Overview

• Value of a Pharmacopoeia
• Manufacturer Compendial Affairs
• Manufacturer Challenges
• Recommendations for Manufacturers
• Collaboration for High Quality Standards
• Future Considerations
• Summary
• Acknowledgements
• Pharmacopoeias are sources of public standards for pharmaceutical products, ingredients, and components
  – Bring consistency to medicines
  – Provide common methodologies
  – Simplify and maintain registrations
Value of a Pharmacopoeia

- A recognized common practice
  - Contain thousands of analytical methods and specifications
    - The manufacturer defines the specifications to control product quality
    - Public standard are minimum requirements for drug acceptable quality
  - Contain general requirements which apply to manufacturing, storage, labeling, and other aspects

- Enforced by regulatory agencies
  - Minimum quality standard to be met by all manufacturers
• Monitor changes in compendia
  – Identify topics that affect products, ingredients, or processes

• Review topics for appropriateness and impact
  – Company practices considered, but science and public health are principle criteria

• Interact with pharmacopoeia
  – Provide information and support

• Implement changes on time
Roles:

• Compendial Liaison
  – Communicate with pharmacopoeias
  – Develop monograph as needed

• Lead Reviewer
  – Manage global process for review and implementation
  – Elevate global issues as needed

• Compendial Trainer
  – Design training courses for internal use
  – Teach courses as needed
Example of Compendial Change Process with Manufacturer Participation

### Pharmacopoeia Process
- Proposal for improvements from pharmacopoeia, government, Lilly and other Industry, Academia
- **Pharmacopoeial Journal**
- Comments Evaluated -Expert group-
- Official Change in Supplement

### Company Process
- **Proposal Submission**
  - Company proposals through Correspondent
- **Proposal Review**
  - Lead Reviewer
  - Pharmacopoeial Review Team
  - Lead Reviewer Issue Leader
  - Review Team & Technical Experts
  - Management
  - Correspondent

### Change Implementation
- Lead Reviewer
- Pharmacopoeial Review Team
- Responsible persons
Example of Manufacturer Compendial Change Implementation Process

**Journal publication**

Compendial Team Members initial review

Identify issues and assignments -team meeting / other communications-

Initial Report

Technical Expert performs detailed review

Determine Implementation conclusions

Final Report

Lead Reviewer identifies changes with impact

Follow up Report

Summary Report

Unresolved issues

Issues communicate to pharmacopoeia as needed

Prepare to implement as needed
Manufacturer Challenges

• **Implement a compendial change or revision on time**
  – Lack of interactions on background information for changes on the compendial requirements
  – Change that does not address or support broad application to affected companies
  – Lack of adequate internal compendial change notification and implementation process

• **Monitor and meet global compendial requirements**
  – Lack of system/process knowledge to address conflicts with compendial requirements
  – Different requirements and interpretation among regulators and pharmacopoeias
  – Lack of benchmarking channels to share concerns and learning
Recommendations for Manufacturers

• Include compendial activities in your business processes
  • Formal processes for compendial monitoring, change implementation
• Engage and participate in the public standard setting and change processes
• Consider sponsoring a new monograph
  
  You will provide
  – Methodology and limits to form the basis of monograph
  – Validation data supporting methods
  – Batch data supporting limits
  – Reference standard materials
Monograph submissions:

• Costs:
  – Resources to prepare submission
  – Technical support during proposal stage
  – Technical support after adoption
  – Reference standard donation
  – Future changes require submission to both regulator and pharmacopoeia

• Benefits:
  – Contribute to public health
  – Avoid competitive disadvantage!
Collaboration for High Quality Standards

- Collaboration effort among regulator, industry, and pharmacopoeias on standards to benefit public health
  - Effective communication on issues and concerns facing each group on setting up public standards
  - Industry especially innovators:
    - Allocate resources and engage in the public standard setting process
  - Pharmacopoeias:
    - Ensure sound scientific basis of specifications and methods
    - A process for monograph submission that is transparent
    - An open system to encourage industry participation
U.S. Midwest Compendial Discussion Group (MWCDG)

- Industry meets six times a year to share knowledge and experiences on general pharmacopoeial requirements and learn future changes
  - Membership open to innovators, generics, and contract laboratories
  - Representatives of the group were invited to present in global pharmacopoeial conferences

- Pharmacopoeias (USP, PhEur, and JP) have interacted with the group to reach out multiple companies through MWCDG members
• In the U.S., USP, FDA, and Industry come together twice a year at the Prescription/Non-Prescription Stakeholder Forum to share views and learning
  – Project Teams are created to lead collaborations on specific topics such as Elemental Impurities, Residual Solvents
    • One team (members from Industry and FDA) works on process issues with USP to provide input on how changes will impact the FDA and Industry before they are implemented
  – Ensure a common understanding that allows changes to be implemented in a manner that is beneficial to all parties
Pharmacopoeias may obtain monographs from innovator

- USP: Wants monographs as soon as possible
  - Innovator submissions are preferred (Policy Statement)
- PhEur: Wants monographs ideally timely before first generic submission (e.g. 5 years after first approval)
  - Single source procedure (preferred):
    Monographs available at time of patent expiry support harmonized regulatory review of generics and strengthen quality of generic products
  - Multi-source procedure:
    after patent expiry, all sources on the market are considered
    > more complex and demanding in terms of resources and time
**Biotech Product:** Proteins (including antibodies) and nucleic acids (DNA, RNA or antisense oligonucleotides)
- Produced by recombinant or non-recombinant cell cultures
- Complexity/diversity of the molecules: Mixture of active ingredients

**Quality Standard Challenges for Biotech Products:** Need extensive characterization (Physicochemistry and Bioassay) and clinical testing to establish quality standards individually

**Establish a high quality public standard:** Manufacturer got involved by submitting technical information based on practical experiences to pharmacopoeias
Future Considerations – Monograph Acquisition

• Develop a process for monograph acquisition that is transparent to improve public standards
  – Encourage industry participation by having an open system
  – Work with industry on monograph development
  – Consider product experience in selecting monograph partners from industry
  – Handle data confidentially
Future Considerations – Pharmacopoeia Harmonization

• Develop common global public standards
  – Goal of the “ideal pharmacopoeia”: A single, global pharmacopoeial standard
  – Possibility of new improved collaboration among the various pharmacopoeias
Collaboration among regulator, industry, and pharmacopoeias is crucial to provide a benefit to public health, both regional and international.
Acknowledgements

- Members of the U.S. Midwest Compendial Discussion Group (MWCDG)
  - Barbara Ferguson, Merck/MSD
  - Joseph Garber, AstraZeneca
  - Scott Messner, Abbott Laboratories
  - Philip Travis, Pfizer
  - Mark Wiggins, Merck/MSD
