Excipient Nomenclature - Industry Perspective

USP Excipient Stakeholder Forum
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Excipient Nomenclature Policy

- Benefit to standardized approach
- Stakeholders involvement needed in the development phase
Nomenclature & labeling

“The name of an inactive ingredient should be taken from the current edition of one of the following reference works (in the order of precedence):

1. the USP or NF
2. USAN and the USP Dictionary of Drug Names
3. CTFA Cosmetic Ingredient Dictionary
4. FCC”

If not in one of these, “common or usual name (the name generally recognized by consumers or health-care professionals) or, if no common or usual name is available, by its chemical or other technical name.”

If the excipient has a USP-NF monograph, that name is used to label the product along with any other monograph labeling requirements.
RIGHT?
Nomenclature References

**USAN**

- Formula, name and chemical information is the same as USP
- Represents the ideal molecule vs USP monograph which includes the substance + impurities + water content, etc.

**CAS Registry Numbers**

- May not meet regulatory needs, not generated confidentially, not designed to be ID standards and may be ambiguous and inadequate for capturing differences (e.g. polydispersion) needed for pharma.

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(1) Andrzej Wilk, USP, “USP Perspective Excipients Nomenclature – Overview and Updates”, USP Excipient Nomenclature Workshop, Aug. 2018

(2) Frank Switzer, FDA, “Introduction and Overview of GSRS and SRS”, USP Excipient Nomenclature Workshop, Aug. 2018
GSRS/IID and USP Nomenclature

- **Consistency needed**
  - Resolve naming discrepancies between monographs & GSRS/UNII
    - Generic chemical names not tradenames
    - Monographs focus on key attributes to support quality and safety & cover the entire product family (one monograph, several grades)
    - UNII are assigned based on a substance’s molecular structure and/or descriptive information (unique UNII for each grade)
    - Current discrepancies need one-on-one discussion to determine best path forward
  - Establish nomenclature linkage and **verification** between the drug application, the GSRS and the monograph name
  - Decide if pharmacopeia nomenclature (and listed synonyms) should be adopted by FDA as the ‘official’ names in the GSRS
Exciipient Nomenclature

Linked to the FDA Global Substance Registration System (GSRS) database, preferred substance names & UNII codes

Should include preferred name and synonyms – common, generic, compendia, cosmetic, brand and trade names

CAS#

GSRS database still needs to be reviewed & updated
Product packaging & labeling is not always for a single market – nomenclature & labeling must often meet multiple regulations.
What’s in a name?
That which we call a rose,
By any other name...
## How Should this Product be Labeled?

<table>
<thead>
<tr>
<th>Ref.</th>
<th>Primary Name</th>
<th>Synonyms</th>
</tr>
</thead>
<tbody>
<tr>
<td>USP</td>
<td>Sodium carboxymethyl cellulose</td>
<td></td>
</tr>
</tbody>
</table>
| Ph. Eur. | Carmellose sodium                                     | Carmellose natricum  
Carboxymethylcellulose sodium |
| FCC   | Cellulose gum                                          | Sodium carboxymethyl cellulose  
CMC  
Modified cellulose |
| JECFA | Sodium carboxymethyl cellulose                         | Sodium cellulose gylcolate  
Na CMC  
Cellulose gum  
CMC  
INS No. 466 |
|       | All of these are CAS# 9004-32-4 but carboxymethyl cellulose is CAS# 9000-11-7 |                                                                          |
| EFSA  | E466                                                   | Sodium carboxymethyl cellulose  
Carboxymethyl cellulose  
Cellulose gum |
| GSRS  | Carboxymethyl cellulose sodium                         | All of above except carboxymethyl natricum                              |
## Or this Product?

<table>
<thead>
<tr>
<th>Ref.</th>
<th>Primary Name</th>
<th>Synonyms</th>
<th>CAS#</th>
</tr>
</thead>
<tbody>
<tr>
<td>NF</td>
<td>Microcrystalline cellulose</td>
<td>Cellulose</td>
<td></td>
</tr>
<tr>
<td>FCC</td>
<td>Cellulose gel</td>
<td>Microcrystalline cellulose</td>
<td>9004-34-6</td>
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<tr>
<td>JECFA</td>
<td>Microcrystalline cellulose</td>
<td>INS 460(i) Cellulose gel</td>
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<tr>
<td>EFSA</td>
<td>E460(i)</td>
<td>Microcrystalline cellulose Cellulose gel Powdered cellulose</td>
<td>9004-34-6</td>
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<td></td>
<td>E460(ii)</td>
<td></td>
<td></td>
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<tr>
<td>GSRS</td>
<td>Powdered cellulose</td>
<td>E460</td>
<td>9004-34-6</td>
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<tr>
<td></td>
<td></td>
<td>No reference to microcrystalline cellulose</td>
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</tr>
<tr>
<td>GSRS</td>
<td>Microcrystalline cellulose</td>
<td>Cellulose gel</td>
<td>9004-34-6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Crystalline cellulose</td>
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<tr>
<td></td>
<td></td>
<td>Dispersible cellulose</td>
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</tr>
<tr>
<td></td>
<td></td>
<td>NO reference to “powdered cellulose”</td>
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</tr>
</tbody>
</table>

**CAS# 9000-11-7** Powdered cellulose
What is “Modified Cellulose” on a Label?

- Listed as a synonym in FCC for MC, HPMC, HPC, NaCMC and EC

- Cosmetic Ingredient Dictionary => “Cellulose & Related Polymers” – safety assessment includes cellulose and ‘modified cellulose polymers’ HEC, HPC, HPMC, MC, MCC and NaCMC

Which one do I pick? I’m so confused!
Strive for consistency among different uses/markets/countries

Determine how to handle differences between pharmacopeia (e.g. Ph. Eur. Macrogol vs. USP Polyethylene glycol)

Address differences between pharma & food compendia

Establish rules/roles for using/referencing other nomenclature, e.g. CAS RN, USAN
Nomenclature Changes

For excipients with well established names and history of use, justification is needed prior to making ANY change in the name, since ANY name change would impact product labeling and regulatory filings.

- Historical nomenclature should only be changed when a major issue (safety, patient, etc.) is identified.

- All name changes require significant resources & time.

- Changes often require more than 6 months to implement.
Considerations

- What should the policy & process consider?
  - Naming consistency
  - Existing names with a long history of use vs. those being developed
  - Impact on labeling
  - International impact
    - Pharmaceutical companies use these references when intending to market the same drug in other countries.
    - The EU has agreed to use the GSRS
Recommendation

- Start with an Advisory Panel
  - Need more than expert committee members
  - Include appropriate industry representation - makers & users
    - Address impact of a “simple” name change and potential ramifications/unintended consequences
  - Nomenclature should be aligned with industry’s uses
    - Industry can not meet FDA expectations if information is incomplete or inaccurate
    - Global view
Thank You!

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Questions?