GLOBAL ORGANIZATION FOR EPA AND DHA OMEGA-3S

Advice to Amazon on proper storage and distribution conditions for omega-3 EPA/DHA dietary supplements

GOED, the Global Organization for EPA and DHA Omega-3s, is a member-based organization representing the global omega-3 industry. Our membership includes producers of EPA+DHA oils as well as contract manufacturers and supplement brands. We have polled our members on the topic of applicable storage conditions in order to assist Amazon in continuing to offer quality omega-3 dietary supplements to consumers.

Omega-3 dietary supplements containing EPA and DHA are heat-sensitive products. They are designed and formulated according to their stability with respect to the conditions of certain climatic zones (link), as defined by the ICH (International Conference for Harmonization). The assigned zone for the United States (US) is zone II, characterized by the following conditions: a temperature of 25°C ± 2°C and a relative humidity of 60% ± 5%.

Formulation of omega-3 products is accompanied by stability testing for those conditions where the product is sold. Stability testing is necessary to prove the product is fit for use. In the US, the FDA requires under the Current Good Manufacturing Practice (CGMP) in Manufacturing, Packaging, Labeling, or Holding Operations for Dietary Supplements (21 CFR 111) (XVII. Subpart M – Holding and Distribution - link) that dietary supplements be held under appropriate conditions of temperature, humidity, and light so that the identity, purity, strength, and composition of the components and dietary supplements are not affected (21 CFR 111.455(a)), and that components, dietary supplements, packaging, and labels under conditions are held under conditions that do not lead to the mix-up, contamination, or deterioration of components, in-process materials, dietary supplements, packaging, and labels (21 CFR 111.455(c)).

For omega-3 products, normal use is the climatic zone for which products are developed. The maximum temperature that our members have indicated is compatible with a product that remains within specification is 25-30°C. Humidity outside the packaging is not considered of influence.

For temperatures above 25-30°C. the quality of products sold in the US cannot be guaranteed and will certainly suffer. In particular, three quality aspects of omega-3 product quality cannot be guaranteed at temperatures above 25-30°C:

i) Oxidative quality will not stay below the limits that industry specifies (primary oxidation parameter Peroxide Value max 5 meq O_2/kg) and secondary oxidation parameter para-Anisidine Value max 20). In general, the rate of oxidation doubles with each 10°C rise in temperature, meaning that above 25-30°C rancidity can develop and reach an unacceptable level in an exponential manner.

ii) capsule integrity – Many omega-3 products are sold in encapsulated form, most often in gelatin capsules. Above 25-30°C the gelatin becomes soft and sticky, leading to the clumping of capsules.

iii) EPA/DHA omega-3 content - Whereas the content of fatty acids is not expected to be affected in the short run (weeks to a few months), it is likely that exposure to temperatures above 40°C over a prolonged period of time (months to years) will also affect the nutrient levels (as a result of the developing rancidity).

GOED recommends the following temperature conditions for storage and distribution of omega-3 EPA/DHA dietary supplements. Maximum 25-30°C, corresponding to the temperature range for which products are designed to be

used in the US, under low light conditions. A responsible retailer guarantees the storage and distribution conditions for which dietary supplements were developed and tested, and follows the FDA DS CGMP rule. A temperature for storage and distribution condition that ranges up to 155 degrees Fahrenheit (i.e. 68.3°C), as a permissible temperature excursion by Amazon, is not suitable for omega-3 EPA/DHA dietary supplements. Even for omega-3 products for which no expiration date is provided, such harsh conditions are not compatible with acceptable product quality.

As additional background, stability testing of nutritional finished products is carried out by contract manufacturers and brands by one of the following guidelines:

- ICH guidelines
  - International Conference on Harmonization (ICH) – Guidance for Industry: Q1A(R2) Stability Testing of New Drug Substances and Products - https://www.fda.gov/media/71707/download
  - ICH Guideline Q1D – Bracketing and Matrixing Designs for Stability Testing of New Drug Substances and Products – https://www.fda.gov/media/71720/download
  - ICH Guideline Q1E – Evaluation of Stability Data - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/q1e-evaluation-stability-data

  These ICH guidelines have been developed for pharmaceutical products, but they are widely employed for dietary supplements around the world.

Lighting conditions should also be considered (in general, omega-3 products should be stored under dim light conditions, as strong incident light can augment oxidation reactions).

Acceptable results from long-term shelf-life studies may be used to justify increasing the shelf-life claim (expiration date) for a dietary supplement.

Product developers frequently use accelerated studies that last three to six months, as a means of predicting product shelf-life for up to two years. The following storage conditions are recommended for products with no special storage conditions specified on the label: 40°C ± 2°C and 75% ± 5% relative humidity. Alternative storage conditions and/or tolerances may be used, as appropriate. Accelerated studies are not 100% predictive of real time product behavior under a certain condition, and the stability of a product must be evaluated under real time conditions.

In summary, storage and distribution should be aligned with the formulation for the zone for which it was designed and tested, and used under normal conditions. That means, for this condition, the quality of the product is guaranteed for the indicated shelf life duration.

Sincerely,

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