Annex C: Minimum Information Requirements for Stability Testing Protocols and Reports

Table 1. Stability study testing parameters and frequency for vitamin A soft gelatin capsules:
The below table indicates minimum requirements

Storage		Testing parameters						
		General appearance		Assay of capsule contents/fill			Functionality	Level of microbial contamination[1]
Testing interval	Condition	Vit. A oil[2 or 3]	Soft gel caps[4]	Vit.A[5 or 6]	Vit. E	Uniformity of dosage units	Hardness	
Specifications		Pass/ fail	Pass/ fail	90.0-120.0% of labeled amount of Vit. A *Report in IU and %*	Limits (min. and max. as % LC) of Vit. E	Meets USP <905> requirement or Meets Ph. Int. Uniformity of deliverable dose (single-dose container) requirement	Limits (min. and max. in Newtons) to be provided by mfrs	Total viable count (NMT10^4/g) Yeast- mold (NMT 10^2/g) Entero bac. (NMT 10^2/g) Absence of E.Coli, Staph.aureus, Salmonella
Initial*		X	X	X	X	X	X	X
Accelerated								
1 Month	40ºC ± 2ºC/75% RH ± 5% RH	X	X	X	X	X	X	X
2 Months		X	X	X	X	X	X	X
3 Months		X	X	X	X	X	X	X
6 Months		X	X	X	X	X	X	X
Long-term								
3 Months	30ºC ± 2ºC/65% or 75% RH ± 5% RH	Δ	Δ	Δ	Δ	Δ	Δ	
6 Months		Δ	Δ	Δ	Δ	Δ	Δ	
9 Months		Δ	Δ	Δ	Δ	Δ	Δ	
12 Months		Δ	Δ	Δ	Δ	Δ	Δ	
18 Months		Δ	Δ	Δ	Δ	Δ	Δ	Δ
24 Months		Δ	Δ	Δ	Δ	Δ	Δ	
36 Months		Δ	Δ	Δ	Δ	Δ	Δ	Δ

*Time point "0" (TP0), the initial time point, should correspond to the study start date, i.e. the day the product is placed in the appropriate stability chamber. Subsequent time points indicate the time at which the samples are removed from the stability chamber in reference to TP0 as described above.

[1] Ph. Eur 6th Total viable count 2.6.12/2.6.13 Tests for specified microorganisms (Pharmaceuticals products which contain excipients/APIs of animal origin).
[2] Current official version of USP – VA OLP monograph (Identification)
[3] Current official version of Int. Ph. – Retinol Oral Solution monograph (Identity test)
[4] To be defined by mfrs to meet NI/UNICEF technical specification – Look for organoleptic properties such as leaking, clumping, melting, etc.
[5] USP – VA OLP monograph (Assay Vit A). As per official correspondence with the USP, the Dietary Supplements Dosage Forms Subcommittee members have agreed to support the request to reduce the lower limit of vitamin A from NLT 95.0% to NLT 90.0% of labeled claim. This change was reflected in the April, 2013 publication of the USP Revision Bulletin.
[6] Current official version of Int. Ph. – Retinol Oral Solution monograph (Assay).

Evaluation of data required

A systematic approach should be adopted for the presentation and evaluation of the stability information, which should include, as appropriate, results from the physical, chemical, biological and microbiological tests, including particular attributes of the dosage form *(for example, hardness for softgel capsules where an oral solution is the dosage form)*. Stability studies should be presented in an appropriate format (e.g. tabular, graphical and narrative).
In addition to *Table 1,* above, the stability study reports need also to include:

- FPP: Ingredients & formulation, dosage strength, batch number, size and mfg date;
- API: Ingredients & formulation, manufacturer and batch number;
- Packaging: Description, materials used, and no. of units per container;
- Study start date, individual time points and total duration of the study;
- Specification reference / Acceptability limits for each parameter tested;
- For quantitative tests, actual numerical results should be provided (avoid using terms like “within limits” or “conforms”);
- Information on analytical procedures used to generate the data and validation of these procedures (if applicable);
- Information on characterization of impurities;
- Study conclusions.

Any variation introduced to the FPP such as changes in the formulation, manufacturing process, container closure system, properties of the packaging materials etc. that could adversely affect the stability of the product and/or where the existing data no longer supports the quality, safety or efficacy of the varied product throughout its shelf life must be reported to NI and UNICEF for assessment.