Update on OTC Drug Products Working Group

Donna Seibert, Ph.D., Perrigo Company
Senior Manager
Estimated >100,000 OTC drug products on the market

Photo credit: Kylen Whitaker
The Problem

- Lack of a framework to provide quality standards for OTC medicines regulated under FDA OTC Drug Monograph Review

- A need for a concerted effort to resolve longstanding science, policy and compliance issues and to set forth a framework to facilitate legally marketed quality OTC medicines under the FDA OTC Monograph Drug Review
2017-2018- CHPA-FDA-USP Round Tables
  • Sept. 19, 2017
  • March 15, 2018
  • October 29, 2018

OTC Drug Products Working Group
  • Nine meetings (October 2017 – September 2018)
  • Six Drug Products Sub-team meetings (November 2017 – April 2018)
## Potential Compendial Approaches (options) to Developing USP Standards

<table>
<thead>
<tr>
<th>Option Number</th>
<th>Proposed Option Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Referee (Traditional)</td>
</tr>
<tr>
<td>II</td>
<td>Flexible</td>
</tr>
<tr>
<td>III</td>
<td>Performance-Based</td>
</tr>
<tr>
<td>IV</td>
<td>General Chapter</td>
</tr>
<tr>
<td>V</td>
<td>Tool Kit</td>
</tr>
<tr>
<td>VI</td>
<td>Specification-only (Refers to acceptance criteria and not procedures)</td>
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</tbody>
</table>
New Strategy will apply **only to OTC drug products** marketed thru OTC Drug Review. Drug substances will continue to follow the traditional USP monograph requirements.

Traditional approach is still applicable while the new approach is intended for complex products.

Drug products monographs could list only specified impurities, with unspecified & total impurities being referred to <476> (when official).

A compendial procedure (example method) is needed for a public standard (which may not be suitable to test all marketed products) while providing flexibility to the manufacturers. Companies “may” use the compendial method or may use an independent method (validated per <1225>).

FDA needs a procedure that is easily optimizable and suitable for surveillance (or screening)
### Current monograph vs. Proposed monograph

<table>
<thead>
<tr>
<th><strong>Current</strong></th>
<th><strong>Proposed</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Definition</strong></td>
<td>Same as current</td>
</tr>
<tr>
<td><strong>Identification</strong></td>
<td>Same as current</td>
</tr>
<tr>
<td><strong>Assay</strong></td>
<td>Same as current</td>
</tr>
<tr>
<td><strong>Performance tests</strong></td>
<td>TBD</td>
</tr>
<tr>
<td><strong>Organic Impurities:</strong></td>
<td>One procedure that may or may not be used for surveillance</td>
</tr>
<tr>
<td><strong>one or more compendial</strong></td>
<td>An additional easily modifiable procedure for surveillance/screening</td>
</tr>
<tr>
<td><strong>procedures and acceptance</strong></td>
<td>Acceptance criteria for specified, unspecified, and total impurities will</td>
</tr>
<tr>
<td><strong>criteria for specified,</strong></td>
<td>be provided in the monograph, and/or are referred to applicable GC.</td>
</tr>
<tr>
<td><strong>unspecified,</strong></td>
<td></td>
</tr>
<tr>
<td><strong>and total impurities</strong></td>
<td></td>
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</table>
How is it different from current alternative procedures-
General Notices 6.30 (Official May 1, 2018)

GN: 6.30. Alternative and Harmonized Methods and Procedures
An alternative method or procedure is defined as any method or procedure other than the compendial method or procedure for the article in question. The alternative method or procedure must be fully validated (see Validation of Compendial Procedures (1225)) and must **produce comparable results to the compendial method** or procedure within allowable limits established on a case-by-case basis. Alternative methods or procedures can be developed for any one of a number of reasons not limited to simplification of sample preparation, enhanced precision and accuracy, improved (shortened) run time, or being better suited to automation than the compendial method or procedure. **Only those results obtained by the methods and procedures given in the compendia are conclusive.**

For evaluation as a potential replacement or addition to the standard, alternative methods and procedures should be submitted to USP.

Certain general chapters contain a statement…//…

**Proposed concept:** Manufacturers have the option of using an alternative but suitably validated method to test their products without having to compare against the compendial method.
• General Principles Document—related to the analytical procedure for Organic Impurities in the OTC Drug Product Monograph under the FDA OTC Drug Review
  – Analytical methods in the monograph and use of the method by the industry
  – Reference to applicable to OTC GNs to allow flexibility
  – All acceptance criteria for impurities must be met
• USP OTC Drug Product Mock up—an example based on Diphenhydramine Oral Solution
• OTC General Notices aligned with General Principles
OTC Drug Products Work Group Members

CHPA
Amy Ellefsen
Saul Gylys
Walter Hirth
John Punzi
Phil Travis
Catherine Vicente
Mike Wisser

FDA
Steve Adah
Scott Furness
Pallavi Nithyanandan
Jingyue (Jan) Yang

USP Volunteers (CHM6 EC)
Tim Gilmor (Chair)
Phil Nethercote
Raphael Ornaf
Donna Seibert
Reinhard Walter (Observer)
Kylen Whitaker

USP
Clyde Anthony
Jennifer Devine
Paul Kanjeemkattu
Elizabeth Miller
Lynette Nguyen
Sujatha Ramakrishna
Ravi Reddy
Leonel Santos

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Thank You

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