HPUS Homeopathic Drug Stability Guidelines

Introduction

1. Homeopathic drugs are drugs within the meaning of the United States Food, Drug and Cosmetic Act and are subject to compliance with the Current Good Manufacturing Practices (GMPs) for manufacture and quality. Drug product stability is an integral part of product quality and assures that the drug product will perform as intended throughout its period of use.
2. Homeopathic drugs are exempt from expiration dating under the FDA Compliance policy Guide Sec. 400.400 Conditions Under Which Homeopathic Drugs May be Marketed (CPD 7132.15), however market forces and GMPs dictate the necessity and practicality of providing shelf life information for homeopathic drugs.
3. Manufacturers of homeopathic drugs and contract marketers are responsible for assessing the stability and conformance to written specifications for all homeopathic starting materials, tinctures, triturates, potencies and finished dosage forms which they manufacture and /or market in conformance with HPUS and FDA cGMP requirements and specifications.
4. Risk analysis or product matrixing may be appropriate in instances of a) small scale production, b) a wide variety of active ingredients with similar physicochemical characteristics and prepared in similar attenuations, or c) products with active ingredient attenuations beyond the limits of analytical detection.
5. Testing methodologies other than those prescribed in the HPUS, USP or other official compendia must be validated and conform to established laboratory controls for GMP (as per CFR 211.Subpart I).
6. Expiration Dating and Retesting specifications are HPUS monographed substance specific, unless the manufacturer can demonstrate that different homeopathic starting materials, intermediates or finished products have the same or very similar physicochemical properties and can show that stability data can be extrapolated to different products of the same dosage forms, at additional attenuations beyond the limits of analytical detection.
7. Retesting is appropriate for any material for which the manufacture can demonstrate conformance to specifications. A retest of previously approved materials which demonstrates “no change from initial testing” supports the continued use of the material for up to one year or no more than an additional 50% of the initial stability period if less than 1 year.

Starting Materials

1. Starting materials including botanicals, active drug substances and excipients must have assigned periods of use and be subject to retesting as needed to confirm suitability for use.
2. Botanicals
    a. Fresh plants have a stability period of 72 hours, unless the collector or manufacturer has established a longer time period based on quality testing.

b. Fresh plant material preserved in alcohol should be processed as soon as possible.

c. Dried plant material, in well sealed containers and protected from light, have a stability period of 3 years. Extended shelf lives beyond this period must be supported by the manufacturer's quality testing prior to use.

d. Microbiological limits: refer to [*Insert final name of GMP Document here*]: Raw Materials of Botanical Origin 5.1.8 g.

3. Chemical Substances: Pure chemicals and minerals utilize the manufacturer's expiration dates if provided. If no expiration date is provided the material should be retested using the most appropriate methods for conformance to HPUS or manufacturer's established specifications.

4. Mixtures of chemical or homeopathic constituents, with or without impurities, should be evaluated and retested after 2 years and 4 years and then prior to each use utilizing the most appropriate methods.

5. Freeze dried zoological materials (Sarcodes, Nosodes, Microorganisms) have an initial two year period of use which may be extended with annual retesting or immediately prior to use with the most appropriate methods, for conformance to HPUS monograph or manufacturer's established specifications.

6. Frozen materials: Freezing should be considered a short term or temporary measure to preserve a material for further processing. Frozen materials should be qualified with testing for compliance with the monograph.

Tinctures, Low Attenuations

1. Analytical methods for tinctures and first attenuations; for example 2X, 3X and 2C are based on analytical methods published in HPUS or otherwise demonstrated to be appropriate by the manufacturer. These methods may also be applicable for the assessment of homeopathic intermediates and attenuations.

2. Alcoholic HPUS tinctures and low attenuations are generally considered to be stable for 3-5 years when stored in well-sealed containers and protected from light.

3. Tinctures and low attenuations should be retested at 3 years of storage and thereafter annually or immediately prior to use for conformance with all relevant HPUS stability indicating parameters and specifications.

4. In the cases of tinctures and low attenuations that do not have HPUS published quality testing requirements, manufacturers must establish specifications consistent with HPUS testing methodologies or other reliable analytical methods. Tinctures and low attenuations are tested for conformance with manufacturer-established specifications, at 3 years and thereafter every 2 years or immediately prior to use.

Triturates and Subsequent Triturations

1. Triturates should be tested after 5 years of storage and every 2 years or immediately prior to use for conformance with established specifications including assays where applicable.

2. In the cases of triturates that do not have HPUS published quality test requirements manufacturers must establish specifications. When available, quality and/or assay testing consistent with HPUS testing methodologies or other reliable analytical methods may be done.
3. Subsequent 2X, 3X and 2C and possibly higher triturations should be tested for conformance with established specifications consistent with HPUS testing methodologies or other reliable analytical methods. First attenuations are tested for conformance with manufacturer-established specifications, at 3 – 5 years and every 2 years thereafter or prior use.

Intermediates, Attenuations and Triturations

1. Homeopathic intermediates, attenuations and triiturations which are manufactured from tinctures or starting materials are considered to be separate entities and are tested or assessed for stability and appropriate shelf lives independent of the starting material or tincture.
2. When feasible, the stability of intermediates, attenuations and triiturations should be tested using HPUS methodologies and their stability evaluated based on the container and closure system used for storage. These materials should be tested for stability using a schedule similar to that used for the tincture or first trituration. Alternate analytical methods, where available and validated, may also be used to assess stability.
3. The stability of attenuations and triiturations, beyond the limits of current quantitative analytical methodologies, should be established based on the stability of the vehicles and the specifications of the dosage form. Testing should establish that there 'has been no change in the established specifications' under normal storage conditions and packaged in the container and closure system used for storage or marketing.

Finished Products

1. Homeopathic marketed dosage forms must meet the requirements for drug product stability in 21 CFR 211.166 with a written assessment of stability based on testing or examination of the product.
2. Finished products must have established specifications for the product's physical, microbiological, and chemical characteristics.
3. Stability assessment must be performed on drug products in the same container and closure systems in which the product is marketed.
4. Shelf lives, when established, are independent of the use life of the starting material or tincture.
5. Finished Goods stability testing should be conducted to determine ingredient compatibility and 'no change' in manufacturer established characteristic and critical or marker specifications, from the initial testing at the time of manufacture, to demonstrate stability.
6. Stability assessment should establish the suitability of all packaging components.