Update on Plastics Packaging Working Group:

<661>, <661.1>, <661.2>, <1661>

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Common Goal – GLOBAL PATIENTS
Purpose

- To present the perspective of the pharmaceutical industry with respect to the USP Plastics Working Group activities
  - Information in this presentation is not reflective of any one pharmaceutical company or industry group
  - Information provided is based on non-proprietary information provided by numerous pharmaceutical companies and industry groups
  - Presentation will not focus on many technical issues

- Provide an example of an industry implementation timeline
- Summarize industry needs to develop an effective implementation date
What changes were made to the chapters?

- **Added component tests per <661.1>:**
  - Bioreactivity (For dosage forms other than Oral and Topical)
  - Identity (IR or DSC)
  - Absorbance
  - Acidity/Alkalinity
  - Extractable Metals
  - Total Organic Carbon

- **Eliminated component tests**
  - Heavy Metals
  - Non-Volatile Residue
  - Residue on Ignition
  - Colorant Extraction

- **Added packaging system tests per <661.2>**
  - Bioreactivity
  - Absorbance
  - Acidity/Alkalinity
  - Total Organic Carbon
  - Extractable/Leachable Safety Assessment
  - Spectral Transmission Requirements for Light-Resistant Containers
Implementation Timeline of 01-May-2018 not feasible

- Impact of <661> Exemption Removal
  - Created a huge impact for currently approved packaging items
- Amount of additional testing/information gathering resources needed
- Change Control & Regulatory activities
- Questions concerning Chapter Requirements
- Competing Company Priorities - Numerous simultaneous USP changes
  - Limited Industry resources

Plastics Working Group created Due to Industry Difficulties

“If you want to go fast, go alone. If you want to go far, go together.”
Met from June 2018 – October 2018

Objective: Gain consensus (not 100% agreement) on the timeline for implementation of the USP plastics packaging general chapters

All groups members...

- Provided process insights from all parties
- Answered and asked questions of each other
- Challenged each other (in a collaborative manner)
INDUSTRY ESTIMATE OF REQUIRED TIMELINE FOR COMPLIANCE WITH UPDATED USP<661> CHAPTERS

**Scoping** 18 mnths

**Verification** 6-24 Months

**Data Processing** 12-24 Months

**Resin change (if needed)** (new item/potential failure) 18-24 mnths

**Stability** 12 – 40 mnths

**US Filing** 6+ mnths

**ROW Filing** Up to 60 mnths

**Change Control Process** (timing dependent of HA approval)

**ESTIMATED TIME:** 18 months

**DRIVERS:**
- Allocation of resources and budget
- Scanning of complete portfolio of packaging systems

**INTERDEPENDENCIES:**
- Scoping efforts will vary within the industry depending on portfolio. Current estimate of 18 months is for a broad and diverse portfolio.

**ESTIMATED TIME:** 6-24 months

**DRIVERS:**
- Allocation of resources and budget
- Verification of Risk Based Recommendation: compliance of complete portfolio of packaging systems

**INTERDEPENDENCIES:**
- Availability of USP<661.1> certificates from raw material suppliers
- Capacity of external laboratories for new analysis
- Capacity of toxicologists Risk Based Recommendation: Leverage historical E&L data to comply with USP<661.2>

**ESTIMATED TIME:** 12-24 months

**DRIVERS:**
- Allocation of resources and budget
- Change control process
- Identification of compliant resin
- Validation of equipment at packaging component supplier
- Validation in factory
- Validate compliance of new CCS with USP<661.1> and USP<661.2> - worst case will include full E&L testing (+6mnths)

**INTERDEPENDENCIES:**
- Capacity of suppliers to handle requests for compliant resins.
- Availability of USP<661.1> compliant alternative resins
- Availability of USP<661.1> certificates from raw material suppliers
- Capacity of external laboratories for analysis and E&L testing

**ESTIMATED TIME:** 12 – 40 months

**DRIVERS:**
- Allocation of resources and budget
- Registration stability requires full stability evaluation over projected shelf life
- Report creation

**INTERDEPENDENCIES:**
- None

**QUESTION for time reduction:** Will filing with accelerated stability data be accepted?

**ESTIMATED TIME:** Min. 6 months

**DRIVERS:**
- Filing preparation
- Filing submission to FDA

**INTERDEPENDENCIES:**
- Available regulatory resources
- Available capacity of FDA to review and approve filing updates

**ADDITIONAL COMPLEXITY**
- Impacted items must be controlled until regulatory approval is granted (for PAS changes)

**ESTIMATED TIME:** Up to 60 months

**DRIVERS:**
- Filing preparation
- Filing submission to Health Authorities
- HA’s interpretation of the requirements

**INTERDEPENDENCIES:**
- Available regulatory resources
- Available capacity of FDA to review and approve filing updates

**ADDITIONAL COMPLEXITY**
- Impacted items must be controlled until regulatory approval is granted (for PAS changes)
Meeting perceptions

We hoped for meetings like this...

To avoid situations like this...

So all parties wouldn’t feel like this...

Our meetings were more like this...

Which led to an outcome like this...
Implementation Date

January
2025

February

March

April

May

June

July

August

September

October

November

December
Industry Recommendations to facilitate on-time compliance with the revised deadline
Industry Recommendations to facilitate implementation

- Creation of Proactive Working Groups for general chapter updates to determine implementation timelines, impact to industry, clarification
  - Significant chapter rewrites
  - Introduction of new methodology
  - Other general chapter updates that can have major impact (i.e. revising general chapter name/number)

- Creation of FAQs listing responses given to working group questions
  - Will assist and benefit implementation activities through visibility/transparency to all users
  - Eventually moving towards incorporation of responses to the chapters as clarifications
  - How were limits derived? Were they based on laboratory testing or based on toxicological information?

- Inclusion of Scope clarification information in chapter
  - Addition of clarification language concerning risk assessments requirements, etc.
  - Inclusion of language in <661> that compliance with the chapter may be met by either: Testing the Materials of Construction (MOC) by <661.1> and/or testing the Packaging System by <661.2>
  - Additional clarifying language consideration to facilitate implementation in Ex-US markets
  - Incorporation of additional “end-user-centric” language in chapters
  - Components and Systems that are in and out of scope
Industry Recommendations to facilitate implementation

✓ Considerations for potential difficulties during assessment verification due to stringent Limits
  i.e. HDPE Bottles
  • Absorbance – borderline results obtained
  • Total Organic Carbon (TOC) – borderline results obtained
  • Extractable Metals – Nickel & Cobalt results exceeded USP limits
  • Are there opportunities to widen limits (i.e. Absorbance limits for light sensitive items)

✓ Alignment of general chapter scope with current regulatory guidance
  • Current general chapter wording alludes that expanded testing of packaging systems would be typical
  • Assessments to establish suitability should include extractables and leachables testing only for higher risk dosage forms, which would align with the 1999 FDA guidance: “Container Closure Systems for Packaging Human Drugs and Biologics”

✓ Removal of extractable/leachable testing for low risk dosage forms
  • Solid oral dosage forms
Industry Questions for FDA & other health authorities

✓ Will current registrations indicating compliance to <661> suffice?
  • Guidance concerning notification of compliance to FDA & other Health Authorities
  • i.e. Annual Reportable, PAS, etc.

Note: Updates to registrations or agency notification may take more effort for industry to inform agencies as to how they comply with <661>. This could extend the time to implement.
Thank you