ANNEX III

SPECIFIC REQUIREMENTS TO BE SATISFIED BY THE DOSSIER PROVIDED FOR IN ARTICLE 3 WITH RESPECT TO CERTAIN CATEGORIES OF ADDITIVES OR CERTAIN PART ICULAR SITUATIONS, AS PROVIDED FOR IN ARTICLE 7(5) OF REGULATION (EC) No 1831/2003

Regulation (EC) No 1831/2003 foresees additional assistance for the preparation of dossiers, where necessary, for each category of additives or for other particular aims according to Article 7(5) of Regulation (EC) No 1831/2003.
List of the specific requirements for establishing dossiers for:

(1) Technological additives

(2) Sensory additives

(3) Nutritional additives

(4) Zootechnical additives

(5) Coccidiostats and histomonostats

(6) Extrapolation from major to minor species

(7) Pets and other non food-producing animals

(8) Additives already authorised for use in food

(9) Modification of authorisations

(10) Renewal of authorisations

(11) Re-evaluation of certain additives already authorised under Directive 70/524/EEC.

Any applications may be submitted following more than one of the specific requirements listed above.
General conditions

Reasons shall be given for the omission from the dossier of any data prescribed in these sections.

1. TECHNOLOGICAL ADDITIVES

1.1. Section I: summary of the dossier

The whole of the Section I of Annex II applies.

1.2. Section II: identity, characterisation and conditions of use of the additive; methods of analysis

The Section II of Annex II applies as following:
— for additives not subject to a specific holder of the authorisation the paragraphs 2.1.2, 2.1.3, 2.1.4, 2.1.4.2, 2.2, 2.3.1, 2.3.2, 2.4.1, 2.4.2, 2.4.4, 2.5, 2.6 apply;
— for other additives subject to a specific holder of the authorisation, the whole of Section II applies.

1.3. Section III: studies concerning the safety of the additive

Subsections 3.1, 3.2 and 3.4 of Annex II do not apply to silage additives where it can be demonstrated that:

— no detectable amounts of the active substance(s) or relevant metabolites or the active agent(s) survive in the final feed; or
— the active substance(s) and agent(s) occur as normal constituents of silage and use of the additive does not substantially increase their concentration compared to silage prepared without use of the additive (i.e. where there is no substantial change in exposure).

In the other cases the whole of Section 3 of Annex II applies.

1.3.1. Studies concerning the safety of use of the additive to the target animals

For xenobiotic[1] substances: the full subsection 3.1 of Annex II applies.

1.3.1.1. Tolerance studies for the target species

For silage additives:
— the product shall be added to a basal diet and results compared to a negative control with the same diet. The basal diet may contain a single source of silage prepared without the use of an additive.
— the dose selected for the tolerance studies shall be a multiple of the concentration present in the ensiled material at the time of normal use where this can be conclusively established. Particular consideration shall be given to product containing viable micro-organisms and their capacity for survival and multiplication during ensiling.

Tolerance studies can usually be limited to a ruminant species, normally the dairy cows. Studies involving other species are required only when the nature of the ensiled material makes it more appropriate for use with non-ruminants.

Other substances:

for the other substances requesting authorisation as technological additives not already authorised for feed use the absence of harm to animals at the highest proposed level shall be demonstrated. This demonstration may be limited to one experiment in one of the most sensitive target species or in one laboratory animal species.

1.3.1.2. Microbial studies

The whole of subsection 3.1.2 of Annex II applies.

1.3.2. Studies concerning the safety of use of the additive for consumers

1.3.2.1. Metabolic and residue studies

Metabolic and residue studies are not required if:

(1) the substance or its metabolites are not present in the feedingstuff at time of feeding; or

(2) the substance excreted unchanged, or its metabolites can be demonstrated to be essentially not absorbed; or

(3) the substance is absorbed in the form of physiological compounds; or

(4) the active component(s) of the additive consists only of micro-organisms or enzymes).

Metabolic studies also are not required if the substance is naturally present in significant amounts in food or feedingstuffs or the substance is a normal constituent of body fluids or tissues. However, in these cases, there is a requirement for residue studies which can be

limited to the comparison of the tissues/products levels in an untreated group and in the group supplemented with the highest recommended dose.

1.3.2.2. Toxicological studies

Toxicological studies are not required if:

(1) the substance or its metabolites are not present in the feedingstuff at time of feeding; or

(2) the substance is absorbed in the form of physiological compound(s); or

(3) the product consists of micro-organisms commonly encountered in ensiled materials or those already used in food; or

(4) the product consists of enzymes with a high degree of purity arising from micro-organisms with a history of documented safe use.

For micro-organisms and enzymes not excluded above, genotoxicity studies (including mutagenicity) and a subchronic oral toxicity study are required. Genotoxicity studies shall not be made in the presence of living cells.

For xenobiotic substances, not exempted above, the whole of subsection 3.2.2 Annex II applies.

For other substances a case by case approach shall be taken, taking into account the level and means of exposure.

1.3.2.3. Assessment of consumer safety

The whole of subsection 3.2.3 of Annex II applies for additives requested for food producing animals.

1.3.3. Studies concerning the safety of use of the additive for users/workers

The whole of subsection 3.3 of Annex II applies. Additives containing enzymes and micro-organisms are assumed to be respiratory sensitisers unless convincing evidence to the contrary is provided.

1.3.4. Studies concerning the safety of use of the additive for the environment

The whole of subsection 3.4 of Annex II applies. For silage additives, the effects of the additive on the production of effluent from clamp or silo during ensiling shall be considered.

1.4. Section IV: studies concerning the efficacy of the additive

Technological additives are intended to improve or stabilise the characteristics of feed but have generally no direct biological effect on animal production. Evidence of the efficacy of the additive must be provided by means of appropriate criteria as reflected in recognised acceptable methods, under the intended practical conditions of use in comparison with appropriate control feed.

Efficacy will be assessed by *in vitro* studies, with the exception of substances for control of radionuclide contamination. The appropriate end-points are indicated in the following table for the various functional groups.

END-POINTS FOR DIFFERENT TECHNOLOGICAL ADDITIVES

Functional group	**End-points for demonstration of efficacy**

(a)	Preservatives	Inhibition of microbial growth, particularly that of biotic and spoilage organisms. The period for which a preserving effect is claimed shall be demonstrated.
(b)	Antioxidants	Protection against oxidative damage of key nutrients/components during feedingstuff processing and/or storage. The period for which a protecting effect is claimed shall be demonstrated.
(c)	Emulsifiers	Formation/maintenance of stable emulsions of otherwise immiscible or poorly miscible feed ingredients.
(d)	Stabilisers	Maintenance of the physico-chemical state of feedingstuffs.
(e)	Thickeners	Viscosity of the feed materials or feedingstuffs.
(f)	Gelling agents	Formation of a gel resulting in a change in the texture of the feedingstuff.
(g)	Binders	Pellet durability or performance of pellet formation.
(h)	Substances for control of radionuclides	Evidence of reduced contamination of food of animal origin.
(i)	Anti-caking agents	Flow ability. The period for which an anti-caking effect is claimed shall be demonstrated.
(j)	Acidity regulators	pH and/or buffering capacity in feedingstuffs.
(k)	Silage additives	— Improved production of silage; — Inhibition of undesirable micro-organisms; — Reduction of effluents; — Improved aerobic stability.
(l)	Denaturants	Indelible identification of feed materials.

Silage additives

Separate tests shall be made to demonstrate the effect requested on ensiling process[(2)]. The trials shall be performed with one example of each of the following categories (where all or unspecified forages are involved):

— easy to ensile forage: > 3 % soluble carbohydrates in fresh material (e.g. whole plant maize, ryegrass, brome grass or sugar beet pulp),

— moderately difficult to ensile forage: 1,5—3,0 % soluble carbohydrates in the fresh material (e.g. meadow grass, fescue or wilted alfalfa);

— difficult to ensile forage: < 1,5 % soluble carbohydrates in the fresh material (e.g., orchard grass or leguminous plants).

Where requests are restricted to sub-categories of forage described in terms of dry matter (DM), the dry matter range shall be explicitly stated. Three tests shall then be made with material representative of the range, where possible using examples of different botanical origin.

Specific tests are required for the particular feedingstuffs.

The duration of the study normally shall be 90 days or longer at a constant temperature (recommended range 15—25 ^{o}C). Use of a shorter duration must be justified.

As a rule measurements of the following parameters shall be provided in comparison to the negative control:

— dry matter and calculated dry matter losses (corrected for volatiles),
— pH- decrease,
— concentration of volatile fatty acids (e.g. acetic, butyric and propionic acids) and lactic acid,
— concentration of alcohols (ethanol),
— concentration of ammonia (g/kg of total nitrogen), and
— content of hydro-soluble carbohydrates.

In addition, other microbiological and chemical parameters shall be included as appropriate to substantiate the specific claim made (e.g. numbers of lactate assimilating yeasts, numbers of Clostridia, numbers of Listeria and biogenic amines).

An effect sought for effluent reduction will be judged against the total volume of effluent produced over the entire experimental period, taking into account the likely effect on the environment (e.g. ecotoxicity of the effluent or biological oxygen demand). Reduction of effluent production shall be demonstrated directly. The capacity of the silo shall be sufficient to allow effluent to be released with the application of pressure. The duration of the study shall normally be 50 days. If a different period is used, this shall be justified.

Improved aerobic stability shall be demonstrated in comparison with a negative control. Stability studies shall be of at least seven days duration after exposure to air and additive shall provide evidence of stability for at least two days longer than that shown by untreated control. It is recommended that the experiment is made at an ambient temperature of 20 ^{o}C and a rise in temperature of 3 ^{o}C or more above background taken as indicative of instability. Temperature measures may be replaced by measurement of CO_2 production.

1.5. Section V: post-market monitoring plan

This section shall apply under provision of Article 7(3)(g) of Regulation (EC) No 1831/2003. That is, a post-market monitoring plan is required only for additives that are GMOs or are produced from GMOs.

2. SENSORY ADDITIVES

2.1. Colourants

2.1.1. Section I: summary of the dossier

The whole of Section I of Annex II applies.

2.1.2. Section II: identity, characterisation and conditions of use of the additive; methods of analysis

The Section II of Annex II applies as following:

— for additives not subject to a specific holder of the authorisation the paragraphs 2.1.2, 2.1.3, 2.1.4, 2.1.4.2, 2.2, 2.3.1, 2.3.2, 2.4.1, 2.4.2, 2.4.4, 2.5, 2.6 apply;

— for other additives subject to a specific holder of the authorisation, the whole of Section II applies.

2.1.3. Section III: studies concerning the safety of the use of the additive

Subsection 3.3 of Annex II applies fully for every additive.

(1) For substances which, when fed to animals, add colours to food of animal origin Section III subsections 3.1, 3.2 and 3.4 of Annex II apply in full.

(2) For substances that add or restore colour in feedingstuffs, studies concerning Section III subsection 3.1 shall be performed on animals receiving the additive at the recommended dose. Evidence can also be provided by reference to existing scientific literature. Section III subsections 3.2 and 3.4 of Annex II apply.

(3) For substances which favourably affect the colour of ornamental fish or birds, studies concerning Section III subsection 3.1 of Annex II are required and shall be performed on animals receiving the additive at the recommended dose. Evidence can also be provided by reference to existing scientific literature. However, subsections 3.2 and 3.4 are not required.

2.1.4. Section IV: studies concerning the efficacy of the additive

The whole of Section IV of Annex II applies.

(a) For substances which, when fed to animals, add colour to food of animal origin:

changes of the colour of products obtained from animals receiving the additive at the recommended conditions of use shall be measured using the appropriate methodology. It shall be demonstrated that the use of the additive does not adversely affect product stability or organoleptic and nutritional qualities of the food. In principle, if effects of a particular substance on the composition/characteristics of animal products are well documented, then other studies (e.g. bioavailability studies) may provide adequate evidence of efficacy.

(b) For substances that add or restore colour in feedingstuffs:

evidence of efficacy shall be provided by adequate laboratory studies reflecting the intended conditions of use in comparison with control feedingstuffs.

(c) For substances which favourably affect the colour of ornamental fish and birds:

studies demonstrating the effect(s) shall be performed on animals receiving the additive at the recommended levels of use. Colour changes shall be measured using the appropriate methodology. Evidence of efficacy may also be provided by other experimental studies (e.g. bioavailability) or by reference to scientific literature.

2.1.5. Section V: post-market monitoring plan

This section shall apply under the provision of Article 7(3)(g) of Regulation (EC) No 1831/2003. That is, a post-market monitoring plan is required only for additives that are GMOs or are produced from GMOs.

2.2. Flavouring compounds

2.2.1. Section I: summary of the dossier

The whole of Section I of Annex II applies.

2.2.2. Section II: identity, characterisation and conditions of use of the additive; methods of analysis

In general, in the case of the group 'natural products', whole plants, animals and other organisms and parts of these or products thereof resulting from very limited processing such as crushing, grinding or drying (e.g. many herbs and spices), shall not be considered as falling under this functional group flavourings of the category sensory additives.

For the purposes of the evaluation of applications of these products, flavourings are classified as follows:

1. Natural products:

   1.1. Natural products — botanically defined.

   1.2. Natural products — non-plant origin.

2. Natural or corresponding synthetic chemically defined flavourings

3. Artificial substances.

   The relevant group, to which the product object of the application belongs, shall be indicated. In case the product does not fit into any of the above groups, this shall be mentioned and justified.

2.2.2.1. Characterisation of active substance(s)/agent(s)

The whole of the subsection 2.2 of Annex II applies.

In addition:

For all groups of flavourings, the relevant identification number(s) (such as FLAVIS[3], Council of Europe[4], JECFA, CAS[5] or any other internationally accepted numbering system) used specifically for the identification of flavouring products in feed and food shall always be provided when available.

(1) Natural products — botanically defined

The characterisation of the natural botanically defined products shall include the scientific name of the plant of origin, its botanical classification (family, genus, species, if appropriate subspecies and variety) and the common names and synonyms in as many European languages as possible or other language(s) (such as the one(s) of the place(s) of cultivation or origin) where available. The parts of the plant used (leaves, flowers, seeds, fruits, tubers, etc) and for lesser known plants the place of cultivation, identification criteria, and other relevant aspects of these plants shall be indicated. The major components of the extract shall be identified and quantified and its range or variability provided. Special attention shall be given to impurities as mentioned in subsection 2.1.4 of Annex II. The concentrations of substances of toxicological concern[6] for humans or animals which may occur in the plant from which the extract is produced shall also be reported.

The pharmacological or related properties of the plant of origin, its parts or of derived products thereof shall be fully investigated and reported.

(2) Natural products — non plant origin

An equivalent approach to the above may be used.

(3) Natural or corresponding synthetic chemically defined flavourings

Besides the general requirements of subsection 2.2.1.1 of Annex II, the origin of the flavouring shall be specified.

2.2.2.2. Method of production and manufacture

The whole of the subsection 2.3 of Annex II applies.

In the case of non chemically well defined natural products, usually complex mixtures of many compounds obtained by an extraction process, a detailed description of the extraction process shall be provided. It is recommended to use in the description the relevant terminology such as essential oil, absolute, tincture, extract and related terms[7] widely used for botanically defined flavouring products to describe the extraction process. The extraction solvents used shall be specified, the precautions taken to avoid residues of the solvents, and the levels of residues where these are of toxicological concern if their presence would be unavoidable. The terms used to characterise the extract may include a reference to the method of extraction.

2.2.2.3. Methods of analysis

(1) For natural products (either botanically defined or non-plant origin) which do not contain substances of toxicological concern for humans or animals, the standard requirement for methods of analysis of subsection 2.6 of Annex II may be replaced by a simpler qualitative method of analysis fit for the purpose for major or characteristic components of the product.

(2) For natural or corresponding synthetic chemically defined flavourings which are not substances of toxicological concern for humans or animals the standard requirement for methods of analysis of subsection 2.6. of Annex II may be replaced by a simpler qualitative method of analysis fit for the purpose.

The whole of subsection 2.6 of Annex II applies for all other flavourings, such as those natural extracts which contain substances of toxicological concern, natural or corresponding synthetic chemically defined flavourings which are substances of toxicological concern themselves and artificial flavourings.

2.2.3. Section III: studies concerning the safety of the additive

For all flavourings, animal exposure and intake calculations both from natural exposure and following addition of the flavouring to feedingstuffs shall be provided.

For flavouring belonging to the group artificial substances, the whole of Section III of Annex II applies.

2.2.3.1. Studies concerning the safety of use of the additive for target animals

(1) Natural products (either botanically defined or non–plant origin)

The safety of these products may be assessed on the basis of its major and characteristic components and also considering known substances of toxicological concern. If the major or characteristic components are not already authorised as chemically defined flavourings or as feed additives, then it has to be verified whether they are substances of toxicological concern for humans or animals, and its toxicological properties have to be provided in accordance with subsection 3.1 of Annex II.

(2) Natural or corresponding synthetic chemically defined flavourings

If these substances are authorised flavourings for humans, the safety for target species may be assessed taking into account the comparison between the level of intake by the target species from feed proposed by the applicant with that by humans from food. Metabolism and toxicological data on which the assessment for human used was made shall be submitted.

In all other cases different from the case where both levels of intake are similar, such as where the level of intake by the target animal proposed be the applicant is substantially higher than that by human from food or where the substance is not authorised in food, the safety for the target animals may be assessed by taking into account the following data: the principle of threshold of toxicological concern[(8)], available toxicological and metabolism data for related compounds, and chemical structural alert consideration (following by analogy of the Commission Regulation (EC) No 1565/2000 of 18 July 2000 laying down the measures necessary for the adoption of an evaluation program in application of Regulation (EC) No 2232/96 of the European Parliament and of the Council)[(9)].

Tolerance studies are needed only where threshold values are exceeded or cannot be determined.

2.2.3.2. Studies concerning the safety of use of the additive for consumers

Evidence that the metabolites of the flavouring do not result in an accumulation in the animal of products of toxicological concern for humans shall be provided. In the case that the use of the requested flavouring product as a consequence of its addition to feedingstuffs results in residues in food of animal origin, detailed calculation of consumer exposure shall be provided.

(a) Metabolic and residue studies

(1) Natural products (either botanically defined or non–plant origin)

The safety of these products for humans when used as flavourings in feed, as regards its metabolism, may be based on the metabolism (in the target animal) and residues studies of their major and characteristic components and the absence of substances of toxicological concern in the extract.

If the major or characteristic components are not already authorised as chemically defined flavourings or if the level of intake by the target animals from feed is substantially higher than that by humans from food, the whole of subsection 3.2.1 of Annex II is required.

(2) Natural or corresponding synthetic chemically defined flavourings

If these products are not authorised as flavourings for humans or if the level of intake by the target animal from feed as proposed be the applicant is substantially higher than that by human from food, available data on metabolic fate shall be provided and used to assess the potential accumulation in edible tissues and products according to subsection 3.2.1 of Annex II.

(b) Toxicological studies

(1) Natural products (either botanically defined or non–plant origin)

The safety of these products for humans when used as flavouring in feed may be based on the toxicological data of their major or characteristic components and the absence of substances of toxicological concern in the extract.

A toxicological package is required when the metabolic studies of the major or characteristic compounds show that there is accumulation in animal tissues or products and the threshold of toxicological concern for the target animal is exceeded. This toxicological package shall comprise genotoxicity studies, including mutagenicity and a subchronic oral toxicity study, according to subsection 3.2.2 of Annex II.

(2) Natural or corresponding synthetic chemically defined flavourings

A toxicological package comprising genotoxicity studies, including mutagenicity and a subchronic oral toxicity study, according to subsection 3.2.2 of Annex II, is required when the metabolic studies of these products show that there is accumulation in animal tissues or products and the threshold of toxicological concern for the target animal is exceeded.

2.2.3.3. Studies concerning the safety of use of the additive for users/workers

The whole of subsection 3.3 of Annex II applies.

2.2.3.4. Studies concerning the safety of use of the additive for the environment

The whole of subsection 3.4 of Annex II applies.

2.2.4. Section IV: studies concerning the efficacy of the additive

Evidence of the flavouring properties, usually on the basis of the published literature, shall be provided. This may also be demonstrated by experience of practical use, where available, otherwise animal studies may be required.

It has to be fully investigated and reported if the product object of the application exerts other functions in the feed, animal or food of animal origin besides the one in the definition of flavouring compounds in Annex I of Regulation (EC) No 1831/2003.

2.2.5. Section V: post-market monitoring plan

This section shall apply under provision of Article 7(3)(g) of Regulation (EC) No 1831/2003. That is, a post-market monitoring plan is required only for additives that are GMOs or are produced from GMOs.

3. NUTRITIONAL ADDITIVES

3.1. Section I: summary of the dossier

The whole of Section I of Annex II applies.

3.2. Section II: identity, characterisation and conditions of use of the additive; methods of analysis

The Section II of Annex II applies as following:

— for additives not subject to a specific holder of the authorisation the paragraphs 2.1.2, 2.1.3, 2.1.4, 2.1.4.2, 2.2, 2.3.1, 2.3.2, 2.4.1, 2.4.2, 2.4.4, 2.5, 2.6 apply;

— for other additives subject to a specific holder of the authorisation, the whole of Section II applies.

3.3. Section III: studies concerning the safety of the additives

3.3.1. Studies concerning the safety of use of the additive for the target species

3.3.1.1. Tolerance of the target species

1. No studies are required for urea, and amino acids, their salts and analogues authorised by Directive 82/471/EEC and compounds of trace elements and vitamins, pro-vitamins and chemically well-defined substances having similar effect which do not have a potential to accumulate already authorised as feed additives under Directive 70/524/EEC.

2. For those additives that fall within the functional group ‘vitamins, pro-vitamins and chemically well-defined substances having similar effect’ and having a potential to accumulate, tolerance will only be required to be demonstrated for compounds for which potency is expected or has been demonstrated to be different from that of the well established vitamin(s). In certain cases elements of the tolerance test (design or criteria) could be combined with one of the efficacy trials.

3. Tolerance will be demonstrated for urea derivatives amino acid analogues and compounds of trace elements not previously authorised. The fermentation products will be requested by tolerance demonstration, unless the active substance is separated from the crude fermentation product and highly purified, or the production organism has a history of apparent safe use and well known about its biology to exclude a potential for the production of toxic metabolites.

4. Where the application is for all animal species/categories, one tolerance study on the most sensitive species (or even an appropriate laboratory animal) under the most recent knowledge is sufficient.

3.3.1.2. Microbial studies

The whole of subsection 3.1.2 of Annex II applies.

3.3.2. Studies concerning the safety of use of the additive for consumers

3.3.2.1. Metabolic and residue studies

Metabolic studies normally are not required. For urea derivatives, ruminal metabolism shall be studied in the efficacy trials.

Residue or deposition studies are only required for those additives that fall within the functional group ‘vitamins, pro-vitamins and chemically well-defined substances, having similar effect’ that have a potential for accumulation in the body and for the functional group of compounds of trace elements where bioavailability has been enhanced. In that case, the procedure described in subsection 3.2.1 of Annex II does not apply. The requirement is limited to the comparison of the levels in the tissues or products between the group supplemented with the highest dose of the substance claimed and a positive control (reference compound).

3.3.2.2. Toxicological studies

These are required for fermentation products and additives not already authorised. For fermentation products, genotoxicity and subchronic toxicity studies must be provided unless:

1. the active substance is separated from the crude fermentation product and is highly purified; or

2. the production organism has a history of apparent safe use and there is sufficient knowledge of its biology to exclude a potential for the production of toxic metabolites.

Where the production organism belongs to a group in which some strains are known to produce toxins, their presence shall be specifically excluded.

3.3.2.3. Assessment of consumer safety

The whole of subsection 3.2.3 of Annex II applies.

3.3.3. Studies concerning the safety of use of the additive for users/workers

The whole of subsection 3.3 of Annex II applies

3.3.4. Studies concerning the safety of use of the additive for the environment

The whole of subsection 3.4 of Annex II applies for new active substances belong to the compound of trace elements.

3.4. Section IV: studies concerning the efficacy of the additive

Efficacy studies are not required for urea, amino acids, amino acid salts and analogues already authorised as feed additives, compounds of trace elements already authorised as feed additives and vitamins, pro-vitamins and chemically well-defined substances having similar effect already authorised as feed additives.

A short term study is required to support efficacy for urea derivatives, amino acid salts and analogues not already authorised as feed additives, compounds of trace elements not already authorised as feed additives and for vitamins, pro-vitamins and chemically well-defined substances having similar effect not already authorised as feed additives.

For other substances for which a nutritional effect is requested at least one long term efficacy study under provisions of Section 4 of Annex II is requested.

Where required, studies shall demonstrate that the additive can provide the animals' nutritional requirements. Tests shall include a test group with a diet that contains the nutrient at concentrations below the animals' requirements. However, trials using a severely deficient control group shall be avoided. Generally, it will be sufficient to demonstrate efficacy in a single animal species or category including laboratory animals.

3.5. Section V: post-market monitoring plan

This section shall apply under provision of Article 7(3)(g) of Regulation (EC) No 1831/2003.

4. ZOOTECHNICAL ADDITIVES

4.1. Zootechnical additives other than enzymes and micro-organisms

4.1.1. Section I: summary of the dossier.

The whole of Section I of Annex II applies.

4.1.2. Section II: identity, characterisation and conditions of use of the additive; methods of analysis

The whole of Section II of Annex II applies.

4.1.3. Section III: studies concerning the safety of the additives

4.1.3.1. Studies concerning the safety of use of the additive for target animals

The whole of subsection 3.1 of Annex II applies.

4.1.3.2. Studies concerning the safety of use of the additive for consumer

(1) Metabolic and residue studies

These studies are not required if:

— the substance or its metabolites can be demonstrated to be excreted unchanged and essentially to be not absorbed; or

— the substance is absorbed in physiological form and physiological level of compound(s).

No metabolic studies are needed if the substance is naturally present in significant amounts in food or feedingstuffs or if the substance is a normal constituent of body fluids or tissues. However, in these cases, there is a requirement for residue studies which can be limited to a comparison of the levels in the tissues or products in an untreated group to the levels found in the group supplemented with the highest recommended dose.

In all other cases the whole of subsection 3.2.1 of Annex II applies.

(2) Toxicological studies

Toxicological studies are not required if the substance is absorbed in the form of physiological compound(s).

For xenobiotic substances the whole of subsection 3.2.2 of Annex II applies.

For other substances, a case by case approach shall be used, taking into account the level and means of exposure, and any omission of data prescribed in this section must be fully justified.

(3) Assessment of consumer safety

The whole of subsection 3.2.3 of Annex II applies for food producing animals.

4.1.3.3. Studies concerning the safety of the additive for users/workers

The whole of subsection 3.3 of Annex II applies.

4.1.3.4. Studies concerning the safety of the additive for the environment

The whole of subsection 3.4 of Annex II applies

4.1.4. Section IV: studies concerning the efficacy of the additive

The whole of Section IV of Annex II applies.

(1) Additives favourably affecting animal production, performance or welfare and for the functional group ‘other zootechnical additives’.

The effects can only be demonstrated in relation to each target animal species or category. Depending on the properties of the additive, outcome measures may be based either on performance characteristics (e.g. feed efficiency, average daily gain, increasing of animal products), carcass composition, herd performance, reproduction

parameters or animal welfare. Evidence of the mode of action can be provided by short term efficacy studies or laboratory studies measuring relevant end-point.

(2) Additives favourably affecting the environmental consequences of animal production

For these additives which favourably affect the environment (e.g. reduced nitrogen or phosphorus excretion or reduced methane production, off-flavours), evidence of efficacy for the target species can be given by three short term efficacy studies with animals showing significant beneficial effects. The studies shall take into consideration the possibility of an adaptive response to the additive.

4.1.5. Section V: post-market monitoring plan

This section shall apply under provision of Article 7(3)(g) of Regulation (EC) No 1831/2003.

4.2. Zootechnical additives: enzymes and micro-organisms

4.2.1. Section I: summary of the dossier

The whole of Section I of Annex II applies.

4.2.2. Section II: identity, characterisation and conditions of use of the additive; methods of analysis

The whole of Section II of Annex II applies.

4.2.3. Section III: studies concerning the safety of the additives

4.2.3.1. Studies concerning the safety of use of the additive for the target animals

The whole of subsection 3.1.1 of Annex II applies.

Applicants are encouraged to use, wherever possible, at least a 100-fold overdose in the experimental group and consequently reduce the number of end-points required. A concentrated form of the additive can be used for this purpose. Concentration shall be adjusted by reducing the amount of carrier present but the ratio of active agent(s)/substance(s) to the other fermentation products must remain the same as in the final product. For enzymes, the diet shall provide the appropriate substrate(s).

The whole of subsection 3.1.2 of Annex II applies for all micro-organisms and for those enzymes with a direct catalytic effect on elements of the microbiota or which otherwise are claimed to affect the gut microbiota.

Where there is novel exposure or a substantial increase in the extent of exposure to micro-organisms, additional studies may be necessary to demonstrate the absence of adverse effects on the commensal microbiota of the digestive tract. For ruminants, direct counts of the microbiota will be necessary only if indicted by evidence of an adverse change to rumen function (measured in vitro as a change in volatile fatty acid concentrations, reduction in propionate concentration or reduced cellulolysis).

4.2.3.2. Studies concerning the safety of the additive use for consumer

(1) Metabolic and residue studies are not required.

(2) Toxicological studies, according to subsection 3.2.2 of Annex II.

Enzymes and micro-organisms form only a part of the whole additive which, in most cases, can include other components originated from the fermentation process. Consequently, it is necessary to test the additive to ensure it does not contain mutagenic or otherwise materials

that can harm human consumers of food derived from animals feed with feedingstuffs or water treated with these additives.

However, most viable bacteria intended for direct or indirect ingestion by mammals (including humans) are selected from groups of organisms with a history of apparent safe use or from groups where the toxic hazards are well defined. Similarly, the hazards associated with micro-organisms currently used for the production of enzymes generally are well recognised and substantially reduced by modern production methods. Therefore, for enzymes from microbial sources and for micro-organisms with a history of apparent safe use and where the components of fermentation process are well defined and know, toxicity tests (e.g. oral toxicity or genotoxicity testing) are not considered necessary. However, for both live organisms and those used for the production of enzymes, the specific concerns in section 2.2.2.2 of Annex II shall always be addressed.

When the organism or its application is novel and insufficient is known about the biology of the (production) organism to exclude a potential for the production of toxic metabolites, genotoxicity and oral toxicity studies made with additives containing viable micro-organisms or enzymes shall be introduced. In this case, they shall take the form of genotoxicity studies including mutagenicity and a subchronic oral toxicity study. It is recommended that such studies are performed with the cell-free fermentation broth or in the case of a solid state fermentation, an appropriate extract.

4.2.3.3. Studies concerning the safety of the additive for users/workers

The whole of subsection 3.3 of Annex II applies except:

— enzymes and micro-organisms, as proteinaceous substances, are assumed to be respiratory sensitisers unless convincing evidence to the contrary is provided. Therefore, no direct testing is required.

— the formulation of the product (e.g. micro-encapsulation) may obviate the need for some or all tests. In such cases, appropriate justification shall be provided.

4.2.3.4. Studies concerning the safety of the additive for the environment

The whole of subsection 3.4 of Annex II fully applies for micro-organisms which are not of gut origin or are not ubiquitous in the environment.

4.2.4. Section IV: studies concerning the efficacy of the additives

The whole of Section IV of Annex II applies.

(1) Additives favourably affecting animal production, performance or welfare and for the functional group ‘other zootechnical additives’.

The effects can only be demonstrated in relation to each target animal species or category. Depending on the properties of the additive, outcome measures may be based either on performance characteristics (e.g. feed efficiency, average daily gain, increasing of animal products), carcass composition, herd performance, reproduction parameters or animal welfare. Evidence of the mode of action can be provided by short term efficacy studies or laboratory studies measuring relevant end-point.

(2) Additives favourably affecting the environmental consequences of animal production.

For these additives which favourably affect the environment (e.g. reduced nitrogen or phosphorus excretion or reduced methane production, off-flavours), evidence of efficacy for the target species can be given by three short term efficacy studies

with animals showing significant beneficial effects. The studies shall take into consideration the possibility of an adaptive response to the additive.

4.2.5. Section V: post-market monitoring plan

This section shall apply under provision of Article 7(3)(g) of Regulation (EC) No 1831/2003.

5. COCCIDIOSTATS AND HISTOMONOSTATS

5.1. Section I: summary of the dossier

The whole of Section I of Annex II applies

5.2. Section II: identity, characterisation and conditions of use of the additive; methods of analysis

The whole of Section II of Annex II applies

5.3. Section III: studies concerning the safety of the additives

5.3.1. Studies concerning the safety of use of the additive for target animals

The whole of the subsection 3.1 of Annex II applies

5.3.2. Studies concerning the safety of use of the additive for consumer

The whole of the subsection 3.2 of Annex II applies

5.3.3. Studies concerning the safety of use of the additive for users/workers

The whole of the subsection 3.3 of Annex II applies

5.3.4. Studies concerning the safety of use of the additive for environment

The whole of the subsection 3.4 of Annex II applies

5.4. Section IV: studies concerning the efficacy of the additive

These additives protect the animals from the results of an invasion of *Eimeria* spp. or *Histomonas meleagridis*. Importance shall be attached to evidence of the 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.

The required efficacy data shall derive from three types of target animal experiments:

— artificial single and mixed infections
— natural/artificial infection to simulate use conditions
— actual use conditions in field trials

Experiments with artificial single and mixed infections (e.g. battery cages for poultry) are intended to demonstrate the relative effectiveness against the parasites and do not require replication. Three significant results are required for studies simulating use conditions (e.g. floor pen studies with poultry, battery cage studies with rabbits). Three field studies in which a degree of natural infection is present are also required.

5.5. Section V: post-market monitoring plan

This section of Annex II shall apply under provision of Article 7(3)(g) of Regulation (EC) No 1831/2003.

6. EXTRAPOLATION FROM MAJOR TO MINOR SPECIES

Minor species are defined in Article 1(2) of this Regulation.

A more limited submission will normally be accepted for a proposed extension of the authorised use to a species which is physiologically comparable to one in which the use of the additive has already been granted.

The following requirements apply only to requested authorisations for minor species of additives already authorised for major species. For requested authorisations for new feed additives requested only for minor species, all sections fully apply, depending on the category/functional group of the additive (see corresponding specific requirements of Annex III).

6.1. Section I: summary of the dossier

The whole of Section I of Annex II applies.

6.2. Section II: identity, characterisation and conditions of use of the additive; methods of analysis

The Section II of Annex II applies as following:

— for additives subject to a specific holder of the authorisation, the whole of Section II applies,

— for other additives the paragraphs 2.1.2, 2.1.3, 2.1.4, 2.1.4.2, 2.2, 2.3.1, 2.3.2, 2.4.1, 2.4.2, 2.4.4, 2.5, 2.6 apply.

6.3. Section III: studies concerning the safety of the use of the additive

6.3.1. Studies concerning the safety of use of the additive for the target animals

6.3.1.1. Tolerance of the target species

The requirements for the different categories/functional groups of additives apply.

In principle, tolerance studies for minor species are not required if the additive showed a wide margin of safety (at least a factor of 10) in the relevant physiologically similar major species.

If three major target species (including monogastric and ruminant mammals and poultry) showed a similar and wide margin of safety, no additional tolerance studies would be required for non-physiologically similar minor species (e.g. horses or rabbits). Where tolerance is required, the duration of the studies for minor species (except rabbits) shall be at least 28 days for growing animals and 42 days for adult animals. For rabbits, the following durations apply: rabbits for fattening: 28 days; breeding does: one cycle (from insemination to the end of the weaning period). If rabbits suckling and weaned are applied for, a period of 49 days (beginning one week after birth) would be considered sufficient and must include the does until weaning. For fish (other than salmonidae) a 90-day period is required.

6.3.2. Studies concerning the safety of use of the additive for the human consumers

6.3.2.1. Metabolic studies

The requirements for the different categories and functional groups of additives apply.

In addition, metabolic studies are not required if the additive is already authorised for use in a species which is physiologically comparable to the minor species for which the authorisation is sought. In the absence of physiological similarity, a comparison of metabolic profile based on *in*

vitro studies (e.g. performed in hepatocytes using labelled compound) is considered sufficient to assess metabolic proximity.

If the minor species is not physiologically similar to a major species, then an indication of the metabolic fate of the additive shall be obtained in the minor species.

6.3.2.2. Residue studies

Only marker residue quantification in edible tissues and products is needed when metabolic proximity is given or demonstrated. In all other cases, subsection 3.2.1.2 of Annex II fully applies.

6.3.2.3. Assessment of consumer safety

Proposal for Maximum Residue Limits (MRLs)

Setting of MRLs can be done by assuming that no significant differences in the content of residues occur in the edible tissues of minor species compared to a similar major species.

MRLs can be extrapolated within classes of animals as follows:

— from major growing ruminants to all growing ruminants;
— from milk of dairy cows to milk of other dairy ruminants;
— from pigs to all monogastric mammals, excluding horses;
— from chickens or turkeys to other poultry;
— from laying hens to other laying birds; and
— from Salmonidae to all fin fish.

MRLs for horses could be extrapolated when MRLs for a major ruminant and a major monogastric mammal exist.

If identical MRLs were derived in cattle (or sheep), pigs and chicken (or poultry), which represent major species with different metabolic capacities and tissue composition, the same MRLs can also be set for ovine, equidae and rabbits, which means an extrapolation is considered possible to all food-producing animals except fish. Considering the Committee for Medicinal Products for Veterinary Use (CVMP) guideline[10] on the establishment of MRLs for *Salmonidae* and other finfish, which already allows an extrapolation from MRLs in muscle of a major species to *Salmonidae* and other finfish provided that the parent substances is acceptable as marker residue for the MRL in muscle and skin, MRLs can be extrapolated to all-food-producing animals.

Analytical methods shall be available for monitoring residues in edible tissue and products of all food-producing animals.

6.3.3. Studies concerning the safety of use of the additive for users/workers

The whole of subsection 3.3 of Annex II applies.

6.3.4. Studies concerning the safety of use of the additive for the environment

Environmental risk assessment can be extrapolated from the assessment performed for the physiologically comparable major species. For additives intended to be used in rabbits, the whole section applies taking into consideration the requirements for each category/functional group of additives.

6.4. Section IV: studies concerning the efficacy of the additive

Where the additive is already approved for a physiologically comparable major species for the same function and where the mode of action of the additive is known or demonstrated, evidence of the same mode of action in the minor species can be taken as evidence of efficacy. Where no such link can be made, efficacy shall be demonstrated following the general rules for Section IV in Annex II. In some cases it may be appropriate to combine animal species in the same productive stage (e.g. goats and sheep used for milk production). Significance should be demonstrated in each study ($P \leq 0,1$) or, if possible, by meta-analysis ($P \leq 0,05$).

If efficacy demonstration is required, the duration of efficacy studies shall be analogous to the comparable production stages of the physiologically comparable major species. In other cases, the minimum study duration shall follow the relevant provisions in subsection 4.4 of Annex II and Annex IV.

6.5. Section V: post-market monitoring plan

This section of Annex II shall apply under provision of Article 7(3) (g) of Regulation (EC) No 1831/2003.

7. PETS AND OTHER NON FOOD-PRODUCING ANIMALS

Pets and other non food-producing animals are defined in Article 1(1) of this Regulation.

7.1. Section I: summary of the dossier

The whole of Section I of Annex II applies.

7.2. Section II: identity, characterisation and conditions of use of the additive; methods of analysis

The Section II of Annex II applies as following:

— for additives subject to a specific holder of the authorisation, the while of Section II applies

— for other additives the paragraphs 2.1.2, 2.1.3, 2.1.4, 2.1.4.2, 2.2, 2.3.1, 2.3.2., 2.4.1, 2.4.2, 2.4.4, 2.5, 2.6 apply.

7.3. Section III: studies concerning the safety of the additive

7.3.1. Studies concerning the safety of use of the additive for the target animals

The requirements for the different categories/functional groups of additives apply. Where a tolerance study is required, its duration shall be at least 28 days.

A tolerance study is not required if the additive has shown a comparable and wide margin of safety in three major species (including monogastric and ruminant mammals and poultry).

7.3.2. Studies concerning the safety of use of the additive for consumers

This subsection is not usually required. Consideration shall be given to the safety of the owner.

7.3.3. Studies concerning the safety of use of the additive for users/workers

The whole of subsection 3.3 of Annex II applies.

7.3.4. Studies concerning the safety of use of the additive for the environment

Subsection 3.4 of Annex II is not required.

7.4. Section IV: studies concerning the efficacy of the additive

The requirements for the different categories/functional group of additives apply.

When the additive, for which animal studies are required, has been previously authorised for other physiological similar species, no further demonstration of efficacy is required provided the requested effect and mode of action are the same. If the additive has not been previously authorised, the requested effect, or the mode of action are different than former authorisation, efficacy shall be demonstrated following the general rules for Section IV in Annex II.

The duration of the long term efficacy trials shall be at least 28 days.

7.5. Section V: post-market monitoring plan

This section of Annex II shall apply under provision of Article 7(3) (g) of Regulation (EC) No 1831/2003.

8. ADDITIVES ALREADY AUTHORISED FOR USE IN FOOD

8.1. Section I: summary of the dossier

The whole of Section I of Annex II applies.

8.2. Section II: identity, characterisation and conditions of use of the additive; methods of analysis

The Section II of Annex II applies as following:

— for additives subject to a specific holder of the authorisation, the whole of Section II applies,

— for other additives the paragraphs 2.1.2, 2.1.3, 2.1.4, 2.1.4.2, 2.2, 2.3.1, 2.3.2., 2.4.1, 2.4.2, 2.4.4, 2.5, 2.6 apply.

8.3. Section III: studies concerning the safety of the additives

The most recent formal assessments of the safety of the food additive shall be included and shall be supplemented with any subsequently produced data.

For those additives which are authorised as food additives or approved as components for foodstuffs in the European Union without any restriction, studies concerning the safety for the consumer and the workers are generally not necessary.

Subsections 3.1, 3.2 and 3.3 of Annex II shall be provided considering the present knowledge on the safety of these substances when used in food. Accordingly, such substances also used in food can be classified as:

— ADI not specified (without an explicit indication of the upper limit of intake, assigned to substances of very low toxicity),

— ADI or UL established, or

— no ADI allocated (applicable to substances for which the available information is not sufficient to establish their safety).

8.3.1. Studies concerning the safety of use of the additive for the target animals

If the use level as for the feed additive is similar to that used in food, the safety for target species can be assessed based on the *in vivo* toxicological data available, a consideration of chemical structure and the metabolic capacity of the target species. If the use level in feed is considerably higher than the corresponding use in food, a tolerance study in the target animal may be required, depending on the nature of the substance.

8.3.2. Studies concerning the safety of use of the additive for consumers

If the use as a feed additive results in a higher consumer exposure, or to a different pattern of metabolites than that resulting from use in food, then further toxicological and residue data will be required.

8.3.2.1. Food additives for which an ADI is not specified

Assessment of the safety for consumers is not required, except when the use of the additive in feed leads to a different pattern of metabolites than when used in food.

8.3.2.2. Food additives with an established ADI or UL

Consumer safety must be assessed taking into consideration the additional exposure from feed use, or specific exposure related to metabolites arising from the target species. This can be done by extrapolating residue data from literature.

Where residue studies are necessary, the requirement is limited to a comparison of the tissue or product levels in an untreated group to the group supplemented with the highest dose that is claimed.

8.3.2.3. Food additives for which no ADI is allocated

The reasons why an ADI was not allocated shall be clearly specified. If concerns arise from this, and the use of the additive in feed would contribute to a significant increase in consumer exposure, a full toxicological evaluation is required.

Additional exposure from feed use can be extrapolated from residue data from the literature.

Where residue studies are necessary, the requirement is limited to a comparison of the levels in tissues or products in an untreated group with the group supplemented with the highest dose that is claimed.

8.3.3. Studies concerning the safety of use of the additive for users/workers

The whole of the subsection 3.3 of Annex II applies.

Precautionary measures set for handling these substances used in food shall be taken into account when considering user safety for the feed additive.

8.3.4. Studies concerning the safety of use of the additive for the environment

Subsection 3.4 of Annex II is required.

8.4. Section IV: studies concerning the efficacy of the additive

Where the function requested for feed is the same as that used in food, no further demonstration of efficacy might be necessary. Otherwise the requirements for efficacy are as those shown in Section IV of Annex II.

8.5. Section V: post-market monitoring plan

This section of Annex II shall apply under provision of Article 7(3)(g) of Regulation (EC) No 1831/2003.

9. MODIFICATION OF THE AUTHORISATIONS

Since reliance can be placed on the evaluation of the data supplied for previous authorisations, a dossier prepared for an application under Article 13(3) of Regulation (EC) No 1831/2003 needs to comply only with the requirements listed below.

An application for modification of the terms included in an existing authorisation Regulation, such as the identification, the characterisation or the conditions of use of the additive, shall demonstrate that the modification does not have any harmful effect on the target species, the consumer, the user or the environment. An additive can be considered as identical for this purpose if the active substance(s) or agent(s) and the conditions of use are the same, its purity is essentially similar and no new components of concern have been introduced. For such products an abridged application may be submitted as it will normally not be necessary to repeat studies to demonstrate the safety for the target species, the consumer and the environment and efficacy.

The application shall address the following requirements:

1. the whole of Annex I applies — this includes details of the modification requested;

2. the whole of Section II of Annex II applies;

3. data must be provided indicating that the, chemical or biological characteristics of the additive are essentially the same to those of the established product;

4. where appropriate, evidence for bioequivalence shall be provided either by specification, or by published literature or from specific studies. Where bioequivalence is not fully demonstrated, conformity of the withdrawal period with the MRL has to be demonstrated;

5. evidence shall be presented that in the light of current scientific knowledge that the additive remains safe under the approved conditions for target species, consumers, workers and the environment;

6. a report on the results of the post-market monitoring, if such monitoring requirements are included in the authorisation, shall be provided; and

7. the specific data supporting the request for change must be submitted in compliance with the relevant parts of Sections III, IV and V of Annex II.

10. RENEWAL OF AUTHORISATIONS

Applications for renewal of authorisation under Article 14 of Regulation (EC) No.1831/2003 shall comply with the following requirements:

10.1. Section I: summary of the dossier

The whole of Section I of Annex II applies. A copy of the original Community authorisation for placing the feed additive on the market, or the last renewal of authorisation, shall be provided. An updated dossier shall be prepared according to the most up-to-date requirements and a list providing all variations since the original authorisation, or the last renewal of authorisation shall be submitted. The applicant has to provide a summary of the dossier, detailing the scope of the application, and any new information that has become available since the previous authorisation/ renewal in terms of identity and safety.

10.2. Section II: identity, characterisation and conditions of use of the additive; methods of analysis

The Section II of Annex II applies as following:

— for additives subject to a specific holder of the authorisation, the whole of the Section II applies,

— for other additives the paragraphs 2.1.2, 2.1.3, 2.1.4, 2.1.4.2, 2.2, 2.3.1, 2.3.2, 2.4.1, 2.4.2, 2.4.4, 2.5, 2.6 apply.

Evidence shall be presented to show that the additive has not been significantly changed or altered in composition, purity or activity in respect of the additive that was authorised. Any change in the manufacturing process shall be reported.

10.3. Section III: studies concerning the safety of the additives

Evidence shall be presented that in the light of the current knowledge the additive remains safe under the approved conditions for target species, consumers, workers and the environment. A safety update for the period since the original authorisation, or the last renewal of authorisation with information on the following items shall be presented:

— reports on adverse effects including accidents (previously unknown effects, severe effects of any type, increased incidence of known effects) for target animals, consumers, users and the environment. The report on adverse effects shall include the nature of the effect, number of affected individuals/organisms, outcome, conditions of use, and causality assessment,
— reports on previously unknown interactions and cross-contaminations,
— data from residue monitoring, where appropriate,
— data from epidemiologic and/or toxicological studies,
— any other information concerning the safety of the additive and risks of the additive to animals, humans, and environment.

If no further information is provided on any of these issues, the reasons for this shall be clearly identified.

A report on the results of the post-market monitoring program shall be provided, if such a monitoring requirement is included in the previous authorisation.

Where, as provided for in Article 14(2)(d) of Regulation (EC) No 1831/2003, the application for renewal of the authorisation includes a proposal for amending or supplementing the conditions of the original authorisation, *inter alia,* the conditions concerning future monitoring, the specific data supporting the proposal for amendment must be submitted in compliance with the relevant parts of Sections III, IV and V of Annex II.

11. RE-EVALUATION OF CERTAIN ADDITIVES ALREADY AUTHORISED UNDER DIRECTIVE 70/524/EEC

The additives concerned by this point 11 are additives which were authorised under Directive 70/524/EEC and are to be re-evaluated in accordance with Article 10(2) of Regulation (EC) No 1831/2003 and which belong to the following groups:

— antioxidant substances,
— flavouring and appetising substances,
— emulsifying and stabilising substances, thickeners and gelling agents,
— colourants, including pigments,
— preservatives,
— vitamins, provitamins and chemically well-defined substances having similar effect,
— trace elements,
— binder, anti-caking agents and coagulants,
— acidity regulators, and
— radionuclide binders.

The level and quality of risk evaluation for these additives shall be similar to other additives. However, due to their long history of safe use, data from studies already published may be used,

under provisions provided by this Regulation, to show that the additive remains safe under the approved conditions for the target species, consumers, users and the environment.

11.1. Section I: summary of the dossier

The whole of Section I of Annex II applies.

11.2. Section II: identity, characterisation and conditions of use of the additive; methods of analysis

The Section II of Annex II applies as following:

— for additives not subject to a specific holder of the authorisation the paragraphs 2.1.2, 2.1.3, 2.1.4, 2.1.4.2, 2.2, 2.3.1, 2.3.2, 2.4.1, 2.4.2, 2.4.4, 2.5, 2.6 apply;

— for other additives subject to a specific holder of the authorisation, the whole of Section II applies.

11.3. Section III: studies concerning the safety of the additives

Where an additive has been assessed for safety for target species, consumers, users/workers and the environment, a summary of the safety studies submitted for the previous authorisation, plus any new information arising since the previous authorisation shall be provided. Where a formal safety assessment has not been undertaken for the use of the substance as a feed additive, studies and data from the scientific literature can be used provided it is equivalent to that which would be required in a new application. Otherwise, a complete set of safety studies shall be provided.

11.4. Section IV: studies concerning the efficacy of the additive

Where appropriate, the compliance with the requirement of efficacy provided for in Article 5(3) of Regulation (EC) No 1831/2003 may be demonstrated by submission of material other than studies, in particular relating to the long history of use.

11.5. Section V: post-market monitoring plan

This section of Annex II shall apply under provision of Article 7(3) (g) of Regulation (EC) No 1831/2003.

(**1**) A xenobiotic is a chemical substance which is not a natural component of the organism exposed to it. It can also cover substances which are present in much higher concentrations than are usual.

(**2**) For purpose of this Regulation, 'ensiling process' means process by which natural deterioration of organic matter is controlled by acidification in anaerobic condition resulting from natural fermentation or/and addition of silage additives.

(**3**) Identification number for chemically defined flavouring substances used in FLAVIS, the EU Flavour Information System, the database used within the Commission Regulation (EC) No 1565/2000 of 18 July 2000 (OJ L 180, 19.7.2000 p. 8) laying down the measures necessary for the adoption of an evaluation programme in application of Regulation (EC) No 2232/96 of the European Parliament and of the Council (OJ L 299, 23.11.1996, p. 1).

(**4**) CoE no.: Council of Europe number used for botanically defined flavouring products in the Council of Europe's Report no. 1 on 'Natural sources of flavourings', Volume I, Strasbourg, 2000 and its subsequent volumes.

(**5**) CAS Number (CAS No) Chemical Abstracts Service Registry Number, unique identifier for chemical substances widely used in chemical inventory listings.

(**6**) For the purpose of this section of this Regulation, 'substance of toxicological concern' means a substance with a tolerable daily or weekly intake (TDI or TWI), an ADI, or with a restriction in its use, or an active principle as defined in Council Directive 88/388/EEC relating to flavourings for use in foodstuffs and to source materials for their production, or an undesirable substance.

(**7**) Defined in Appendix 4 of the Council of Europe's Report no. 1 on 'Natural sources of flavourings', Volume I, Strasbourg, 2000.

(**8**) JECFA (FAO/WHO, 1996, Food additive series 35, IPCS, WHO Geneva) corresponding threshold for target animal should be adjusted to take into account of animal weight and feed intake.

(**9**) OJ L 180, 19.7.2000, p. 8.

(**10**) Note for guidance of the establishment of maximum residue limits for *Salmonidae* and other fin fish. The European Agency for the Evaluation of Medicinal Products. *Veterinary Medicines Evaluation Unit.* EMEA/CVMP/153b/97-FINAL.