Excipient Nomenclature - Industry Perspective

USP Excipient Stakeholder Forum
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Priscilla Zawislak,
Immediate Past-Chair, IPEC-Americas
Global Regulatory Affairs Advocacy Manager,
DuPont Nutrition & Biosciences

Multiple stakeholders; **one objective.**

International Pharmaceutical Excipients Council

Collaborative solutions for excipient industry stakeholders

Disclaimer

The views, thoughts, and opinions expressed in the presentation belong solely to the author, and not necessarily to the author's employer, organization, committee or other group or individual.

Excipient Nomenclature Policy

- Benefit to standardized approach
- Stakeholders involvement needed in the **development** phase

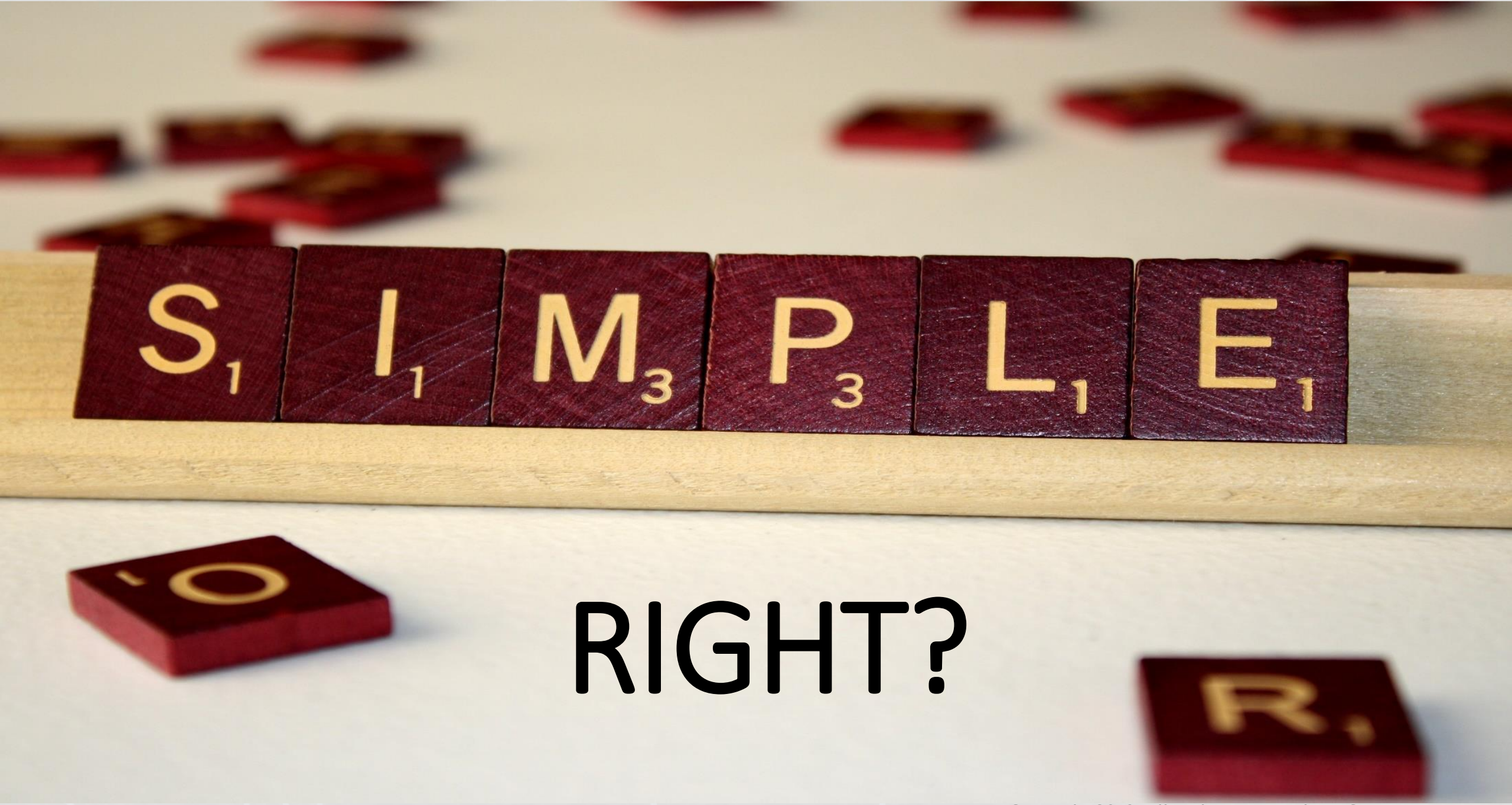
<1091> Labeling of Inactive Ingredients

- 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



Nomenclature References

USAN[1]

- 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. polydispersity) needed for pharma.[2]

[1] Andrzej Wilk, USP, "USP Perspective Excipients Nomenclature – Overview and Updates", USP Excipient Nomenclature Workshop, Aug. 2018

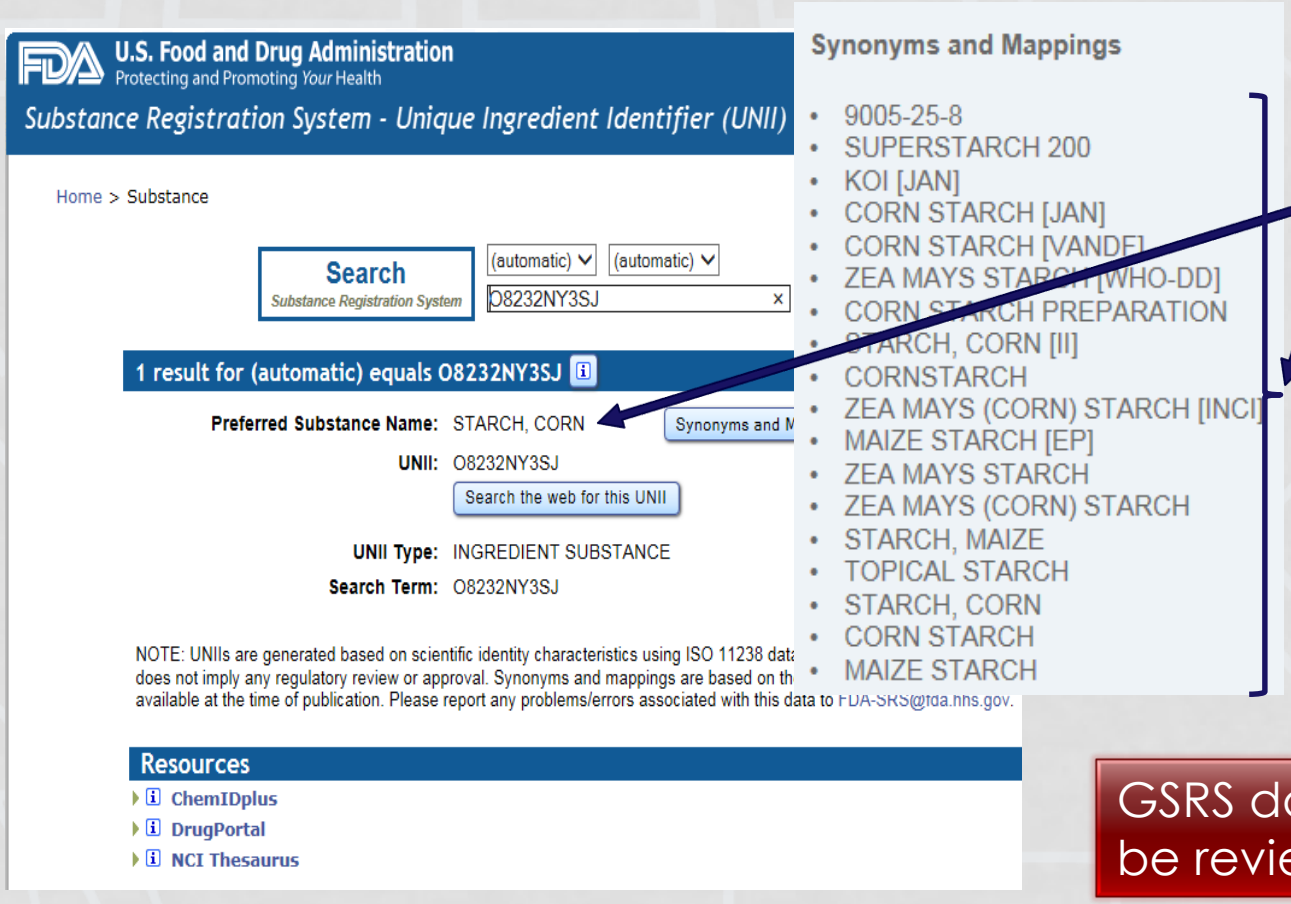
[2] Frank Switzer, FDA, "Introduction and Overview of GSRS and SRS", USP Excipient Nomenclature Workshop, Aug. 2018

GSRS/IID and USP Nomenclature

- **Consistency needed**
  - Resolve naming discrepancies between monographs & GSRS/UNIIs
    - Generic chemical names not tradenames
    - Monographs focus on key attributes to support quality and safety & cover the entire product family (one monograph, several grades)
    - UNIIs 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

Excipient 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

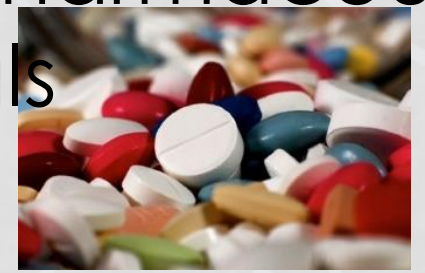
Excipient Nomenclature & Labeling

Excipient

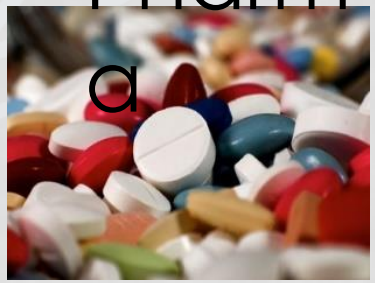
Chemical Compa

Product packaging & labeling is not always for a single market – nomenclature & labeling must often meet multiple regulations

Pharmaceuticals



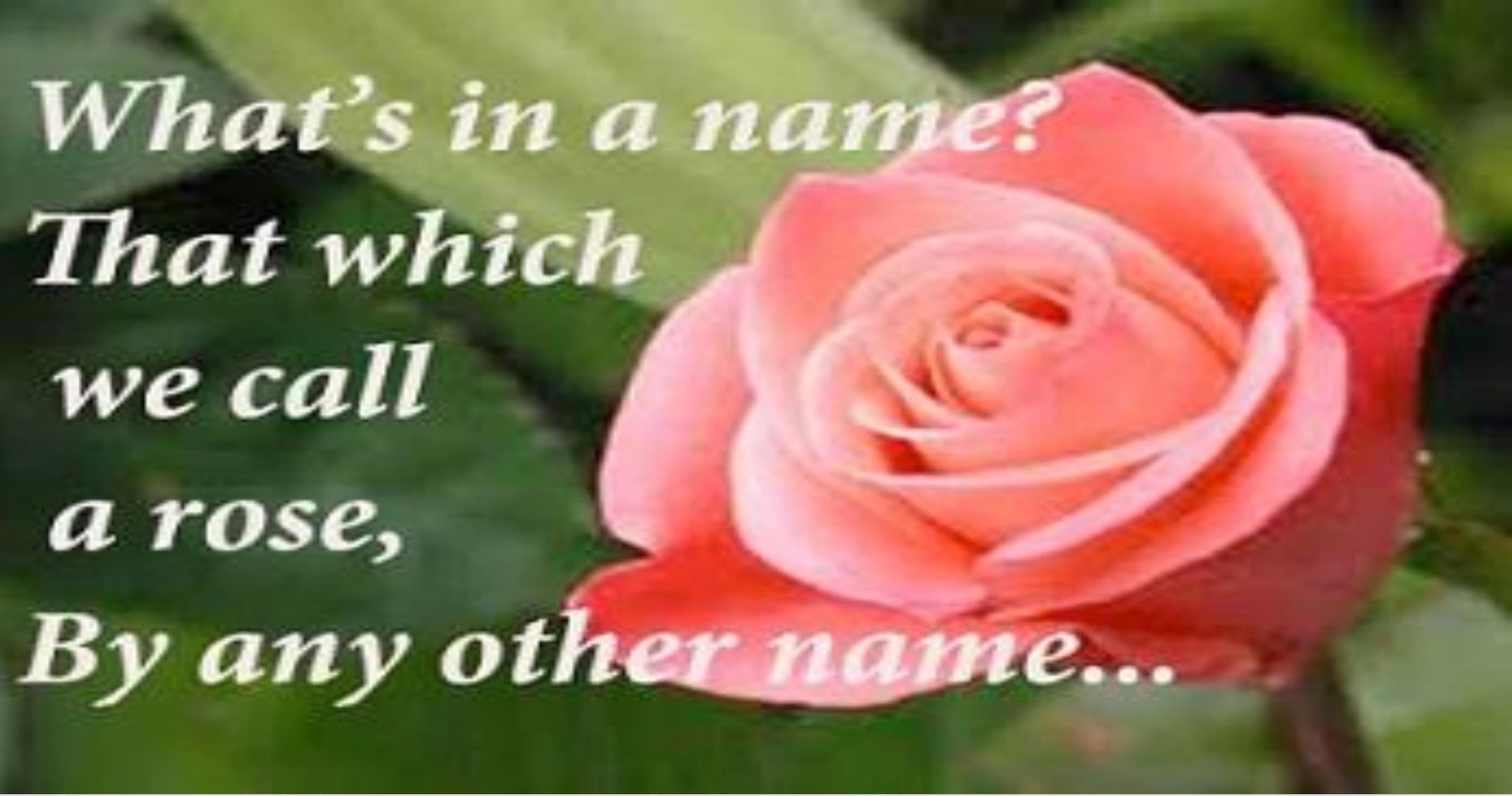
Pharma



Food

Personal Care

Industrial



How Should this Product be Labeled?

Ref.	Primary Name	Synonyms
USP	Sodium carboxymethyl cellulose	
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
EFSA	E466	Sodium carboxymethyl cellulose Carboxymethyl cellulose Cellulose gum
GSRS	Carboxymethyl cellulose sodium	*All of above except carmellose natricum*

All of these are CAS# 9004-32-4 but carboxymethyl cellulose is CAS# 9000-11-7

Or this Product?

Ref.	Primary Name	Synonyms
NF	Microcrystalline cellulose	Cellulose
FCC	Cellulose gel	Microcrystalline cellulose
JECFA	Microcrystalline cellulose	INS 460(i) Cellulose gel
EFSA	E460(i) E460(ii)	Microcrystalline cellulose Cellulose gel Powdered cellulose
GSRS	Powdered cellulose	E460 No reference to microcrystalline cellulose
GSRS	Microcrystalline cellulose	Cellulose gel Crystalline cellulose Dispersible cellulose NO reference to "powdered cellulose"

CAS # 9004-34-6

CAS# 9004-34-6

CAS# 9004-34-6

→ 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

Nomenclature Consistency

- 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

General brainstorm on excipient nomenclature

- 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?