29 January 2015

Dr. Desmond Hunt
United States Pharmacopeial Convention
12601 Twinbrook Parkway
Rockville, MD 20852-1790 USA

Dear Dr. Hunt,

The International Pharmaceutical Aerosol Consortium on Regulation and Science (IPAC-RS), submits these comments on the USP chapter <1661>, in follow up to the IPAC-RS comments on the draft <661>, <661.1>, and <661.2>. IPAC-RS is an international consortium of innovator and generic companies that develop, manufacture, and market orally inhaled and nasal drug products for the treatment of diseases such as asthma, chronic obstructive pulmonary disease, and diabetes, and is committed to advancing consensus-based, scientifically driven standards and regulations for inhalation products, with the purpose of facilitating the availability of high-quality, safe, and efficacious drug products to patients.

We support text in <1661> that clarifies the applicability of chapters <661>, <661.1>, and <661.2>. Further it is helpful to have clarification regarding responsibilities and legacy/predicate packaging. Additionally, the explanation of non-interacting materials is useful and should be incorporated into the scope statement of 661. Our other comments to <1661> are similar to and support the IPAC-RS comments made to <661>, <661.1>, and <661.2>, i.e.,

- Concepts contained in the chapter are not appropriate for a range of diverse drug product types including, e.g., inhalations and solid orals.
- Use of alternate methods should be acceptable as long as it can be demonstrated that they meet the same analytical figures of merit as those put forth in the USP.
- Performance of extractables testing on a material of construction for purposes of material characterization and selection is redundant with component testing. Component testing takes into consideration the extractables profile from not only the material but also the fabrication process. For purposes of biological reactivity evaluation, component testing is appropriate (and preferable to material of construction testing) since it incorporates consideration of the fabrication process. Performing extractables studies on a system may not allow for tracing the source of a leachable to a specific component, which is a common avenue of mitigation by a pharmaceutical manufacturer.
- The use of leachable testing, or simulated leachables testing where necessary, is appropriate for safety evaluation of the packaging system.
- The definition of polyolefins is not consistent with the polymer literature and should be revised.

We are happy to discuss these further with you directly, and/or provide further information if needed.

Sincerely,

Susan Holmes, GlaxoSmithKline
Chair, IPAC-RS Board of Directors

Robert Berger, Merck & Co
Vice-Chair, IPAC-RS Board of Directors