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

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[(1)] 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.

(**1**) 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.