POLICY AND PROCEDURES

Office of Pharmaceutical Quality

Acceptability of Standards from Alternative Compendia (BP/EP/JP)

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PURPOSE

- This MAPP provides clarification to Office of Pharmaceutical Quality (OPQ) reviewers on the appropriate use of quality standards for excipients, drug substances, and drug products found in alternative compendia, specifically the British Pharmacopoeia (BP), the European Pharmacopoeia (EP), and the Japanese Pharmacopoeia (JP), during chemistry, manufacturing, and controls (CMC) review of drug applications (i.e., investigational new drug applications (INDs), new drug applications (NDAs), and abbreviated new drug applications (ANDAs)).

- This MAPP is not intended to establish the BP, EP, and/or JP as official compendia in place of or in addition to the *United States Pharmacopeia/National Formulary* (USP/NF).

- This MAPP is not intended to preclude any current efforts to establish a process for evaluation and regulatory acceptance of harmonized analytical procedures and/or acceptance criteria.

BACKGROUND

- It is common for drug sponsors and applicants to propose specifications (i.e., attributes, analytical procedures, and acceptance criteria) for the excipients, drug

substances, and drug products in their applications based on quality standards in the British Pharmacopoeia (BP), the European Pharmacopoeia (EP), or the Japanese Pharmacopoeia (JP). However, because the *United States Pharmacopeia/National Formulary* (USP/NF) is a drug compendium officially recognized in the United States, reviewers have been reluctant to accept BP, EP, or JP quality standards as part of the drug application review process, even when the standards in the BP, EP, or JP are equivalent to or better than the corresponding USP/NF standards. In the past, reviewers gave varying advice to the pharmaceutical industry about the use of these standards in applications. Some have informed companies that standards in USP/NF monographs must be used as the specifications; others have said that the standards in the BP/EP/JP monographs could be used, but the USP/NF monographs would be considered the official standards. This MAPP is intended to clarify OPQ's policy on this topic.

POLICY

- It is reasonable to accept an applicant's proposal to use a quality standard from the BP, EP, or JP as part of the specifications for an excipient, drug substance, or drug product in the drug application, if the standard in the BP, EP, or JP is equivalent to or better than the corresponding standard in the USP/NF. Equivalent standards have the same acceptance criteria and make use of analytical procedures based on similar principles (e.g., chromatographic, spectroscopic, titration) and performance characteristics (e.g., specificity, accuracy, precision).

  A standard can be considered better than a corresponding standard for a number of reasons, including narrower ranges for acceptance criteria or superior performance of the analytical procedure (e.g., improved specificity, greater accuracy).

- Although specifications (i.e., test, analytical procedure, and acceptance criteria) in the General Chapters of the USP/NF are applicable only if there is a monograph in the USP/NF for the excipient, drug substance, or drug product being tested; these specifications may be accepted, if appropriate, in the absence of a monograph.

  In such cases, if the applicant proposes to use an analytical procedure from the BP, EP, or JP in lieu of the corresponding analytical procedure in the General Chapters of the USP/NF, the procedure is considered an alternative analytical procedure and may be used provided it is equivalent to or better than the corresponding analytical procedure in the USP/NF. In this circumstance, the acceptance criteria in the BP, EP, or JP monograph should be accepted only if deemed appropriate for the product under review.

- The USP/NF monographs are the official standards when excipients, drug substances, or drug products are tested for compliance with the USP/NF monograph.

- This MAPP applies to the product quality assessment of drug applications performed by the CDER/OPQ.

RESPONSIBILITIES AND PROCEDURES

- It is the responsibility of the applicant to justify the use of a standard from the BP, EP, or JP in lieu of the USP/NF standard in the application. The applicant should also provide a copy of the referenced BP, EP, or JP monograph or analytical procedure and a statement acknowledging the corresponding USP/NF monograph as the official standard or the corresponding analytical procedure as the regulatory analytical procedure.

- The OPQ product quality reviewer should assess the proposed specification to determine whether it can be considered to be equivalent to or better than the corresponding USP/NF standard.

- The respective OPQ Branch Chief and Division Director are responsible for the appropriate application of this MAPP.

DEFINITIONS

- **Official Compendium:** The Federal Food, Drug, and Cosmetic Act (the Act) uses this term to mean the official USP, the official NF, or the official Homeopathic Pharmacopeia of the United States or any supplement to them.

- **Pharmacopeia:** A book containing the official standards for drug quality, published by the authority of a government or a medical or pharmaceutical society. The most referenced pharmacopeias are the British Pharmacopoeia (BP), the European Pharmacopoeia (EP), the Japanese Pharmacopoeia (JP), and the United States Pharmacopeia (USP).

- **British Pharmacopoeia (BP):** The official standards for medicinal and pharmaceutical substances in the United Kingdom. The standards are legally enforceable in the United Kingdom and in most of the Commonwealth (http://www.pharmacopoeia.co.uk/).

- **European Pharmacopoeia (EP):** The official standards for medicines in Europe, including bulk drug substances, chemical and biological analytical methods, and reagents. It is maintained and distributed by the European Directorate for the Quality of Medicines (http://www.pheur.org).

- **Japanese Pharmacopoeia (JP):** The official Japanese standards for the description and quality of excipients, drug substances, and drug products. It is maintained and distributed by the Pharmaceuticals and Medical Devices Agency (PMDA) (https://www.pmda.go.jp/english/rs-sb-std/standards-development/jp/0019.html) and the Ministry of Health, Labor, and Welfare of Japan (MHLW).

- **United States Pharmacopeia/National Formulary (USP/NF):** The official compendia of the United States of America for excipients, drug substances, and drug products. It is published every year by the United States Pharmacopeial Convention (http://www.usp.org/).

EFFECTIVE DATE

This MAPP is effective on October 13, 2017.

CHANGE CONTROL TABLE

Effective Date	Revision Number	Revisions
2/21/2007	N/A	Original
11/3/2007	N/A	Administrative Changes
1/26/2017	N/A	Updated to reflect Office of Pharmaceutical Science change to Office of Pharmaceutical Quality reorganization
10/13/2017	Rev. 1	Policy clarification
12/8/2022	N/A	Recertified: no changes