**Paper No.: 13**

**Paper Title: FOOD ADDITIVES**

**Module – 34: Legal aspects, ADI and GRAS status of food additives**

## 34.1 Legal Aspects of Food Additives

The data provided by Joint Expert Committee on Food Additives & Contaminants (JECFA) by Acceptable Daily Intake (ADI) and maximum level of use of additives is based on dietary pattern of a region and thus taking into account the total intake of a particular additive through all sources which should be below ADI. Same principle is also adopted for Maximum Residue Level (MRL) of Pesticide & Toxins etc. We can ensure safety by adoption of Food Safety Management System GHP/GMP/HACCP so that food additives do not present a hazard to health while serving a technological function. Safety is ensured through Principle of Risk Assessment System.

### 34.1.1 International Scenario

#### 34.1.1.1 *Codex (definitions)*

- **Food** means any substance, whether processed, semi-processed or raw, which is intended for human consumption, and includes drinks, chewing gum and any substance which has been used in the manufacture, preparation or treatment of "food" but does not include cosmetics or tobacco or substances used only as drugs.
- **Ingredient** means any substance, **including a food additive**, used in the manufacture or preparation of a food and present in the final product although possibly in a modified form.
- **Food Additive** means any substance not normally consumed as a food by itself and not normally used as a typical ingredient of the food, whether or not it has nutritive value, the intentional addition of which to food for a technological (including organoleptic) purpose in the manufacture, processing, preparation, treatment, packing, packaging, transport or

holding of such food results, or may be reasonably expected to result, (directly or indirectly) in it or its by-products becoming a component of or otherwise affecting the characteristics of such foods. The term does not include "contaminants" or substances added to food for maintaining or improving nutritional qualities.

- **Contaminant** means any substance not intentionally added to food, which is present in such food as a result of the production (including operations carried out in crop husbandry, animal husbandry and veterinary medicine), manufacture, processing, preparation, treatment, packing, packaging, transport or holding of such food or as a result of environmental contamination.
- **Processing aid** means a substance or material not including apparatus or utensils and not consumed as a food ingredient by itself, intentionally used in the processing of raw materials, foods or its ingredients to fulfill a certain technological purpose during treatment or processing and which may result in the non-intentional but unavoidable presence of residues or derivatives in the final product.

**34.1.1.2 Carry-Over of Food Additives into Foods**

**Compliance with the carry-over principle** (Other than by direct addition)

An additive may be present in a food as a result of carry-over from a food ingredient, subject to the following conditions:

- The additive is permitted in the raw materials or other ingredients (including food additives) according to this General Standard.
- The amount of the additive in the raw materials or other ingredients (including food additives) does not exceed the maximum amount so permitted.
- The food into which the additive is carried over does not contain the food additive in greater quantity than would be introduced by the use of the ingredients under proper technological conditions or manufacturing practice.

**Ingredients and raw materials as carriers for additives**

An additive is permitted in a raw material or other ingredient if the raw material or ingredient is used exclusively in the preparation of a food, which is in conformity with the provisions of the standard.

### 34.1.2 Indian Scenario (FSSAI Act & Rules)

FOOD ADDITIVE APPROVAL PROCESS – INDIA

- Application in a structured format
- Details of additive requested:
- Name of food categories
- Level of usage
- Technological justification
- Current status under local regulations
- JEFCA and other safety evaluations
- Codex Approval Status
- Approval by other regulatory authorities
- Questionnaire to include information on:
- Technical information such as chemical name, CAS No., chemical & structural formula
- Specification for identity & purity of the substance
- Chemical & physical properties
- Method of analysis

## 34.2 GRAS

GRAS substances are a group of additives regarded by qualified experts as ‘‘generally recognized as safe’’. These substances are considered safe because their past extensive use has not shown any harmful effects.

Under Federal Food, Drug, and Cosmetic Act, any substance that is intentionally added to food is a food additive, that is subject to premarket review and approval by FDA, unless the substance is generally recognized, among qualified experts, as having been adequately shown to be safe under the conditions of its intended use, or unless the use of the substance is otherwise excluded from the definition of a food additive.

The use of a food substance may be GRAS either through scientific procedures or, for a substance used in food, through experience based on common use in food.

- General recognition of safety through scientific procedures requires the same quantity and quality of scientific evidence as is required to obtain approval of the substance as a food additive and ordinarily is based upon published studies, which may be corroborated by unpublished studies and other data and information.

- General recognition of safety through experience based on common use in foods requires a substantial history of consumption for food use by a significant number of consumers.

***GOOD MANUFACTURING PRACTICE (GMP)***

All food additives subject to the provisions of this Standard shall be used under conditions of good manufacturing practice, which include the following:

- The quantity of the additive added to food shall be limited to the lowest possible level necessary to accomplish its desired effect;
- The quantity of the additive that becomes a component of food as a result of its use in the manufacturing, processing or packaging of a food and which is not intended to accomplish any physical, or other technical effect in the food itself, is reduced to the extent reasonably possible;
- The additive is prepared and handled in the same way as a food ingredient.

## 34.3 ADI (Acceptable Daily Intake)

Assessments of safe limits are based on reviews of all available toxicological studies, including observations in human and in a given model. Data are analyzed to arrive at a maximum level of an additive that has no demonstrable toxic effect. The "no-observed-adverse-effect level" is used to determine the Acceptable Daily Intake (ADI) for each food additives. The ADI provides a large margin of safety which denotes the amount of a food additive that can be consumed daily in the diet, over a life time, without any adverse effect on health. The expert committees working on food additives safety also study the range of intakes across a population by consuming too much of or too many products containing a particular food additive. The JECFA have developed guidelines for food safety titled 'General Standards for Food Additives' with the purpose of establishing a harmonized level for acceptance by member countries signing world trade agreements for export purposes.

***Acceptable Daily Intake (ADI)*** is an estimate by JECFA of the amount of a food additive, expressed on a body weight basis that can be ingested daily over a lifetime without appreciable health risk.

***Acceptable Daily Intake "Not Specified" (NS)*** is a term applicable to a food substance of very low toxicity for which, on the basis of the available data (chemical, biochemical, toxicological, and other), the total dietary intake of the substance, arising from its use at the levels necessary to achieve the desired effect and from its acceptable background levels in food, does not, in the opinion of JECFA, represent a hazard to health.

For the above reason, and for reasons stated in individual JECFA evaluations, establishment of an acceptable daily intake expressed in numerical form is not deemed necessary by JECFA. An additive meeting the above criterion must be used within the bounds of good manufacturing practice.

***Maximum Use Level*** of an additive is the highest concentration of the additive determined to be functionally effective in a food or food category and agreed to be safe by the Codex Alimentarius Commission. It is generally expressed as mg additive/kg of food. The maximum use level will not usually correspond to the optimum, recommended, or typical level of use. Under GMP, the

optimum, recommended, or typical use level will differ for each application of an additive and is dependent on the intended technical effect and the specific food in which the additive would be used, taking into account the type of raw material, food processing and post-manufacture storage, transport and handling by distributors, retailers, and consumers.

### 34.3.1 Approval Procedure for Food Additive

The manufacturer of food additive files an application on the prescribed Performa to the food regulatory authority by providing convincing evidence that the proposed additive performs the intended function and that it will not cause harmful effects at expected levels of human consumption. Animal experiments using large doses of the additive for long periods are often necessary to substantiate the claim. Studies of the additive in humans are also desirable. The Food Regulatory Authority may advise the government food laboratories to conduct independent risk assessment trials before deciding whether an additive should be approved. The agency considers the composition and properties of the substance, the amount likely to be consumed, its probable long term effects and various safety factors. It may be stated that absolute safety of any substance can never be proven. However, best scientific knowledge available should be used to determine whether the addition is safe.

The Ministry of Health, Govt. of India after the recommendations of the Food Additive Sub Committee of the Central Committee for Food Standards (CCFS) through the Gazette Notifications invites objections from the public, trade associations, NGO's, industry users, etc. The comments received within stipulated notified time are scrutinized by the expert group. The approval is given for its use as a food additive indicating maximum amount which can be incorporated. Methods of tests are also prescribed.

### 34.3.2 Determination of Safety Margins

The toxicological tests required by the regulatory authorities include lifetime feeding studies and multigenerations that determines how the body reacts to the additive. The starting point for establishing ADI is the determination of no observed adverse effect level (NOAEL) in the most sensitive animal species. NOAEL is expressed in *mg* of additive per kg of body weight per day. This is then divided by a safety factor of 100. This gives a large margin of safety since

the test is conducted on animals. Man is more sensitive than the most sensitive test animals. Moreover, the reliability of tests is limited by the number of animals tested. The uncertainty factor of 100 is based on a 10-fold factor for differences between animals and an average human, and a 10-fold factor to allow the differences between the sensitive sub groups of humans (pregnant women, children, elderly).

### 34.3.3 Setting the Acceptable Daily Intake (ADI)

The quality/value of the data that can be used in risk assessment varies according to the set of data obtained from epidemiology, animal experiments and short term tests. When a food additive is already on the market it is very difficult to detect adverse effects. That is the reason for the extensive requirements for safety testing before a new food additive is permitted to be used on the market. From the results in the toxicological file submitted by the petitioner, the Scientific Committee on Food (SCF) calculates the ADI-value for each additive. For the safety evaluation of pesticides and contaminants an "acute reference dose" is used to detect levels where toxic effects appear after a single dose. This "acute reference dose" has been used as a bench mark for a short-term ADI. Such a dose and evaluation is not applicable for food additives since the safety should cover daily intake during the whole life time, i.e. the acceptable daily intake (ADI). In 1987 the WHO defined the ADI as "An estimate by JECFA of the amount of food additive, expressed on a body weight basis, that can be ingested daily over a lifetime without appreciable health risk". The "safe" dietary level or daily intake for animals is known as the "no observable effect level", NOEL. The ADI is calculated from the NOEL as follow:

$$\text{ADI (mg/kg bw/day)} = \frac{\text{NOEL}}{\text{Safety Factor}}$$

Man may be more sensitive than the most sensitive species tested in the toxicological studies, or certain specific individuals and subgroups may show a greater sensitivity than the general population. Uncertainty or safety factors are used to extrapolate from a group of animals to an average human and from average humans to potentially sensitive groups. To allow for these

possibilities a large "uncertainty factor" is applied to the NOEL, normally 100, i.e. a safety factor of 10 is applied for intra-species differences and another factor of 10 for interspecies differences.

This means that the average daily intake (ADI) will not exceed one-hundredth of that which has been shown to be without observed effects in animal tests. The need for an extra safety factor depending on the nature of toxicity has been debated. However, this safety factor can be reduced. When human data are available it is possible to accept a safety factor of 10, whereas when animal data are less convincing a safety factor of 1000 may be applied. Thus, a flexible approach, using additional factors, is adopted in order to perform risk assessments.

### 34.4 Modern Technology in Producing New Additives

Requests are being received to use ingredients that would replace fat or sugar in foods. Biotechnology allows the use of simple organisms to produce additives. FDA approved the first bioengineered enzyme (rennin) for use in making cheese. Rennin has traditionally been extracted from fourth stomach of the calves or the microorganisms.

JECFA reviews hundreds of fresh requests from various member countries each year. Proposals are identified as *high priority* or *on priority* for evaluation. The Codex Committee on Food Additives has developed a diagram that illustrates the procedures for consideration of the entry and review of food additives for the benefit of member countries. The codex has also developed the International Numbering System (INS) for food additive.