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U.S. Pharmacopeial Convention

The USP Excipients Stakeholder Forum
Meeting #1
June 7, 2013

Excipient Monograph Modernization

Lawrence H. Block, Ph.D,
Chair , Excipients Expert Committee

Topics

- USP Excipients Expert Committee
- USP Monograph Modernization Initiative
  - Background
- USP Monograph modernization strategy and approaches
- FDA Modernization Task Group (MMTG)/FDA ORA
  - Review the FDA Lists of priority excipients
- USP Monograph modernization
  - Progress on NF Excipients
  - Collaborative efforts with stakeholders
- How Stakeholders Can Contribute

USP Monograph Modernization

- Primary driver is maintaining up-to-date quality standards to support USP's commitment to public health
- Need for modernization
  - Monographs have been official for many years, decades in some cases
  - Content does not reflect current expectations for procedures and acceptance criteria
  - Complaints from the public
  - General lack of specificity
- Modernization is a subset of USP's ongoing revision work, started using the term "modernization" in 2009
- FDA Modernization Task Group (Nov. 2010)
  - List of priority excipients - most recent, July 2012 list of 13.

FDA Monograph Modernization Task Group (MMTG)

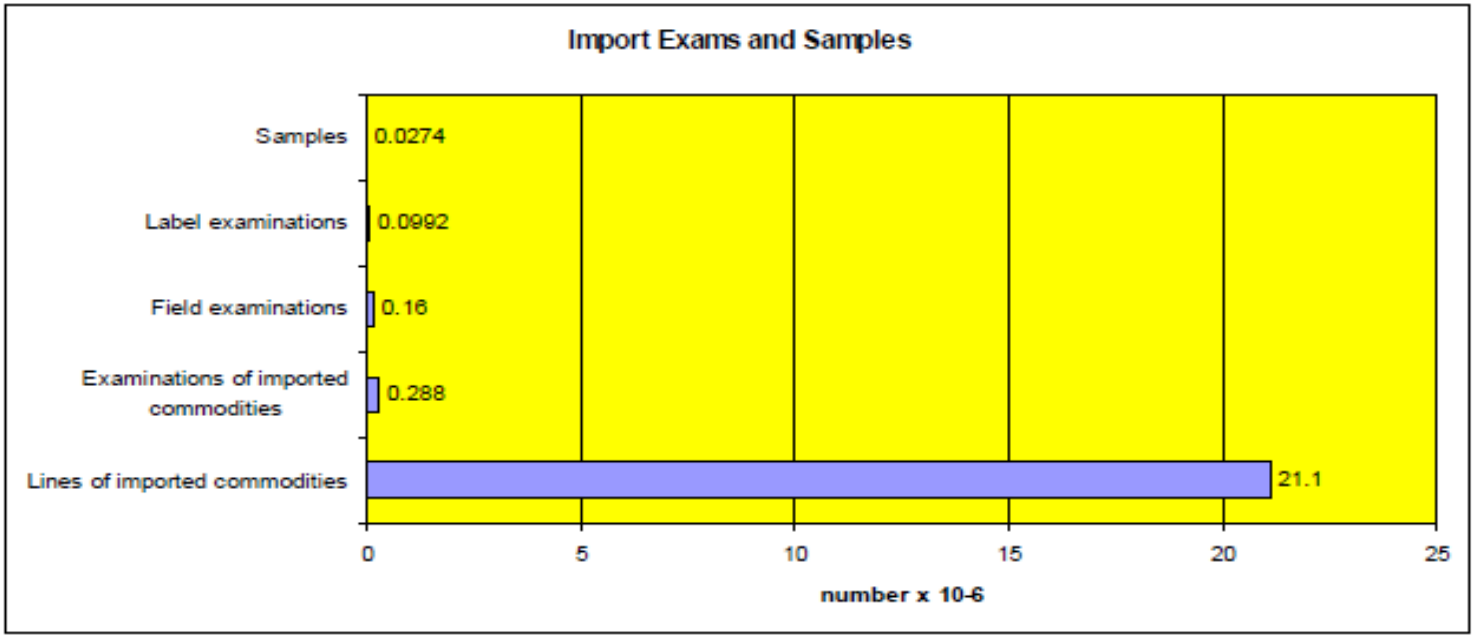
- The FDA MMTG was established within the FDA Pharmaceutical Quality Standards Working Group, whose purpose it is to :
  - Identify *USP-NF* monographs in need of modernization and is especially focused on monographs with outdated or inadequate ID tests or analytical methods that may make the drug or excipient vulnerable to economically-motivated adulteration (EMA).
  - Facilitate monograph modernization and monograph prioritization activities of FDA.
  - This is in keeping with resolutions adopted by USP at its April 2010 Convention to work to modernize its monographs as a priority in its work plan for the next five years.
  - Develop a science- and risk-based approach for ongoing prioritization and oversight of USP monograph modernization efforts.
  - Focus ongoing efforts for USP monograph modernization on those monographs and general chapters whose improvement would most greatly benefit public health by reducing potential risks.
  - Provide any evolved recommendations in writing to USP.

USP Monograph Modernization

- Benefits
  - Strengthens the public standards
  - Moves from non-specific to specific procedures
  - Considers practical factors
    - Removes unnecessary tests
    - Addresses safety/environmental issues such as eliminating use of chlorinated solvents
    - Hard-to-find equipment
    - Elimination of empirical methodology that does not adequately address QbD-related issues
  - Increases consistency across monographs

U.S. Food and Drug Administration
Protecting and Promoting Public Health
www.fda.go

Relatively Small Percentage of Imports of FDA-Regulated Articles Receive Scrutiny



Source: FDA Strategic Plan Item 2.2
Strengthen the Safety and Integrity of the Global Supply Chain
http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/ucm227527.htm

Glycerin: History of Adulteration with Diethylene Glycol (DEG)

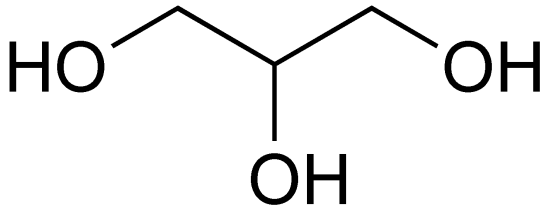
Country	Year	Incident
USA	1937	"Elixir sulfanilamide" – 107 deaths *Resulted in the implementation of the1938 Amendment to the FFD&C Act*
South Africa	1969	Sedative formulated with DEG – 7 deaths
Italy	1985	DEG in wines from Austria – no known deaths
India	1986	Medicinal glycerin laced with DEG – 14 deaths
Nigeria	1990	Acetaminophen pediatric syrup compounded containing DEG – 40 deaths APAP (some sources say 200 deaths)
Bangladesh	1990-2	Acetaminophen pediatric syrup containing DEG – 339 deaths
Haiti	1995/6	Cough medicine containing DEG – 85 deaths
Panama	2006	Cough and anti-allergy syrup manufactured by Panamanian government containing DEG – 46 deaths (116 or 365 according to other sources)
USA	2006/7	Imported toothpaste from China containing DEG – no deaths
Panama	2007	Toothpaste containing DEG – no deaths reported
Nigeria	2008/9	Teething formula contaminated with DEG from propylene glycol – 84 deaths
Bangladesh	2009	Paracetamol syrup to children adulterated with diethylene glycol. 24 children reported dead

The Problem: Even to the Trained Professional…

Ethylene Glycol ("Antifreeze")
POISON!

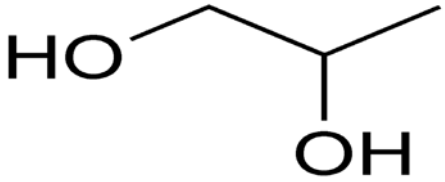
- Light colored
- Slightly viscous liquid at room temp.
- Sweet taste
- Known nephrotoxin and hepatotoxin

Glycerin (Glycerol)
Edible and GRAS



- Light colored
- Slightly viscous liquid at room temp.
- Sweet taste

Propylene Glycol
Edible and GRAS



- Light colored
- Slightly viscous liquid at room temp.
- Sweet taste

Diethylene Glycol ("Antifreeze")
POISON!

- Light colored
- Slightly viscous liquid at room temp.
- Sweet taste
- Known nephrotoxin and hepatotoxin

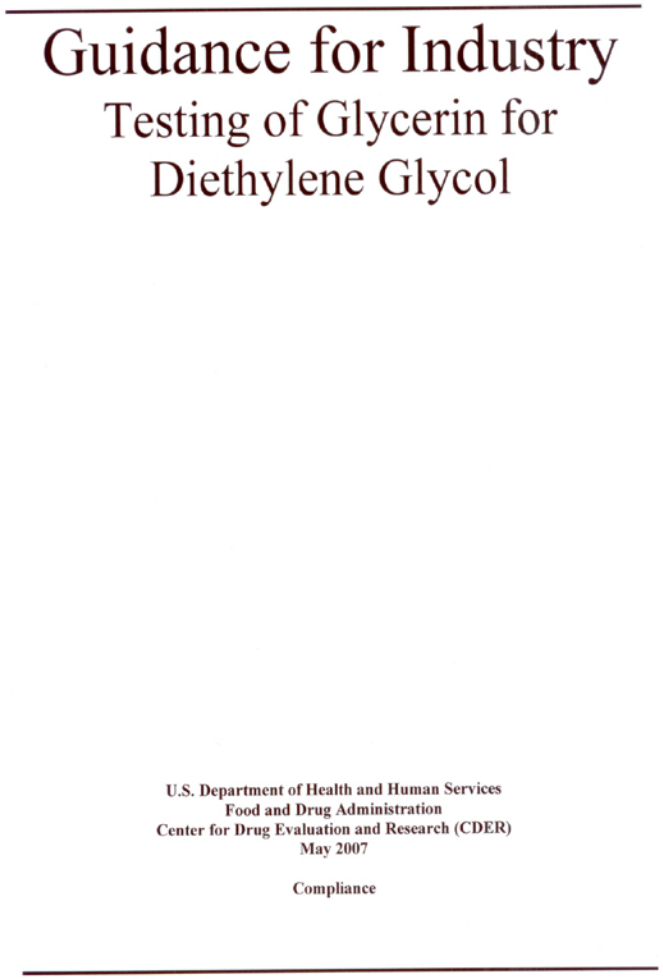
Reference: Albinus D'Sa, Ph.D., FDA, 2008 USP ASM , Kansas

USP Glycerin Monograph Modernization- Background

- **April 2007:** FDA request to USP to revise the Glycerin monograph's IDENTIFICATION section. Revision includes: adding
  - Identification test B. LIMIT OF DIETHYLENE GLYCOL AND ETHYLENE GLYCOL to detect and quantify DEG/EG in Glycerin.
    - Is no longer part of the impurity testing, "*Limit of DEG and Related Compounds".*
    - Introduces a capillary gas-chromatographic (GC) method with flame ionization detection (FID).
    - Limit of NMT 0.10% each for diethylene glycol and ethylene glycol is found.
    - Official date: **May 1, 2009**
- **Jan. 2009:** FDA letter requested modernization of both Sorbitol Solution and Propylene Glycol consistent with the update to the USP Glycerin Monograph
- **Rationale:** GMPs allow the use of Identification testing alone, by dosage form manufacturers, for raw material(s) qualification
  - CGMP regulations at 21 C.F.R. § 211.84(d)(l) would require that manufacturers of drug products detect and quantify any DEG/EG present.
  - manufacturers could therefore not deviate from the DEG/EG limit since this would be an aspect of identity.
- Consistent with FDA Guidance, Testing of Glycerin for Diethylene Glycol.

May 2007 FDA Guidance: DEG Contamination of Glycerin

- Perform a specific identity test that includes a limit test for DEG per cGMPs (NMT 0.10%).
- Reiterates §211.84(d)(2) requirement for specific ID testing when not performing full USP testing.
- Testing for Glycerin has to be capable of detecting DEG in every container.
- Reliance on COA is not sufficient to ensure quality of glycerin.
- Recommends intimate knowledge of the supply chain. Traceability is critical.
- Applies to all recipients of Glycerin USP, not only those who formulate or compound.


Guidance for Industry

Testing of Glycerin for Diethylene Glycol

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
May 2007

Compliance

USP Glycerin GC Method Development Summary

- Developed a capillary GC FID method for the identification/quantification of EG and DEG in glycerin.
- Proposed GC method and limit to be NMT 0.10% each for DEG and EG
- The USP Lab validation study showed that the proposed method is specific, sensitive, precise, and accurate.
- The results were compared to those obtained by TLC and showed greater sensitivity and specificity.
- Provides industry with a compendial standard that could be met with a commonly used analytical technology
- The limit provides adequate protection from adulteration
- USP Outreach:
  - Shared results of TLC and GC method with FDA and Stakeholders at 2008 USP Annual Science Meeting
  - Posted updates on the USP Hot Topics web page
  - Announced the proposed GC method and limit at the 2008 PNP Stakeholder Forum

FDA "High Priority" Monograph Revisions for Limit of DEG and EG

- **Glycerin**
  - Official date **May 1, 2009 (*USP* 31-*NF* 26-2S)**
- **Sorbitol Sorbitol Solution**
- **Sorbitan solution**
- **Noncrystallizing sorbitol solution**
- **Maltitol Solution**
  - Official date **August 1, 2010** (***USP* 34-*NF* 29**)
- **Propylene glycol**
  - Official date **February 1, 2010 (*USP* 33-*NF*28 Reissue-1S)**
- **Hydrogenated Starch Hydrolysate**
  - Official date **May 1, 2012 (*USP* 35-*NF* 30)**

USP–NF Fixed Oil Monographs Modernization

- The 2010-2015 EC's examination of *USP–NF* fixed oil monographs developed several decades earlier, demonstrated that similar outdated monograph specifications were applied throughout all these old fixed oil monographs.
  - In general, no *Identification* and *Assay* in fixed oil monographs
  - Incomplete understanding and limited characterization studies of the fixed oil substances when the monographs were developed prior to 2005
  - Change the tests (*Ester Value*, *Hydroxyl Value*, *Iodine Value*, and *Saponification Value*) which assess fat and oil structure indices to the tests (*Fatty Acid Composition* and *Sterol Composition*) which determine fat and oil compositions
- 31 oil excipient monographs include vegetable oils (edible), petrochemical oils, and essential oils. All vegetable oils are termed "fixed oils" in *USP–NF*. The term *fixed oils* distinguishes them from the relatively volatile petrochemical oils and essential oils.

8 Newly Developed and 8 Modernized Fixed Oil Monographs

No	Monograph	Revision Type	No	Monograph	Revision Type
1	Canola Oil	New	1	Almond Oil	Modernization
2	Coconut Oil	New	2	Corn Oil	Modernization
3	Hydrogenated Palm Oil	New	3	Cottonseed Oil	Modernization
4	Palm Kernel Oil	New	4	Soybean Oil	Modernization
5	Fully Hydrogenated Rapeseed Oil	New	5	Olive Oil	Modernization
6	Superglycerinated Fully Hydrogenated Rapeseed Oil	New	6	Peanut Oil	Modernization
7	Hydrogenated Coconut Oil	New	*7*	*Castor oil*	*In progress*
8	Palm Oil	New	*8*	*Hydrogenated Castor oil*	*In progress*

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PLUS: FDA on GMP Inspection Trends : USP on Fixed-Oil Excipients : Pharmacopeial Harmonization

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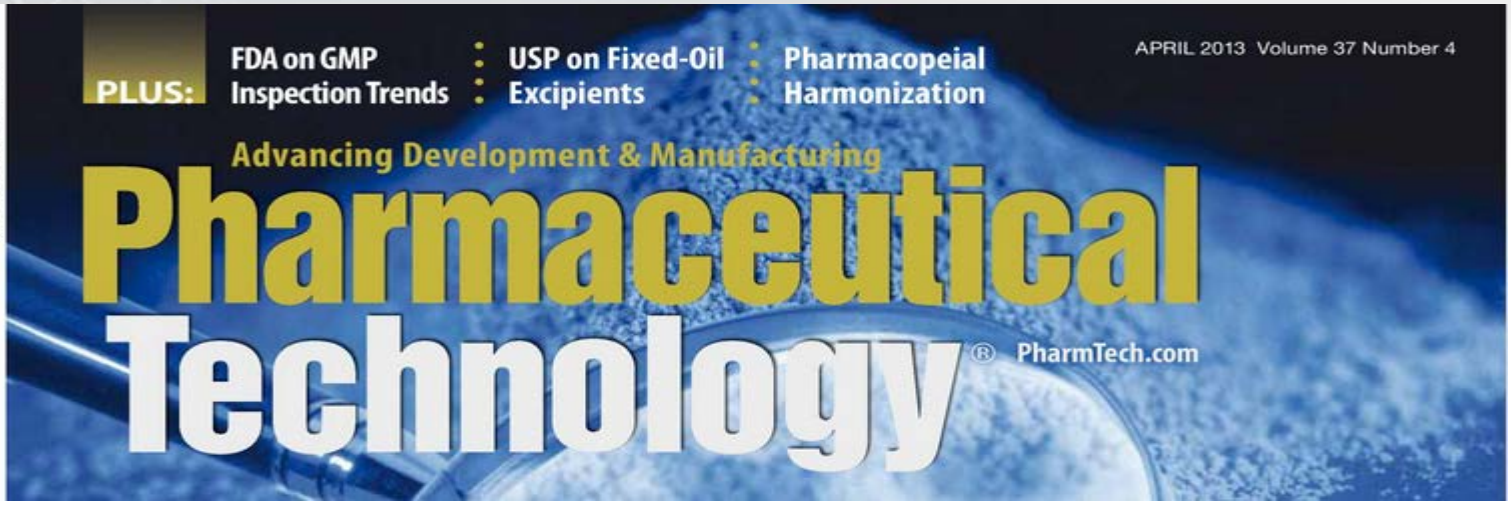

REFERENCE STANDARDS

Fixed-Oil Excipient Monographs

Development of USP Fixed-Oil Reference Standards

Hong Wang, Catherine Sheehan, Lawrence H. Block, Richard C. Moreton, Richard H. Wendt, Shireesh P. Apte, and Eric J. Munson

This article summarizes the development and modernization of the *United States Pharmacopeia–National Formulary* (*USP–NF*) fixed-oil excipient monographs. Fats and fixed oils are processed from natural sources and have complex chemical compositions. As part of the public standards-setting processes, USP staff and the Excipients

The US Pharmacopeia (USP) Monographs—Excipients Expert Committee (EXC EC) for the current 2010–2015 revision cycle is responsible for the 31 *United States Pharmacopeia–National Formulary* (*USP–NF*) monographs with "oil" in the monograph title (see **Table I**) in *USP 35–NF 30* through the Second Supplement (1). The 31 oil excipients include vegetable oils (edible), petrochemical oils, and essential oils. All vegetable oils are termed "fixed

USP Monograph Modernization

- *USP's greatest challenge is obtaining updated procedures and acceptance criteria—manufacturers are encouraged to submit proposals to USP*
- Pace of monograph modernization is linked to availability of procedures
- Excipient monograph modernization is a major initiative in the 2010-2015 revision cycle.
- USP is devoting resources to this effort -
  - USP expansion includes establishment of global laboratory sites.
- Collaboration with FDA, industry and other stakeholders is key to advancing the work.

Monograph Modernization Strategy and Approaches

Continued Collaboration with FDA and Industry

- Prioritization
- Timing considerations

USP Monograph Modernization Process

- Modernization of monographs achieved by
  - *Replacing* outdated technology and methodology with more current procedures
  - *Adding* critical tests to the monograph
  - *Deleting* non-value added tests, as needed (e.g., odor test, melting point)
- Follows the USP standards-setting process (i.e., with publication in PF for 90-day comment period)
- FDA to provide input to USP on prioritization (FDA MMTG and ORA lists)
- Other considerations
  - Use procedures from other pharmacopeias
  - May need RS materials
  - Revising the monograph “family”, as needed

Excipient Monograph Modernization: Prioritization of Categories

- No Identification or non-specific Identification procedures
- No Assay or non-specific Assay procedures
  - Stainless steel/packed column GC procedures
  - Titration to GC/HPLC where appropriate
- No impurity test, (e.g., Povidones and peroxides)
- Safety-related concerns (e.g., chlorinated solvents).
- Labeling deficiencies , e.g., when used in parenteral/injectable grade applications
  - Missing specific tests to control quality (e.g., Microbial/BE)

Monograph Updating Strategies

Monograph and Reference Material Procurement and Development

- Traditional donor model (‘externally sourced’)
  - Very difficult to engage sponsors
- USP laboratories (‘internally sourced’)
  - New technologies in Rockville labs (eg, UPLC, High Res. MS)
  - Extensive testing facilities in India for reference procedure development
  - Collaborative testing sites in India, China and Brazil (in addition to Rockville)
  - MOU with China - excipient monograph development
- FDA (CRADA: ORA Labs)
- Adapt/Adopt (Other Pharmacopeias e.g. B.P., ChP)

Excipients FDA High Priority List – Monograph Modernization Task Group (MMTG) list			
Monograph	**List**	**FDA recommend**	**Modernization progress**
Povidone Crospovidone Copovidone	Letter 1 Nov 2010	*Replace non-specific N determination Assay <461> Kjeldahl method* *Add Peroxide test*	Povidones Expert Panel formed June 2011. PDG S6 – Peroxide , hydrazine tests added
Talc	Letter 1 Nov 2010	*Replace Limit of Asbestos and update Definition and Labeling*	Talc Expert Panel formed Aim: publish Stim article in PF 39(6)
Butylated Hydroxyanisole	Letter 3 Jul 2012	*Lack of specific ID test*	
Butylated Hydroxytoluene			USP labs – Add Chromatographic Assay – ID test add RT agreement
Dextrose Excipient			
Silicon Dioxide (Colloidal)			
Titanium Dioxide			
Croscarmellose Sodium (Croslinked CMC sodium)			USP labs – IR test
Carboxymethylcellulose Sodium (CMC sodium)			
Gelatin			PDG Stage 6 published as RB
Guar Gum			USP labs: ID: chem. comp. by TLC
Microcrystalline Cellulose			USP labs – ID by IR test
Pregelatinized Starch			
			USP labs – ID:IR and TLC methods
Shellac			
Calcium Stearate			Harmonization with PDG S6 Mg (St)2 Published in PF 39(4)

FDA High Priority Excipients - ORA list of deficiencies -		
Monograph	**Deficiency**	**Modernization progress**
Aspartame	"*Replace non specific assay titration and add impurities test*"	HPLC Procedure For **LIMIT OF 5-BENZYL-3,6-DIOXO-2-PIPERAZINEACETIC ACID .** USP Labs: **EVALUATE FOR USE IN ASSAY**
Titanium Dioxide (also on MMTG list)	*"Assay method is out of date, involves digestion with concentrated acids, etc."* FDA recommendation: Use advanced methods for quantitation of TiO2 (Ref: "A novel volumetric method for quantitation of titanium dioxide in cosmetics," Journal of Cosmetic Science, Volume 57, Issue 5, Pages377-383, 2006).	USP Labs: evaluate method
Glycerin	"*Current assay method for glycerin is out of date (periodate method)).*" FDA recommendation. Replace periodate method with quantitative GC method (USP method for determination of quantities of Diethylene Glycol and Ethylene Glycol is a GC method).	Glycerin Expert Panel formed in Dec. 2012 PDG monograph USP labs: evaluate method
Crospovidone (also on MMTG list)	*"Test method for Peroxides is outdated"* FDA recommendation: Quantitative determination of trace levels of hydrogen peroxide in crospovidone and a pharmaceutical product using HPLC with coulometric detection." International Journal of Pharmaceutics, Volume 375, Issues 1–2, 2009, Pages 33–40).	Povidones Expert Panel formed in Jan. 2011 PDG monograph USP Labs: evaluate method

FDA MMTG Nov.16, 2010 Letter Requested Revisions

- **USP Povidone, NF Crospovidone, NF Copovidone:**
  - 3 Povidones not consistent w.r.t. impurity specifications. Should be harmonized within USP and to the EP monographs (Limit of Hydrazine; Limit of aldehydes; Peroxides; Heavy metals.
  - Nitrogen assay test (<461> Nitrogen Determination (by Kjeldahl method)) is non-specific. Prefer a more specific method due to concerns about economically motivated adulterants, e.g., melamine.
    - Expert Panel formed, January 2012.
- **USP Talc:**
  - Labeling statement should be revised to match the statement from the FCC monograph's description thereby assuring that Talc is not sourced from mines that are known to contain asbestos.
  - USP should consider revising the current test for *Absence of asbestos* to ensure adequate specificity.
  - Talc Expert Panel formed, May, 2011.

FDA MMTG List: Povidones

- **Povidone:** PDG Stage 6 adoption includes the addition of tests for
    - Limit of hydrazine, Limit of aldehydes, Peroxides
- **Crospovidone:** PDG Stage 6 adoption includes the addition of tests for
    - Peroxides, Limit of monomers (vinylpyrrolidinone)
    - Both Stage 6 posted on harmonization website on Feb. 25, 2011, Official Dec. 1, 2011 (Second Supplement to *USP* 34–*NF* 29)
- **Copovidone:** PDG Stage 4 Official Inquiry
    - *PF* 37(4) [July – Aug. 2011] . Scheduled for ***USP* 35-*NF* 30-2S** publication
        - Addition of Test for Lead.
        - Revision of Limit of Monomers (change from titration,(0.1%) to HPLC (0.001%)
- **Povidone:** PDG Stage 6 adoption
    - *PF* 38(2) [Mar. – Apr. 2012]. Scheduled for ***USP* 36-*NF* 31-1S** publication
        - Revision of Identification test to include an FTIR spectroscopy test. EP monograph includes this test.

Povidones Expert Panel Challenges and Progress

- Melamine is not the only intentional adulterant that may be introduced into pharmaceutical ingredients supply chain.
- USP Expert Panel Conclusions:
  - Determine what level of detection can be established through existing USP compendial tests (s) or other procedures to be established.
  - Monograph unable to detect all potential known and unknown EMAs at levels as stated in the FDA Melamine guidance of 2.5ppm (0.00025%)
  - Current compendial tests can control adulteration at levels greater than 5%, but are mostly inconclusive at levels below.
  - NOT to focus specifically on individual adulterants such as melamine .
  - Explore ways to control BOTH known and unknown intentional adulterants.

Povidones Expert Panel Challenges and Progress

- Consensus from Povidones EP is not to replace Kjeldahl Assay, but instead introduce a series of orthogonal ID and other tests to strengthen monograph.
- Proposed methods for introduction
  - HPLC as a specific test to control organic impurities. Method was developed using an ELSD detector; currently testing to see if conventional UV detector can be used.
  - CHN as an Identity method. Working with industry representatives on panel to establish appropriate limits.
  - Ash test as an identity method to control for inorganic adulterants
  - Eliminate non-value added chemical identity methods where information is already provided in IR Identification.
- Proposal to be discussed at PDG June 2013 Strasbourg meeting

Talc Expert Panel Challenges and Progress:

Pure Talc (hydrated magnesium silicate, $Mg_3Si_4O_{10}(OH)_2$)

- Request from FDA to revise Labeling statement and revise the current test for Absence of Asbestos to ensure adequate specificity.
- Expert Panel (EP) Accomplishments: No one single method is sufficient to adequately control asbestos contamination.
- As a result, EP considering the possibility that the monograph be revised as follows:
  - Submit the EP/EXC EC update to PDG on the development of a Stimuli Article to solicit stakeholder feedback to the appropriate methodologies and specifications for a compendial standard. Educate users who are not familiar with the unique geological challenges of Talc.
  - Strengthen the X-Ray Diffraction (XRD) methodology to include RS and eliminate IR test. Development of orthogonal microscopy methods (Polarized Light Microscopy (PLM), Scanning Electron Microscopy (SEM), Transmission Electron Microscopy (TEM)).
- Labeling statement language to be addressed following finalization of methodology.

Glycerin Expert Panel

- Panel Formed in March 2013 with the goal to provide a global Stage 3 draft proposal to present to PDG.
- Provide a consensus on which methods should be included and which existing methods may not have value
- Three Subteams have been formed to work on different parts of the monograph
  - Definition, Assay, ID, and Water
  - Organic impurities, related compounds, aldehydes, chlorinated compounds, fatty acids, and esters
  - ROI, Chloride, sulfate, heavy metals, Color

Excipient Modernizations for USP 37-NF 32

Monograph Completed	*PF*	Sponsor	Modernization	Priority
Compressible Sugar	*PF*38(6)	**USP Lab/Industry**	*ID* by FTIR, *Assay by* HPLC	USP weblist
Confectioner's Sugar	*PF*38(6)	**USP Lab**	*ID* by Spec Rot, *Assay by HPLC Content of Sucrose*	USP weblist
Sugar Spheres	*PF*38(6)	**USP Lab**	*ID* by Spec Rot, *Assay by* HPLC	USP weblist
Lecithin	*PF*38(6)	**USP Lab/Industry**	ID by updated TLC for chem comp. *Assay*, add *Content of Phospholipids* by HPLC-ELSD. Update the *Labeling* requirements	USP weblist
Squalane	*PF*38(6)	**USP Lab**	ID by RT agreement with *Assay. Assay* by GC.	USP weblist
Ascorbyl Palmitate	*PF*38(6)	**USP Lab**	ID by RT agreement with *Assay* *Assay* from titration to HPLC	USP weblist
High Fructose Corn Syrup	*PF*39(1) (IRA)	**USP Lab/Industry**	*Content of Fructose*	USP weblist
Succinic Acid	*PF*39(2)	**USP Lab**	ID by RT agreement with *Assay.*Assay from titration to a HPLC	USP weblist
Cholesterol	*PF*39(3)	**USP Lab**	Add ID by FTIR	USP weblist
Purified Stearic Acid	*PF*39(1)	PDG S6 Stearic acid	ID by RT agreement with Assay. Assay by GC cap	USP weblist
Sodium Stearate	*PF*39(3)	Mg (St)2 PDG S6/**USP lab**	ID by RT agreement with Assay. Assay by GC cap	USP weblist
Calcium Stearate	*PF*39(3)	Mg (St)2 PDG S6/**USP lab**	ID A from wet-chemistry to FTIR ID by RT agreement with Assay. Assay by GC cap	USP weblist/ MMTG llist
Gelatin (H6)	PF37(1) Revision Bulletin	EP/JP/USP (PDG)	Stage 6 posted on USP website/harmonization Sept 2012, official April 2013	USP weblist/ MMTG llist

Excipient Modernizations in Development

Monograph	Modernization in progress	Stakeholder	Priority list
Methylparaben sodium	Add Assay and related substances	**USP Lab**/PDG S6	USP weblist
Propylparaben sodium	Add Assay and related substances	**USP Lab**/PDG S6	USP weblist
Mannitol (H)	Introduce FTIR in ID test	**USP Lab**/EP	USP weblist
Polysorbate 80	Introduce FTIR in ID test	**USP Lab**/EP	USP weblist
Anise oil	Update Definition /Assay by GC	**USP Lab**/EP	USP weblist
Sucrose	Introduce FTIR in ID test	**USP Lab**	USP weblist
Potassium Sorbate	Introduce FTIR in ID test. Replace Assay by titration with GC	**USP Lab**	USP weblist
Microcrystalline Cellulose	Introduce FTIR in ID test	**USP Lab**	USP weblist/MMTG llist
Croscarmellose Sodium (Croslinked CMC sodium)	Introduce FTIR in ID test	**USP Lab**	USP weblist/MMTG llist
Carboxymethylcellulose Sodium (CMC sodium)	Introduce FTIR in ID test	**USP Lab**	USP weblist/MMTG llist
Guar Gum	Update ID	**USP Lab**/EP/Industry	USP weblist/MMTG llist
Shellac	Introduce FTIR and chemical composition TLC in ID test	**USP Lab**/Industry	USP weblist/MMTG llist
Butylated Hydroxytoluene	Introduce ID by RT . Add Assay -HPLC /GC methods under evaluation	**USP Lab**	USP weblist/MMTG llist
Glycerin	Expert panel formed to develop S3 draft	Industry	FDA ORA list
Aspartame	Replace Assay titration with HPLC	**USP Lab**	FDA ORA list

Chinese Pharmacopoeia Commission – USP MOU

- Chinese Pharmacopoeia Commission (ChP) - USP MOU Working group #1
  - *Documentary standards and Reference Materials* – Excipients
  - 13th meeting of MOU discussion. USP first visit to China in 1990. Initial MOU signed 2005
  - Cooperate to develop quality standards for excipients in the global supply chain
  - Establish the 22 nd Medicines Expert Committee East Asia Expert committee (EAEC) to work on development of excipient monographs to support the Medicines Compendium and for potential adoption by both ChP and NF.
    - Dr Jiasheng Tu serves as Chair of the ChP Commission Expert Committee on Excipients and a member of the Expert committee of Center for Drug evaluation, SFDA. He is also Chair of the USP EAEC, China and a member of the USP Excipient EC, USA.
    - Ms. Han Peng is the ChP liaison to the MCEA EC.
  - Provincial lab support.

ChP-USP Work on Excipient Modernization

- ChP also modernizing several excipients in ChP 2010 that appear on the USP web list
- ChP reviewed USP's Excipient modernization web list
- USP Excipient Expert Committee agree to start work on the following excipients
  - Calcium Stearate (USP Lab work complete)
  - Calcium Sulfate
  - Carnauba Wax
  - Cholesterol (USP Lab work complete)
  - Diethyl Phthalate
  - Ethyl Acetate
  - Hydrogenated Castor Oil (USP Lab in dev.)
  - Maltodextrin (Working with Industry)
  - Monobasic Potassium Phosphate
  - Sulfuric Acid
  - White Wax
  - Xanthan Gum (USP Lab in dev.)

ChP-USP Work on Excipient Monograph Development

- USP Rockville reviewed the ChP list of 150 monographs targeted for development in ChP 2015 edition
- USP and ChP selected 15 new excipient monographs for development
- 8 monographs published for development in MC:
  - Sodium Bisulfite
  - Potassium Stearate
  - Aluminum Stearate
  - Sodium Oleate
  - Cholic Acid
  - Nutmeg Oil
  - Sodium Caseinate
  - Turpentine Oil
    - Dr Tu will provide additional details

Moving Forward

- USP efforts
  - USP will continue to use its lab resources and engage stakholders
  - Sourcing procedures from other compendia, literature, other
  - Form Expert Panels, as needed, to address specific topics

- Collaboration
  - Explore possible lab support from CRADA with the FDA
  - Collaborate with FDA MMTG, refine priorities as needed
  - ChP - USP list of 15 new monographs and12 modernizations
  - Engage with other stakeholders

Conclusion

- Excipient monograph modernization is a major initiative in the 2010-2015 revision cycle
- USP is devoting resources to this effort – new laboratory capabilities
- Collaboration with FDA, industry, and other stakeholders is key to advancing the work
- Long-term goal is to implement a regular monograph review process to monitor the needs for further modernization
- USP's Challenges
  - Obtaining procedures and acceptance criteria
  - Prioritizing and requesting submissions - with FDA involvement , the hope is that industry is much more likely to come to the table

Thank You