4. 毒性データ

4.1 毒性試験

食品酵素の毒性試験の必要性については、酵素の基原、その組成や特性、既知の毒性試験、食品中での酵素の利用についての記録のある履歴などの既知情報や推定曝露レベルに基づいて判断すること。

原則的には毒性試験は必要であるが、例外もある（4.1.2 に詳細）。

4.1.1 毒性試験データセット

毒性試験データに必須なデータセットは以下のとおりである。

i. 遺伝毒性の評価

遺伝毒性の評価は、遺伝子突然変異と染色体異常(構造異常および数的異常)の両方をカバーする *in vitro* 試験から開始すること。

通常、2 種類の *in vitro* 試験が必要とされる（以下）。

- 細菌を用いる遺伝子突然変異誘発性試験（Ames 試験; OECD 指針 471）。Ames 試験が適切でない場合には、哺乳類細胞を用いた遺伝子突然変異誘発性試験、望ましくは、コロニーサイズ解析のあるマウスリンパ種 TK（thymidine kinase）試験（OECD 指針 476）に換えることができる。
- 染色体異常を指標とする *in vitro* 試験（OECD 指針 473）、または小核試験（OECD 指針 487 ドラフト）、またはコロニーサイズ解析のあるマウスリンパ種 TK 試験（OECD 指針 476）。

いかなる場合でも、少なくとも 2 つの *in vitro* 試験を実施すること。

上記の *in vitro* 試験のいずれかで陽性となった場合には、その食品酵素や食品酵素に存在する可能性のある残留成分、分解生成物および製造工程由来の物質が変異原性を持つことが示唆される。遺伝毒性試験における陽性反応は、*in vivo* での遺伝毒性が在るかどうか確定するためにさらなる評価が必要となる場合がある。食品に遺伝毒性発癌物質を意図的に添加することは認められない(Barlow 等、2006)。

通常、1 つ以上の *in vitro* 試験で陽性の場合、*in vivo* 試験での追加検討が必要となるが、*in vitro* では陽性の結果であっても *in vivo* では陽性とならない根拠を証明すればこの限りではない。この方針は、変異誘発性試験についての改訂版「WHO/IPCS Harmonized Scheme (Eastmond 等、2009)」に詳述された一般的な検討方針に従っている。

試験により感度の違い、指標の違い、その他の変動要因があるため、適切な *in vivo* 試験を選択することが成功の鍵を握っている。あらゆる有用な情報から個別事案として専門家が判断することが肝要である。このことから、あらかじめ意思決定ツリーを作成して用いるよりも、柔軟性をもって考察しながら進めていくことが望ましい。

in vitro 試験での陽性結果に対する追加試験についての指導書は、近年欧州化学物質庁（ECHA)により発行された指導書文書（ECHA2008、ECB2003）から入手できる。この指導書では、以下の試験のいずれかを実施することを推奨している。

1. げっ歯類の骨髄細胞またはマウス末梢血を用いた小核試験（OECD 指針 474）もしくはげっ歯類の骨髄細胞での染色体異常誘発試験（OECD 指針 475)。
2. コメットアッセイ（単細胞ゲル電気泳動）
3. 全ての組織に存在するレポーター遺伝子（例えば *lacI*、*lacZ* または cII）を用いたトランスジェニックげっ歯類モデルにおける遺伝子突然変異試験。
4. ラット肝不定期 DNA 合成（UDS）テスト

この ECHA 指導書によれば、「*in vivo* 試験を選択する際に *in vitro* 応答（すなわち、遺伝子突然変異、染色体の構造異常および数的異常）の本質を考慮すること」と記載されている。 例えば被験物質が *in vitro* 試験で染色体異常誘発の事実を示した場合、小核試験、染色体異常試験、またはコメットアッセイのいずれかを追加試験として実施するのが最適であろう。しかしながら、*in vitro* の小核試験で陽性が観察された場合には、げっ歯動物での小核試験が、染色体異常誘発性および異数性誘発性を最もよく調べられるという点で、適当であろう。

遺伝子突然変異を特異的に誘発すると考えられる物質に対しては、コメットアッセイおよびトランスジェニック試験も適切であるが、ラット肝臓 UDS テストが適切と考えられる（Speit、2008)。 コメットアッセイおよびトランスジェニック試験により、その物質の薬物動態（毒性試験における全身的曝露の評価）や薬物動力学の既知情報に基づいて、より変動が大きく、最も顕著に結果が出る可能性がある組織群がわかる。UDS 試験およびコメットアッセイは、推定される DNA 傷害の検出を指標とした試験であることに注意すること。 対照的に、トランスジェニック試験は永久的な変異を測定する（ECHA2008)。Pfuhler 等（2007） により示された通り、単一の試験において *in vivo* 小核試験とコメットアッセイを組合せて試験することも可能である。

他の試験法（例えば DNA 付加体試験）も、遺伝毒性のメカニズムを明確にするために実施する意義があるかもしれない。

これらの試験法の感度（発癌物質であれば陽性と判定できる）と特異性（非発癌物質であれば陰性と判定できる）が、最近 Kirkland と Speit（2008）により解析されたので、是非参考にされたい。

ii 全身毒性評価

亜慢性経口毒性試験は、OECD 指針 408（OECD、2000a）に従って実施すべきである。

可能な限り、毒性試験は国際的に合意されたプロトコルを用いて実施すべきである。OECD および欧州法のその他の条項に書かれた試験法が推奨される。 試験指針の最新版に従って実施すべきである。試験は、欧州指令 2004/10/EC[13] および 2004/09/EC[14] に示されている優良試験所規範（GLP）に従って実施され、実験室での試験の実施にあたり GLP コンプライアンスの陳述書に従って実施されること。

毒性試験は、製剤化のための成分を添加する前のものを被験物質（食品酵素のバッチ）として実施すること。

場合によっては、上記の指導内容から逸脱することが適切であるかもしれない。この逸脱とは、特定の試験の免除、代替のプロトコルの使用、あるいは代替の分析方法等を指す。逸脱が許可される条件として、その科学的正当性が示される必要があり、別途考察やメカニズムの実証が求められることがある。

[13] OJ L 50, 20.2.2004, p. 44

[14] OJ L 50, 20.2.2004, p. 28

もし、毒性試験が不十分な場合、食品酵素の分子学的また機能的な特性、食品中や消化管中での消滅、あるいは潜在的に曝露される程度に関わる入手可能な知識に因り、個別に安全性評価の追試験が要求されることがある。

例えば、長期間摂取による、消化管での影響を含む健康への影響の可能性に関する試験が必要とされる場合があり、又食品酵素のアレルゲン性の可能性に関する追加試験が要求される場合がある(4.2 項参照)。追加試験が必要かどうかの決定は EFSA によって個別に行われる。

4.1.2 毒性試験が不必要な場合

安全性評価に諮る全ての食品酵素については、適正な技術的データの提出が原則であるが、毒性データについての要求は、場合により減免されたり全く免除されることがある。毒性データの提出が免除されるには、以下のような理由があればよい。

- その食品酵素の基原の安全性、その組成や、特性およびその食品での使用について根拠のある歴史が明らかであること。その中で、何らかの毒性試験によって、摂取によるヒトの健康への有害作用がないことを示すこと。例えば、その酵素が動物や（非 GM）植物の可食部に含有される等、評価する上での根拠となるものは EFSA に提供しなければならない。
- QPS（適格な安全性の推定）標準に適合した微生物生産による食品酵素であること。これには、あらゆる残留物、分解生成物および製造工程由来の成分に関して全く懸念がないことを示すこと(EFSA, 2005)。
- その食品酵素について、同じ菌株由来のものが完全に試験済みであり、その酵素の製造工程が、当該菌株から製造される他の食品酵素と大して違いはない場合、この食品酵素についての一連の試験は免除される。この判断は個別になされる。

（上記の）正当性の根拠をドシエの中で詳述すること。ただし、さらなる説明を EFSA が求めることがある。

4.1.3 データの報告

標準的な毒性試験についてのデータは、関連する OECD 指針に示された推奨書式に則って報告すること。実施された各試験について漏れなく記載され、被験物質が間違いなくドシエに記載されたその食品酵素であることが、第 3.1.2.2 の規格に則した分析データにより支持されなければならない。

4.1.4 毒性および曝露データのレビューと結論

各毒性試験において、重要な所見があればそれを強調し、無作用量（NOEL）又は無毒性量（NOAEL)、及び他の関連情報と合わせて記載すること。もし動物で所見が見られる場合、所見が見られる用量と食品酵素の使用による食事からの推定曝露量との相関について、十分な安全マージンを設定するために議論すること。いかなる所見についてもそれを無視する場合はその理由を慎重に説明すること。その所見が有意である場合、その有意性についての解釈を結論に付記すること。

4.2 アレルゲン性

現時点で、経口摂取された際の酵素タンパク質やその分解物のアレルゲン性を正しく予測できる試験方法はない。しかし、遺伝子組換え植物に存在する新規発現タンパク質の安全性評価に用いられているアプローチを応用することで、食品酵素の潜在的なアレルゲン性についていくつかの情報を得る事ができる（EFSA, 2006a; FAO/WHO, 2001)。食品酵素の基原のアレルゲン性は考慮に入れるものとし、また可能であればアミノ酸配列や発現タンパク質と既知のアレルゲンとの構造類似性の検索を実施すること。もし、この一次スクリーニングにより懸念される要因があれば、たとえば、遺伝子組換え植物やそれを使用した食品や飼料のリスク評価に関する遺伝子組換え生物についての科学的パネルによる指導書に記載されているさらなる解析が必要である場合がある(EFSA, 2006a)。

他では、現場での安全性の評価など、他の目的のために実施された安全性評価（例えば感受性試験）の中で、適当なものがあれば提出すること。

5. 結論

個別の試験における選択や除外基準についての論理的根拠や、試験品と販売されている製品の規格の違いや既知のアレルゲンとの構造類似性についてなどの妥当性や不確実性についての議論を含めて、安全性情報および毒性試験について総括的な評価を行い、提出すること。推定されるヒトへの既知の曝露量を用いて、ヒトにおける潜在的なリスクについて総括的評価をすること。

6. ドシエの参考文献一覧

ドシエを提出する際に、完全な参考文献一覧を入れること。また、参考文献の全文コピーを提供すること。参考文献は、以下のように引用すること。

i. 公開情報

- 雑誌: 全著者名（全氏名とイニシャルを含む完全なリスト)、日付、論文の表題、雑誌名、巻数、ページ番号
- 図書: 著者、章または本の表題、編者(該当する場合)、発行人、所在地、日付、ページ番号(該当する場合)
- インターネット: 組織名、記事の表題、ウェブサイト、アクセス日

ii. 未発表データ

- 申請者の氏名、レポートの表題、参考文献(ある場合)、研究者氏名、研究室名、研究室の住所、日付

iii. 添付文書および研究報告

- 安全性評価に必要な引用文献の全文コピーをドシエに入れること。

iv. 全ての未発表の研究報告書の全文コピーを提出すること。未発表の研究の概要や要旨では不十分である。

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略語

AFSSA	フランス食品衛生安全局
CAS	化学情報検索サービス機関
COT	英国・食品・消費者製品・環境中化学物質・毒性委員会
DVFA	デンマーク獣医食品局
EC	欧州委員会（酵素委員会の場合も有る）
EC/IUBMB	国際生化学・分子生物学連合の酵素委員会
EFSA	欧州食品安全機関
EINECS	欧州既存化学物質リスト
ELINCS	欧州届出化学物質リスト
EU	欧州連合
FAO	国連食糧農業機関
FEEDAP	飼料添加物・飼料製品・飼料物質に関するパネル
GLP	優良試験所規範
GMM	遺伝子組換え微生物
GMO	遺伝子組換え生物
GMP	優良製造規範（製造管理および品質管理）
IUBMB	国際生化学・分子生物学連盟
JECFA	FAO/WHO 合同食品添加物専門家委員会
NOAEL	無毒性量
NOEL	無作用量
OECD	経済協力開発機構
QPS	適格な安全性の推定
SCF	食品科学委員会
TSE	伝達性海綿状脳症
TOS	総有機固形分
WHO	世界保健機関

附則 I：定義

酵素活性単位(U) - 標準条件下で、1 分間に 1 μmole の基質の変化を触媒する酵素の量(IUPAC、1974)

酵素活性単位(kat) –Katal は 1 秒間に 1mole の基質の変化を触媒する酵素の量を示す SI 活性単位である。 Katal は 1978 年に酵素活性単位(U)の代替として提案された。

1 kat = 60×10^6 U。

酵素活性 - 単位重量あたりの酵素活性単位 (U)または SI 単位 (kat)

食品酵素 [15] - 植物、動物、微生物から得られる産物、又は微生物を用いた醗酵工程により得られる生産物を含み、特定の生化学反応を触媒することのできる一つ又はそれ以上の酵素を含有し、技術的目的のために、食品の製造、加工、製剤化、処理、包装、輸送、保管のいずれかの工程で加えられる産物。

食品酵素剤 [16] - 一つ又はそれ以上の食品酵素と、食品添加物及び/又は食品成分から成り、保管、販売、標準化、希釈、溶解を容易にした製剤。

微生物 - 原核生物、原虫、微細藻類、およびすべての菌類(カビ、酵母、および糸状菌を含む)を指す言葉。 ただし、菌性の担子菌類子実体/菌糸は植物源と考えられている。

基原物質- 食品酵素の生産に用いられる動物、植物、担子菌類子実体/菌糸や微生物

全有機固形分(TOS) – 酵素剤中の基原物質に由来する部分と、製造工程で意図的に加えられる配合成分に関連する部分を区別するために、全有機固形分(TOS)は以下ように計算される。

%TOS=100-(A+W+D)

ただし、A = % 灰分、W = % 水分、D = % 希釈剤やその他の賦形剤

1) 食品酵素に関する EC 規則 No.1332/2008 にて定義

[15] 食品酵素に関する EC 規則 No.1332/2008 にて定義

[16] 食品酵素に関する EC 規則 No.1332/2008 にて定義

I

(Acts adopted under the EC Treaty/Euratom Treaty whose publication is obligatory)

REGULATIONS

REGULATION (EC) No 1331/2008 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 16 December 2008

establishing a common authorisation procedure for food additives, food enzymes and food flavourings

(Text with EEA relevance)

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty establishing the European Community, and in particular Article 95 thereof,

Having regard to the proposal from the Commission,

Having regard to the opinion of the European Economic and Social Committee [1],

Acting in accordance with the procedure laid down in Article 251 of the Treaty [2],

Whereas:

(1) The free movement of safe and wholesome food is an essential aspect of the internal market and contributes significantly to the health and well-being of citizens, and to their social and economic interests.

(2) A high level of protection of human life and health should be assured in the pursuit of Community policies.

(3) In order to protect human health, the safety of additives, enzymes and flavourings for use in foodstuffs for human consumption must be assessed before they are placed on the Community market.

(4) Regulation (EC) No 1333/2008 of the European Parliament and of the Council of 16 December 2008 on food additives [3], Regulation (EC) No 1332/2008 of the European Parliament and of the Council of 16 December 2008 on food enzymes [4] and Regulation (EC) No 1334/2008 of the European Parliament and of the Council of 16 December 2008 on flavourings and certain food ingredients with flavouring properties for use in and on foods [5] (hereinafter referred to as the sectoral food laws) lay down harmonised criteria and requirements concerning the assessment and authorisation of these substances.

(5) It is envisaged, in particular, that food additives, food enzymes and food flavourings, to the extent that the safety of food flavourings must be assessed in accordance with Regulation (EC) No 1334/2008 [on flavourings and certain food ingredients with flavouring properties for use in and on foods], must not be placed on the market or used in foodstuffs for human consumption, in accordance with the conditions laid down in each sectoral food law, unless they are included on a Community list of authorised substances.

(6) Ensuring transparency in the production and handling of food is absolutely crucial in order to maintain consumer confidence.

(7) In this context, it appears appropriate to establish for these three categories of substances a common Community assessment and authorisation procedure that is effective, time-limited and transparent, so as to facilitate their free movement within the Community market.

(1) OJ C 168, 20.7.2007, p. 34.

(2) Opinion of the European Parliament of 10 July 2007 (OJ C 175 E, 10.7.2008, p. 134), Council Common Position of 10 March 2008 (OJ C 111 E, 6.5.2008, p. 1), Position of the European Parliament of 8 July 2008 (not yet published in the Official Journal) and Council Decision of 18 November 2008.

(3) See page 16 of this Official Journal.

(4) See page 7 of this Official Journal.

(5) See page 34 of this Official Journal.

(8) This common procedure must be founded on the principles of good administration and legal certainty and must be implemented in compliance with those principles.

(9) This Regulation will thus complete the regulatory framework concerning the authorisation of the substances by laying down the various stages of the procedure, the deadlines for those stages, the role of the parties involved and the principles that apply. Nevertheless, for some aspects of the procedure, it is necessary to take the specific characteristics of each sectoral food law into consideration.

(10) The deadlines laid down in the procedure take into account the time needed to consider the different criteria set in each sectoral food law, as well as allowing adequate time for consultation when preparing the draft measures. In particular, the nine-months deadline for the Commission to present a draft regulation updating the Community list should not preclude the possibility of this being done within a shorter period.

(11) Upon receipt of an application the Commission should initiate the procedure and where necessary seek the opinion of the European Food Safety Authority (hereinafter referred to as the Authority) established by Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety [1] as soon as possible after the validity and applicability of the application have been assessed.

(12) In accordance with the framework for risk assessment in matters of food safety established by Regulation (EC) No 178/2002, the authorisation to place substances on the market must be preceded by an independent scientific assessment, of the highest possible standard, of the risks that they pose to human health. This assessment, which must be carried out under the responsibility of the Authority, must be followed by a risk management decision taken by the Commission under a regulatory procedure that ensures close cooperation between the Commission and the Member States.

(13) The authorisation to place substances on the market should be granted pursuant to this Regulation provided that the criteria for authorisation laid down under the sectoral food laws are satisfied.

(14) It is recognised that, in some cases, scientific risk assessment alone cannot provide all the information on which a risk management decision should be based, and that other legitimate factors relevant to the matter under consideration may be taken into account, including societal, economic, traditional, ethical and environmental factors and the feasibility of controls.

(15) In order to ensure that both business operators in the sectors concerned and the public are kept informed of the authorisations in force, the authorised substances should be included on a Community list created, maintained and published by the Commission.

(16) Where appropriate and under certain circumstances, the specific sectoral food law may provide for protection of scientific data and other information submitted by the applicant for a certain period of time. In this case, the sectoral food law should lay down the conditions under which these data may not be used for the benefit of another applicant.

(17) Networking between the Authority and the Member States' organisations operating in the fields within the Authority's mission is one of the basic principles of the Authority's operation. In consequence, in preparing its opinion, the Authority may use the network made available to it by Article 36 of Regulation (EC) No 178/2002 and by Commission Regulation (EC) No 2230/2004 [2].

(18) The common authorisation procedure for the substances must fulfil transparency and public information requirements while guaranteeing the right of applicants to preserve the confidentiality of certain information.

(19) Protecting the confidentiality of certain aspects of an application should be maintained as a consideration in order to protect the competitive position of an applicant. However, information relating to the safety of a substance, including, but not limited to, toxicological studies, other safety studies and raw data as such, should under no circumstances be confidential.

(20) Pursuant to Regulation (EC) No 178/2002, Regulation (EC) No 1049/2001 of the European Parliament and of the Council of 30 May 2001 regarding public access to European Parliament, Council and Commission documents [3] applies to documents held by the Authority.

[1] OJ L 31, 1.2.2002, p. 1.

[2] Regulation (EC) No 2230/2004 of 23 December 2004 laying down detailed rules for the implementation of European Parliament and Council Regulation (EC) No 178/2002 with regard to the network of organisations operating in the fields within the European Food Safety Authority's mission (OJ L 379, 24.12.2004, p. 64).

[3] OJ L 145, 31.5.2001, p. 43.

(21) Regulation (EC) No 178/2002 establishes procedures for taking emergency measures in relation to foodstuffs of Community origin or imported from third countries. It authorises the Commission to adopt such measures in situations where foodstuffs are likely to constitute a serious risk to human health, animal health or the environment and where such risk cannot be contained satisfactorily by measures taken by the Member State(s) concerned.

(22) In the interests of efficiency and legislative simplification, there should be a medium-term examination of the question whether to extend the scope of the common procedure to other legislation in the area of food.

(23) Since the objectives of this Regulation cannot be sufficiently achieved by the Member States on account of differences between national laws and provisions and can therefore be better achieved at Community level, the Community may adopt measures, in accordance with the principle of subsidiarity as set out in Article 5 of the Treaty. In accordance with the principle of proportionality, as set out in that Article, this Regulation does not go beyond what is necessary in order to achieve those objectives.

(24) The measures necessary for the implementation of this Regulation should be adopted in accordance with Council Decision 1999/468/EC of 28 June 1999 laying down the procedures for the exercise of implementing powers conferred on the Commission [1].

(25) In particular the Commission should be empowered to update the Community lists. Since those measures are of general scope and are designed to amend non-essential elements of each sectoral food law, *inter alia*, by supplementing it with new non-essential elements, they must be adopted in accordance with the regulatory procedure with scrutiny provided for in Article 5a of Decision 1999/468/EC.

(26) On grounds of efficiency, the normal time-limits for the regulatory procedure with scrutiny should be curtailed for the addition of substances to the Community lists and for adding, removing or changing conditions, specifications or restrictions associated with the presence of a substance on the Community lists.

(27) When, on imperative grounds of urgency, the normal time-limits for the regulatory procedure with scrutiny cannot be complied with, the Commission should be able to apply the urgency procedure provided for in Article 5a(6) of Decision 1999/468/EC for the removal of a substance from the Community lists and for adding, removing or changing conditions, specifications or restrictions associated with the presence of a substance on the Community lists,

HAVE ADOPTED THIS REGULATION:

CHAPTER I

GENERAL PRINCIPLES

Article 1

Subject matter and scope

1. This Regulation lays down a common procedure for the assessment and authorisation (hereinafter referred to as the common procedure) of food additives, food enzymes, food flavourings and source materials of food flavourings and of food ingredients with flavouring properties used or intended for use in or on foodstuffs (hereinafter referred to as the substances), which contributes to the free movement of food within the Community and to a high level of protection of human health and to a high level of consumer protection, including the protection of consumer interests. This Regulation shall not apply to smoke flavourings falling within the scope of Regulation (EC) No 2065/2003 of the European Parliament and of the Council of 10 November 2003 on smoke flavourings used or intended for use in or on foods [2].

2. The common procedure shall lay down the procedural arrangements for updating the lists of substances the marketing of which is authorised in the Community pursuant to Regulation (EC) No 1333/2008 [on food additives], Regulation (EC) No 1332/2008 [on food enzymes] and Regulation (EC) No 1334/2008 [on flavourings and certain food ingredients with flavouring properties for use in and on foods] (hereinafter referred to as the sectoral food laws).

3. The criteria according to which substances can be included on the Community list provided for in Article 2, the content of the regulation referred to in Article 7 and, where applicable, the transitional provisions concerning ongoing procedures are laid down in each sectoral food law.

Article 2

Community list of substances

1. Under each sectoral food law, substances that have been authorised to be placed on the Community market shall be included on a list the content of which is determined by the said law (hereinafter referred to as the Community list). The Community list shall be updated by the Commission. It shall be published in the *Official Journal of the European Union*.

2. 'Updating the Community list' means:

(a) adding a substance to the Community list;

[1] OJ L 184, 17.7.1999, p. 23.

[2] OJ L 309, 26.11.2003, p. 1.

(b) removing a substance from the Community list;

(c) adding, removing or changing conditions, specifications or restrictions associated with the presence of a substance on the Community list.

CHAPTER II

COMMON PROCEDURE

Article 3

Main stages of the common procedure

1. The common procedure for updating the Community list may be started either on the initiative of the Commission or following an application. Applications may be made by a Member State or by an interested party, who may represent several interested parties, in accordance with the conditions provided for by the implementing measures referred to in Article 9(1)(a) (hereinafter referred to as the applicant). Applications shall be sent to the Commission.

2. The Commission shall seek the opinion of the European Food Safety Authority (hereinafter referred to as the Authority), to be given in accordance with Article 5.

However, for the updates referred to in Article 2(2)(b) and (c), the Commission shall not be required to seek the opinion of the Authority if the updates in question are not liable to have an effect on human health.

3. The common procedure shall end with the adoption by the Commission of a regulation implementing the update, in accordance with Article 7.

4. By way of derogation from paragraph 3, the Commission may end the common procedure and decide not to proceed with a planned update, at any stage of the procedure, if it judges that such an update is not justified. Where applicable, it shall take account of the opinion of the Authority, the views of Member States, any relevant provisions of Community law and any other legitimate factors relevant to the matter under consideration.

In such cases, where applicable, the Commission shall inform the applicant and the Member States directly, indicating in its letter the reasons for not considering the update justified.

Article 4

Initiating the procedure

1. On receipt of an application to update the Community list, the Commission:

(a) shall acknowledge receipt of the application in writing to the applicant within 14 working days of receiving it;

(b) where applicable, shall as soon as possible notify the Authority of the application and request its opinion in accordance with Article 3(2).

The application shall be made available to the Member States by the Commission.

2. Where it starts the procedure on its own initiative, the Commission shall inform the Member States and, where applicable, request the opinion of the Authority.

Article 5

Opinion of the Authority

1. The Authority shall give its opinion within nine months of receipt of a valid application.

2. The Authority shall forward its opinion to the Commission, the Member States and, where applicable, the applicant.

Article 6

Additional information concerning risk assessment

1. In duly justified cases where the Authority requests additional information from applicants, the period referred to in Article 5(1) may be extended. After consulting the applicant, the Authority shall lay down a period within which this information can be provided and shall inform the Commission of the additional period needed. If the Commission does not object within eight working days of being informed by the Authority, the period referred to in Article 5(1) shall be automatically extended by the additional period. The Commission shall inform the Member States of the extension.

2. If the additional information is not sent to the Authority within the additional period referred to in paragraph 1, the Authority shall finalise its opinion on the basis of the information already provided.

3. Where applicants submit additional information on their own initiative, they shall send it to the Authority and to the Commission. In such cases, the Authority shall give its opinion within the original period without prejudice to Article 10.

4. The additional information shall be made available to the Member States and the Commission by the Authority.

Article 7

Updating the Community list

1. Within nine months of the Authority giving its opinion, the Commission shall submit to the Committee referred to in Article 14(1) a draft regulation updating the Community list, taking account of the opinion of the Authority, any relevant provisions of Community law and any other legitimate factors relevant to the matter under consideration.

In those cases where an opinion of the Authority has not been requested, the nine-month period shall start from the date the Commission receives a valid application.

2. In the Regulation updating the Community list, the considerations on which it is based shall be explained.

3. Where the draft regulation is not in accordance with the opinion of the Authority, the Commission shall explain the reasons for its decision.

4. The measures, designed to amend non-essential elements of each sectoral food law, relating to the removal of a substance from the Community list, shall be adopted in accordance with the regulatory procedure with scrutiny referred to in Article 14(3).

5. On grounds of efficiency, the measures designed to amend non-essential elements of each sectoral food law, *inter alia*, by supplementing it, relating to the addition of a substance to the Community list and for adding, removing or changing conditions, specifications or restrictions associated with the presence of the substance on the Community list, shall be adopted in accordance with the regulatory procedure with scrutiny referred to in Article 14(4).

6. On imperative grounds of urgency, the Commission may use the urgency procedure referred to in Article 14(5) for the removal of a substance from the Community list and for adding, removing or changing conditions, specifications or restrictions associated with the presence of a substance on the Community list.

Article 8

Additional information concerning risk management

1. Where the Commission requests additional information from applicants on matters concerning risk management, it shall determine, together with the applicant, a period within which that information can be provided. In such cases, the period referred to in Article 7 may be extended accordingly. The Commission shall inform the Member States of the extension and shall make the additional information available to the Member States once it has been provided.

2. If the additional information is not sent within the additional period referred to in paragraph 1, the Commission shall act on the basis of the information already provided.

CHAPTER III

MISCELLANEOUS PROVISIONS

Article 9

Implementing measures

1. In accordance with the regulatory procedure referred to in Article 14(2), within a period of no longer than 24 months from the adoption of each sectoral food law, the implementing measures for this Regulation shall be adopted by the Commission, and shall concern in particular:

(a) the content, drafting and presentation of the application referred to in Article 4(1);

(b) the arrangements for checking the validity of applications;

(c) the type of information that must be included in the opinion of the Authority referred to in Article 5.

2. With a view to the adoption of the implementing measures referred to in paragraph 1(a), the Commission shall consult the Authority, which, within six months of the date of entry into force of each sectoral food law, shall present it with a proposal concerning the data required for risk assessment of the substances concerned.

Article 10

Extension of time periods

In exceptional circumstances, the periods referred to in Article 5(1) and Article 7 may be extended by the Commission on its own initiative or, where applicable, at the Authority's request, if the nature of the matter in question so justifies, without prejudice to Article 6(1) and Article 8(1). In such cases the Commission shall, where appropriate, inform the applicant and the Member States of the extension and the reasons for it.

Article 11

Transparency

The Authority shall ensure the transparency of its activities in accordance with Article 38 of Regulation (EC) No 178/2002. In particular, it shall make its opinions public without delay. It shall also make public any request for its opinion as well as any extension of period pursuant to Article 6(1).

Article 12

Confidentiality

1. Among the information provided by applicants, confidential treatment may be given to information the disclosure of which might significantly harm their competitive position.

Information relating to the following shall not, in any circumstances, be regarded as confidential:

(a) the name and address of the applicant;

(b) the name and a clear description of the substance;

(c) the justification for the use of the substance in or on specific foodstuffs or food categories;

(d) information that is relevant to the assessment of the safety of the substance;

(e) where applicable, the analysis method(s).

2. For the purposes of implementing paragraph 1, applicants shall indicate which of the information provided they wish to be treated as confidential. Verifiable justification must be given in such cases.

3. The Commission shall decide after consulting with the applicants which information can remain confidential and shall notify applicants and the Member States accordingly.

4. After being made aware of the Commission's position, applicants shall have three weeks in which to withdraw their application so as to preserve the confidentiality of the information provided. Confidentiality shall be preserved until this period expires.

5. The Commission, the Authority and the Member States shall, in accordance with Regulation (EC) No 1049/2001, take the necessary measures to ensure appropriate confidentiality of the information received by them under this Regulation, except for information which must be made public if circumstances so require in order to protect human health, animal health or the environment.

6. If an applicant withdraws, or has withdrawn, its application, the Commission, the Authority and the Member States shall not disclose confidential information, including information the confidentiality of which is the subject of disagreement between the Commission and the applicant.

7. The implementation of paragraphs 1 to 6 shall not affect the circulation of information between the Commission, the Authority and the Member States.

Article 13

Emergencies

In the event of an emergency concerning a substance on the Community list, particularly in the light of an opinion of the Authority, measures shall be adopted in accordance with the procedures referred to in Articles 53 and 54 of Regulation (EC) No 178/2002.

Article 14

Committee

1. The Commission shall be assisted by the Standing Committee on the Food Chain and Animal Health established by Article 58 of Regulation (EC) No 178/2002.

2. Where reference is made to this paragraph, Articles 5 and 7 of Decision 1999/468/EC shall apply, having regard to the provisions of Article 8 thereof.

The period laid down in Article 5(6) of Decision 1999/468/EC shall be set at three months.

3. Where reference is made to this paragraph, Article 5a(1) to (4) and Article 7 of Decision 1999/468/EC shall apply, having regard to the provisions of Article 8 thereof.

4. Where reference is made to this paragraph, Article 5a(1) to (4) and (5)(b) and Article 7 of Decision 1999/468/EC shall apply, having regard to the provisions of Article 8 thereof.

The time-limits laid down in Article 5a(3)(c) and (4)(b) and (e) of Decision 1999/468/EC shall be two months, two months and four months respectively.

5. Where reference is made to this paragraph, Article 5a(1), (2), (4) and (6) and Article 7 of Decision 1999/468/EC shall apply, having regard to the provisions of Article 8 thereof.

Article 15

Competent authorities of the Member States

Not later than six months after the entry into force of each sectoral food law, Member States shall forward to the Commission and to the Authority, in relation to each sectoral food law, the name and address of the national competent authority for the purposes of the common procedure, as well as a contact point therein.

CHAPTER IV

FINAL PROVISION

Article 16

Entry into force

This Regulation shall enter into force on the 20th day following its publication in the *Official Journal of the European Union*.

For each sectoral food law, it shall apply from the date of application of the measures referred to in Article 9(1).

Article 9 shall apply from 20 January 2009.

This Regulation shall be binding in its entirety and directly applicable in all Member States.

Done at Strasbourg, 16 December 2008.

For the European Parliament
The President
H.-G. PÖTTERING

For the Council
The President
B. LE MAIRE

REGULATION (EC) No 1332/2008 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 16 December 2008

on food enzymes and amending Council Directive 83/417/EEC, Council Regulation (EC) No 1493/1999, Directive 2000/13/EC, Council Directive 2001/112/EC and Regulation (EC) No 258/97

(Text with EEA relevance)

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty establishing the European Community, and in particular Article 95 thereof,

Having regard to the proposal from the Commission,

Having regard to the opinion of the European Economic and Social Committee [1],

Acting in accordance with the procedure laid down in Article 251 of the Treaty [2],

Whereas:

(1) The free movement of safe and wholesome food is an essential aspect of the internal market and contributes significantly to the health and well-being of citizens, and to their social and economic interests.

(2) A high level of protection of human life and health should be assured in the pursuit of Community policies.

(3) Food enzymes other than those used as food additives are not currently regulated or are regulated as processing aids under the legislation of the Member States. Differences between national laws, regulations and administrative provisions concerning the assessment and authorisation of food enzymes may hinder their free movement, creating conditions for unequal and unfair competition. It is therefore necessary to adopt Community rules harmonising national provisions relating to the use of enzymes in foods.

(4) This Regulation should only cover enzymes that are added to food to perform a technological function in the manufacture, processing, preparation, treatment, packaging, transport or storage of such food, including enzymes used as processing aids (hereinafter referred to as food enzymes). The scope of this Regulation should therefore not extend to enzymes that are not added to food to perform a technological function but are intended for human consumption, such as enzymes for nutritional or digestive purposes. Microbial cultures traditionally used in the production of food such as cheese and wine, and which may incidentally produce enzymes but are not specifically used to produce them, should not be considered food enzymes.

(5) Food enzymes used exclusively in the production of food additives falling within the scope of Regulation (EC) No 1333/2008 of the European Parliament and of the Council of 16 December 2008 on food additives [3] should be excluded from the scope of this Regulation, since the safety of these foods is already assessed and regulated. However, when these food enzymes are used as such in food, they are covered by this Regulation.

(6) Food enzymes should be approved and used only if they fulfil the criteria laid down in this Regulation. Food enzymes must be safe when used, there must be a technological need for their use and their use must not mislead the consumer. Misleading the consumer includes, but is not limited to, issues related to the nature, freshness, quality of ingredients used, the naturalness of a product or of the production process, or the nutritional quality of the product. The approval of food enzymes should also take into account other factors relevant to the matter under consideration including societal, economic, traditional, ethical and environmental factors, the precautionary principle and the feasibility of controls.

(7) Some food enzymes are permitted for specific uses, such as in fruit juices and certain similar products and certain lactoproteins intended for human consumption, and for certain authorised oenological practices and processes. The use of such food enzymes should comply with this

[1] OJ C 168, 20.7.2007, p. 34.

[2] Opinion of the European Parliament of 10 July 2007 (OJ C 175 E, 10.7.2008, p. 162), Council Common Position of 10 March 2008 (OJ C 111 E, 6.5.2008, p. 32), Position of the European Parliament of 8 July 2008 (not yet published in the Official Journal) and Council Decision of 18 November 2008.

[3] See page 16 of this Official Journal.