PRESENTATION OF AN APPLICATION FOR ASSESSMENT OF A FOOD ADDITIVE PRIOR TO ITS AUTHORIZATION

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Document

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PRESENTATION OF AN APPLICATION FOR ASSESSMENT OF A FOOD ADDITIVE PRIOR TO ITS AUTHORISATION

1. INTRODUCTORY REMARKS

(i) The admission of a substance as food additive is dependent on the availability of experimental data, on which an objective evaluation of the material's safety can be made.

(ii) Irrespective of whether the additive is on a Community list or simply subject to national rules each Member State evaluates its safety - firstly, in terms of its acceptability in general and secondly, in terms of the conditions of use within its territory.

(iii) Where the addition of a substance to a Community list is concerned, the Commission consults the EEC Scientific Committee for Food, an independent group of scientists drawn from the Members States with knowledge of food safety matters, prior to the submission of its proposals.

(iv) Member States must also be mindful of the safety in use of a particular additive in the context of its national consumption patterns and each State has its own particular system of evaluation.

2. FORMAT OF THE DOSSIER

(i) The format and contents of a dossier as described in Annex I have been devised by a working party composed of government experts, the Scientific Committee for Food and the Commission services as acceptable for an application for the assessment of food additives. Other formats may also be acceptable to individual authorities. Other legal provisions concerning applications should be discussed with the competent services.

(ii) It is likely that the "EEC" dossier will be the most comprehensive as this takes into account the particular concerns of each Member State.

(iii) Applicants should discuss with individual Member States or the Commission any special submissions for which the extent of information in a particular dossier is less than described. During the evaluation of a dossier, further justified requests by the responsible authority for additional testing cannot be excluded if such tests are necessary to assess the significance of the effects found.

It would be expected that such tests would, as far as possible, be presented in the same format as the initial studies.

3. RESPONSIBLE AUTHORITIES

Dossiers for evaluation by Member States and the Commisison must be submitted to the responsible authority(ies) listed in Annex II.

4. OTHER REQUIREMENTS

Individual responsible authorities have differing requirements for the number of copies of dossier and summaries. These are specified in Annex III.

ANNEX I

DOSSIER

PART I. ADMINISTRATIVE DATA

I.1. The name of the applicant (firm, organisation, etc.), address and other means of communication, e.g. telex, telephone.

I.2. The name of the manufacturer(s) of the substance (if different), address and other means of communication, e.g. telex, telephone.

I.3. The name of the person responsible for the dossier.

I.4. The table of contents of the dossier.

Where the dossier differs from similar dossiers sent to individual Member States by the applicant, this should be indicated.

PART II. TECHNICAL DATA

II.1. Name of the substance

- names in the IUPAC nomenclature;
- other names (usual name, trade name, synonyms, abbrevations);
- CAS number (if this has been attributed).

II.2. Specification of the substance

- composition (%, w/v, mg/kg), e.g. in the case of heterogeneous products);
- empirical and structural formula;
- molecular weight;
- degree of purity (%);
- nature of known impurities;
- percentage of significant and main impurities;
- physical form (liquid, powder, etc.);
- solubility (e.g. aqueous, organic solvents, lipid);
- other data that the applicant believes may be useful to identify the substance (e.g. physico-chemical properties, analytical data on differences between batches),*

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* Applicants are referred to Council Directive 79/831/EEC, amending for the sixth time Directive No 67/548/EEC, on the approximation of laws regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances (OJ L 259 of 15.10.79, p. 10), in particular Annex VII thereof.

- information on the microbiological characteristics, in particular on the possible presence of pathogens and bacterial or myco-toxins.

II.3. Manufacturing process

- information on the method of manufacture (i.e. the process by which the raw materials are converted to the finished product).

Factors such as reaction sequence, side reactions, purification and preparation of the product to be commercialized assist in determining likely impurities and their unfluence on the toxicological evaluation.

II.4. Methods of analysis

- analytical methods to describe the substance, evaluate its purity and measure its physico-chemical and microbiological characteristics;
- analytical methods for the determination of the additive and its degradation products (where relevant), in the foodstuff of which the substance is to form part.

Where the methods used are specified in Part A of Commission Directive 84/449/EEC of 25 April 1984 on the approximation of laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances (OJ L 251 of 19.9.1984, p. 1), these may be given by reference only. Other methods should be given in full unless they are sufficiently well described in scientific literature to make this unnecessary.

II.5. Justification for the additive

- intended use and purpose;
- the quantity to be added to specific foods and the residues in food;
- investigations on the efficacy of the substance for the intended effect at the level proposed;
- documentation on the need for the additive; benefit for the consumer.

A summary of basic principles is included as Annex IV

II.6. Exposure

- likely human exposure (actual or expected) from food and other sources, including route, frequency, duration and other factors influencing exposure (e.g. maximum and average dosage or exposure);

- consumption of the food including variations affecting particular sections of the population (e.g. by age, sex, disease or occupation).

Information on national authorisations (within or outside the Community) with indication of levels in the food in which the substance is used gives useful guidance on possible exposure.

II.7. Reaction and fate in food

- any significant degradation products or reaction products appearing as a result of the storage and preparation of food with the additive;
- any possible effect on nutrients.

PART III. TOXICOLOGICAL DATA

III.1. General principles for the toxicological evaluation of food additives

If the technological need and value to consumer of a food additive have been established, it is necessary to evaluate the implications for the health of the consumer due to the presence of that additive in food. It is necessary to determine by toxicological examination whether the substance, when used in the manner and in the quantities proposed, might be injurious to the health of those population groups whose pattern of food consumption or physiological status makes them most vulnerable, e.g. age, pregnancy. No fixed programme is laid down to be followed rigidly in every case, but a framework is summarized for planning a sequence of steps which enables the safety-in-use of a food additive to be evaluated. It may be possible to use human data derived from medical use, occupational epidemiology, or specific studies, such as studies on volunteers or on critically exposed groups, but in general, one must rely on experimental data derived from investigations in laboratory animals. If the biological action of a substance has been ascertained qualitatively and quantitatively in different laboratory animals, the likely effects on man can then be estimated by careful extrapolation.

Studies will be requested in their entirety or in part depending on the nature of the additive and on the conditions proposed for its use.

In general, this text is intended to apply to the evaluation of new, or the re-evaluation of already established intentional food additives, directly incorporated into food and fulfilling a defined purpose.

The reasons for carrying out unusual studies should be stated, as should the reasons, for not submitting a study of a type that might be expected.

All the important results obtained, favourable or unfavourable, should be presented with the full original data to allow a critical appreciation, independent of the interpretation of the author.

As specified tests are completed, the toxicologist might decide that a decision on safety can already be taken in the light of the results obtained. However, in principle, it is desirable that any food additive should be fully examined for all toxicological potentialities before its safety-in-use can be accepted.

III.2. Protocols

Methods for determining toxicity are described in Commission Directive 84/449/EEC of 25 April 1984, adapting to technical progress for the sixth time, Council Directive 67/548/EEC on the approximation of laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances (OJ L 251 of 19.9.1984, p.1).

Protocols for undertaking studies have also been developed in many international fora (e.g. WHO, OECD). Test requirements are always subject to review, and discussion with regulatory authorities is recommended.

The use of other methods should be justified.

To ensure the mutual recognition by Member States of the data submitted, studies should be carried out according to the principles of Good Laboratory Practice, described in Council Directive 87/18/EEC of 18 December 1986. (OJ No L 15 of 17.1.1987, p. 29). Adequate explanation must be provided for divergences from these principles.

Attention is also drawn to the Council Directive 86/609/EEC of 24 November 1986 (OJ No L 358 of 18.12.1986, p. 1) on the protection of animals used for experimental and other scientific purposes.

III.3. Toxicological section of the dossier

The toxicological section of the dossier should comprise sections as follows.

(a) Acute toxicity

Range-finding studies provide information on dosage for feeding studies and target organs.

(b) Genetic toxicity

It is recommended that any new food additive should be investigated for mutagenic potential by testing procedures which cover both gene and chromosome damage, both *in vitro* and *in vivo*.

In this way, some evidence may be provided upon which a preliminary assessment of a possible mutagenic hazard can be based. This information will be helpful in setting priorities for long-term testing.

(c) Metabolic, including pharmacokinetic studies (alternative terms are toxicokinetics or chemobiokinetics)

These studies are carried out principally to gain an understanding of the absorption, biotransformation, disposition and elimination of an ingested foreign substance after a single and repeated doses. They also provide information about the rate at which these processes occur and the temporal relationship between dose and tissue levels reached.

The information obtained assists :

- in planning studies in laboratory animals;
- in selecting the species, dosing regime and duration of studies;
- in assessing the relative importance of different metabolic pathways;
- in assessing the relationship of species differences to the likely metabolism in man;
- in assessing the extent of and even the need for extensive toxicological testing, e.g. non-absorbed compounds, metabolism to normal body constituents.

In vitro preliminary studies on the effects of acids, bases and hydrolytic enzymes may be followed by investigation of the biodegradation in the gut, of the transformation by tissue cells or perfused organs. The capacity to form chemically reactive metabolites is a key information for the understanding of the toxic effects, species differences and reactions with the genetic material. The possibility of enzyme induction and the determination of major and minor metabolites are also essential as is the assessment of the possibility of placental transfer.

(d) Subchronic studies

Studies in two laboratory species (usually a rodent and a non-rodent) are normally required, generally representing 10% of the life span of the species selected.

The major objective of subchronic studies is the establishment of the spectrum of toxicological effects of the compound, their nature and severity in an animal species in which the metabolic pathways of the same or analogous substances are as similar as possible to those in man.

(e) Reproduction and teratogenicity studies

The purpose of reproduction studies is to provide information about the possible increase, in successive generations, in sensitivity to a substance, the effects on the fertility of male and female animals, the detection of any pre-, peri- and post-natal effects on the embryo, the foetus, and the young, including any teratogenic and mutagenic effects, and the discovery of peri- and post-natal effects on the mother.

Food additives should be tested for teratogenicity in at least two species. The practical possibilities are the mouse, rat or rabbit; in certain circumstances, the hamster and the guinea-pig may be more appropriate.

(f) Chronic toxicity studies and carcinogenicity studies

For food additives it is recommended that combined protocols be used for studying chronic toxicity and carcinogenicity in the same experiment. Most of the procedures for carrying out such chronic studies are relatively standardized but several areas are still considered controversial. The selection of test species is limited by many practical considerations, although the animal model should be biologically appropriate for the toxicological assessment of the possible human risk. This implies that metabolism and pharmacokinetics of the test substance in the species and strains chosen should mimic those in man as closely as possible. For food additives both mice and rats are the traditional species employed because of the relatively short life span, size, cost and extensive experience and availablity of information on their biological characteristics. Both species have to be used in most circumstances unless specific considerations dictate otherwise. Dogs and non-human primates may be useful when the nature of the toxicity or the procedures required necessitate the use of large species.

(g) Allergic, intolerant and other idiosyncratic reactions

At present there exist no validated methods for studies in animals which allow assessment of an additive's potential for causing intolerant and/or allergic reactions in susceptible individuals following oral exposure. However studies relevant to dermal (contact) and inhalational

sensitiation can be performed. These studies may give information relevant to occupational exposure, and could be helpful in assessing consumer safety. As techniques for such studies vary considerably, the reasons for using the particular method(s) should be explained (also in the summary).

Human studies (see below) or other human experience, such as pre-marketing surveys, may give some information about idiosyncratic reactions to a new food additive. Although data may be limited due to a small number of subjects involved, all exposed subjects should be monitored for possible idiosyncratic actions, and any data (positive or negative) should be included in the dossier.

(h) Human studies

When the safety of a new addditive has been adequately demonstrated in animals, clinical studies in volunteers may be undertaken. Such studies are particularly useful in providing pharmacokinetic and metabolic data, but other special studies in humans may sometimes be appropriate. Any studies must satisfy the ethical requirements for investigation in humans, and several national and international guidelines on this subject have been published.

In addition to clinical studies any available information should be presented on observations in humans made during the use of a food additive in a third country, in pre-marketing trials, as a result of occupational exposure or following accidental or deliberate poisoning.

III.4. Data reporting for the toxicological section

The data reported for each study in the toxicological section of the dossier should as far as possible follow the sequence summarized below.

(a) Laboratory diet and husbandry

- a full description of the animal diet used in the biological studies, including composition, the results of analyses for macro- and micro-nutrients, presence or absence of toxicologically important contaminants (e.g. myco-toxins, toxic heavy metals, etc.);
- conditions of husbandry, distribution and environmental circumstances.

(b) Experimental design

(i) Material tested

- analytical data on the batch used should be provided if the specification is different from that given in Part II (e.g. technical grade rather than food grade), the differences should be identified, the reasons explained and the significance discussed.

(ii) Animals

- species, strains, microbiological status, sex, random allocation to groups, group sizes, age and/or weight at the start of the study, type of diet, anti-microbial agents, other drugs or vaccines administered.

(iii) Compound preparation and administration

- route, duration, frequency, dosage (by volume as well as concentration for liquids), estimated total doses (for long-term studies), controls (positive and negative) and vehicle.

(iv) Duration of study if different from duration of dosage.

(v) Any unusual study design considerations such as paired feeding, satellite groups or interim kills should be noted.

(vi) Nature of major observations

- frequency of body weight measurement, timing, volume and site of blood sampling, timing of urine collection, haematological and clinical chemistry parameters measured, methods of killing animals, organs weighed, organs examined macroscopically/microscopically, methods of examining foetuses, etc.

(vii) Statistical analyses employed

- specify methods used including reference to publication of any new or unusual statistical tests used.

(c) Results

The main findings should be summarized and a statement made on whether significant deviations from control and normal values occured.

(i) Clinical condition

- general health, intercurrent disease, behaviour (including the results of specific observations, if undertaken), clinical investigations (including opthalmoscopic findings, palpitation).

(ii) Mortality

- times of death and causes, where known.

(iii) Weight change, food and water consumption, relationship of growth rates to dosage and to any changes in food consumption/utilisation.

(iv) Haematology

- haemoglobin concentration and red cell parameters, white blood cell count and differential; other haematological parameters where appropriate.

(v) Clinical chemistry

- urea and electrolytes, glucose, liver function tests and routine urinalysis; other clinical chemistry studies where appropriate.

(vi) Pathology

- macroscopic abnormalities observed at post-mortem examinations and abnormalities on histological examination should be described. In addition to the current control incidence of lesions, the background incidence may need to be given, e.g. the incidence of tumours in control groups in other experiments carried out in the same strain and sex at a similar time (concurrent controls) or in the past (historical controls). This is of particular importance when it appears that the current control data are atypical. Where special studies (histochemistry, electron microscopy or quantitative histology) have been undertaken, the findings should be described in relation to those from routine histology. In the study summary, the information should be clearly presented in a concise form.

(d) Comment

The significant findings from the study should be highlighted together with the no-adverse-effect level, if one has been determined, and any other relevant information.

(e) Reference

(i) published data

Author, journal, and date.

(ii) unpublished data

Applicant, investigator, laboratory and date.

III.5. Review of results and conclusions

The section should list all significant findings in all studies and seek to make interpretations and draw conclusions, which the submitter would wish the Commission/national administration to consider. The reasons for disregarding any findings should be carefylly explained. Where relevant, attention may be drawn to the extent to which dosage or concentrations are exaggerated and the possible influence of the vehicle used for administering the substance. The conclusion should include an interpretation of the significance of the finding in terms of possible mechanisms of the effect seen in the animal and extrapolation of the animal data to humans. References to known effects (or lack of effect) in human exposure should be given; evidence from recorded experience for occupational exposure, for example, may be informative. The evaluation of potential human hazard should be made in the context of known or likely human exposure, including that from other sources.

PART IV. SUMMARY DOCUMENT

The summary should follow the same order as decribed for the dossier.

Parts I and II need only be completed once for each substance or product. A summary should be completed for each study reported in the toxicological section of the dossier.

The main findings should be summarized and a statement made on whether significant deviations from control and normal values occured.

REFERENCES

Useful guidance can be found in the following documents :

Council for International Organisations of Medical Sciences (1982). Proposed International Guidelines for Biomedical Research Involving Human Subjects. A joint project of the World Health Organization and the Council for International Organisations of Medical Sciences, Geneva.

Refshauge, W. (1977). The place for international standards in conducting research on humans. The Bulletin of the World Health Organization. 55, Supplement 2, 133-145 (Appendices B and C, Helsinki Declarations).

Guidelines for the Testing of Chemicals for Toxicity, Department of Health and Social Security Report of Health and Social Subjects No 27, HMSO, London, 1982.

Reports of the Scientific Committee for Food, 10th Series.

Reports of the Scientific Committee for Food, 12th Series.

Journal Officiel de la République Française No C 8549 of 25 September 1980.

Guidance on the preparation of summaries of data on chemicals in food, consumer products, and the environment. (UK, DHSS Report 30).

Introductory remarks in "List of approved food additives", October 1985 (English translation of document of the NFA of Denmark).

Principles for the Safety Assessment of Food Additives and Contaminants in Food. Environment Health Criteria 70 (World Health Organization, Geneva, 1987).

Report on Food Additives and Contaminants; Technological and Toxicological Guides. Netherlands Nutrition Council, Ministry of Welfare, Health and Cultural Affairs. December 1985.

BILAG ANHANG ΠΑΡΑΡΤΗΜΑ ANNEX ANEXO ANNEXE ALLEGATO BIJLAGE

ANEXO

II

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de los Consumidores
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ANEXO

III

	B	DK	D	E	F	GR	IRL	I	L	NL	P	UK	SCF
*D	2	1	7	3	3		1		1	1		3	2
*S	20	4	7	3	4		5		2	2		25	35
micro-film/ fiche		1	0									2	1

* D = dossier, dokumentationsmateriale, antrag, expediente, processo

* S = summary, résumé, zusammenfassung, resumen, sintesi, samenvatting, resumo

ANNEX IV

General criteria for the use of food additives*

1. Food additives can be approved only provided that

   - there can be demonstrated a reasonable technological need and the purpose cannot be achieved by other means which are economically and technologically practicable,

   - they present no hazard to health of the consumer at the level of use proposed, so far as can be judged on the scientific evidence available,

   - they do not mislead the consumer.

2. The use of food additives may be considered only where there is evidence that the proposed use of the additive would have demonstrable advantages of benefit to the consumer, in other words it is necessary to establish the case for what is commonly referred to as 'need'. The use of food additives should serve one or more of the purposes set out from points (a) to (d) and only where these purposes cannot be achieved by other means which are economically and technologically practicable and do not present a hazard to the health of the consumer :

   (a) to preserve the nutritional quality of the food; an intentional reduction in the nutritional quality of a food would be justified only where the food does not constitute a significant item in a normal diet or where the additive is necessary for the production of foods for groups of consumers having special dietary needs;

   (b) to provide necessary ingredients or constituents for foods manufactured for groups of consumers having special dietary needs;

   (c) to enhance the keeping quality or stability of a food or to improve its organoleptic properties, provided that this does not so change the nature, substance or quality of the food as to deceive the consumer;

   (d) to provide aids in manufacture, processing, preparation, treatment, packing, transport or storage of food, provided that the additive is not used to disguise the effects of the use of faulty raw materials of undesirable (including unhygienic) practices or techniques, during the course of any of these activities.

3. To assess the possible harmful effects of a food additive or derivatives thereof, it must be subjected to appropriate toxicological testing and evaluation. The evaluation should also take into account, for example, any cumulative, synergistic or potentiating effect of its use and the phenomenon of human intolerance to substances foreign to the body.

4. All food additives must be kept under continuous observation and must be re-evaluated whenever necessary in the light of changing conditions of use and new scientific information.

5. Food additives must at all times comply with the approved criteria of purity.

6. Approval for foor additives must :

   (a) specify the foodstuffs to which these additives may be added and the conditions under which they may be added;

   (b) be limited to the lowest level of use necessary to achieve the desired effect;

   (c) take into account any acceptable daily intake, or equivalent assessment, established for the food additive and the probable daily intake of it from all sources. Where the food additive is to be used in foods eaten by special groups of consumers, account should be taken of the possible daily intake of the food additive by consumers in those groups.

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* Annex II in COUNCIL DIRECTIVE 89/107/EEC of 21 December 1988 on the approximation of the laws of the Member States concerning food additives authorized for use in foodstuffs intended for human consumption; OJ L 40 of 11.2.89, p. 27.

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Presentation of an application for assessment of a food additive prior to its authorization

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