Chemical Medicines 6 (OTC) Expert Committee Update

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FDA OTC Drug Monograph Review (21 CFR Part 330) allows marketing of products that are “generally recognized as safe and effective” (GRASE).

Finished OTC products that are in the scope of the FDA OTC Drug Monograph Review can be marketed without a FDA NDA/ANDA/BLA pre-market approval.

Approximately 100,000 drug substance/dosage form/formulation combinations could currently be marketed through the FDA OTC Monograph System.

Products marketed under this system require compliance to the USP monograph, if one is available.
Standards for OTC Products - Challenges

- Many products regulated under FDA OTC Drug Monograph Review are without public quality standards for finished dosage forms.

- These OTC drug products pose unique challenges for product monograph development:
  - e.g. the formulation and development timelines are often fast to react to the constant change in consumer tastes and medicinal needs.

- Longstanding science, policy and compliance issues need innovative, flexible solutions in order to develop a suitable framework to facilitate public quality standards for finished products:
  - Essential to strike reasonable and feasible balance between compliance and regulatory predictability that helps ensure quality.
## 2015-2020 Chemical Medicines Expert Committees

<table>
<thead>
<tr>
<th>Expert Committees</th>
<th>Therapeutic Category</th>
<th>Number of Official Monographs</th>
<th>Total Number of Volunteers</th>
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<tbody>
<tr>
<td>Chemical Medicines 1</td>
<td>Antiviral, Antimicrobials &amp; Antibiotics</td>
<td>608</td>
<td>15</td>
</tr>
<tr>
<td>Chemical Medicines 2</td>
<td>Cardiovascular, Cough, Cold, &amp; Analgesic</td>
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<td>16</td>
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<tr>
<td>Chemical Medicines 3</td>
<td>Gastrointestinal, Renal, Endocrine and Ophthalmology, Oncology, Dermatology &amp; Veterinary</td>
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<td>17</td>
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<td>Chemical Medicines 4</td>
<td>Psychiatric, Psychoactive, Neuromuscular, Aerosol, &amp; Imaging Drugs</td>
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<td>Chemical Medicines 5</td>
<td>Pulmonary &amp; Steroids</td>
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<td>16</td>
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<td><strong>Chemical Medicines 6</strong></td>
<td><strong>Over the Counter (OTC)</strong></td>
<td><strong>458</strong></td>
<td><strong>18</strong></td>
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</tbody>
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CHPA-FDA-USP dialogue

- 2017 - 2018 - CHPA-FDA-USP Round Tables
  - September 19, 2017
  - March 15, 2018
  - October 29, 2018
  - October 17, 2019

- OTC Drug Products Working Group
  - Nine meetings (October 2017 – September 2018)
  - Six Drug Products Sub-team meetings (November 2017 – April 2018)

- CHPA RSQ post meeting – 22 May 2019
CHM6 EC – New Structure for cycle 2020 - 2025

- CHM6 EC was a new EC created for the current 2015 - 2020 cycle to focus on OTC products
- The current CHM6 EC focuses on development of individual OTC monographs
- New CHM6 EC structure for the next cycle
  - Develop methods, approaches and strategy for OTC product standards
  - Will not ballot individual OTC monographs
CHM6 EC will be the driving force to provide the recommendations/ideas for OTC standards development.

The recommendations/ideas are vetted by OTC products stakeholders (FDA, CHPA and OTC manufacturers) through a round table or user forum.

The stakeholders can also provide the ideas/suggestions to CHM6 EC to consider.

CHM6 EC, collaborating with OTC Products Stakeholders, can publish stimuli articles/white papers to seek broader public input.

The final recommendations/ideas are implemented into standard development.

CHM Monograph 1-5 ECs ballot product specific monographs.

CHM6 EC ballots general chapters.
When and how much specificity and/or flexibility?
How to address compliance and enforcement concerns?
What are the most feasible compendial approaches?
Applicability of the approaches in developing standards for different drug products?
How to address acceptance criteria for impurities over ICH threshold/toxicology?
   - Need toxicology reports for justification
How to prioritize standards development?
What is the best process to develop public standards?
How to address labeling issues?
... and others
Subcommittees under the CHM6 EC undertake the opportunities to develop the ideas and make recommendations to the CHM6 EC and/or other CHM ECs
- Advisory experts can be part of the subcommittees
- Subcommittee chairs report back to CHM6 EC
- Other CHM ECs who will approve the standards will be notified as needed

Each subcommittee includes FDA liaison to ensure agency’s perspective is represented

The duration of the subcommittee is not expected to be a long term
Pilot Study under the Current CHM6 EC

- Scope
  - To develop approaches to achieve a compendial “primary” method capable of testing all marketed products
  - To demonstrate the need for flexibility (e.g. performance based approach) and how to implement

- CHM6 EC chair and vice chairs as well as CHPA PQMC Cough & Cold panel recommended **diphenhydramine products** for the first pilot study
  - Presented and endorsed by the Oct 17 Round Table

- Forming a *Diphenhydramine subcommittee* under CHM6 EC to support the pilot study
  - A small group of EC members, reporting back to CHM6 EC
  - To develop and validate primary method for *Organic Impurities test* for diphenhydramine products (particularly for complex formulation, such as oral solution)
    - Focus on the common degradation products