International Special Dietary Foods Industries

Shelf Life Determination for Foods for Special Medical Purposes (FSMPs)

August 2022
Guidance document

DISCLAIMER

This document is intended to provide guidance on shelf life tests of Foods for Special Medical Purposes (FSMP). It is for general information purposes only and does not constitute legal or other professional advice. It does not replace the relevant Codex Standards, ISO or AOAC methods and should be read in conjunction with all the relevant texts at Codex Alimentarius, ISO or AOAC level. This document does not replace any specific requirements already established by specific regulatory bodies.

The information provided is without prejudice to national regulations and national interpretations.

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EXECUTIVE SUMMARY: KEY PRINCIPLES AND RECOMMENDATIONS

The rationale for establishing the key principles highlighted below is further explained in the Guidance document.

Key principles

1. Requirements and guidelines related to drug stability are inappropriate for FSMPs.

2. Shelf life tests should be conducted on the commercial recipe produced in a factory or pilot plant in primary packaging with barrier properties equivalent to the commercial packaging and stored under temperature conditions that simulate typical conditions. Stability tests under controlled humidity conditions are not required because the primary packaging used for FSMPs is impermeable to moisture. Tests performed in more extreme temperature conditions are sufficient (but not required) to justify the shelf life of FSMPs.

3. Temperature is a fundamental parameter to control when performing shelf life tests.

4. The temperature of shelf life tests should reflect the temperature expected during FSMP product shelf life and correspond to the temperature zone of the country in which they will be marketed.

   For FSMPs, the world can be divided into three temperature zones:

   a. Zone I: "Temperate" 21°C +/- 2°C
   b. Zone II: "Subtropical" 25°C +/- 2°C
   c. Zone III: "Hot" 30° +/- 2°C

5. Shelf life duration can be appropriately defined on the sole basis of real-time results obtained, at minimum, at the beginning and end of shelf life. In such cases, the obtention of results at intermediate times is not mandatory.

6. If real-time data at the end of shelf life are not available, intermediate real-time data, accelerated tests, stability studies on similar products and extrapolation of relevant bibliographic and predictive mathematical modelling data may be used to define shelf life. Storage temperatures used for FSMP accelerated shelf life studies should be no more than 10°C above typical, ambient storage temperatures. Excessively high temperatures should be avoided as they can lead to nutrient instability and other changes not reflective of typical conditions. The specific temperatures used for these studies vary depending on the type of FSMP and are determined by the product manufacturer with appropriate justification. Data generated in a single accelerated temperature study may be sufficient to establish product shelf life if the appropriate correlation between accelerated and available real-time stability data is established on the most unstable nutrients by predictive mathematical modelling.

7. Shelf life tests should only include product characteristics that are subject to change during storage and that could affect product quality, safety, nutrient levels, claims or efficacy. Physical stability, organoleptic and sensory properties should be part of shelf life tests when appropriate. They should be adapted to the method of feeding and target patient acceptance of preparation and ingestion (e.g. exclusively tube-fed products do not have to be organoleptically acceptable but must be lump free and display a suitable viscosity).

8. The most labile product parameters and nutrients should be considered as the main determinants of shelf life. Most nutrients remain stable, some will degrade over time at different speeds. Shelf life tests for FSMPs should, therefore, contain a quantitative analysis of one to two nutrients used as tracers or markers. Stable nutrients only need to be analytically quantified once, typically directly after production of the FSMPs. If the FSMP contains probiotics, probiotic counts (number of colony forming units) should also be included in the shelf life test.

9. Monitoring factors typically considered for food safety, including testing for contaminants, pathogens, microbial burden or assessment of sterility is not required when determining FSMP shelf life.

10. Data from one batch are sufficient to define shelf life duration.

11. When a product is stored in different sizes of the same primary packaging, shelf life tests conducted on a single pack size are sufficient to justify the shelf life of the product in all the different pack sizes.

Summary of analyses to be included in FSMP shelf life tests

Since shelf life tests should focus on product characteristics that are subject to change during storage over time and that could affect product quality, safety, nutritional labelling, claims or efficacy (key principle 6), the following analyses are recommended for FSMP shelf life tests:

i. **A quantitative analysis of the following labile nutrient tracers:**

TYPE OF PRODUCTS	TRACER
Powder FSMPs	Vitamin A
Non-acidified liquid and paste FSMPs	Vitamin C
Acidified liquid and paste FSMPs	Vitamin C & Pantothenic acid

ii. **Enumeration of colony forming units, if the FSMP contains probiotics;**

iii. **A qualitative evaluation of product sensory characteristics;**

iv. **A qualitative evaluation of identified product physical properties (including where relevant appropriateness for use with tube feed and sip feed FSMPs).**

Conversely, the following product characteristics are not subject to change during storage, do not affect product quality, safety, nutritional labelling, claims or efficacy and are not required for FSMP shelf life tests:

i. Contaminants;

ii. Sterility, pathogens and microbial counts, provided the packaging remains sealed and intact: testing straight after manufacturing is considered enough. For powder products, ensuring in addition that water activity (a_w) straight after manufacturing is less than 0.6 renders subsequent microbiological tests unnecessary;

iii. Stable nutrients, such as minerals;

iv. Labile non-tracer nutrients;

v. Packaging; and

vi. Specific compositional characteristics (flavours and fibre).

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PURPOSE OF THE GUIDANCE DOCUMENT

This document is intended to provide practical guidance on what should be considered when developing shelf life study protocols to establish or confirm the shelf life duration of Foods for Special Medical Purposes (FSMPs). The content of this guidance is based on unique and extensive knowledge and data accumulated over the years by the medical food industry.

FSMPs, also known as medical foods or medical nutrition, are defined by Codex Alimentarius as *"a category of foods for special dietary uses which are specially processed or formulated and presented for the dietary management of patients and may be used only under medical supervision. They are intended for the exclusive or partial feeding of patients with limited or impaired capacity to take, digest, absorb or metabolize ordinary foodstuffs or certain nutrients contained therein, or who have other special medically-determined nutrient requirements, whose dietary management cannot be achieved only by modification of the normal diet, by other foods for special dietary uses, or by a combination of the two"* (CODEX STAN 180-1991).

FSMPs are highly specialised foods designed to meet the nutritional or dietary needs arising from a wide range of medical conditions that affect patients of all ages from infancy to old age. FSMPs are for the dietary management of patients who have a disease, disorder or medical condition, which either temporarily or permanently affects their ability to achieve a suitable nutritional intake from normal foods alone. FSMPs may be used only under medical supervision and can be consumed in hospitals, other healthcare settings or the patient's home. You can find more information and details on FSMP Codex standards in the ISDI Brochure on Foods for Special Medical Purposes.

FSMPs are highly complex food products with several ingredients and/or nutrients interacting in the matrix that could affect nutrient stability and the overall stability of the product. Together, these multiple nutrients provided by FSMPs improve the quality of life and reduce the morbidity and mortality of the patients who consume them[1]. Pleasant sensory properties of orally consumed (i.e. not tube-fed) FSMPs play a key role in acceptability by the patient, particularly for the sole source ofnutrition FSMPs or when the option of suitable locally available products is very limited. For some products, an appropriate texture is critical to clinical performance (e.g. free from undissolved lumps/particles in tube-fed FSMPs or adequate viscosity for FSMPs intended for dysphagic patients – patients with swallowing difficulties). It is, therefore, of particular importance that shelf life study protocols are appropriately designed and conducted on such products and that they are sufficiently specific to demonstrate that these products remain safe and suitable until their expiration dates.

Although there are numerous treatises and studies found in the scientific literature that discuss the relative stability of single vitamin, lipid or other food ingredients present in FSMPs[2,3], reported results and conclusions are not readily applicable to the stability of the same compounds in FSMP food matrices. Published stability studies for finished general food products are sparse and are not available for FSMPs.

Similarly, guidelines on how to conduct stability tests exist, but they are relevant only to health/food supplements[4,5] or drugs[6]. These existing guidelines, particularly those for drug stability, are inappropriate for FSMPs. The properties and composition of FSMPs and drugs differ widely. Drugs normally contain one or only a few active pharmaceutical ingredients (API). FSMPs do not contain API but often comprise more than 40 nutrients that can interact with each other. Consequently, FSMPs and drugs must comply with different requirements and are regulated differently. This approach impacts shelf life study protocols. Drug stability requirements applied to FSMPs are overly stringent on certain aspects that, although critical for the shelf life determination of a drug, are irrelevant for the shelf life determination of an FSMP. Other aspects (e.g. sensory) that are critical for the shelf life of FSMPs are, on the contrary, not (so) critical for drugs.

In this context, this document aims to provide:

1. Specific guidance on which key principles should guide the design of FSMP stability tests; and,
2. Specific product characteristics that should be monitored.

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[1] See further on this topic:

- WHO Guidelines on Integrated Care for Older People (ICOPE) (https://www.who.int/ageing/publications/guidelines-icope/en/)
- Gomes et al. Association of Nutritional Support With Clinical Outcomes Among Medical Inpatients Who Are Malnourished or at Nutritional Risk An Updated Systematic Review and Meta-analysis. JAMA Network Open. 2019; 2(11):e1915138. doi:10.1001/jamanetworkopen.2019.15138 https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2755665
- Hudson L, Chittams J, Griffith C, Compher C. Malnutrition Identified by Academy of Nutrition and Dietetics/American Society for Parenteral and Enteral Nutrition Is Associated With More 30-Day Readmissions, Greater Hospital Mortality, and Longer Hospital Stays: A Retrospective Analysis of Nutrition Assessment Data in a Major Medical Center. *JPEN J Parenter Enteral Nutr.* 2018;42(5):892-897.
- Smith TR, Cawood AL, Walters ER, Guildford N, Stratton RJ. Ready-Made Oral Nutritional Supplements Improve Nutritional Outcomes and Reduce Health Care Use-A Randomised Trial in Older Malnourished People in Primary Care. Nutrients. 2020 Feb 18;12(2). pii: E517. doi: 10.3390/ nu12020517 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7071441/)

[2] Chapter 26 – The Stability and shelf life of vitamin-fortified foods, in Food and Beverage Stability and Shelf Life; Woodhead Publishing Series in Food Science,Technology and Nutrition; 2011, Pages 743-754

[3] Vitamin C degradation during storage of fortified foods, Journal of Food and Nutrition Research, Vol. 45, 2006, 2, 66-61

[4] ASEAN Guidelines on Stability Study and Shelf life of Health Supplements

[5] IADSA: Stability Testing for the Shelf Life Determination of Supplements

[6] ICH Q1A (R2) Stability testing of new drug substances and drug products

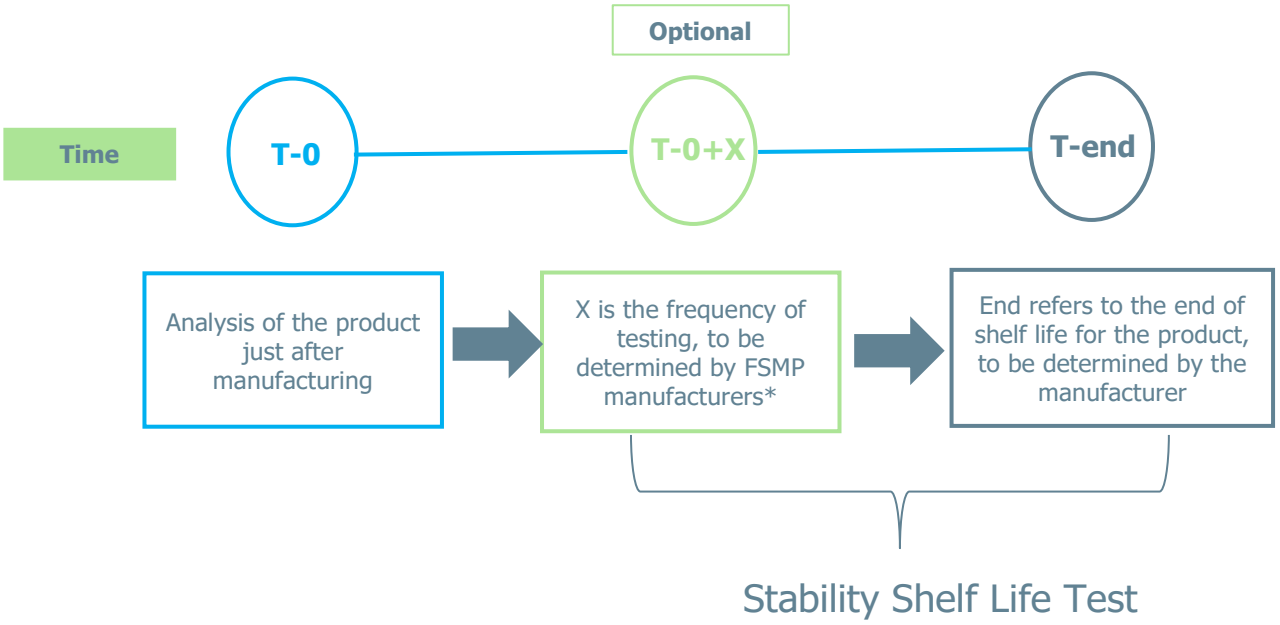
SCOPE OF THE GUIDANCE

Definition and aim of shelf life tests

Shelf life tests are all tests and analyses that are performed over the intended shelf life of a product to ensure that the shelf life duration is adequate – i.e. that the product is safe, suitable and acceptable for consumption up to the end of the shelf life. Shelf life tests should be representative, relevant, fact-based and scientifically driven.

Shelf life test protocols include analyses done after Time 0 (T0) (straight after manufacturing) to Time X (with X to be determined by FSMP manufacturers).

Product Development & Launch



*According to key principle 4, intermediate analyses are not mandatory.

RECOMMENDATIONS ON SHELF LIFE TESTS FOR FSMPs

1. Parameters impacting shelf life

The following factors may impact the composition or stability of FSMPs and therefore their shelf life:

Extrinsic (i.e. environmental) factors:	Intrinsic (i.e. product specific) factors:
• Temperature • Humidity • Light • Oxygen	• Product pH • Product moisture • Degree of protein hydrolysis • Primary packaging • Specific compositional characteristics (flavours and fibre)

The following sections explain how these factors may affect the shelf life of FSMPs and the practical implications they have on the design of FSMP shelf life tests.

1.1 Extrensic (i.e. environmental) factors

a. Temperature and humidity

Temperature during product storage can have an impact on product characteristics such as sensory properties and the physical stability of the formulation. The temperature at which the product is stored can have a significant influence on the rate of degradation of nutrients and other functional ingredients. Generally, higher temperatures increase the rate of chemical reactions responsible for nutrient degradation. Temperature is, therefore, a fundamental parameter to control when performing shelf life tests. FSMP shelf life tests have demonstrated that the following nutrients were sensitive to temperature: tryptophan, pantothenic acid, Vitamin A, C, B12, folic acid and thiamine (see Annex).

Storage conditions used during shelf life tests should reflect those expected during FSMP product shelf life and should correspond to the climatic zone of the country in which they will be marketed.

ISDI notes the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH)[7,8], which divides the world into four climatic zones[9]. Although the ICH is relevant to pharmaceuticals, it is not applicable per se to FSMPs.

Stability tests under controlled humidity conditions are not required for FSMPs because the primary packaging is impermeable to moisture. This is confirmed by the results of FSMP shelf life tests in which no nutrient was affected by the humidity conditions of the tests (see Annex).

Since humidity is not relevant for FSMP stability tests, ISDI considers that the four ICH climatic zones can be simplified to three with stability tests evaluated using the following temperature zones:

Zone I: "Temperate" 21° +/- 2°C
Zone II: "Subtropical" 25° +/- 2°C
Zone III: "Hot" 30° +/- 2°C

Shelf life tests are called real-time tests when they are conducted over the whole expected shelf life of the product and when the product is stored at temperatures representing the temperature zone of the market of sale. Real-time shelf life tests in storage temperatures for a zone with a warmer temperature than the temperature zone in which the FSMP will be marketed are acceptable for justification/validation of shelf life in cooler climatic zones. For example, shelf life tests conducted on an FSMP in Zone II or III are sufficient to justify its shelf life in Zone I.

Accelerated shelf life tests (in higher temperatures than the FSMP will be exposed during shelf life to drive an acceleration in the rate of change, so reducing the duration of the test) are sometimes performed because the determination of product shelf life based on real-time stability data is time-consuming and may delay the availability of products to patients in critical need. However, it should be considered that these tests often result in significant deviations in product texture and taste and are of limited value for predicting the physical stability of FSMPs. In addition, as most vitamin degradation reactions follow first order kinetics[10], a high constant storage temperature (e.g. 30°C) during shelf life study can cause reaction rates that would never occur at low storage temperatures (e.g. 21°C). Storage temperatures used for FSMP accelerated shelf life studies should be no more than 10°C above typical, ambient storage temperatures. Excessively high temperatures should be avoided as they can lead to nutrient instability and other changes that do not reflect typical conditions. The specific temperatures used for these studies vary depending on the type of FSMP and are determined by the product manufacturer with appropriate justification.

Data generated in a single accelerated temperature study may be sufficient to establish product shelf life if the appropriate correlation between accelerated and available real-time stability data is established on the most unstable nutrients by predictive mathematical modelling.

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[7] International Conference of Harmonisation Q1A(R2) and Q1F: (link; accessed on 20 FEB 2021)
[8] World Health Organisation, Technical Report Series, No. 953, 2009 (link; accessed on 20 FEB 2021)
[9] For reference
- Zone I: "Temperate "21°C +/- 2°C / 45% +/- 5% RH
- Zone II: "Subtropical "25°C+/- 2°C / 60% +/- 5% RH
- Zone III: "Hot/dry "30°C+/- 2°C /35 +/- 5% RH
- Zone IVa: "Hot/humid "30°C +/- 2°C / 65% +/- 5% RH
- Zone IVb: "Hot/very humid "30°C +/- 2°C / 75% +/- 5% RH

ISDI recommendations: Temperature and humidity conditions

- Temperature is a fundamental parameter to control when performing shelf life tests.
- Storage conditions used during shelf life tests should reflect those expected during FSMP product shelf life and should correspond to the temperature zone of the country in which they will be marketed.
- In the case of FSMPs, stability tests under controlled humidity conditions are not required because the primary packaging is impermeable to moisture.
- For FSMPs, the world can be divided into three temperature zones:
  - Zone I: "Temperate" 21°C +/- 2°C
  - Zone II: "Subtropical" 25°C +/- 2°C
  - Zone III "Hot" 30° +/- 2°C
- Real-time shelf life tests performed in a climatic zone hotter than the climatic zone in which the FSMP will be marketed are acceptable for justification/validation of shelf life in cooler climatic zones.
- Storage temperatures used for FSMP accelerated shelf life studies should be no more than 10°C above typical, ambient storage temperatures. Excessively high temperatures should be avoided as they can lead to nutrient instability and other changes not reflective of typical conditions. The specific temperatures used for these studies vary depending on the type of FSMP and are determined by the product manufacturer with appropriate justification.
- Data generated in a single accelerated temperature study may be sufficient to establish product shelf life if the appropriate correlation between accelerated and available real-time stability data is established on the most unstable nutrients by predictive mathematical modelling.

b. Light

Light, especially ultra-violet light (wavelengths < 460nm), can lead to degradative loss of vitamins. Product exposure to visible light can also compromise the product's organoleptic quality (e.g. accelerating free radical reactions that lead to fat degradation). Most FSMP primary or secondary packagings have good light barrier properties. Light is therefore not a parameter of concern for shelf life tests.

c. Oxygen

Oxygen content within the primary packaging is a critical factor in determining the stability of functional ingredients and nutrients found in FSMPs. Degradation is typically first-order and dependent on the amount of oxygen present[11]. Fats and oils are also susceptible to oxidation, which can cause rancidity via the generation of hydroperoxides, leading to smaller, volatile aldehydes and ketones and associated "off" flavours/odours. From a nutritional point of view, vitamin C in FSMP shelf life tests was the only nutrient the degradation of which was accelerated when inert gas was not used to flush the oxygen out of the headspace (see Annex). This was observed in paste and liquids but not in powders.

1.2 Intrinsic (i.e. product specific) factors

a. Degree of protein hydrolysis

FSMP shelf life tests have demonstrated that vitamin D & vitamin C were sensitive to the degree of protein hydrolysis in liquid FSMP. Degree of protein hydrolysis had no impact on the level of any nutrient in powder FSMP.

b. Product pH

pH can only be measured in liquid and is therefore not a relevant parameter in powder. Product pH can impact product organoleptic quality, as well as nutrient and component stability. Some vitamins are particularly susceptible to degradative loss in low pH conditions[12]. This is of particular relevance for low pH or acidified FSMPs (i.e. FSMPs that have a pH of 4.6 or below)[13], such as acidified milk-based FSMPs or FSMPs containingfruit-based ingredients. FSMP shelf life tests have demonstrated that the following nutrients were sensitive to an acidic pH in liquid FSMP (i.e. pH below 4.6): some amino acids (cystine, histidine, tryptophan), some vitamins (vitamin C, D, folic acid, pantothenic acid). Conversely, vitamin A was sensitive to high pH (i.e. >4,6) in liquid FSMP – see Annex.

[10] Effect of Storage Temperature on the Chemical Stability of Enteral Formula; Advance Journal of Food Science and Technology 4(5): 235-242,2012
[11] Factors influencing the stability of ascorbic acid in total parenteral nutrition infusions; J Clin Hosp Pharm. 1984 Jun;9(2):75-85.

c. Product moisture

Moisture content is a significant contributor to many of the processes responsible for nutrient loss or degradation over the product's shelf life. Product moisture is kept at a very low level in powder FSMP for safety considerations (see Product Safety paragraph below).

Vitamin A was the only nutrient to display significant losses in powder FSMPs. In contrast, several nutrients degrade in liquid FSMPs: some amino acids (cystine, histidine, tryptophan), some vitamins (Vitamin A, B12, C, D, Folic Acid, pantothenic acid, thiamine), sugars, glucose and lactose (see Annex). Pastes show nearly comparable degradation for vitamins like liquid FSMPs (Vitamin C, Folic acid, pantothenic acid, thiamine). As the data set was limited, no more evaluations about the degradation of other nutrients could be made.

d. Type of Primary packaging

Primary packaging used for FSMPs can be classified under the following categories:

- Metal cans;
- Opaque plastic bottles;
- Composite cans (cans made of multilayered materials, such as LDPE, PE, aluminum and paper);
- Flexible packaging (i.e. collapsible tubes, flexible plastic bags, sachets, pouches and stick packs); and,
- Cartons

Shelf life tests should be conducted using primary packaging with barrier properties equivalent to the commercial product. The materials that compose the packaging protect the product from the above-mentioned extrinsic factors through several barrier properties that vary from one type of packaging to another (i.e. different abilities to prevent external light, ultra-violet light, oxygen and humidity). The type of packaging used can impact the quality and shelf life of an FSMP product. However, no difference in nutrient degradation was observed between different packaging types in FSMP shelf life tests (see Annex). There is therefore no need to repeat shelf life tests for the same recipe in different types of packaging.

e. Influence of Packaging Headspace and size

Headspace is the portion above the FSMP product level (brim volume minus fill volume). This headspace is filled with air or with an inert gas (e.g. nitrogen). If the headspace is filled with an inert gas (e.g. nitrogen), oxidation reactions in the product can be prevented or decelerated. When the headspace is filled with air, the oxygen it contains may impact the stability of some nutrients and/or the sensory properties of the product. This was observed for vitamin C in liquid FSMP shelf life tests.

Packaging size may impact the shelf life of the product. When oxygen drives nutrient losses, the higher the headspace/product ratio is, the higher the risk the shelf life duration of the product may be reduced [Ref: Commission Regulation (EU) 2017/752 of 28 April 2017 Article (12)]. Also, when the barrier properties of the primary packaging materials do not fully protect the product from the external environmental factors, the higher the packaging surface/product volume ratio will be, the higher the risk that the shelf life duration of the product may be reduced [Ref: Commission Regulation (EU) 2017/752 of 28 April 2017 Article (12)].

Shelf life test results indicate that the packaging size does not affect the stability of any nutrient except marginally for Vitamin C. In this case, the smallest the packaging is, the highest the vitamin C degradation is. However, the impact of the packaging size on the amplitude of vitamin C losses is small compared to other factors such as temperature and pH (see Annex).

Since small packaging size presents the highest headspace/product ratio and packaging surface/product volume ratios and the worst-case scenario, it is not surprising that higher losses of vitamin C are observed in smaller packaging sizes [Ref: Commission Regulation (EU) 2017/752 of 28 April 2017 Article (12)].

When a product is stored in different sizes of the same primary packaging, shelf life tests conducted on a single pack sizes are sufficient to justify the shelf life of the product in all the different pack sizes.

ISDI recommendations: Packaging

- Shelf life tests should be conducted using primary packaging with barrier properties equivalent to the commercial product
- There is no need to repeat shelf life tests for the same recipe in different types of packaging.
- When a product is stored in different sizes of the same primary packaging, shelf life tests conducted on a single pack size are sufficient to justify the shelf life of the product in all the different pack sizes.

f. Specific compositional characteristics (flavours and fibre)

FSMP shelf life tests have demonstrated that flavours and absence or presence of fibre does not impact the stability of any nutrient as shown in Appendix V.

ISDI recommendations: flavours and fibre

- It is not relevant nor required to conduct distinct shelf life tests for recipes that only differ by their flavours or their fibre content.

2. Recommended analyses for determining FSMP shelf life

Each FSMP is defined by its key attributes, including:

- Product safety parameters;
- Nutrients and functional ingredient content; and,
- Organoleptic and physical (including product stability) properties.

While all these attributes must be maintained at the end of shelf life, some do not change (at all or significantly) over time and should therefore not be included in stability tests. Shelf life tests should focus on product characteristics that are likely subject to change during storage over time and that could affect the product quality, safety, nutrient levels, claims or efficacy, and therefore define product shelf life. The present chapter lists the analyses that should be part of FSMP shelf life tests and the ones that are not required.

ISDI recommendations: Scope of shelf life analyses

- Shelf life tests should focus on product characteristics that are subject to change during storage over time and that could affect product quality, safety, nutrient levels, claims or efficacy.

2.1. Product Safety

Product safety is of critical importance in FSMPs, which are medical foods for the dietary management of critically ill patients. To ensure food safety, manufacturers regularly perform rigorous ingredient qualifications, implement routine ingredient quality monitoring programs and adopt good manufacturing practices (GMP). In addition, ingredients used in the manufacture of FSMPs must conform to local legislation and international standards to ensure products placed on the market are both compliant and safe.

During the manufacture of liquid products, processes such as pasteurisation and Ultra-High Temperature (UHT) treatment kill pathogens that may be present and ensure that the product, when packaged, has been adequately heat treated. Once the product is packed and considered commercially sterile or pasteurised and sealed, food safety is ensured by the primary barrier provided by the packaging to eliminate the introduction of spores, yeasts or pathogens. For liquid products, control of micro-biological load straight after manufacturing is sufficient and monitoring pathogen content and changes during shelf life studies is not required.

Powder FSMPs contain very low moisture content within the formulation, making the environment fundamentally much harsher for pathogen growth than in liquid products. The key microbiological control parameter for powder products is to measure Water Activity (a_w), which is a measure of the free and available water vapour that can support microbial growth. Most organisms require a minimum of 0.6 a_w to grow. For powder products, ensuring that a_w straight after manufacturing is less than 0.614 is sufficient and renders any other microbiological tests unnecessary.

As a consequence, monitoring factors typically considered for food safety, including testing for contaminants, pathogens, microbial burden or assessment of sterility, is not required when determining FSMP shelf life.

[12] Source: (1) The Vitamins, 5th Ed.; Fundamental Aspects in Nutrition and Health; GF Combs, JP McClung, 2017 (2) Food and Beverage Stability and Shelf Life, Woodhead Publishing (2012); Chapter 26; "Factors Affecting the Stability and Shelf Life of Vitamin-Fortified Foods"; pp 743-749.
[13] Section 2.2. from the Codex Code of Hygienic Practice for Low and Acidified Low Acid Canned Foods (CXC 23-1979)
[14] Determination of water activity in food, Public Health England (link; accessed on 3 MAY 2021)

ISDI recommendations: Safety parameters

- Monitoring factors typically considered for food safety, including testing for contaminants, pathogens, microbial burden or assessment of sterility, is not required when determining FSMP shelf life.
- For powder products, ensuring that aw straight after manufacturing is less than 06 is sufficient and renders any other microbiological tests unnecessary.
- For liquid products, control of micro-biological load straight after manufacturing is sufficient and monitoring pathogen content and changes during shelf-life studies is not required.

2.2. Nutrient and functional ingredient content

Not all nutrients have the same susceptibility to, or rate of, degradation over shelf life. As explained in the respective chapters above; temperature, light, oxygen, product pH, degree of protein hydrolysis and product moisture can, to a differing extent, affect nutrient stability.

FSMPs typically contain a complex blend of macro and micro-nutrients. However, the shelf life of FSMPs is primarily defined by the nutrients most prone to degradation. While most nutrients remain stable, other nutrients degrade over time and at different speeds (see Annex). It is these more labile nutrients that define and reduce the shelf life of FSMPs. Nutrients with higher rates of degradation during shelf life can therefore be used as tracers or markers to indicate product nutritional suitability and help define product shelf life. If the levels of these more unstable nutrients remain adequate at the end of shelf life, the levels of the other more stable nutrients will be adequate too.

Typically, therefore, shelf life tests for FSMPs should only require a quantitative analysis of a limited number of identified nutrient tracers[15]. Based on the available results from more than 1400 FSMP shelf life tests conducted by industry and gathered to build this guidance, most nutrients - all minerals, all macronutrients, all fatty acids, total nucleotides, some vitamins and most of amino acids - are stable in all conditions and should be excluded from shelf life tests.

ISDI recommends limiting the analyses of nutrients in FSMP shelf life tests to the following tracers or markers (see Annex for additional justification):

TYPE OF PRODUCTS	TRACERS
Powder FSMPs	Vitamin A
Non acidified liquid and paste FSMPs	Vitamin C
Acidified liquid and paste FSMPs	Vitamin C & Pantothenic acid

If the FSMP contains probiotics, probiotic counts (number of colony-forming units) should also be included in the shelf life test.

ISDI recommendations: Nutrient and functional ingredient analyses

- Most nutrients (all minerals, all macronutrients, all fatty acids, total nucleotides, some vitamins and most of the amino acids) are stable in all conditions and should be excluded from shelf life tests.
- Shelf life tests for FSMPs should only require a quantitative analysis of a limited number of identified nutrient markers or tracers (i.e. nutrients with higher rates of degradation during shelf life used as tracers or markers to indicate product nutritional suitability and product shelf life)
- The following nutrients as tracers or markers should be used:

TYPE OF PRODUCTS	TRACERS
Powder FSMPs	Vitamin A
Non acidified liquid and paste FSMPs	Vitamin C
Acidified liquid and paste FSMPs	Vitamin C & Pantothenic acid

- If the FSMP contains probiotics, probiotic counts (number of colony forming units) should also be included in the shelf life test.

[15] A list of current reference methods can be found within AOAC, ISO and Codex. Other methods can be used. In such cases, method proficiency should be demonstrated using suitable matrices representing FSMPs, preferably with comparison and alignment of results to those generated using reference methods of analysis

[16] Bailey´s Industrial Oil and Fat Products, Sixth Edition, Six Volume Set. Edited by Fereidoon Shahidi, 2005 John Wiley & Sons, Inc

[17] Food Chemistry, Third edition, edited by Owen R. Fennema, 1996 Marcel Dekker, Inc., pages 492-499

[18] S. Martins et al., A review of Maillard reaction in food and implications to kinetic modelling, Trends in Food Science & Technology, 11 (2001), 354-373

2.3. Organoleptic and physical properties

Organoleptic changes during storage of FSMPs include changes in appearance and colour, smell and taste, texture and mouth-feel. These changes can occur in every kind of food during storage. While not all changes of these types will cause unwanted or unpleasant taste or texture, they are nonetheless indicators that the product is showing a degree of instability during shelf life.

These changes are provoked by oxygen, light, moisture, temperature or the ingredients reacting with each other. Major chemical changes include lipid oxidation[16] and enzymatic[17] and non-enzymatic browning[18], and all three can occur simultaneously within an FSMP. Lipid oxidation, for example, produces off-flavour compounds through the generation of peroxides that are converted to alcohols, ketones and aldehydes, as well as free fatty acids. While uncommon in sterile commercial products, enzymatic browning is provoked by lipase and generates free fatty acids that have a distinct off-flavour that can render the taste unacceptable. Finally, non-enzymatic browning (Maillard reaction) is responsible for brown discolouration and flavour changes.

In addition to monitoring sensorial properties over shelf life, the manufacturer will assess the changes in physical parameters and determine what levels of changes are acceptable. The aim is to evaluate the impact on the user experience when preparing (if necessary) and/or consuming the product, as recommended by the manufacturer. This is considered a critical element of shelf life studies since it focuses on the necessary step that determines consumer acceptability and consumption.

Physical properties, such as appearance, sedimentation, absence of lumps, homogeneity and suitability of product use (e.g. pumpability for a tube feed product), may also change during the storage of FSMPs. These changes can be impacted by several factors, such as ingredient composition, product complexity, manufacturing processing, product storageconditions and packaging material.

Overall, physical, organoleptic and sensory evaluations should be adapted to the method of product consumption and target patient acceptance of product preparation and ingestion (e.g. exclusively tube-fed products do not have to be organoleptically acceptable but must be lump free and display a suitable viscosity).

ISDI recommendations: Physical and organoleptic properties

- Overall, physical, organoleptic and sensory evaluations should be adapted to the method of feeding and target patient acceptance of preparation and ingestion (e.g. exclusively tube-fed products do not have to be organoleptically acceptable but must be lump free and display a suitable viscosity).

3. Analysis frequency during shelf life tests

Real-time shelf life tests

Shelf life duration can be appropriately defined on the sole basis of real-time results obtained, at a minimum, at the beginning and end of shelf life. Results at intermediate times are not mandatory.

If real-time data at end of shelf life are not available, intermediate real-time data can be used to define an initial shorter, or preliminary, shelf life. Significant changes in sensory properties, physical properties and nutrient content in real-time (non-accelerated) conditions typically require longer than 3 months to materialise, so a frequency of analysis less than three months is not necessary.

ISDI recommendations: Analysis frequency

- Shelf life duration can be appropriately defined on the sole basis of real-time results obtained, at a minimum, at the beginning and end of shelf life. In such cases, the obtention of results at intermediate times is not mandatory.

Accelerated shelf life tests

The frequency and scope of analyses should be defined on a case-by-case basis and based on the market temperature zone and product type.

The temperature and humidity conditions for conducting shelf life tests are discussed in chapter 1.1.

4. Number of required batches

Product shelf life can be determined by analysing a single batch because the following processes ensure that different batches of the same product recipe do not present significant differences:

1. The Packaging Validation Standard (ISO/TS 22002-4): Specific prerequisite programs for food packaging manufacturing ensure that the barrier properties of a given packaging do not differ from one pack to the next. The physical-chemical processes responsible for product deterioration and for the determination of the product shelf life duration will therefore be qualitatively and quantitatively identical between different manufacturing batches.

2. Manufacturing and hygiene standards: The implementation of Food Good Manufacturing Practices (GMPs) and Hazard Analysis and Critical Control Points (HACCP) ensures that the product composition and properties remain constant across different production batches[19]. The residual and unavoidable small variations in manufacturing between different batches might result in small differences in nutrient content. These differences remain within the legal tolerances and do not affect the shelf life of the product. They might affect the quantity of some nutrients present at the beginning of the shelf life of the product*, although the relative amplitude of loss of each nutrient over time (expressed as a percentage) between batches will not be significantly different.

The implementation of these standards guarantees a small inter-batch variability. Data generated on a single batch arerepresentative of all batches of the recipe and sufficient to define the shelf life duration of the FSMP. The collection of shelf life data on several batches is therefore unnecessary.

ISDI recommendations: Number of batches

- The shelf life of a product can be determined by the analysis of a single batch.

[19] See General Principles of Food Hygiene CAC/RCP 1-1969 (link).

* Once commercially launched, food manufacturers routinely monitor product composition at batch release.

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