: General Principles for Evaluating the Safety of Compounds Used in Food-Producing Animals

<http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/ucm052180.pdf>

GFI 33: Target Animal Safety Guidelines for New Animal Drugs 1989

(Not available on the Internet: may be requested from the Division of Animal Feeds, Center for Veterinary Medicine, FDA)

CVM GFI #53 Evaluation of the Utility of Food Additives in Diet Fed to Aquatic Animals

<http://www.fda.gov/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/ucm053413.htm>

GFI 80: Studies to Evaluate the Utility of Anti-Salmonella Chemical Food Additives in Feeds

<http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/ucm052407.pdf>

GFI: General Principles For Evaluating The Safety Of Compounds Used In Food-Producing Animals

<http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM052180.pdf>

CPG Sec. 683.100 Action Levels for Aflatoxins in Animal

Feeds <http://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm074703.htm>

CPG Sec. 690.800 Salmonella in Animal Feed

<http://www.regulations.gov/#!documentDetail;D=FDA-2010-D-0378-0002>

GFI and FDA: Advisory Levels for Deoxynivalenol (DON) in Finished Wheat Products for Human Consumption and Grains and Grain By-Products Used for Animal Feed

<http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/ChemicalContaminantsMetalsNaturalToxinsPesticides/ucm120184.htm>

GFI: Fumonisin Levels in Human Foods and Animal Feeds

<http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/ChemicalContaminantsMetalsNaturalToxinsPesticides/ucm109231.htm>

GFI: Complementary and Alternative Medicine Products and their Regulation by the FDA

<http://www.fda.gov/RegulatoryInformation/Guidances/ucm144657.htm>

Memorandum of Understanding AAFCO and FDA

http://www.aafco.org/Portals/0/AAFCO/AAFCO-FDA_MOU_2012.pdf

Extension: <http://www.aafco.org/Portals/0/AAFCO/AAFCO-FDA-MOU2015.pdf>

APPENDIX A

BRAZIL: Regulatory Definitions and Submission Requirements for Authorities' Review of Feed Ingredients/Raw Materials

DEFINITIONS:

Ingredient or raw material

Component or part of any combination or mixture used in animal feed, regardless of its nutritional value, which can be of vegetable, animal, or mineral origin, in addition to other organic or inorganic substances.

Feed additive

Substance, micro-organism or preparation, intentionally added to feed, not normally used as feed ingredient, whether or not it has nutritional value, which affects the characteristics of feed or animal products, enhances productivity of healthy animals, supports nutritional needs or prevents coccidiosis.

AUTHORIZATION OF A NEW FEED INGREDIENT

Requirements for the Inclusion of Raw Materials in the Authorization Program for Animal Feed Products of the Brazilian Agricultural Ministry

The company shall forward to the Department of Livestock Inputs Inspection, through the regional office of its jurisdiction, the request for inclusion of the raw material with the following information:

1. Suggested name for the raw material.
2. Category, with the information if the use will be as an ingredient or additive.
3. Characteristics of the ingredient.
 - i) Origin or source from which the ingredient is obtained.
 - List from which material it originated.
 - ii) How the product is obtained
 - Inform with a flow chart and the detailed description of the process, describing the chemical or physical processing and inform the name of chemical agents and the temperature to which the material was submitted, if this is the case.
 - iii) Physical aspects
 - List the physical state: micronized, powder, liquid, granulated, pelletized, extruded, paste, lyophilized, laminated, block, meal, pressed, whole, etc.
 - iv. Purity of the ingredient/active substances
 - v. Presence of eventual contaminants
4. Animal species: List the animal species to which the raw materials are aimed.
5. Restriction: List if there is any restriction of use for a certain animal species;

6. Classification: If the category is "Additive," list the classification (probiotic, prebiotic, adsorbent, palatabilizer, etc., according to Annex I of IN 13/2004.
7. Use objectives: Justify the use objectives in animal nutrition (e.g. as a protein source, fibers or other nutrients or responsible for a functionality other than nutritional to the animal or food).

Observation: For raw material that will have nutritional and/or functional allegations in finished products (complete feed, food, supplements, etc.) that will contain it, indicate the intended allegations and present scientific evidences of the effect of using the ingredient/nutrient and its relation with the allegation, mentioning the minimum daily ingestion to obtain the desired effect.

8. Safety of the ingredient use: Include scientific evidences that support the safe use of the raw material.
9. Intended levels of guarantee
 - 9.1. The intended levels of guarantee shall be based in report of analysis of at least 3 different fabrication lots. The report of analysis must be signed by the lab technician in charge.
 - 9.2. For ingredients: List at least the following parameters: moisture content (max) (g/kg), protein (min) (g/kg), ether extract (min) (g/kg), gross fiber (max) (g/kg), ash (max) (g/kg), Ca (min and max) (g/kg) and P (min) (g/kg).
 - 9.3. For ingredients of animal origin list also the acidity index (max) in mg of NaOH/g.
 - 9.4. For oils and fats, list the moisture content (max) (g/kg), ether extract (min) (g/kg), iodine index (%), saponification index (%), total fatty acids (min) (%), saturated fatty acids (%), linoleic acid (%) (min), unsaponifiable matter (max) (%), acidity index (mg KOH/g), peroxide index (Meq/kg).
 - 9.5. For raw materials aimed to be used as an additive or to supplement processing, the analytical report as in item 9.1 shall be accompanied of the methodology description for the analysis with the inclusion of the method validation parameters.
10. Additional information
 - 10.1. All other references mentioned in the text shall be annexed to the document.
 - 10.2. All annexed documents shall be written in Portuguese, English or Spanish. The published documents published in other languages shall be accompanied of official translation.

AUTHORIZATION OF A FEED ADDITIVE

Annex I 3.2. Authorization.

Any juristic person, duly registered in the Ministry of Agriculture, Livestock and Supply (MAPA), in order to obtain the authorization of an additive for animal feeding, shall present a request to DFIP (Inspection Department of Feed) with the following information and documents:

- I. Name and address of requester.
- II. Denomination.

III. Identification:

- a) Type of additive according to its main purpose (e.g. antimicrobial, flavoring, preservative), including a proposal to classify it according to its category and functional group, according to item 3.5, and giving its specific data.
- b) Qualitative and quantitative composition (active substance, other components and impurities).
- c) Chemical nature, physical state, physical properties: electrostatics, melting point, temperature of decomposition, density, vapor tension, solubility in water and in organic solvents, mass and absorption spectra and any other relevant physical property.
- d) Formula (including the structure), molecular weight. When considering fermentation products, qualitative and quantitative composition of main elements, including residues from fermentation.
- e) When a mixture of active components, describe separately and each main compound chemically defined and its proportion in the mixture.
- f) Register of the chemical substance or basic component in Pharmacopeia, Chemical Abstracts Service (CAS), Food Chemicals Codex (FCC), or other international references or official and scientific publications.

IV. Manufacturing:

- a) Summarized description of production method.
- b) Description of the use of the additive.

V. Control methods:

- a) Description of the methods applied in qualitative and quantitative analysis for routine control of the additive in the premixtures and other products.
- b) Description of the analytical method to determine the additive residues in tissues of the treated animals and/or products to be given to animals.
- c) Description of methods applied in qualitative and quantitative analysis of additive residues in products of animal origin (when applicable), informing the existent method validation.

Note: When referred methods are officially published, the reference will suffice.

- d) Copy of studies and other material that show that criteria in sub item 3.1.1 have been observed.
- e) Proposal for Maximum Residue Limits to be established for related animal origin food or that the authority indicates that it is not necessary to establish an MRL for consumer protection or this has already been established.
- f) Applicable scientific document that proves that product is innocuous to animal health in the proposed quantities.

VI. Physical-chemical and technological properties:

- a) Stability regarding the atmospheric agent (light, temperature, humidity, oxygen and others).
- b) Stability when preparing premixtures and products in special referring to heat, pressure and humidity; eventual decomposition products.
- c) Stability in regard to validity date, in the original packaging, in the usage conditions and during its conservation.

- d) Physical-chemical interactions (incompatibility with products, other additives or medications).
 - e) Other relevant physical-chemical and technological properties, especially its homogeneity in premixtures and feed, dust properties.
- VII. Biological properties:
- a) For zootechnical additives, indication of effects on the animal performance efficiency and on the quality of animal origin products.
 - b) For the coccidiostatic (indication of prophylactic effects), the proof of prophylactic effects shall be based in scientific publications accepted internationally or by company experimentation.
 - c) Eventual contraindication or precautions, including biological incompatibilities, withdrawal periods and scientific proof and justification.
 - d) For additives that contain or are produced from Genetically Modified Organisms (GMO), presentation of applicable documentation for the evaluation and legal authorization for the use in conformity with the current legislation.
- VIII. Conditions for the utilization:
- a) Intended use in animal feeding (species, types of products, usage and withdrawal period and contraindication, when applicable).
 - b) The proposed conditions for marketing the additive, intended concentrations in the premixtures and in the products and, when necessary, prevention measures for the risks and control measures in the production and utilization.
 - c) Qualitative and quantitative indications of eventual residues in the animal origin products, according to the intended use of additives.
- IX. Other relevant characteristics for the identification of the additive.
- X. Name of technician in charge.

Legal Reference IN 13/2004, item 3.2 (Annex I), item 3 to 7 (Annex III)

APPENDIX B

CANADA: Regulatory Definitions and Submission Requirements for Authorities' Review of a Single-Ingredient Feed

The Canadian feed ingredient evaluation process is specific to livestock, defined as horses, cattle, sheep, goats, swine, foxes, fish, mink, rabbits and poultry. There are no approval requirements for feeds or single-ingredient feed for non-livestock species.

The outlined Canadian requirements (below) cover the requirements for unapproved single-ingredient feeds, as regulated by the Canadian Food Inspections Agency (CFIA) [Feeds Regulations](#). The New Drug Submissions approval requirements are found in Part C, Division 8 of the [Food and Drug Regulations](#).

Feed Definition as per the Feeds Act:

“Feed” means any substance or mixture of substances containing amino acids, anti-oxidants, carbohydrates, condiments, enzymes, fats, minerals, non-protein nitrogen products, proteins or vitamins, or pelletizing, coloring, foaming or flavoring agents and any other substance manufactured, sold or represented for use

- (a) for consumption by livestock,
 - (b) for providing the nutritional requirements of livestock, or
 - (c) for the purpose of preventing or correcting nutritional disorders of livestock,
- or any substance for use in any such substance or mixture of substances.

DEFINITIONS (Feeds Regulations, 1983, Part 2)

Single-ingredient feed

Any substance or mixture of substances that is assessed or evaluated as being acceptable for use in feeds and that is described in an item of Schedule IV or V.

Complete feed

A feed that, when used for the kind of livestock and for the purposes stated on the label, will provide all of the nutritional requirements necessary for the maintenance of life or for promoting production except:

- (a) water, in the case of monogastric animals other than horses, and
- (b) water or roughage, in the case of ruminant animals and horses.

Supplement

A feed that is used with another feed to improve the nutritive balance of the total and that is intended to be:

- (a) fed undiluted as a supplement to other feeds,
- (b) offered free choice with other parts of the ration separately available, or
- (c) further diluted and mixed to produce a complete feed that is acceptable for registration.

Medicating ingredient

(a) A substance that is intended for use in the prevention or treatment of disease in livestock, or

(b) a substance, other than a feed, that is intended to affect the structure or any function of the body of the livestock, and that has assigned to it a drug identification number pursuant to the Food and Drugs Act.

AUTHORIZATION REQUIREMENTS

SAFETY

All feeds must be safe for animals and humans (food safety and worker/bystander safety) and the environment. As per Section 3.(3) of the [Feeds Act](#): No person shall manufacture, sell or import into Canada in contravention of the regulations any feed that may adversely affect animal or human health.

The Canadian approach to the safety assessment is a weight of evidence approach; the specific requirements for a new ingredient may vary depending on the nature of the ingredient.

SAFETY INFORMATION (as necessary)

Scientific investigations concerning, but not limited to, chemical analyses and/or harmful residues and/or toxicological evaluation and/or animal feeding study and/or tissue residue analysis, etc., presented in support must be:

- Carried out by qualified research personnel.
- Carried out using suitable methods.
- Designed to facilitate statistical analysis.
- Analyzed by appropriate statistical methods.
- Conducted under conditions similar to those that may be expected to occur in Canada. ([RG-1](#), Ch. 2.3 and 2.4)

TARGET ANIMAL SAFETY

Mammalian toxicological data and pertinent livestock toxicity data are referenced for both target animal and human safety. Data requirements as listed in RG-1, Ch. 2.3, 2.4, 2.5, 2.6, and/or 2.7 (depending on the nature of the ingredient)

HUMAN FOOD SAFETY

Mammalian toxicological data and pertinent livestock toxicity data are referenced for both target animal and human safety.

RATE AND DEGREE OF ABSORPTION

Distribution, Metabolism and Elimination Data:

- Acute toxicity
- Acute median lethality
- Skin/eye irritation

- Skin sensitization
- Mutagenicity
- Short-term toxicity
- Teratogenicity
- Developmental toxicity
- Reproductive toxicity
- Carcinogenicity
- Epidemiological studies
- Chemical interaction

In particular for food safety, the following studies are required in the event that a residue may be present in the food produced -- i.e., meat, milk, eggs, fish.

- Suggested Maximum Residue Limit (MRL) or Tolerance
- Livestock Metabolic Fate and Residue Studies
- Metabolic Fate and Elimination Studies
- Residue Studies for the Parent Compound and Its Possible Metabolites

Should it be determined that the use for the ingredient may result in residues, CFIA will consult with Health Canada for support of the safety determination. (Data requirements as listed in RG-1, Ch. 2.3, 2.4, 2.5, 2.6, and/or 2.7, depending on the nature of the ingredient.)

WORKER SAFETY

Human Exposure Data and Exposure Estimation

- Major routes of exposure
- Amount of product handled by workers and consumers
- Frequency and duration of exposure
- Exposure concentrations
- Exposure studies

(Data requirements as listed in RG-1, Ch. 2.3, 2.4, 2.5, 2.6, and/or 2.7, depending on the nature of the ingredient)

Material Safety Data Sheet (MSDS) required; labeling requirements when needed

ENVIRONMENTAL SAFETY

Feed may not be introduced that:

- Has or that may have an immediate or long-term harmful effect on the environment.
- Constitutes or that may constitute a danger to the environment on which human or animal life depends.
- Constitutes or that may constitute a danger in Canada to human or animal life or health. (Feed Regs, Sec. 2(2).)

DETERMINATION OF ENVIRONMENTAL FATE AND EFFECTS (studies required)

- Vapor pressure and volatilization
- Hydrolysis

- Photodegradation
- Adsorption-Desorption
- Biotransformation in Soil
- Biotransformation in aquatic systems
- Biochemical oxygen demand
- Toxicity to aquatic organisms
- Toxicity to soil organisms
- Toxicity to birds
- Toxicity to wildlife

(Data requirements as listed in RG-1, Ch. 2.3, 2.4, 2.5, 2.6, and/or 2.7, depending on the nature of the ingredient)

ADDITIVES' EFFECT ON LIVESTOCK PRODUCT EVALUATION

Studies must be conducted to determine if significant changes in the chemical or physical composition of livestock products are produced when the feed is used (Feeds Regs)

Description of Additive:

- Clear identification of the ingredient
- Physicochemical data
- Composition of the ingredient
- Consideration of contaminants

(Data requirements as listed in RG-1, Ch. 2.3, 2.4, 2.5, 2.6, and/or 2.7 and for specific product types, Ch. 3, depending on the nature of the ingredient).

UTILITY/EFFICACY

Data to demonstrate the “conditions and the prevalence of such conditions under which the feed would be efficacious for its intended purposes” (Feeds Regs). Specific requirements depend on the intended purpose of the new ingredient, but typically a minimum of three scientific studies in support of a nutritional purpose carried out by qualified research personnel, using suitable methods, designed to facilitate statistical analysis, analyzed by appropriate statistical methods, and conducted under conditions similar to those that may be expected to occur in Canada. Certificates of analysis and analytical methodology substantiating the guarantee in the ingredient as well as in a mixed feed matrix may be required. (RG-1, Ch. 2.3; for some product types, see Ch. 3.).

MANUFACTURING

A general description of the production and formulation processes, identifying raw materials, chemical reactions, techniques, and any other parameters which may influence the specifications, quality, or safety of a product. A flow-chart diagram accompanying the description is recommended. (See the appropriate RG-1 chapters for more specifics -- depends on ingredient type.)

SPECIFICATIONS

The exact formulation of a particular product may vary, depending upon the manufacturer. A precise description of ingredients, including contaminants, is needed to

properly assess product safety. Examples of acceptable analytical methods for contaminant detection include Nuclear Magnetic Resonance (NMR) spectrums or Gas Chromatography (GC) profiles. (See the appropriate RG-1 chapters for more specifics -- depends on ingredient type.)

ANALYTICAL METHODS

An acceptable test method for the analysis of the product must be provided. (RG-1, Ch. 2.3) Suitable methodology needed for the detection of significant amounts of any ingredient, compound, substance or organism that is intentionally incorporated into the feed or that occurs as a contaminant of the feed.(Feeds Regs)

Certificates of analysis are required in support of the label guarantee using the proposed methodology. Also for safety, may require analytical methods for inherent contaminants or ingredient in final feed (RG-1, Ch. 2.4 and 2.5)

STABILITY

This is the length of time the product can be stored without alterations to its chemical or biological integrity. This includes storage times under ideal conditions, a description of the factors affecting shelf life, what happens when the product degrades or decays, how one can tell if degradation has occurred, whether this creates a particular hazard, and how the manufacturer has substantiated its estimation of shelf life. Shelf life should be determined based upon sensory/quality assessment, nutrient loss profiles, and perishability time. (See the appropriate RG-1 chapters for more specifics -- depends on ingredient type.)

HOMOGENEITY IN FEEDS

Not typically required, but depends on the ingredient (personal communication, CFIA). A More of a concern with low inclusion products and feeds intended to provide nutrition above normal levels (Feed Regs Section 5).

POST-MARKETING PLANS

Not generally required for typical feed ingredients; however, needed for some specialty feeds such as diluted drug premixes (personal communication, CFIA).

SAMPLES TO BE PROVIDED

Typically, requests sample for a new ingredient

WITHDRAWAL PERIODS

The feed ingredient registration may provide restrictions for use based on physiological status or age of animal. Feed Ingredients are not typically assigned withdrawal period. (personal communication/CFIA)

APPENDIX C

CHINA: Regulatory Definitions and Submission Requirements for Authorities' Review for Authorization for a New Feed or Feed Additive

DEFINITIONS:

There is no definition of Feed Ingredient in China, but the concept of the Codex Alimentarius Commission (CAC) definition is acceptable, and it is further classified as feed materials and feed additives in China.

Feed material

Substances that do not belong to feed additives and are used to manufacture feed product, originating from animals, plants, micro-organisms or minerals (see State Council Decree No.609, Feed and Feed Additive Administrative Regulation, Articles 2 and 49).

Within the scope of feed materials, substances that are processed or manufactured industrially are defined as **single feed**. Single feed also falls into the category of feed product, and its production requires a permit.

Feed additive

The micro or trace amount of substances added during the processing, manufacturing and use of feed, including nutritional feed additives and general feed additives (State Council Decree No. 609, article 2).

- **Nutritional feed additive:** The small or trace amount of substances added into feed for nutrition purpose, including feed-grade amino acids, vitamins, trace minerals, enzymes, Non-Protein Nitrogen (NPN), etc. (State Council Decree No.609, article 49)
- **General feed additive:** The small or trace amount of substances added into feed for the purpose of maintaining or improving feed quality, or improving feed efficiency. (State Council Decree No.609, article 49)

APPLICATIONS

Any applicant seeking an authorization for a new feed or feed additive shall submit an application for approval to the Ministry of Agriculture (MOA). Once the application passes the review, MOA shall issue the certificate for new feed or feed additive to the applicant and issue an announcement on MOA website that allows the new feed or new feed additive be used as feed or feed additive.

However, apart from the new-feed and new-feed-additive application, there are several other conditions in which pre-market authorization is needed. In these cases, the government will not issue a new feed and feed additive certificate, only issue an announcement to permit the usage and production:

- To enlarge the application scope of authorized feed additive.
- To make the active substance content lower than the required ones in [Practice for Safely Usage](#) of Feed Additive, except where the feed additives are prepared with carriers or diluents based on a certain proportion.

- To change processing method of authorized additives fundamentally.
- In case an approved new feed or new feed additive is not put into production three years after such new feed or new feed additive certificate is issued, and any other enterprise applies for the production of such new feed or new feed additive. (MOA Decree No. 4, 2012)

The MOA is responsible for the approval of new feeds and new feed additives. The MOA-established National Feed Assessment Committee -- consisting of scientists in different backgrounds such as animal nutrition, toxicology, chemistry, veterinary, etc. -- is responsible for scientific assessment of the application, evaluating the safety, effectiveness and impact on the environment of product. (State Council Decree No. 609 and MOA Decree No. 4, 2012)

REQUIREMENTS

Requirements for application materials for new feed and new additive (see MOA Announcement No. 611) and the procedure of feed administrative license (see MOA Announcement No. 517). The requirements for application materials for new feed and new additive are being revised; the revised version will be released soon.

In addition to the above-mentioned announcements, the MOA has published several technical guidances for the applicants, concerning:

- Stability test of feed additive.
- Efficacy studies in livestock target animal.
- Efficacy studies in aquatic target animal.
- Tolerance studies in livestock target animal.
- Tolerance studies in aquatic target animal.
- Extrapolation of data from major livestock species to minor livestock species regarding the assessment of feed and feed additive.
- Procedures and methods for toxicological assessment of food (GB 15193-2003)

The list of information for a new ingredient to be used in the country includes (based on the revised version not published yet):

- Application form.
- Summary of application materials: a brief summary for each chapter concerning safety, efficacy, quality manageability and impact to environment.
- Name of product and naming basis.
- Purpose of developing the product.
- Product composition and identification report, physical and chemical properties and Material Safety Data Sheet information, composition includes effective components (active substance) and other components.
- Function, scope and method of use, including the animal species, growth stage, the recommended dosage, the usage precautions, and the maximum limit in compound feed or total mixed ration where necessary.
- Production process and manufacturing methods, including process flow chart and correspondent text descriptions, focusing on the key technical parameters

(such as the temperature, pressure and reactive time, pH, etc.), various steps of the raw material equipment and production process et al.

- Stability test report, including influencing factor test, acceleration test and long-term stability test, conducted in accordance with relevant technical guidance as published by MOA.
- Quality standard (specifications) draft and compilation description and inspection report. The quality standard draft should comply with Directives for Standardization, Part 1: Rules for the Structure and Drafting of Standards. (GB/T 1.1). When there is the maximum limit, the analysis method of the active substance in compound feed shall be provided, and the analysis method of the active substance in concentrated feed, supplemental feed or premix shall also be provided according to the scope of the application.
- Evaluation report for efficacy, including feeding study (in vivo) and in vitro studies based on different function of product. The feeding study shall be conducted by the institution designated by MOA and according to relevant technical guidance issued by MOA.
- Evaluation report for safety, including target animal tolerance evaluation, toxicology safety evaluation, metabolism and residue evaluation and strain safety evaluation. Report shall be provided by institutions designated by MOA; study will be done according to technical guidance issued by MOA or national and industrial standard.
 - Target animal tolerance evaluation: All feed additive applicants shall provide a target animal tolerance evaluation report, except a situation in which, based on MOA technical guidance data, extrapolations can be used. Tolerance studies may be combined with efficacy studies.
 - Toxicology safety evaluation, including acute toxicity test, genetics toxicity test, traditional teratogenesis test, 30-day feeding test, sub-chronic toxicity test and chronic toxicity test (including carcinogenesis). Toxicology data published by international authorities (such as Joint FAO/WHO Expert Committee on Food Additives, Organization for Economic Cooperation and Development) or data published by a Good Laboratory Practices laboratory is acceptable.
 - Metabolism and residue evaluation report: Chemical synthesized product shall carry out metabolism and residue evaluation, except the several exemption provisions.
 - Strain-safety evaluation report: for microorganism and its fermentation products, a strain-safety evaluation is needed, except for strains whose safety has been approved and recognized by public.
- Impact on human health analysis report: to evaluate and analyze the impact of the additive on human health based on the results of the efficacy and safety evaluations and the consultation of relevant data, by making reference to the methods of risk assessment.
- Label's format, package requirement, storage conditions, shelf life and attentions.
- Summary of the pilot production, including the time and location of the pilot production, the number of batches (minimum five consecutive batches), etc.

- Report of discharges (gas, liquid and solid discharges) treatment, assessing the impact of production on the environment.
- The joint application agreement should involve both parties in the product development of the research and the development unit or manufacturing enterprises.
- Genetically modified products should provide a copy of genetically modified products approval document issued by the relevant departments.
- Reference Materials

In addition to the above new-feed and new-feed-additive application, the new product holder shall apply for a production license before marketing. The list of information for a new ingredient to be manufactured in the country is as follows:

- Application form: applicant's general information, including but not limited to applicant's name, address, business license; the name of the legal representative, fixed asset, institutional departments and its composition; briefing of the company, including production capacity and equipment, etc.
- Product's general information, including but not limited to product's name and its production capacity, raw materials, equipment list, analysis instrument list.
- Registration form of management and technical staff.
- Organizational chart.
- Contract of institutional chief and specialty workers.
- Certificate of specialty workers.
- Layout of the establishment.
- Processing flow chart and correspondent text descriptions.
- Layout of analysis laboratory.
- Product standard (specifications).
- Analysis method for the active substance.
- Management document of the company.
- Certificate by the environmental authority at local level approving the production.
- Certificate of the microorganism origin.
- New-feed or new-feed additive certificate.

REQUIREMENTS FOR A FOREIGN MANUFACTURER

The additional information is as follows (based on the revised version not published yet):

- Letter of authorization indicating that the foreign manufacturer has authorized the representative agency in China to go through the import registration procedures for the imported product.
- Qualification certificates of the representative agency: a) If the application for import registration is entrusted to its representative office resident in China by a foreign enterprise, the copy of the Registration Certificate of Representative Offices of Foreign Enterprises Resident in China shall be provided; b) If the application is entrusted to other representative agency, the copies of the

Business License of Enterprise Legal Person and the Organization Registration Code Certificate of the representative agency shall be provided.

- Certificate of approval to manufacture in producing country, issued by the official authority of the producing country to permit manufacture of the product pursuant to local laws and regulations.
- Certificate of free sale, issued by the official authority of the producing country, indicating that there are no restrictions to the manufacture, sales and utilization of the imported product in the producing country.
- The documentary evidence certifying that the registered product and its components are permitted to be manufactured and used as feeds or feed additives in the producing country.
- If the product has acquired the import license in other countries, relevant documentary evidence or the copy of the registration license shall be provided as references.

NOTES: The official documentary evidence shall be confirmed by an embassy or consulate of the People's Republic of China in the producing country. In case that the official documentary evidence is not in English, the translations both in Chinese and English issued by the official translating organization of the producing country shall be offered; the original version and the translation version shall be jointly notarized.

APPENDIX D

EUROPEAN UNION: Regulatory Definitions and Submission Requirements for Authorities' Review of a New Feed Additive and Feed Materials

DEFINITIONS

Feed additive

Substances, micro-organisms or preparations, other than feed material and premixtures, which are intentionally added to feed or water in order to perform, in particular, one or more of the functions mentioned in Article 5(3). ([EC No 1831/2003](#))

Categories

- (1) Technological additives
- (2) Sensory additives
- (3) Nutritional additives
- (4) Zootechnical additives
- (5) Coccidiostats and histomonostats
- (6) Feed materials and feed additives consisting, containing or produced from a

GMO

Feed materials

Products of vegetable or animal origin, whose principal purpose is to meet animals' nutritional needs, in their natural state, fresh or preserved, and products derived from the industrial processing thereof, and organic or inorganic substances, whether or not containing feed additives, which are intended for use in oral animal-feeding either directly as such, or after processing, or in the preparation of compound feed, or as carrier of premixtures. ([EC No. 767/2009](#))

Processing aids

Any substance not consumed as a feedingstuff by itself, intentionally used in the processing of feedingstuffs or feed materials to fulfill a technological purpose during treatment or processing which may result in the unintentional but technologically unavoidable presence of residues of the substance or its derivatives in the final product, provided that these residues do not have an adverse effect on animal health, human health or the environment and do not have any technological effects on the finished feed. (EC No 1831/2003)

NEW FEED MATERIALS

The European Union has no system of premarket authorization of feed materials. The distinction between feed materials and feed additives is established on the basis of the various definitions contained in Regulations (1831/2003, 767/2009, 178/2002). The European Commission has also published a recommendation ([2011/25/EU](#)) providing guidelines for the distinction between feed materials, feed additives, biocidal products,

and veterinary medicinal products. (An unofficial advisory [tool](#) developed on this basis is publicly available on the FEFANA website).

The placing on the market of a feed material is covered by the general safety requirements established by the Food Law (178/2002), in particular the requirements of Article 15 (Feed shall not be placed on the market or fed to any food-producing animal if it is unsafe) and Article 17 (Feed business operators shall ensure that feeds satisfy the requirements of food law). The Regulation [767/2009](#) has resulted in the establishment of two lists: the Catalog of Feed Materials and the Register of Feed Materials. As far as the Catalog of Feed Materials is concerned, this is a non-exhaustive inventory of materials, whose main purpose is to be a support for proper labeling. It does not establish that the products it contains have been authorized (no positive list value) or even that the products contained in it are always feed materials. Its use is voluntary, but if an operator decides to use it, it shall use the terminology as provided in the list. In addition, processing aids used in the original manufacture/processing of the feed material may only appear in the feed material in compliance with the specific tolerances set out in the Catalogue of Feed Materials. This has, in effect, rendered the use of the Catalogue compulsory for such materials. This Regulation 767/2009 also provides that new feed materials, which are placed on the market after the entry into force of the regulation, must be included in the register. It might be relatively difficult to determine the novelty of a feed material, since the baseline reference used is the first Catalogue of Feed Material, which was a non-exhaustive list. The register has taken the form of a website where any operator can freely list its product(s).

FEED ADDITIVES

The European Union review for a new feed additive is based on EC Regulation No. [429/2008](#) and requires the use of a form and of a technical dossier.

The submission must be by interested person located in the European Union, independent of where the additive is manufactured domestically or imported. In either case, the requirements of the submission do not differ. The [European Food Safety Authority](#) (EFSA) provides additional not legally binding guidance providing more detailed information on what is required.

The general areas that must be covered in a submission for a new feed additive are the following:

SAFETY

Feed additives shall not have an adverse effect on animal health, human health or the environment (Art. 5, Reg 1831/2003)

Safety is based on studies intended to demonstrate the safety of the use of the additive in relation to:

- (a) The target species at the highest proposed levels of incorporation in the feed or water.

(b) Consumers who ingest food products obtained from animals that have received the additive, its residues or its metabolites.

In this case, safety might be ensured by the setting of Maximum Residue Limits (MRLs) and possible withdrawal periods. MRLs may be based on an Acceptable Daily Intake (ADI).

(c) Persons likely to be exposed to the additive by respiratory, mucosal, eye or cutaneous contact while handling the additive or incorporating it into premixtures or complete feed or water or using feed or water containing the additive concerned.

(d) Animals and humans with respect to the selection and spread of antimicrobial resistance genes.

(e) The environment, as a result of the additive itself or products derived from the additive, either directly and/or as excreted by animals.

Where an additive has multiple components, each one may be separately assessed for consumer safety, then consideration may be given to the cumulative effect (where it can be shown that there are no interactions between the components). Alternatively, the complete mixture shall be assessed.

For micro-organisms, a system called QPS (Qualified Presumption of Safety) is also inducing reduced requirements in the evaluation by the European Food Safety Agency (EFSA), based on body of knowledge available.

TARGET ANIMAL SAFETY

Tolerance tests must be conducted to provide evidence for safety for each of the target species/animal categories for which an application for authorization is made. Tolerance studies provide an evaluation of toxicity of the additive to the target animals and are used to establish a margin of safety, if the additive is consumed at higher doses than recommended. Tolerance studies may be combined with efficacy studies. The main characteristics of the tolerance studies to be carried out (dosages, duration etc.) are established in Regulation 429/2008.

Exemptions are provided for additives, e.g. vitamins which are not accumulating. Possibility of extension to minor species is provided, if tolerance tests are provided for species with the same metabolism and physiology, e.g. minor poultry species (ducks) based on tolerance tests in chickens for fattening, turkeys for fattening and laying hens.

CONSUMER SAFETY/HUMAN FOOD SAFETY

The evaluation process takes into account if the product is also authorized in food, especially to address the human health part of the assessment and not the animal health or the environmental aspects.

Metabolic and residue studies

The establishment of the metabolic fate of the additive in the target species is a determinant step in the identification and quantification of the residues in the edible

tissues or products. Studies must be submitted concerning the absorption, distribution, metabolism and excretion of the substance (and its metabolites).

Metabolic Studies

Metabolic balance following a single-dose administration of the active substance at the doses proposed for use (total amount corresponding to the daily intake) and possibly a multiple dose (if justified) to assess an approximate rate and extent of the absorption, distribution (plasma/blood) and excretion (urine, bile, feces, milk or eggs, expired air, excretion via gills).

Metabolic profiling, identification of the metabolite(s) in excreta and tissues and distribution in tissues and products shall be established following repeated dose administration of the labeled compound to animals to the steady state (metabolic equilibrium) identified by plasma levels.

Residue Studies

Residue Studies are required when residues are not a significant natural constituent of the body or fluids.

- For major species, studies shall simultaneously evaluate the total residues of toxicological significance and identify the marker residue of the active substance in edible tissue (liver, kidney, muscle, skin, skin plus fat) and products (milk, eggs and honey).
- Withdrawal studies are described by animal number in the guidance.
- Metabolic and disposition studies.
- Bioavailability of residues.

Toxicological studies

- (1) Acute toxicity
- (2) Genotoxicity (mutagenicity, clastogenicity)
- (3) Sub-chronic oral toxicity
- (4) Chronic oral toxicity/carcinogenicity
- (5) Reproduction toxicity, including teratogenicity
- (6) Other studies.

A toxicological *No Observed Adverse Effect Level* (NOAEL) must be established.

- Proposal of an Acceptable Daily Intake (ADI) for the active substance. For micronutrients such as minerals and vitamins, it is usually more appropriate to use the concept of ULs (Tolerable Upper Level) rather than ADIs.
- Calculation of consumer exposure.
- Comparison of the ADI or the UL with consumer exposure considering all possible sources of the additive.

Transfer of Resistance to Antimicrobials and Shedding of Enteropathogens

Studies shall be provided to determine the ability of the additive to induce cross-resistance to antibiotics used in human or veterinary medicine, to select resistant bacterial strains under field conditions in target species, to give rise to effects on

opportunistic pathogens present in the digestive tract, to cause shedding or to excrete zoonotic micro-organisms.

ESTABLISHMENT OF WITHDRAWAL PERIODS

Proposal of withdrawal period and Maximum Residue Levels must be provided by the applicant where appropriate.

WORKER SAFETY

Toxicological risk assessment for user/worker safety (inhalation, dermal, mucosal, allergenicity, optic, and toxicity (from consumer safety data).

- Exposure assessment.
- Mitigating measures.

Material Safety Data Sheet (MSDS) required.

Labeling requirements when needed.

Specific labeling requirements for microorganisms that are greater than Biosafety Level 1.

ENVIRONMENTAL SAFETY

To determine if the additive or its metabolites may be excreted and exert an adverse impact on the environment, an approach based in different steps is used. Predicted Environmental Concentration (PEC) may be required to be calculated.

Phase I serves to identify those additives that do not need further testing (natural or physiological substance with no increase in the environment, substance intended for nonfood-producing animals, or when the PEC is very low). For the other situations a second phase (Phase II) assessment is needed to provide additional information, based upon which further studies may be considered necessary.

Phase II is to assess the potential for additives to affect non-target species in the environment, including both aquatic and terrestrial species or to reach groundwater at unacceptable levels. The Phase II assessment is based on a risk quotient approach, where the calculated PEC and Predicted No Effect Concentration (PNEC) values for each compartment shall be compared. A $PEC/PNEC > 1$ requires a full environmental risk assessment.

ADDITIVES' EFFECT ON LIVESTOCK PRODUCT EVALUATION

Meat, milk, egg, honey, quality studies may be required unless adequately justified to be not needed.

Description of Additive

Identity of the Additive

- Name of the additive
- Qualitative and quantitative composition (active substance/agent, other)
- Physical state
- Purity

-- Proposal for classification

Physical and chemical properties shall be given. Dissociation constant, pKa, electrostatic properties, melting point, boiling point, density, vapor pressure, solubility in water and in organic solvents, Kow and Kd/Koc, mass spectrometry and absorption spectra, NMR data, possible isomers and any other appropriate physical properties shall be provided, where appropriate.

Specific requirements for chemical substances; mixtures in which the constituents cannot be described by a single chemical formula; enzyme and enzyme preparations; substance produced via fermentation, micro-organisms are described in (EC) No. 429/2008.

For Genetically Modified Organisms (GMOs), the description of the genetic modifications shall be given. The unique identifier for each GMO, as referred in Commission Regulation (EC) No 65/2004 establishing a system for the development and assignment of unique identifiers for genetically modified organisms, shall be included.

UTILITY/EFFICACY

Based on studies intended to demonstrate the efficacy of an additive in terms of the aims of its intended use (function requested by the applicant) as defined in Article 6 (1) and Annex I of Regulation (EC) No 1831/2003. (EC) No 429/2008. Studies are specific to species and class of animal.

- In vitro studies are usually sufficient for all technological and some sensory additives affecting the characteristics of feed.
- Short-term efficacy studies, e.g. bioavailability studies, digestion/balance studies, or other as justified. Long-term efficacy studies (two different locations). Duration is specified in guidelines (No 1831/2003, Annex IV).
- For zootechnical additives at least two geographical locations are required, and generally long-term studies unless otherwise justified.
- Coccidiostats and histomonostats: specific effects of the additive (e.g. species controlled) and its prophylactic properties (e.g. reduction in morbidity, mortality, oocyst count and lesion score). Information on the effect on growth and feed conversion (fattening birds, replacement layers and rabbits), effects on hatchability (breeding birds) shall be provided, as appropriate. (EC) No 429/2008

MANUFACTURING

To identify the critical points of the process that may have an influence on the safety of the additive, a description of the manufacturing process shall be given.

A listing of all raw materials used in the manufacture of the ingredient as well as the accompanying MSDS is required.

SPECIFICATIONS

Applicant submits a proposal for specification.

Concerns as based on type of substance, these may include:

- For micro-organisms: microbiological contamination, mycotoxins, heavy metals.
- For fermentation products (not containing micro-organisms as active agents): They shall follow the same requirements as for micro-organism products (see above). The extent to which spent growth medium is incorporated into the final product shall also be indicated.
- For plant-derived substances: microbiological and botanical contamination (e.g. castor oil plant, weed seeds, rye ergot in particular), mycotoxins, pesticide contamination, maximum values for solvents and, where appropriate, substances of toxicological concern known to occur in the original plant.
- For animal-derived substances: microbiological contamination, heavy metals and maximum values for solvents, where appropriate.
- For mineral substances: heavy metals, dioxins and PCBs.
- For products produced by chemical synthesis and processes: All chemicals used in the synthetic processes and any intermediate products remaining in the final product shall be identified and their concentrations given. The selection of mycotoxins for analysis shall be made according to the different matrices, where appropriate.

ANALYTICAL METHODS

- Are validated in-house according to international harmonized guidelines. In the case of additives resulting in residues on food of animal origin, the method(s) to be used for the analysis for the official controls of its metabolites in food of animal origin shall be included.
- Validated methods of analysis for the active substance for use in the product, premix and the feed.
- When an MRL is required, a validated methods of analysis for residues of the additive or of its metabolites in food. In the case of coccidiostats and histomonostats which are also authorized as veterinary drugs, the MRLs and the methods of analysis are the same ones reviewed by European Medicines Agency (EMA).
- Validated methods of the analysis relating to the identity and characterization of the additive, when required (EC) No 429/2008. Methods must follow the format of International Organization of Standards (ISO) 78-2.

STABILITY

The stability of each formulation of the additive, on exposure to different environmental conditions (light, temperature, pH, moisture, oxygen and packing material) shall be studied. Expected shelf-life of the additive as marketed should be based on at least two model situations covering the likely range of use conditions (e.g., 25 oC, 60% relative air humidity (HR) and 40 oC, 75% HR).

HOMOGENEITY IN FEEDS

The capacity for homogeneous distribution of the feed additive (other than flavoring compounds) in premixtures, feedingstuffs or water must be demonstrated.

POST-MARKETING PLANS

In the case of substances that are recognized antibiotics and its use shown to select resistant bacterial strains, field studies to monitor for bacterial resistance to the additive have to be undertaken as part of postmarket monitoring.

For coccidiostats and histomonostats, field monitoring of *Eimeria* spp. and *Histomonas meleagridis* resistance have to be undertaken.

Marketing of products consisting of, containing or produced from GMOs also must include a proposal for post-market monitoring.

SAMPLES TO BE PROVIDED

3 samples (EC) No 429/2008. In addition applicant shall maintain reference samples valid for the entire period of the authorization of the feed additive by supplying new reference samples to the Community Reference Laboratory (CRL) to replace those expired.

PROPRIETARY NATURE

All technological, sensory and nutritional additives have nonholder-specific authorizations, unless they are consisting, containing or produced from GMOs (in that latter case, the authorization is holder specific (proprietary)). Note that for additives produced by fermentation, the authorization contains the strain collection culture identification number, which renders the nonholder-specific authorization proprietary.

Authorizations for zootechnical additives, for coccidiostats, and histomonostats are “holder-specific authorizations” (proprietary).

APPROVAL PERIOD

Ten years of authorization, with renewal after the 10 years on the basis of specific application

The outlined European requirements are specific to feed additives as defined in Regulation 1831/2003. These requirements are not required for processing aids and veterinary medicinal products (defined in Directive 2001/82/EC) as they are excluded from the scope of Regulation 1831/2003 on feed additives. Coccidiostats and histomonostats are included in the scope of Regulation (EC) No 1831/2003 on feed additives and have specific requirements under Regulation 429/2008.

APPENDIX E

JAPAN: Regulatory Definitions and Submission Requirements for Authorities' Review of a New Feed or Feed Additive

DEFINITIONS (Law Concerning Safety Assurance and Quality Improvement of Feeds. No. 35, 1953 article 2)

Feeds

Those used to supply nutrients to domestic animals, etc.

Feed additives

Those used in feeds by methods such as addition, mixture and infiltration to prevent deterioration of quality of feeds and to attain other uses specified by ordinance of the Ministry of Agriculture, Forestry and Fisheries, which are designated by the minister of Agriculture, Forestry and Fisheries after consultation with the Agricultural Materials Council.

AUTHORIZATION REQUIREMENTS

Based on the [Law Concerning Safety Assurance and Quality Improvement of Feeds](#), the [Safety Evaluation Criteria and Evaluation Procedure for Feeds](#) (in Japanese only) have been established for feeds and the [Standards for Evaluation of Feed Additives](#) for feed additives.

Prefectures are responsible for making judgments about the safety of feed (including individual feed ingredients that will be used as raw materials in the manufacture of formula feed), but the federal Ministry of Agriculture, Forestry and Fisheries (MAFF) will step in to make a judgment when the prefecture is unable to. The Agricultural Materials Council, which serves as an advisory body to the minister of Agriculture, Forestry and Fisheries, is responsible for judging the safety and effect of feed additives.

However, a company wishing to manufacture or import a new feed additive that is not currently designated as such in Japan would need to consult closely with regulatory authorities in advance (specifically, the Animal Products Safety Division of the Food Safety and Consumer Affairs Bureau at the Ministry of Agriculture, Forestry and Fisheries) and seek instruction from them.

The evaluation standards define individual test methods but do not constitute a guide on how to have a substance designated a feed additive. Concerning feed (including individual feed ingredients that will be used as raw materials in the manufacture of formula feed), there are safety evaluation standards for feed that define how safety is evaluated and the test methods and other procedures used to do so. Here, too, it is necessary to seek guidance from the prefectural government or MAFF in order to determine which documentation listed in the standard should be submitted. As with the

evaluation standards, the available information does not constitute a guide. [This information](#) is available on the website of the Food and Agricultural Materials Inspection Center (FAMIC), although only in Japanese.

COMPANION ANIMAL FEED VS. LIVESTOCK FEED

Because livestock animals given livestock feed are consumed by humans, the safety of livestock feed must be assured not only for the livestock eating the feed, but also as food products for human consumption. Consequently, feed (including individual feed ingredients that will be used as raw materials in the manufacture of formula feed) and feed additives used for livestock are subject to strict regulation.

However, pet food is less strictly regulated than livestock feed because only the safety of pets eating the food needs be considered, as reflected in the Act on Ensuring of Safety of Pet Animals Feed. This law was enacted following several incidents of pet food contamination with melamine. The Act does not distinguish between feed and feed additives, and a ministerial ordinance only sets forth upper limits for substances such as agricultural chemicals, mycotoxins, and heavy metals in pet food (final products). Under the Act, feed additives can be used in pet food. In fact, food additives, feed additives, and other substances whose safety has been verified are likely used in this way. Because large amounts of pet foods are imported into Japan in the form of the final product, additives that are used in the EU and U.S. can also be used in pet food manufactured in Japan.

EVALUATION OF NEW FEED ADDITIVES (not previously authorized feed additive)

Summary of required information for establishment of new Feed additives is provided in the MAFF documents [Establishment of the Standards for Evaluation of Feed Additives](#). A summary of the required information includes:

REQUIREMENTS ON EFFICACY

- Feed additives shall be effective for the purposes specified in Article 1 of the Regulations for Enforcement of the Law Concerning the Safety Assurance and Quality Improvement of Feed (Ministry of Agriculture and Forestry Ordinance No. 36 of 1976, hereinafter called “the Regulations for Enforcement”).
- The efficacy of antibacterial substances as feed additives shall not be intended for purposes other than the following:
 - Prevention of deterioration of feed quality due to growth of fungi and other causes.
 - Promotion of livestock growth (animals as specified in Article 1 of the Enforcement Ordinance for the Law Concerning the Safety Assurance and Quality Improvement of Feed [Government Ordinance No. 198 of 1976, hereinafter called “the Enforcement Ordinance”] and so on) (in principle, restricted to young livestock) and improvement of feed efficiency.
 - Prevention of reduction of productivity of young livestock due to specific pathogenic parasites.

- The effectiveness of the new feed additives intended for purposes similar to those previously designated shall be at least equivalent to that of the previously designated ones.

REQUIREMENTS ON RESIDUES

Antibiotics intended as feed additives shall not be detectable in products of livestock fed a diet containing such substances by adequately sensitive methods of quantitative analysis.

REQUIREMENTS ON SAFETY

- Feed additives shall not produce harmful animal products (meat, milk and other edible products of livestock that may be harmful to human health) as a result of using feed containing these additives or hinder the production of animal products (products of livestock) by harming the livestock.
- Safety of new feed additives that have similar structures and mode of actions, etc., to those previously designated, shall be at least equivalent to that of the previously designated ones.
- Feed additives shall have an adequate safety margin for use in livestock.
- Feed additives shall not, in principle, be poisonous or dangerous drugs based on the Pharmaceutical Affairs Law (Law No. 145 of 1960) or poisonous or deleterious substances designated under the Poisonous and Deleterious Substances Control Law (Law No. 303 of 1950).
- Veterinary medical care shall not be negatively influenced by the use of feed containing additives.

OTHER REQUIREMENTS

- Feed additives shall, in principle, be available for quantitative analysis by physical, chemical, or biological means from feed containing such additives.
- Addition of feed additives shall not lower the quality of the feed or the effectiveness of the feed additives.

The cited MAFF document provides very specific information on when data requirements are waived and the experimental design of the required studies.

The Feed Additive Application outlines the following items and provides specific tables for the summary and analysis of the required data:

- Details of origin or discovery and status of approval, usage, etc. in foreign countries
- Specifications
 - Name
 - Chemical structure
 - Manufacturing process
 - Biological and physicochemical properties
 - Properties
 - Identification test

- Purity test
 - Content and assay procedure
- Method of quantitative analysis in feed
- Change with time
- Efficacy
 - Basic studies proving effectiveness
 - Field trial studies proving effectiveness
- Residue
 - Residue studies using target animals
- Safety
 - Toxicity test
 - General toxicity test
 - Single-dose toxicity
 - Repeated-dose toxicity (short-term)
 - Repeated-dose toxicity (long-term)
 - Special toxicity test
 - Multi-generation reproduction
 - Teratogenicity
 - Carcinogenicity
 - Mutagenicity
 - Other toxicity test (local toxicity, inhalation toxicity)
 - Pharmacology
 - Metabolism
 - Feeding studies using target animals
 - Studies regarding development of resistant bacteria
 - Other Studies
 - Studies on environmental impact (plant toxicity, fish toxicity, and environmental pollution)
 - Others
 - Samples are required in some cases

The MAFF documents also provide specific data requirements for probiotics (direct fed microbials), which require additional bacteriological properties as well efficacy tests with feed containing antibacterial feed additives.

APPENDIX F

SOUTH AFRICA: Regulatory Definitions and Submission Requirements for Authorities' Review

DEFINITIONS:

Farm feed

(A) (1) Any substance obtained by a process of crushing, gristing or grinding, or by the addition to any substance or the removal therefrom of any ingredient; or

(2) any condimental food, vitamin or mineral substance or other substance which possesses or is alleged to possess nutritive properties; or

(3) any bone product, intended or sold for the feeding of domestic animals or livestock; or

(B) any stock lick or substance which can be and is used as a stock lick, whether or not such stock lick or substance possesses medicinal properties, but does not include straw, chaff, unground hay, silage, any cereal in the grain or any substance which would otherwise be a farm feed but has been ground, crushed, gristed or prepared for any person, in accordance with his directions for his own use, unless the minister has by notice in the *Gazette* declared such substance a farm feed for the purposes of this act.

Feedstuff

A product of vegetable or animal origin, in its natural state, fresh or preserved; a product derived from the industrial processing thereof; and an organic or inorganic substance, whether or not used as a carrier in a mixture. Feedstuff has the same meaning as raw material, feed ingredient or any words of similar connotation.
(Farm Feeds Regulations)

Registration requirements are published in the [Farm Feeds Regulations](#) and the [Farm Feeds Guidelines](#) and the [application forms for registration](#) are published on the website of the [Department of Agriculture, Forestry and Fisheries](#) (DAFF).

The application requires:

- Two copies, at least one copy in English with or without another official language, of a typed version of the details relating to the particular farm feed that will be marked on the immediate container in which it will be sold, or will be attached to the label of such immediate container, or an example of an actual label that will be used for that product.
- A certificate of product analyses, which was obtained in the current year of application for registration.
- When required by the registrar, two samples each containing at least 100 ml, in case of a liquid, or 100g in case of dry product.
- When required by the registrar, a risk assessment satisfying that the animal feed has no adverse effect on animal health, human health or environment.

- In case of an additive, also submit a description of the method of production, manufacturing and intended uses, method of analyses of the additive or premix in feed according to its intended use and, where appropriate, method of analyses for the determination of residue levels of the additive or its metabolite in food.
- In the case of an animal feed being manufactured in facilities that are being used for the first time for the purpose of manufacturing by the animal feed applicant, the application to register the product should only be made after there has been a full inspection of the facilities by the registrar and the registrar is satisfied that the facilities are suitable and adequate for the manufacture of the animal feed concerned and fully meet the requirements for establishments set out elsewhere in the Farm Feeds Regulations. Where the facility has previously produced animal feed and is being taken over by a new company or is no longer operated by the same legal entity that previously operated it, it shall be re-inspected before continuing operations.

APPLICATION REQUIREMENTS FOR FEED ADDITIVES

Part 1: Application Overview

- Product rational
- Active substance/substances

Part 2: Chemistry and Manufacture

- Identity of Additive
 - Proposed propriety name(s)
 - Type of additive according to its main function
 - Qualitative and quantitative composition (active substance, other components, impurities)
 - Physical state, particle size
 - Manufacturing process, including any specific processing process
- Specifications Concerning Active Substance
 - Name according to main active as described by IUB/IUPAC, EINECS and CAS Number
 - The biological origin, the activities toward relevant chemically pure model substrates and other physicochemical characteristics
 - Purity (checking the level of contaminating microorganisms, heavy metals, absence of toxins relevant to the source organism as shown by suitable method, absence of antibiotic activity at feed concentration level as determined by a suitable method, and composition of the non-active components (i.e. Total Organic Solids)
 - Optimal pH, purification process and media used
- Physiochemical, Technological and Biological Properties if the Additive
 - Stability on exposure to environmental conditions such as light, temperature, pH, moisture, and oxygen. Expiry date
 - Stability during the preparation of premixtures and feedingstuff, in particular stability to heat, pressure and moisture. Possible decomposition product

- Stability during the storage of premixtures under defined conditions (Storage time under defined condition). Shelf life
- Other appropriate physicochemical, technological or biological properties such as stability to obtain homogenous mixtures in premixtures and feedingstuffs, dust-forming properties, assessment of resistance to degradation or loss of biological activity in the digestive tract or by system of stimulation in vitro
- Physicochemical or biological incompatibilities or interactions (e.g. with feedingstuffs, other approved additives or medicinal products)
- Control Methods
 - Description of the methods used for the determination of the criteria required for:
 - Qualitative and quantitative composition
 - Purity
 - Optimum pH and purification process
 - Stability testing for feed additive (expiry date)
 - Stability testing during the preparation of premixtures and feedingstuffs;
 - Stability for storage of premixtures (shelf-life); and
 - Properties to ascertain physicochemical, technological, or biological properties to determine mixability, dust-formation assessment of resistance to degradation, or loss of biological activity in any in vivo or in vitro tests.
 - Description of the qualitative and quantitative analytical methods for routine control of the additive in premixtures and feedingstuffs

Part 3: Toxicology

- Studies on laboratory animals (when the active substance is a non-photogenic micro-organism found naturally these types of studies may not be necessary)
- Acute toxicity
 - Acute inhalation toxicity
 - Skin and eye irritancy
- Mutagenicity
 - Ames/Salmonella test
 - Chromosomal aberration test
- Pharmacokinetics aspects
- Subchronic toxicity
- Chronic toxicity/carcinogenicity
- Reproductive toxicity

Part 4: Metabolism and Toxicokinetics

Part 5: Residues

Part 6: Regulatory Status in Other Countries

Part 7: Occupational Health and Safety

Part 8: Environmental Studies

Part 9: Efficacy and Safety

- Studies Concerning the Efficacy of the Additive
 - Broiler trials
 - Layer hen trials
 - Turkey trials
 - Piglet trials
 - Fattening pig trials
 - Sow trials
 - Ruminant trials
 - Other relevant trials
- Studies Concerning the Safety of the Target Animal
 - Chicken for fattening
 - Laying hens
 - Turkey for fattening
 - Piglets
 - Sows
 - Ruminant trials
 - Other relevant trials

Part 10: Other Trade Aspects

- Studies concerning the quality of the animal produce

APPENDIX G

UNITED STATES: Regulatory Definitions and Submission Requirements for Authorities' Review for a Food Additive Petition, Association of American Feed Control Officials (AAFCO) Ingredient Definition, and Generally Recognized As Safe (GRAS) Notification

DEFINITIONS

Food

(1) Articles used for food or drink for man or other animals; (2) chewing gum; (3) articles used for components of any such article. (*Federal Food, Drug, and Cosmetic Act*[FFDCA] 201(f))

Food Additive

Any substance, the intended use of which results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food (including any substance intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food; and including any source of radiation intended for any such use), if such substance is not generally recognized, among experts qualified by scientific training and experience to evaluate its safety, as having been adequately shown through scientific procedures (or, in the case of a substance used in food prior to January 1, 1958, through either scientific procedures or experience based on common use in food) to be safe under the conditions of its intended use; except that such term does not include:

- (1) a pesticide chemical residue in or on a raw agricultural commodity or processed food.
 - (2) a pesticide chemical.
 - (3) a color additive.
 - (4) any substance used in accordance with a sanction or approval granted prior to September 6, 1958, pursuant to this chapter, the Poultry Products Inspection Act [21 U.S.C. 451 et seq.] or the Meat Inspection Act of March 4, 1907, as amended and extended [21 U.S.C. 601 et seq.].
 - (5) a new animal drug.
 - (6) an ingredient described in paragraph (ff) in, or intended for use in, a dietary supplement.
- (FFDCA, 201 (s))

Animal feed

An article which is intended for use for food for animals other than man and which is intended for use as a substantial source of nutrients in the diet of the animal, and is not limited to a mixture intended to be the sole ration of the animal. (FFDCA, 201(w))

General Recognized as Safe

A substance not generally recognized, among experts qualified by scientific training and experience to evaluate its safety, as having been adequately shown through scientific procedures (or, in the case of a substance used in food prior to January 1, 1958, through either scientific procedures or experience based on common use in food) to be safe under the conditions of its intended use. (Paraphrased FFDCA, 201(s)).

AUTHORIZATIONS FOR NEW FEED INGREDIENTS

There are three potential methods to seek authorization for a new feed ingredient. The regulatory path is determined by what data are available to demonstrate the safety and utility (intended use) of the product, and the perceived safety of the ingredient, and sometimes preference by the submitter. Only the food additive and GRAS notification process are recognized as legal ingredients by the FDA under U.S. law. Successful completion of the food additive petition process results in a codified food additive regulation (21 CFR 573); and use is not revocable except through notice and comment rule-making. GRAS notification process is based on published data. Successful completion of a GRAS notification procedure for an intended use of a feed ingredient results in the listing of the ingredient and GRAS notice on the FDA webpage. The AAFCO feed ingredient process results in a definition in the AAFCO OP, however, it represents a use of enforcement discretion by FDA (not a formal approval). FDA coordinates the AAFCO definition process with AAFCO when no safety concerns are identified with the ingredient.

The table below provides a description and comparison of the requirements for each approach.

SAFETY

Food Additive Petition	AAFCO Definition Support	GRAS Notification
Safe or safety means that there is a reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use. It is impossible in the present state of scientific knowledge to establish with complete certainty the absolute harmlessness of the use of any substance. Safety may be determined by scientific procedures or by general	Safe or safety means that there is a reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use. It is impossible in the present state of scientific knowledge to establish with complete certainty the absolute harmlessness of the use of any substance. Safety may be determined	Safe or safety means that there is a reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use. It is impossible in the present state of scientific knowledge to establish with complete certainty the absolute harmlessness of the use of any substance. Safety

<p>recognition of safety. In determining safety, the following factors shall be considered:</p> <p>(1) The probable consumption of the substance and of any substance formed in or on food because of its use.</p> <p>(2) The cumulative effect of the substance in the diet, taking into account any chemically or pharmacologically related substance or substances in such diet.</p> <p>(3) Safety factors which, in the opinion of experts qualified by scientific training and experience to evaluate the safety of food and food ingredients, are generally recognized as appropriate.</p> <p>(Title 21, Code of Federal Regulations (CFR) Part 570.3(i))</p>	<p>by scientific procedures or by general recognition of safety.</p>	<p>may be determined by general recognition of safety. (FDA interprets this as information from the published literature).</p>
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TARGET ANIMAL SAFETY

Food Additive Petition	AAFCO Definition Support	GRAS Notification
<p>When currently available data are not persuasive to the determination of target animal safety, FDA will require a safety study conducted under Good Laboratory Practices (GLPs) (or equivalent Organization for Economic Cooperation and Development [OECD] guidance) that meets the guidance such as a 0, 1X, 3X, and 5X dose study where toxicology-endpoints are assessed. (CVM Guidance For Industry [GFI] 33(1998), 21 CFR 571.1)</p>	<p>Often safety of AAFCO defined ingredients is based on general recognition of safety, which is described in white papers developing the safety assessment. However, for some ingredients, FDA has required studies to demonstrate Target Animal Safety (TAS) (see food additive requirements)</p>	<p>For GRAS notified substances, the safety determination must be based on published data. There must also be a basis to establish general recognition, such as the use of GRAS panels. . FDA requests that any published data be from peer-reviewed journal and published at least 6 months prior to submission to support the notification. The determination of safety must be described in detail and explain how the published studies</p>

Companion Animal Safety requires reproduction and growth studies in the target species at multiple levels of exposure.		demonstrate the use of the substance is GRAS.
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HUMAN FOOD SAFETY

Food Additive Petition	AAFCO Definition Support	GRAS Notification
<p>Human food safety is required to be addressed for all substances intended for use in food-producing animals. If an understanding of safety based on currently available data are not sufficient a series of toxicological, metabolic and residue studies may be requested (this is typical for animal drugs). In addition FDA will request consideration of antimicrobial resistance issues in the feed and the gastro-intestinal tract (for known antimicrobials). No human food safety assessment is needed for products restricted to non-food animals.</p> <p>Studies that may be required include: Metabolism Studies In Target Animals Total Residue Depletion Study Metabolism Studies In Laboratory Animals</p>	<p>To be considered for the AAFCO ingredient process, significant safety concerns cannot exist. Therefore, in most cases human food safety is based on a white paper developing the safety assessment and demonstrating that no formal assessment is required.</p> <p>No human food safety assessment is needed for products restricted to non-food animals.</p>	<p>Human food safety is required to be addressed for all substances intended for use in food-producing animals. If an understanding of safety based on currently available data is not sufficient a series of toxicological, metabolic and residue studies may be required. (See the food additive section of the table for a description of the studies that may be required). These studies must be published in peer-reviewed journals for adequate support. Alternatively support can be from a review article that evaluates the required safety studies.</p> <p>No human food safety assessment is needed for products restricted to non-food animals.</p>

WORKER SAFETY

Food Additive Petition	AAFCO Definition Support	GRAS Notification
If warranted, FDA may	This issue is not typically	This issue is not typically

require information on the label regarding worker safety issues, as specified in Material Safety Data Sheet (MSDS), in support of food additives. Generally data is required only in new animal drug applications.	addressed in an AAFCO Definition request.	addressed in a GRAS notification.
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ENVIRONMENTAL SAFETY

Food Additive Petition	AAFCO Definition Support	GRAS Notification
Either the requirement for a full environmental assessment can be waived under specific categorical exclusions (21 CFR 25.30, 25.32, or 25.33) or if no exclusion, an Environmental Assessment (EA) must be provided in the submission that covers the use and disposal of the ingredient. The EA is a public document for which FDA requests public input. FDA must issue in response to the filing of either a Finding Of No Significant Impact (FONSI) or an Environmental Impact Statement. (21 CFR 25.40, 25.41, and 25.42).	A statement of environmental safety is required.	Environmental Safety Assessment is not required to support a GRAS notification.

DESCRIPTION OF ADDITIVE

Food Additive Petition	AAFCO Definition Support	GRAS Notification
<p>IDENTITY OF THE ADDITIVE:</p> <ul style="list-style-type: none"> -- Chemical identity -- Composition of the food additive, its physical, chemical, and biological properties, and specifications prescribing the minimum content of the desired component(s) and 	<p>Description of the Ingredient:</p> <ul style="list-style-type: none"> -- Chemical identity -- Proposed AAFCO Definition -- Composition of the ingredient, its physical, chemical, and biological properties, and specifications prescribing 	<p>Description of the Ingredient:</p> <ul style="list-style-type: none"> -- Chemical identity -- Composition of the ingredient, its physical, chemical, and biological properties, and specifications prescribing the minimum content of the desired component(s) and

identifying and limiting the reaction byproducts and other impurities. (21 CFR 571	the minimum content of the desired component(s) and identifying and limiting the reaction byproducts and other impurities	identifying and limiting the reaction byproducts and other impurities
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UTILITY/EFFICACY

Food Additive Petition	AAFCO Definition Support	GRAS Notification
<p>Sufficient data to establish that the food additive will have the intended physical or other technical effect or that it may reasonably be expected to become a component, or to affect the characteristics, directly or indirectly, of food and the amount necessary to accomplish this. These data should include information in sufficient detail to permit evaluation with control data. (21 CFR 571.1)</p> <p>To address this requirement, FDA requires sufficient well-designed and carried out scientific studies to support that the additive can be expected to serve its intended use under various feed and animal systems in the US, and studies must cover all the requested animal species, and if “all animals” must cover the major species. Specific studies may be required to cover aquaculture or companion animals. Historically FDA has requested three studies in separate geographical locations, but that requirement is being phased out.</p>	<p>Sufficient data to establish that the ingredient will have the intended physical or other technical effect or that it may reasonably be expected to become a component, or to affect the characteristics, directly or indirectly, of food and the amount necessary to accomplish this. Depending on the ingredient, the data is similar to that required for a food additive.</p>	<p>Sufficient data to establish that the GRAS substance will have the intended physical or other technical effect or that it may reasonably be expected to become a component, or to affect the characteristics, directly or indirectly, of food and the amount necessary to accomplish this. Depending on the ingredient, the data are similar to that required for a food additive. FDA/CVM requires that this data be published in peer-review journals for support. FDA has stated it is reconsidering the requirement for published data to support a GRAS notification.</p>

MANUFACTURING

Food Additive Petition	AAFCO Definition Support	GRAS Notification
The petition shall supply a list of all substances used in the synthesis, extraction, or other method of preparation, regardless of whether they undergo chemical change in the process. Each substance should be identified by its common English name and complete chemical name, using structural formulas when necessary for specific identification. If any proprietary preparation is used as a component, the proprietary name should be followed by a complete quantitative statement of composition. Reasonable alternatives for any listed substance may be specified. (21 CFR 571.1) In addition FDA requires a full understanding of each control point in the manufacture and specifications for all ingredients (AAFCO PPT, Manufacturing Chemistry).	The request will supply a list of all substances used in the synthesis, extraction, or other method of preparation, regardless of whether they undergo chemical change in the process. Each substance should be identified by its common English name and complete chemical name, using structural formulas when necessary for specific identification. If any proprietary preparation is used as a component, the proprietary name should be followed by a complete quantitative statement of composition. Reasonable alternatives for any listed substance may be specified. (21 CFR 571.1) In addition FDA requires a full understanding of each control point in the manufacture and specifications for all ingredients (AAFCO PPT, Manufacturing chemistry).	The notification must provide enough information on the manufacturing that an adequate safety assessment can be made. It should include a general description of the manufacturing process generally based on published information. FDA generally wants all raw materials identified and specifications for these. Final specifications for the GRAS substance.

SPECIFICATIONS

Food Additive Petition	AAFCO Definition Support	GRAS Notification
Based on compositional testing and what is known regarding the additive. Generally based on 3-5 production batches.	Based on compositional testing and what is known regarding the ingredient. Generally based on 3-5 production batches.	Based on compositional testing and what is known regarding the additive.

ANALYTICAL METHODS

Food Additive Petition	AAFCO Definition Support	GRAS Notification
-- Validated method of analysis for the ingredient	Validated method of analysis for the substance	Validated method of analysis for the substance

-- Validated methods of analysis for determination of substance in the complete feed -- Validated methods of analysis for residues in milk, meat or eggs required only for assessment of residue potential.	-- Validated methods of analysis for determination of substance in the complete feed -- Validated methods of analysis for residues in milk, meat or eggs required only for assessment of residue potential.	-- Validated methods of analysis for determination of substance in the complete feed -- Validated methods of analysis for residues in milk, meat or eggs required only for assessment of residue potential.
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STABILITY

Food Additive Petition	AAFCO Definition Support	GRAS Notification
-- Stability of the additive in the intended marketed container -- Stability of the additive once mixed into feed (AAFCO PowerPoint Presentations (AAFCO PPT), Manufacturing Chemistry)	-- Stability of the additive in the intended marketed container -- Stability of the additive once mixed into feed (AAFCO PPT, Manufacturing Chemistry)	-- Stability of the additive in the intended marketed container -- Stability of the additive once mixed into feed (AAFCO PPT, Manufacturing Chemistry)

HOMOGENEITY IN FEEDS

Food Additive Petition	AAFCO Definition Support	GRAS Notification
Required testing batches of feed to demonstrate the mixability of the additive in feed(AAFCO, PPT-Manufacturing Chemistry; 21 CFR 514.1 (b)(5))	Required testing batches of feed to demonstrate the mixability of the additive in feed(AAFCO, PPT-Manufacturing Chemistry; 21 CFR 514.1 (b)(5))	Required testing batches of feed to demonstrate the mixability of the additive in feed. FDA has indicated that this data must be from published sources.

POST-MARKETING PLANS

Food Additive Petition	AAFCO Definition Support	GRAS Notification
None are required for food additives, required for approved animal drugs (21 CFR 514.80)	None	None

WITHDRAWAL PERIODS

Food Additive Petition	AAFCO Definition Support	GRAS Notification
The food additives may require restrictions for use based on physiological status or age of animal, do not generally provide a	No withdrawal periods may be provided for an AAFCO defined ingredient. However restrictions on physiological status or age	GRAS substances would not typically have a withdrawal period. However restrictions on physiological status or age of animal may

withdrawal period. Withdrawal periods are used for pharmaceutical products, approved under a New Animal Drug Application, as listed in 21 CFR 558	of animal may be provided within the definition.	be provided within the notification.
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PROPRIETARY

Food Additive Petition	AAFCO Definition Support	GRAS Notification
All food additives are non-proprietary.	All products covered under AAFCO ingredient definitions are non-proprietary.	GRAS Notifications are specific to the notifier. However, others may rely on the information within the GRAS notification to form their own GRAS determination (and voluntary notification).

APPROVAL MECHANISMS

Food Additive Petition	AAFCO Definition Support	GRAS Notification
Letter sent to the petitioner and codified in Title 21 of the Code of Federal Regulations, part 573	Publication as Defined Feed Ingredient in the Official Publication of the American Association of Feed Control Officials	Letter sent to notifier and placed on the CVM/FDA GRAS website

APPROVAL PERIOD

Food Additive Petition	AAFCO Definition Support	GRAS Notification
Until the regulation/non-objection is found to be invalid or unsafe and FDA removes it.	Should FDA or the states object to the definition as it is found to be invalid or unsafe , it can be removed by the AAFCO Board of Directors by vote.	Should FDA subsequent to not objecting to the notification determine that substance unsafe and find the notification not substantiated, such a letter would be placed on the FDA GRAS website.

The outlined Food Additive Petition (FAP), US requirements cover the general requirements for substances that must be approved for use through a which are similar and breadth for a New Animal Drug Application (NADA). FDA relies on a number of the animal drug guidance for the safety evaluation of feed ingredients. FDA also has an MOU with AAFCO in which FDA must issue a letter of concurrence regarding the suitability of the feed ingredient for its proposed use from FDA prior to adopting new feed ingredient definitions or amending existing ones. The FDA provides this scientific

review through an informal procedure. This procedure is only used when there are no significant safety concerns for the product; as such the safety submission does not always conform to what is provided in the table above; also FDA does not generally require a full battery of utility studies to support these definitions (AAFCO PPT: Feed Ingredient Utility). Also is the newly adopted voluntary GRAS notifications that are based on published literature, these outlined requirements will not be strictly followed (75 FR 31800). Plant-based material for genetically altered plants has its own specific process not described in this table (May 29, 1992 FR). Color additives for animal feed use are evaluated by the Center for Food Safety and Applied Nutrition, under the regulations 21 CFR 73, and submission requirements do not follow the outline provided above.