

2.1.P.8 Stability

Shelf-Life and Storage Conditions:

An initial twelve-month 'shelf-life' for storage below 25°C will be based on three-month stability data at 30°C/65%RH.

Stability Program:

A rolling stability testing programme (POV, p-AV and fatty acid analysis) at 25°C and 30°C was commenced in July 2014.

Stability testing is being performed by ALS Food and Pharmaceutical (<http://www.als-testing.co.uk>) at their GMP compliant Chatteris facility.

Testing protocol is as follows:

- Product to be stored – 1 batch of concentrated omega-3 EPA fish oil encapsulated and blistered in boxes of 60.
- Product to be stored at 25°C/60%RH for 36 months in accordance with ICH guidelines.
- Product to be stored at 30°C/65%RH for 18 months in accordance with ICH guidelines.

The table below summarises the time point/condition at which product is to be tested:

Condition/Time Point (months)	0	3	6	9	12	15	18	21	24	27	30	36	Spares
25°C / 60%RH	A,B*	A,B	A,B	A,B	A,B	A,B	A,B	A,B	A,B	A,B	A,B	A,B	24
30°C / 65%RH		A,B	A,B	A,B	A,B	A,B	A,B						12
Minimum number of sample blisters required per batch	2	4	4	4	4	4	4	2	2	2	2	2	36

The following tests are to be performed, at the time points indicated in the above table:

Suite ID: A = Anisidine value (p-AV), Peroxide value (POV)

 B = Fatty acid Profile (excluding cis / trans breakdown)

Note: B* - sample will be tested after storage for five weeks at 25°C/60%RH. Testing of all following time points will be conducted as per schedule.

Test	Method	Specification	Result 0M time point, 25°C/60%RH
POV (Peroxide Value)	AM/C/112 (Attachment 12).	Max 5.0meq/kg	2.5
p-AV (Anisidine Value)	ISO 6885	Max' 20.0	16
TOTOX (2xPOV +p-AV)	(Derived value)	Max' 26.0	21
Fatty acid analysis	GOED Omega -3 Voluntary Monograph (v. 4) (Attachment 11)	NLT EPA _≥ 90%	<i>Not yet available.</i>

0M test certificate provided in Attachment 13 (excluding Fatty acid analysis which is being tested after storage for 5 weeks).

Note: Suite A individual test parameter results will be reported as obtained. TOTOX value will be derived as follows: TOTOX = 2POV + p-AV.

Shelf-Life Extension Program:

A review of the stability programme and supporting data for shelf life assignment will be carried out by the head of R&D, Quality Control North West (QCNW), on behalf of Stockport Pharmaceuticals.

Shelf life extension will be carried out following the receipt of satisfactory data at each time point during the on-going stability test program.

The three-month stability data will be available in mid-October 2014 and will be submitted to the MHRA to gain approval for an initial 12-month shelf-life.

This will be followed by repeat stability testing at 30°C/65%RH every three months allowing extension of the shelf-life in a stepwise manner (see table below), thus taking the maximum shelf-life to 36 months (which will enable the trial to recruit to target and complete the intervention for all participants by July 2017). Ongoing three-month stability testing at 25°C/60%RH will continue through to 36 months and confirm stability stored below 25°C.

30°C/65%RH Stability data within specification	Assigned shelf life at 'store below 25°C'
3 months	1 year
6 months	2 years
9 months	30 months
12 months	3 years