

Effective innovation in development, manufacture, and quality assurance would be expected to answer the following questions:

- What are the mechanisms of degradation, drug release, and absorption?
- What are the effects of product components on quality?
- What sources of variability are critical?
- How does the process manage variability?

This guidance facilitates innovation in development, manufacture, and quality assurance by focusing on process understanding. These concepts are applicable to all manufacturing situations.

3.3.2 Phytomedicines

In January 2004, the U.S. FDA issued a guideline for botanical products and a revised draft in 2016. The information discussed in section VII.A.1 of the guideline pertains to the initiation of characterization of the drug substance. Also, it should be provided for all products. It is important for the safe conduct of clinical trials to ensure the proper identity of botanical raw materials used in the trials. As there is no history of experience in the United States with botanical raw materials marketed only outside the United States, a certificate of authenticity of the plant and plant parts should be provided for such materials. A trained professional who is competent to determine authenticity should sign this certificate. This information should also be provided, if available, for a botanical raw material marketed in the United States.

The general method of preparation (e.g., pulverization, decoction, expression, aqueous extraction, and ethanolic extraction) is provided under §312.23(a)(7)(iv)(a). This is especially important where more than one process exists in the literature on which the safety of the botanical drug substance is based.

The European Medicines Agency (EMA) provides the following guidelines for herbal (botanical, as listed in United States) products:

- Patient Leaflet template concerning advice on the preparation of herbal teas as (traditional) herbal medicinal products by end-users
- Public statement on the interpretation of the term 'external use' for use in the field of traditional herbal medicinal products
- Public statement on CPMP List of Herbal Drugs with serious risks, dated 1992
- HMPC statement on environmental risk assessment of herbal medicinal products

A comprehensive specification for each herbal drug must be submitted, even if the starting material is a herbal drug preparation. This also applies if the applicant is not the manufacturer of the preparation. In the case of fatty or essential oils used as active substances of herbal medicinal products, a specification for the herbal drug is required, unless fully justified. The scientific names of the parent plant and its part(s) also need to be stated.