The Director General

Maisons-Alfort, 5 August 2015

# OPINION
# of the French Agency for Food, Environmental and Occupational Health & Safety

## on the guidelines for preparing industrial dossiers on food for special medical purposes

*ANSES undertakes independent and pluralistic scientific expert assessments.*
*ANSES's public health mission involves ensuring environmental, occupational and food safety as well as assessing the potential health risks they may entail.*
*It also contributes to the protection of the health and welfare of animals, the protection of plant health and the evaluation of the nutritional characteristics of food.*

*It provides the competent authorities with the necessary information concerning these risks as well as the requisite expertise and technical support for drafting legislative and statutory provisions and implementing risk management strategies (Article L.1313-1 of the French Public Health Code).*

*Its opinions are made public.*
*This opinion is a translation of the original French version. In the event of any discrepancy or ambiguity the French language text dated 5 August 2015 shall prevail.*

On 20 March 2014, ANSES issued an internal request to identify and harmonise the scientific information needed for preparing industrial dossiers on food for special medical purpose (FSMPs).

## 1. BACKGROUND AND PURPOSE OF THE REQUEST

### 1.1. Regulatory background

FSMPs are very specific foods intended for sick people who are unable to eat conventional products. They may be consumed temporarily (in the case of malnutrition, dehydration or after surgery, for example) or permanently for incurable diseases, such as inherited amino acid metabolism disorders. FSMPs are either complete foods, i.e. they constitute the only source of food, whose composition may or may not be adapted to a pathology (enteral nutrition, child nutrition), or they are incomplete foods consumed as a supplement to other common foods (nutrition rehabilitation, rehydration, inherited metabolic diseases).

In France, operators must notify the General Directorate for Competition Policy, Consumer Affairs and Fraud Control (DGCCRF) when an FSMP is first placed on the market. They must attach a copy of the product label to this notification.
Although no prior authorisation is necessary, the regulations nevertheless require the authorities to be notified when the product is first placed on the market (Article 7 of the Order of 20 September 2000). When it deems necessary, the DGCCRF may ask the body responsible for placing the product on the market to send it any scientific information likely to justify the FSMP status of the

product and may then request ANSES to instruct its CES on Human Nutrition to conduct an assessment.
Any subsequent change in composition and/or labelling should also be declared.

The assessment, carried out by the CES on Human Nutrition, can thus take place after the product concerned has been placed on the market. This assessment does not therefore cover the basic requirements in terms of hygiene and safety, which apply to all foods intended for human consumption[1].

### 1.2. Scientific background

For the preparation of their dossiers, industrial companies currently have common guidelines for all dossiers submitted to the CES on Human Nutrition, dating back to 2001 (AFSSA). Nevertheless the quality of the dossiers submitted for assessment by ANSES varies greatly. ANSES therefore deemed it necessary to adapt guidelines to the preparation of dossiers for these specific products.

## 2. ORGANISATION OF THE EXPERT APPRAISAL

The expert appraisal was carried out in accordance with French Standard NF X 50-110 "Quality in Expert Appraisals – General Requirements of Competence for Expert Appraisals (2003)".

The collective expert appraisal was carried out by the Expert Committee (CES) on Human Nutrition, which met on 11 September 2014, 16 October 2014, 28 November 2014, 18 December 2014, 17 April 2015 and 26 June 2015, on the basis of initial reports drafted by five expert rapporteurs of the CES and review reports by three experts outside the CES.

ANSES analyses the links of interest declared by the experts prior to their appointment and throughout the work, in order to avoid potential conflicts of interest with regard to the matters dealt with as part of the expert appraisal.
The experts' declarations of interests are made public via the ANSES website (www.anses.fr).

To conduct this expert appraisal, the CES based its work on:

- all of the regulatory texts governing the marketing of FSMPs at European and French level;
- the current guidelines (AFSSA, 2001);
- previous opinions written by ANSES on FSMPs;
- minutes of meetings with the DGCCRF;
- minutes of hearings with the main French industrial companies marketing FSMPs.

[1] On this point, one of the CES experts, Mr Belegaud, wished to express a dissenting position: "*The European regulatory texts regard FSMPs as foods for a particular purpose that have to meet the regulatory requirements for food and are therefore not subject to authorisation before they are placed on the market. These guidelines, which have been discussed in great depth, amended and which represent a significant advance compared to the currently existing ones should, from my point of view, be applied when the FSMPs are first placed on the market and not "a posteriori". Speaking personally, as a rapporteur and member of the CES on Nutrition, I can only abstain on the validation of this text given that it does not sufficiently take into account either the* ***safety of patients,*** *who are often being treated for fairly serious disorders by drugs with a high therapeutic index and who cannot be equated to mere consumers, or the* ***quality*** *of the FSMP product.*"

## 3. ANALYSIS AND CONCLUSIONS OF THE CES

### Guidelines for the preparation of industrial dossiers for FSMPs

These guidelines have been designed to enable operators to prepare an informative dossier containing all the necessary data for a complete and thorough assessment of the product, in order to avoid processing of formal requests being delayed due to a lack of information.

Listed below are all the elements that the CES deems necessary in principle for its assessment of products. The absence of any of these elements must be duly justified. If such justification is not provided, ANSES reserves the right to return the dossier not complying with these guidelines to the administration that sent it.
This list is not exhaustive, and the applicant may provide any additional data that it considers useful to justify its application.

The CES stresses the importance of consistency between the different elements of the dossier and in particular regarding what appears on the product labelling.

During the scientific assessment of the dossier, the CES may request additional information.

*The following must be presented at the beginning of the dossier:*

- the nature of the application (product type, target population, pathology);
- a summary of the dossier (approximately one page);
- the administrative data characterising the applicant;
- the table of contents and page numbering for the document.

*The different parts below must then be provided as follows:*

#### 1. Introduction, current state of knowledge

1.1. Scientific context

This part will present the relevant data available in the scientific literature, concerning:

- the pathology(ies) or physiological functions specifically concerned by the products;
- the specific nutritional needs of the target population and the inadequate or excessive nutritional intakes;
- the recommendations and/or good practices in terms of dietary management of the pathology(ies) concerned (French National Authority for Health - HAS, learned societies, etc.).

If the product has been assessed by a health agency in another country, the expert report (translated into French where appropriate or, failing that, in English) must be attached to the applicant's dossier.

1.2. Regulatory context

The applicant must demonstrate that its product meets the definition of an FSMP in regulatory terms and state the regulatory category to which the product belongs. It will make reference to all the applicable French and EU regulatory and legal texts that specifically govern the placing on the market of the product(s) concerned.

## 2. Product presentation

2.1. Product description

- the form of the product as consumed (e.g. beverage, biscuit, cream dessert);
- the packaging;
- the mode of consumption: dose and frequency of consumption recommended according to age and possibly physiological status (e.g. children, pregnant women) or pathophysiological status (e.g. the form or stage of the pathology), recommended duration of consumption and criterion for interrupting consumption of the product;
- the claimed indications (pathologies);
- the claimed properties (health claims).

Concerning FSMPs for which there are already comparable common foods on the market, the applicant must present the unique characteristics of the product that justify its FSMP status.

2.2. Target population

The applicant should make a precise argument for the benefit of using an FSMP in the indicated target population. The dossier must show the existence of a correspondence between the product's composition and the needs of this particular population.

The target population must be defined by:

- its age group;
- the characteristics of its pathology;
- its nutritional status and specific needs in order to justify the product's composition.

If several populations are specifically targeted, it must be possible to apply the justification to each one.
Thus, if the product is intended for a broad target population, the product's benefits should be justified for all of the populations proposed.

*Examples*

- *For patients with swallowing disorders, specify the type of disorder (i.e. concerning liquid, solid or mixed foods).*
- *For a malnourished population, state the causes of the malnourishment.*
- *For the elderly, state the nutritional situations in which the product may be prescribed (malnutrition, sarcopenia, etc.).*
- *For subjects with inherited metabolic disorders, low-protein FSMPs cannot, unless precisely justified, claim to be indicated for the management of other diseases such as renal or hepatic impairment.*

## 3. Composition and nutritional analysis of the product

### 3.1. Nutritional composition

The description of the product's composition must be in accordance with the regulatory context mentioned in point 1.2.

Depending on the nature of the product, its indication and the associated claims, detailed information should be included on the levels of amino acids, fatty acids, sugars and fibres, according to the modes of expression used in the regulatory texts, or other details that may be necessary.

The use of any ingredient or the addition of any nutrient or substance whose presence is not required to cover the needs of the population should be justified.

In the case of liquid food (or food intended to be reconstituted in liquid form), the osmolarity should be stated.

### 3.2. Comparison of the composition of vitamins and minerals with the regulatory values

The dossier must present a table documenting the product's levels of vitamins and minerals, for 100 kcal, as well as the regulatory minimum and maximum values.

### 3.3. Comparison with products on the market

A table comparing the product with equivalent FSMPs present on the market will provide useful data for the expert appraisal.

### 3.4. Justifications of the doses used and possible instances where the upper regulatory and safety limits may be exceeded

The dossier must present simulation data on consumption of the product concerned. This simulation must be carried out in the context of the target population's normal food consumption, on the basis of the most accurate estimates of nutrient intakes from this population's normal diet, in order to assess the total nutrient intake during consumption of the product.
The applicant must compare these intakes to the upper regulatory and safety limits and the nutritional references for each of the targeted populations.
Any instance where limits are exceeded must be duly justified.

### 3.5. Studies conducted with the product

The applicant must make an argument for the product's acceptability and tolerance in terms of data obtained with the product itself or, failing this, with products of similar composition.

If the product's composition responds to a specific need of the target population that could not be estimated from scientific data already published, a clinical efficacy study must be presented to justify this composition.

*Examples*

- *Tests of acceptability of texture are in particular essential for products intended for patients with swallowing disorders, because they determine the product's benefits and safety of use in the case of swallowing disorders concerning liquids.*
- *For oral nutritional supplements for which there is no direct evidence of clinical efficacy with the product considered, it will be necessary to provide evidence that their use can effectively increase total energy intake.*

## 4. Technological data

### 4.1. Raw materials: list, origin and traceability

The dossier must present the technical data sheets for all the ingredients.

### 4.2. Stability of the nutritional properties

Where the manufacturing processes and the storage method could potentially change the product's nutritional properties, the dossier must present data that can be used to ascertain its stability.

For example, for products containing significant quantities of n-3 fatty acids, data on the peroxidability of the n-3 fatty acids within this product must be presented.

If necessary, the applicant shall specify the storage conditions needed to preserve the product's stability.

## 5. Proposed labelling

The dossier must present the draft text of the labelling, i.e., the label of the product and all the documents that accompany its marketing. The documents submitted must be legible.

In addition to the statements required according to the regulations, if the product has high osmolarity, the labelling should include a statement advising consumers to drink water between doses.

## References cited

All the references cited by the applicant must be presented rigorously in a list, and the complete corresponding articles must be attached to the dossier in electronic form, in PDF format.

The applicant shall make reference to data in the literature as a whole, without omitting recent references.

## 4. AGENCY CONCLUSIONS AND RECOMMENDATIONS

The French Agency for Food, Environmental and Occupational Health & Safety adopts the guidelines proposed by the CES on Human Nutrition. As a result, the dossiers sent to ANSES for assessment by the CES must henceforth comply with the requirements of this document. Applications for which the associated dossiers are incomplete in terms of the expectations laid down in these guidelines, thereby hindering a comprehensive and reasoned assessment, may be deemed non-admissible by ANSES.

These guidelines, presenting the list of elements needed by the CES to carry out a complete and thorough assessment of FSMPs, will enable industrial companies to prepare a comprehensive argument to demonstrate the nutritional benefit of the products they wish to propose.

Marc Mortureux

## KEYWORDS

FSMPs, guidelines, update, industrial dossier

## ANNEX

List of elements to be included in applicants' dossiers

| | Chapters | Criteria | Y/NA[2] | P, L[3] |
|---|---|---|---|---|
| | | Presentation of the application | | |
| | | Summary of the dossier | | |
| | | Administrative information | | |
| | | Contents and page numbering | | |
| Introduction | 1.1 | Scientific context | | |
| | 1.2 | Regulatory context | | |
| Product description | 2.1 | Form of the product as consumed | | |
| | | Packaging | | |
| | | Mode of consumption | | |
| | | Claimed indications (pathologies) | | |
| | | Claimed properties (health claims) | | |
| | | Benefit compared to similar common foods | | |
| Target population | 2.2 | Age | | |

[2] Yes/Not Applicable
[3] Page, Line

| | | | | |
|---|---|---|---|---|
| | | Characteristics related to its pathology | | |
| | | Nutritional status and specific nutritional needs | | |
| | | Justification for all of the populations considered | | |
| Composition and nutritional analysis | 3.1 | Product composition (regulatory format) | | |
| | | Additional nutritional information (depending on the nature of the product or whether claims have been made) | | |
| | | Justification for the presence of ingredients that are not necessary for the specific needs of the target population | | |
| | 3.2 | Composition in vitamins and minerals for 100 kcal | | |
| | | Comparison of the composition in vitamins and minerals with regulatory values | | |
| | 3.4 | Simulations of nutritional intakes for normal consumption of the product and comparisons with reference values (needs and upper limits) | | |
| | 3.5 | Acceptability studies | | |
| | | Studies of digestive tolerance | | |
| | | Study of clinical efficacy | | |
| Technological data | 4.1 | Technical data sheets for all ingredients | | |
| | 4.2 | Stability data | | |
| | 5 | Proposed labelling | | |
| References | | Relevant recent references | | |
| | | References cited in full in electronic form | | |