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Position paper of the Working Group Food Biotechnology
on 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 of the EUROPEAN PARLIAMENT and of the COUNCIL

Situation

Regulation EG 1331 of the EUROPEAN PARLIAMENT and of the COUNCIL introduces a „common authorisation procedure for food additives, food enzymes and food flavourings". The working group supports the aims, as cited in the recital clauses and in Art. 1(1) of REGULATION (EC) No 1331/2008 of 16 December 2008, in particular the aim of "a high level of protection of human health and to a high level of consumer protection including the protection of consumer interests". To assure this, „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" (3. recital). Sector regulations (EC No 1332, 1333 und 1334) „lay down harmonised criteria and requirements concerning the assessment and authorisation of these substances" (4. recital). This procedure „must be founded on the principles of good administration and legal certainty and must be implemented in compliance with those principles" (8. recital). The „various stages of the procedure, the deadlines for those stages, the role of the parties involved and the principles that apply" are defined (9. recital). The final step is the publication of a "Community list of authorised substances" (5. recital). This includes enzymes for food processing.

Simplification of the Procedure according to Regulation (EC) 1331

Numerous formulations, particularly in the recital clauses, explain that the EUROPEAN PARLIAMENT and the COUNCIL attempted to weaken the often heard criticism of an excessive bureaucratisation by introducing well considered regulations. For example

- the Commission will „seek the opinion of the European Food Safety Authority *where necessary*" (11. recital);

- „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*" (10. recital);

- „It is recognised that, in some cases, …. other legitimate factors relevant to the matter under consideration may be taken into account, including *societal, economic, traditional, ethical and environmental factors* ….. (14. recital)

- „ 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 …… " (26. recital).

- „ 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. " (Art. 3(2)).

Common authorisation procedure: The practical embodiment

The interest of the EUROPEAN PARLIAMENT and of the COUNCIL in efficiency and legislative simplification is endorsed. On the medium-term, the Commission plans to examine the possibility "to extend the scope of the common procedure to other legislation in the area of food" (22. recital). However, the Working Group, recognizing the *substantial differentness of enzymes* compared to food additives and flavouring substances, pleads for establishing a *reasonable and practical embodiment of the authorisation procedure*. Undue and new bureaucratic hurdles for the application of food enzymes should be avoided in order not to needlessly impede the future development of these economically and ecologically most favorable catalysts.

Differences between Enzymes *vs.* Food Additives/Flavouring Compounds

Occurrence

Enzymes are globular proteins with catalytic properties build from amino acid modules. Some of them require co-substrates, such as Adenosine Triphosphate (ATP) or Nicotinamide Adenine Dinucleotide (NAD) to unfold their catalytic function. Hundreds of enzymes and the matching co-substrates *occur in food as genuine constituents*, even though in usually lower concentrations than in typical technical applications. Very few foods are completely devoid of any enzymes.

Traditional and Safe History of Use (cf. 14. recital)

Modern food biotechnology originates from empirical processes, which were supposedly used thousands of years before the invention of writing. Enzymes of yeasts inevitably change untreated must of fruits, like enzymes from lactic acid formers acidify moist cereal flour, left-over milk, or minced meat and vegetables. If consumed in moderation, fermented food offer a high level of chemical and microbial safety (cf. 2. recital); some of them are even discussed as functional foods, maintaining a robust intestinal status and reducing the susceptibility to infection (Yoghurt, Kefir etc). The metabolites formed by extra- and intracellular enzymes are mainly the same as they arise from a deliberate addition of technical enzymes to food, because the mechanisms of catalysis are the same. Not a single case of a human intoxication by the consumption of an enzyme has become known.

Societal, Economic, Ethical and Environmental Aspects (14. recital)

The only producer of enzymes is the living cell. Where enzymes are formed, neither exogenous organic contaminants nor heavy metals are present in live-threatening concentrations; otherwise the producer itself would not survive. In combination with appropriate state-of-the-art isolation and purification techniques it is safe to conclude that technical enzymes are devoid of toxicologically relevant contaminants. Although technical enzymes are never chemically pure, they have to be concentrated and purified to gain standardized, storable and transportable products. Among the procedures used are mechanical (membrane) processes, precipitation with non-toxic salts, such as $(NH_4)_2SO_4$, or more rarely chromatographic steps. *Only safe substances are used*, because enzymes, as

complex bio-molecules, are sensitive towards any chemical which may damage their spatial structure and, thus, the desired catalytic activity. In contrast, the chemosynthesis of flavouring compounds or food additives often does not get along without catalysts, solvents, and substances which may harm human health if they remain in the final product. Further, flavouring compounds or food additives must remain intact in the final food product. These differences should affect *the depth of toxicological evaluation* of technical enzymes *vs* flavourings or additives by the authorities.

Food enzymes are usually extracted from a fermentation broth or from a tissue. To unfold their activity they are added to food as such, usually in an early step of processing. The effects are fully known and well reproducible, if the enzyme was sufficiently standardized. Thus, the consequences of an enzyme addition to a mixture of substances, here called food, are *well controllable and predictable*. If they were not, enzymes would not have found such widespread uses.

Enzymes are formed and are active in a cell under ambient conditions. Therefore enzyme catalysis works best under mild conditions of pH, pressure and temperature. The resulting energy saving and environmentally friendly processes, summarized under the recent term „White Biotechnology“, enjoy particular promotion and sponsorship by the EUROPEAN PARLIAMENT and the COUNCIL. The gentle operational conditions enabled by using *enzymes protect the constituents of food better than any other alternative process*.

Enzymes show the same endogenous catalytic effects in the cells/foods, from which they were derived, as in isolated form after exogenous supplementation. For example, baking enzymes are added to dough just to compensate for endogenous deficiencies caused by unfavourable weather conditions. Hence, the *possible health risks* associated with the use of food enzymes must be estimated *very low*. In contrast: Numerous prominent applications i*mprove digestibility and lower health risks of food*. Examples are the enzymatic hydrolysis of Lactose (Lactose intolerance) or of Gluten (coeliac disease).

Most processed foods receive a final thermal treatment to assure microbial stability. As all other proteins, the enzymes present are denatured, i.e. inactivated. The appropriate technology will thus limit the function of the enzyme to the desired time and place, and the consumer absorbs and digests the enzyme *like any other protein*, hydrolysing it during the intestinal passage into smaller peptides and eventually free amino acids.

The *allergenic potential* of orally consumed enzymes is lower than that of other typical food proteins. Technical enzymes are well water-soluble globular structures and *rapidly degradable* by hydrolysis during gastrointestinal passage.

Enzymes from Genetically Modified Microorganisms (GMMO)

The working group supports explicitly the safe and sustainable use of genetic engineering for the food industry. Previously quoted scientific concerns, for example as to remaining marker genes coding for antibiotics resistance have been overcome and invalidated by advanced protocols (construction of vectors, food grade production stains). Enzymes generated by modern GMMO basically *bear even less risk than those from often less well-characterized enzymes from wild strains*. Genetic engineering protocols depend on knowing the exact amino acid sequence of the enzyme. The over-producing GMMO accumulates mainly the target enzyme as the inducer controlled gene product, and all other proteins typically occur in lower concentrations. This facilitates purification of the recombinant enzyme from the very beginning, resulting in very low contents of undesired accessory substances. Enzymes from GMMO are typically pure proteins and may thus require a shortened evaluation only.

Recombinant enzymes, such as *Chymosin* for the clotting of cheese dairy milk, contribute since many years to increased diversity and quality, but also the safety of our food choice. The use of food enzymes looks back on *long-standing positive experiences* resulting in an *undisputed strong acceptance by the European societies*. This includes green and alternative political groups. It is just environmental concerns which unavoidably lead to the preference for gentle “white” bioprocesses.

To enumerate a few out of many more examples existing: Lactases enable an increasing number of patients suffering from Lactose intolerance the untroubled consumption of milk products rich in essential nutrients. Lipases produce natural flavours, such as fruit esters and lactones. Hydrolysed vegetable proteins and soy sauce enable vegetarians to enjoy products with the taste and smell of meat broth (umami, kokumi). Asparaginases reduce the concentration of the precursor of acrylamide in baked or roasted foods, such as toast bread, crackers or potato chips, thereby dramatically lowering the formation of a potentially carcinogenic compound.

Summary

The working group pleads for an evaluation of food enzymes according to Art. 5 und 9 (1)c) of REGULATION (EC) No 1331/2008, which is *appropriate to the particular properties* of this group of substances, and which exhausts the simplifications of procedure provided by the COMMISSION.

Food biotechnology with its ancient origins affords foods offering a high level of inherent sanitary and toxicological safety. Key to this result are enzymes which are proteins produced by and contained in any living cell. Enzymes are thus *genuine constituents of foods*. Toxins or heavy metals do not occur in the sources of enzymes. Standard processes of production and isolation do not use critical processing aids. Thus, technical enzymes are devoid of critical contaminants. Substrate and reaction specificity and activity under mild conditions predestine enzymes for applications in mixed substrate systems, such as foods („Bio-economy"). The thermal inactivation of enzymes in the last step of processing destroys their catalytic activity; enzymes then equal physiologically any other food proteins. The *allergenic potential* of enzymes is lower than that of other food proteins, as they are rapidly digested in the human intestine.

Risks associated with enzymes derived from GMMO are generally even lower than those associated with less well-characterised activities from wild strains, because the GMMO accumulates mainly the recombinant enzyme, and the concentrations of side-products remain minimal. Meanwhile, a number of recombinant enzymes show quite a *long history of safe use*, contributing to quality and safety of food. The long-term positive experience has resulted in *strong societal and political* acc*eptance*. Thoroughly evaluating the circumstances of formation, the procedures of isolation and purification, the substrate and reaction specific mode of action in food and the physiological behaviour after consumption, the potential risks involved in using technical enzymes for food must be estimated extremely low.

Enzymes hold a hardly to over-estimate potential of innovation for the future production of safe, tasteful and well-digestible food. The policy of the COMMISSION as expressed by its framework programs clearly demonstrates that it is well aware of the *vast opportunities of bio-catalysis*. The practical execution of the regulations of (EC) No 1331/2008 should not counteract this policy, but promote the future research and development in the field of food enzymes through a prudent embodiment appreciating the fascinating properties of nature´s most capable catalysts.

Hannover, 27 May 2010, Prof. Dr. Dr. R. G. Berger