10 March 2025

Shelf-life Determination of Foods for Special Medical Purposes (FSMP)

Position Paper – Factors around Humidity, Temperature & Climatic Zones

Summary

- 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.

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Introduction

In 2019, following a literature review that emphasized the lack of relevant references and studies, the International Special Dietary Industry (ISDI) launched a multiyear project to develop guidance on shelf-life tests for Food for Special Medical Purpose (FSMP).

The major global manufacturers of FSMPs (Abbott, Fresenius, Nestlé Health Science, Nutricia, Reckitt) participated in the Stability Guidelines Task Force. Available stability data on FSMPs were gathered to be analysed and used to provide recommendations on which nutrients should be included in stability tests to determine the shelf-life of foods for special medical purposes.

The data collected comprised 32,798 data points and 1,471 datasets (or recipes) covering 67 nutrients. The datasets were categorized into 9 categories (physical state, temperature, humidity, pH of the product, level of protein hydrolysis, presence/absence of fat, adult vs infant FSMP, type of packaging and protective atmosphere) with 28 subcategories. For each nutrient, statistical analyses were performed to identify which factors among these 28 subcategories were responsible for losses and to which extent.

The recommendations applicable to FSMP would be the same for other Foods for Special Dietary Uses (FSDU) that are manufactured in a similar way, such as for example, infant formula or follow-up formula.

Results

Temperature during product storage can have an impact on product characteristics such as sensory properties and the physical stability of the formulation. In addition, 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.

The shelf-life analyses of the FSMPs performed by the ISDI Stability Guideline Task Force demonstrates (see Appendix):

- in non-acidified liquid FSMPs, 3 nutrients displayed losses much larger than the others (by decreasing amplitude of losses: vitamin C, thiamin and vitamin D -for this nutrient losses were only observed in products with hydrolyzed proteins).
- in acidified liquid FSMPs, 5 nutrients displayed losses much larger than the others (by decreasing amplitude of losses: pantothenic acid, vitamin C, folic acid, thiamin and vitamin D -for this nutrient losses were only observed in products with intact proteins).
- in powder FSMPs, the only nutrient displaying losses was vitamin A.

Observed losses in amino acids and in total sugars, glucose and lactose are likely due to Maillard reducing reactions.

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.

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ISDI notes the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH)[1],[2] which divides the world into four climatic zones[3]. 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 the shelf-life analyses of the FSMPs performed by the ISDI Stability Guideline Task Force in which no nutrient was affected by the humidity conditions of the tests.

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 performed at 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[4], 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

[1] International Conference of Harmonisation Q1A(R2) and Q1F: (link; accessed on 10 March 2025)

[2] World Health Organisation, Technical Report Series, No. 953, 2009 (link; accessed on 10 March 2025)

[3] 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

[4] Effect of Storage Temperature on the Chemical Stability of Enteral Formula; Advance Journal of Food Science and Technology 4(5): 235-242,2012

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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.

APPENDIX

Average percentage of degradation after one year in liquid FSMPs.

Nutrient	Non-acidified liquid FSMPs		Acidified liquid FSMPs	
	20°C	25/30°C	20°C	25/30°C
Vitamins				
Pantothenic acid (B5)	stable	-10%	-53%	-72%
Vitamin C[1)]	-20% (with flushing) -46% (no flushing)	-55% (with flushing) -65% (no flushing)	-35% (intact protein) -49% (amino acid based/hydr.)	Not enough data (intact protein) -68% (amino acid based)
Folic Acid (B9)	-11%	-16%	-35%	-56%
Thiamin (B1)	-20%	-50%	-20%	-50%
Vitamin D	Stable with intact proteins -33% (extensively hydrolysed proteins)		-28% (with intact proteins)	
Vitamin B12	-11%	-17%	-11%	-17%
Vitamin A	Stable	-15%	stable	
Amino acids				
Tryptophan	stable		-21%	-31%
Cysteine	stable		-20%	
Histidine	stable		-19%	
Sugars				
Glucose	-19%			
Lactose	-10%			
Total Sugars	-7%		-14%	

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