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LIFE FORWARD

DOE 2017 MO-99 TOPICAL MEETING

The Drug Regulatory Pathway to LEU Conversion

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PURPOSE AND AGENDA

PURPOSE: to provide a brief Regulatory perspective on planning and conversion of HEU to LEU

AGENDA:

- Global Submissions
- Critical Activities for Regulatory Success
- Cross Functional and Readiness Considerations

REGULATORY APPROVALS

Key Country/Region	RA Submissions to Health Authority (Master File + Variation / Supplement)	Approval Date
EU	16-January-17	25-April-17
Switzerland	16-January-17	Pending
US	31-January-17	27-April-17
Canada	21-March-17	31-May-17
Asia	31-May- 17	21-June-17

Experiences from previous drug regulatory submissions

EU - Work sharing with National MA. Grouped submissions. ASMF and Type IB Variation as prospectively agreed by Reference Authority.

US – DMF and Prior Approval Supplement

Canada – DMF and Notifiable Change

The commitment and collaboration between Global Drug and Nuclear governing bodies was outstanding and served as a solid foundation for LEU regulatory success

CRITICAL ACTIVITY FOR REGULATORY SUCCESS

Collaboration with Health Authorities

- Example - FDA / Health Canada Joint Meeting in 2012
- Prospective discussions on submission type
- Provide periodic program updates
- Notification to Authorities prior to submission
- Polite contact when allowed during review

Common Technical Document (CTD) Content Recommendations

- DOSSIER CONCEPT = LEU **“new”** to applicant’s drug products
- DOSSIER CONTENT - Importance of LEU Target design, elution, specifications, controls, and impurity profile

CRITICAL ACTIVITY FOR REGULATORY SUCCESS

Global Regulatory Planning - Focus on the Basics of Approval and Implementation Requirements

1. Define **Regional/Country** requirements
2. Compile into **Global RA Requirements**
3. Drug requirements and data availability

   Health safety requirements — **executable**

   Estimated time to drug and safety approvals — **dossier plan**

CRITICAL ACTIVITY FOR REGULATORY SUCCESS

**Global Regulatory Planning - ** Focus on the Basics of Approval and Implementation Requirements (continued)

4. Understand regional process differences in order to **define Region/Country Dossier Filing Sequence** (for example Asia following EU/US)
5. **Globally Track** filings rather than by region/county alone
6. **CRITICAL =** Regulatory and Program Leadership alignment on Data, Approval timing and implementation

CRITICAL ACTIVITY FOR REGULATORY SUCCESS

Managing LEU Module 3 / Master File content

- Meet Regional/Country expectations while maintaining global content
- Understand use CTD Module 3 CTD verse Master File for LEU data location

Health Authority Review Questions

- Maintain “Global Regulatory Memory” when responding to review questions from multiple Authorities
- Be alert to question similarities and differences and understand corresponding relationship to global data set and process controls
- **Reminder: utilize process data and process knowledge while compiling response**

CROSS FUNCTIONAL AND READINESS CONSIDERATIONS

- Process knowledge gains from Cold Testing
- New LEU Analytical Methods
- Nuclear Safety License and Safety Approvals
- Process Validation
- Cross functional factors that contribute to LEU conversion date
- Inventory management, LEU conversion and potential clinic and patient management


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QUESTIONS
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