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Proposal for a

COUNCIL DIRECTIVE

on the fixing of guidelines for the assessment of certain products used in animal nutrition

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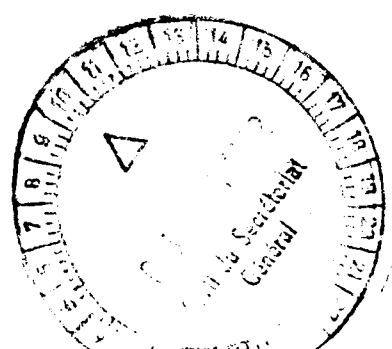
(submitted to the Council by the Commission)

COM(82) 615 final



COM 615

EXPLANATORY MEMORANDUM

On 30 June 1982, the Council adopted Directive 82/471/EEC concerning certain products used in animal nutrition on account of their protein content.

The purpose of that framework directive was to authorize - under certain conditions - the production and use of bioproteins for animal feeding. More particularly, the purpose was to control not only the use of certain well-known products such as amino acids, non-protein nitrogenous compounds and certain yeasts, but above all the use of novel proteins obtained from algae, fungi and the culture of micro-organisms (bacteria, yeast) on substrates of various origins such as petroleum or methanol.

In order to establish every possible guarantee ensuring the safeguard of human and animal health and protection of the environment, the Council decided to make protein products obtained from bacteria, yeasts, algae and inferior fungi subject to a very severe authorization procedure, under which the Commission will be required to consult the Scientific Committee for Animal Nutrition and the Scientific Committee for Food, and to obtain the opinion of the Standing Committee for Feedingstuffs.

Furthermore, to ensure compliance with the provisions on human and animal health in the framework Directive, Article 7 provides that, for each product, the Member State concerned must send a dossier officially to all the other Member States and to the Commission and to the members of the Scientific Committees. This dossier must be drawn up in accordance with guidelines which the Council undertook to adopt in time for them to apply as from the date of application of the basic Directive.

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Accordingly, the purpose of the present Directive is to lay down the said guidelines for the presentation of the product dossiers referred to in Article 7 of Directive 82/471/EEC. These guidelines will be used as a reference for assessing the products concerned in the light of current scientific knowledge and for ensuring that such products meet the basic criteria laid down for their authorization.

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THE COUNCIL OF THE EUROPEAN COMMUNITIES,

Having regard to the Treaty establishing the European Economic Community,

Having regard to Council Directive 82/471 /EEC of 30 June 1982 concerning certain products used in animal nutrition [1], and in particular Article 7 thereof,

Having regard to the proposal from the Commission,

Whereas Directive 82/471/EEC provides that the products belonging to certain groups must be examined on the basis of a dossier forwarded officially to the Member States and the Commission ;

Whereas such dossiers must make it possible to verify that the products in question comply with the general principles laid down in the Directive in respect of the inclusion of new products in the Annex ;

Whereas it has been found necessary to provide for the dossiers to be compiled in accordance with common guidelines defining, for each principle, the scientific data which make it possible to identify and characterize the products concerned and the studies necessary in order to evaluate their nutritional properties and biological effects ; whereas these guidelines must be applicable on the date on which Directive 82/471/ EEC itself enters into force ;

Whereas the guidelines are intended primarily as a general guide ; whereas, depending on the nature of the product or its conditions of use, the extent of the studies necessary in order to evaluate its properties or its effects may vary ;

Whereas the guidelines have been drawn up on the basis of present scientific and technical knowledge and they may be adapted if necessary to any developments in this sphere,

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(1) J.O. Nº L 213, 21.7.1982, p. 8.

HAS ADOPTED THIS DIRECTIVE :

Article 1

Member States shall prescribe that the dossiers on the products listed in points 1.1. and 1.2. of the Annex to Directive 82/471/EEC are to be compiled in accordance with the guidelines set out in the Annex hereto.

Article 2

Member States shall bring into force on 13 July 1984 the laws, regulations or administrative provisions necessary in order to comply with this Directive. They shall forthwith inform the Commission thereof.

Article 3

This Directive is addressed to the Member States.

Done at Brussels, For the Council

GUIDELINES FOR THE ASSESSMENT OF CERTAIN PRODUCTS USED IN ANIMAL NUTRITION

GENERAL ASPECTS

This document is intended as a guide for establishing dossiers on products listed in item 1 of the Annex of Council Directive 82/471/EEC of 30 June 1982 concerning certain products used in animal nutrition (1), which have been obtained from culturing microorganisms and which are proposed as a new source of proteins in animal nutrition. These dossiers should enable an assessment of such products based on the present state of knowledge and should ensure their compliance with the fundamental principles laid down for permitting their use, which are the subject of the provisions of Article 6(2) of the abovementioned Directive.

All the studies outlined in this document may be required and, if necessary, additional information may be requested. As a general rule, all the information necessary to establish the identity of the microorganism and the composition of the culture medium, and also the manufacturing process, characteristics, presentation, conditions of use, methods of determination and nutritional properties of the product must be provided. The same applies to the information necessary to assess the tolerance of the product by the target species and the risks for man and the environment, which could result directly or indirectly from the use of the product. The toxicological studies required for this purpose will depend on the nature of the product, the animal species concerned and the metabolism of the product in laboratory animals.

The documentation to be provided should include detailed reports, presented in the order and with the numbering proposed in these guidelines and should be accompanied by a summary. The omission of any proposed studies should be justified. The publications quoted as references should be attached.

OBSERVATIONS

The term "product", as used in these guidelines, refers to any proteinaceous product in the state in which it will be presented as feedingstuff or component of a feedingstuff.

Any modification in the manufacturing process or in the conditions of use of a product will require notification and, if necessary, additional documentation for a new assessment.

The guidelines will be updated as new scientific knowledge develops.

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(1) OJ No L 213, 21.7.1982, p. 8

PRESENTATION OF STUDIES

I. Microorganism, culture medium and manufacturing process, characteristics of product, presentation and conditions of use, methods of determination.

II. Studies on the nutritional properties of the product.

III. Studies on the biological consequences of the use of the product in animal nutrition.

IV. Other relevant studies.

SECTION I : MICROORGANISM, CULTURE MEDIUM AND MANUFACTURING PROCESS, CHARACTERISTICS OF PRODUCT, PRESENTATION AND CONDITIONS OF USE, METHODS OF DETERMINATION

1. MICROORGANISM

1.1. Classification, morphology, biological properties, any genetic manipulation.

1.2. Innocuity, possible survival outside the fermenter and environmental consequences.

1.3. Constancy and purity of strains cultivated. Methods used to check these criteria.

2. CULTURE MEDIUM AND MANUFACTURING PROCESS

2.1. Composition of substrate, added substances, etc.

2.2. Manufacturing and purification processes. Methods used to check the constancy of composition of the culture product and the detection of any chemical and biological contamination during production.

2.3. Technical processes of preparation for use.

3. CHARACTERISTICS OF PRODUCT

3.1. Physical and physico-chemical properties : macro- and micro-morphology, particle size, density, specific weight, hygroscopicity, solubility, solution characteristics (pH, rheological characteristics), electrostatic properties, etc.

3.2. Chemical composition :

3.2.1. Content of moisture, crude protein, crude fat, crude fibre, ash, nitrogen-free extract. Limits of variation.

3.2.2. Content of total, ammonium, amide, nitrate and nitrite nitrogen, true protein. Qualitative and quantitative composition of total and free amino acids, nucleic acids (purine and pyrimidine bases).

3.2.3. Qualitative and quantitative composition of total lipids : fatty acids, non-saponifiable matter, lipid soluble pigments, etc.

3.2.4. Qualitative and quantitative composition of carbohydrates and related substances.

3.2.5. Qualitative and quantitative composition of inorganic components.

3.2.6. Qualitative and quantitative composition of vitamins.

3.2.7. Qualitative and quantitative compositon of the other constituents : additives, residues of substrate and solvents, contaminants (in particular, polycyclic aromatic hydrocarbons, nitrosamines), etc.

3.3. Contamination by microorganisms during the manufacturing process.

3.4. Behaviour and stability of the product, as such and when mixed with feedingstuffs in current use, during storage.

4. PRESENTATION AND CONDITIONS OF USE

4.1. Proposed names for marketing the product.

4.2. Proposed formulations for marketing the product.

4.3. Intended use of the product in animal nutrition. Proposed concentrations in complete and complementary feedingstuffs for the animal species concerned.

5. METHODS OF DETERMINATION

Qualitative and quantitative methods for determination of the product in complete and complementary feedingstuffs.

N.B. : Description of these methods should be accompanied by information as to specificity, sensitivity, limits of detection, margin of error, possible interferences by other substances. Samples of the product in its various proposed presentations should be available.

SECTION II : STUDIES ON THE NUTRITIONAL PROPERTIES OF THE PRODUCT

1. ASSESSMENT OF PROTEIN VALUE

1.1. Chemical and/or microbiological studies.

1.2. Studies on laboratory animals (preferably rats) : digestibility, protein efficiency ratio (PER), biological value of the product compared with refcrence proteins.

2. STUDIES ON TARGET SPECIES

The following studies should be performed on each target species in comparison with a control group receiving, under the same conditions of nutritional balance, a diet in current use containing equivalent amounts of protein nitrogen.

2.1. Protein and energy supplementation value of the product in the rations under the proposed conditions of use at various physiological stages of the animals (growing period, pregnancy, laying, etc.).

2.2. Influence of the product under the proposed conditions of use on growth rate, feed conversion rate, morbidity, mortality, etc.

2.3. Optimum levels of incorporation of the product in the rations.

2.4. Effect of the product under the proposed conditions of use on the composition and on nutritive, technological and organoleptic quality of meat, offal, eggs and milk.

3. EXPERIMENTAL CONDITIONS IN THE STUDIES ON TARGET SPECIES

Give a detailed description of the tests performed and provide the following data :

3.1. Species, breed, age and sex of the animals, identification procedure.

3.2. Number of test and control groups; number of animals in each group (the number should be large enough for statistical analysis using suitable statistical parameters).

3.3. Levels of incorporation of the product, qualtitative and quantitative composition of the ration and its analysis.

3.4. Location of each experiment, physiological state and animal health conditions, rearing conditions (these should reflect those used in practice in the Community).

3.5. Exact duration of testing and date of the analyses performed.

3.6. Adverse effects which occured during the experiment and time of their appearance.

SECTION III : STUDIES CONCERNING THE BIOLOGICAL CONSEQUENCES OF THE USE OF THE PRODUCT IN ANIMAL NUTRITION

The studies outlined in this section are intended to permit assessment of the safety in use of the product in the target species, and of the risks for man and the environment which could result directly or indirectly from this use. The toxicological studies required for this purpose will depend on the nature of the product, the animal species concerned and the metabolism of the product in laboratory animals.

1. STUDIES ON TARGET SPECIES

The following studies should be performed on each target species in comparison with a control group receiving, under the same conditions of nutritional balance, a diet in current use containing equivalent amounts of protein nitrogen.

1.1. Maximum incorporation rates of the product in the ration without producing any adverse effect.

1.2. Effects of ingestion of the product under the proposed conditions of use on microorganisms of the flora of the alimentary tract and on colonization of pathogens in the alimentary tract.

1.3. Investigation under the proposed conditions of use of possible residues of the product (substrate, culture medium, solvents, contaminants) in animal products (meat, milk, eggs, etc.).

1.4. Investigation under the proposed conditions of use of possible residues of the product (substrate, culture medium, solvents, contaminants) in excreta.

2. STUDIES ON LABORATORY ANIMALS

2.1. Metabolism

Fate of the product in the animal : absorption, elimination, etc.

2.2. Mutagenicity

Investigations of potential mutagenicity due to contaminants (in particular mycotoxins) or residues of the product (substrate, culture, medium, solvents), including *in vitro* screening tests using metabolic activation systems.

2.3. Toxicological studies

The following studies should be performed in comparison with control groups receiving, under the same conditions of nutritional balance, a diet in current use containing equivalent amounts of protein nitrogen. Toxic effects should be investigated to elucidate their cause and mechanisms and to ascertain that they do not result from nutritional imbalance or from an overdosage of the product in the diet.

2.3.1. Subchronic toxicity (at least 90 days)

In general, these studies should be carried out on two animal species, one of which being a rodent. The product should be administered in the daily ration in at least two levels of incorporation. If possible, these should be chosen so as to determine a no-effect level and a level showing some adverse effect. The experimental groups should contain an adequate number of animals of each sex. A control group should always be included. All relevant biological data should be recorded at appropriate intervals, particularly data on growth rate, feed consumption, haematology, urine analysis, biochemical parameters, mortality, organ weights, gross pathology and histopathology of major organs and tissues. The results should be presented in detail and, as far as possible, should include statistical assessment.

2.3.2. Chronic Toxicity

In general, chronic toxicity studies should be carried out on two animal species, one of which being a rodent. The product should be administered in the daily ration in at least two levels of incorporation. Experiments should extend for a minimum of two years in the rat or 80 weeks in mice. The experimental groups should contain an adequate number of animals of each sex. A control group should always be included. The experiment, if continued beyond the minimum period, should be terminated when survival in any but the group with the highest level of incorporation has fallen to 20 %.
The biological examinations mentioned under item 2.3.1. should be carried out preferably on a small satellite group of animals at appropriate intervals throughout the experiment and on the surviving animals at the end of the experiment. For assessing carcinogenicity, particular attention should be paid to the time of appearance, the histological types of any observed tumours and their incidence. Any effect on the incidence of tumours and/or the incidence or progress of diseases should be assessed by reference to control groups, as indicated in paragraph 2.3. The result should be presented in detail and, as far as possible, should include statistical assessment.

2.4. Other studies

Reproduction studies should extend over at least two filial generations and may be combined with embryotoxicity including teratogenicity studies. Particular attention should be paid to fertility, fecundity and observation on post-natal development of litters.

2.5. Experimental conditions in the studies on laboratory animals

Give detailed description of the tests performed and provide the following data :

2.5.1. Species, breed, strain and sex of animals.

2.5.2. Number of test and control groups, number of animals in each group (the number should be large enough for statistical analysis using suitable statistical parameters).

2.5.3. Levels of incorporation of the product, qualitative and quantitative composition of the ration and its analysis.

2.5.4. General rearing conditions throughout the period of testing.

2.5.5. Exact duration of testing and date of examinations performed.

2.5.6. Rate and timing of deaths for the various test groups.

2.5.7. Pathological incidents which occurred during the experiment and time of their appearance.

3. STUDIES CONCERNING THE ENVIRONMENT

Depending on the nature of possible residues of the product (substrate, culture medium, solvents, contaminants) in excreta of target species, data on the fate of these residues in manure, soil and water and also their effects on soil biology, plant growth and aquatic life may be required.

SECTION IV : OTHER RELEVANT STUDIES

Depending on the nature and the conditions of use of the product, data on allergic effects, on irritation of the skin and mucous membranes of the eye, respiratory or digestive tract may be required to assess possible risks in handling the product and to prevent them.