FDA Public Meeting: Electronic Submission of Regulatory Information, and Creating an Electronic Platform for Enhanced Information Management

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Background Information

- Presenters
  - Nancy Smerkanich: Regulatory Affairs professional with responsibility for submission compilation IND and NDA
  - David Evans: CIO with responsibility for clinical information management and CDISC implementation, conversions and strategies

- Octagon Research Solutions, Inc.

  Software and Service provider to the pharmaceutical and biotech industry primarily focused on electronic submissions and clinical data strategies

- Survey Responders

  Email blast to companies of all sizes/stakeholders with docket questions and follow-up queries

Agenda

- Dockets Questions (1-13) Reorder and grouped as follows:
  - Electronic Submissions
  - Data Standards
  - IT Plan
- Informal Survey Results

Electronic Submissions

Dockets Question #1:

What would help improve the quality of electronic submissions to the agency?

- Making eCTD validation criteria available to the public
- Documenting requirements vs. “nice to have” for navigation
- Provide feedback from reviewers

Electronic Submissions

Dockets Question #2:

What would help improve the quantity of electronic submissions to the agency?

- Mandate according to a schedule
  - Similar to how PLR was handled
- Incentive (e.g. reduced user fee)

Electronic Submissions

Dockets Question #3:

How would you prioritize these quality and quantity improvements?

- Quality over quantity *always*
  - Establish process for building quality into submissions and quantity follows
- Align with global efforts

Electronic Submissions

Dockets Question #11:

What key areas require new or expanded electronic submissions guidance?

- Validation specification
- Granularity and lifecycle management best practices/Q&A/Preferences
  - Document specific for Annual Reports, SURs, QOS
- Dataset compliance specification
  - Needs to encompass information that was in ’99 docs

Data Standards

Dockets Question #4:

What data standards are needed to implement these improvements?

- The data standards (SDTM) needed for implementation are already in place.
- FDA needs to mandate SDTM and announce a date when these standards become effective. Due to the withdrawal of the 1999 guidance for submitting electronic data at the end of this year and SDTM only being recommended in the eCTD guidance, the industry is confused. Mandating SDTM and providing clear direction will be a great benefit to everyone.
- Legacy data conversion will always prove challenging but training and the implementation of SDTM nomenclature into the data lifecycle early will increase the quality and quantity of future electronic data submissions.

Data Standards

Dockets Question #7:

What lead time is needed for stakeholders to respond to and be in alignment with FDA initiatives?

- Late-stage SDTM conversion
  - Convert first study: 8 weeks
  - Convert studies ongoing: 3 weeks per study, after 2-6 months to build conversion program development tools
- Integrate SDTM in collection
  - 6-9 months, if presently have a data standard
  - 12-18 months, if not presently have a data standard

Data Standards

Dockets Question #9:

What data standards areas provide the greatest challenge?

- Legacy Data Conversion to SDTM due to:
  - Failure of small and mid-sized companies to adopt data standards
  - Failure of CROs to adopt data standards
  - Lack of standardized CRFs
  - Lack of controlled terminology
  - Familiarity with SDTM is still relatively new
  - Highly defined vertical structure

Data Standards

Dockets Question #10:

What approaches will facilitate the most effective and efficient adoption and implementation of data standards?

- Mandate according to a schedule
  - Similar to how PLR was handled
- Incentive (e.g. reduced user fee)

eSUBs and Data Standards: Informal Survey Results from Stakeholders

Questions from Docket:

5. How should FDA engage stakeholders while developing, testing, and implementing these solutions?
7. What lead time is needed for stakeholders to respond to and be in alignment with FDA initiatives?
8. How should FDA coordinate with stakeholders on the adoption and implementation of data standards?
9. What data standards areas provide the greatest challenge?
11. What key areas require new or expanded electronic submissions guidance?

Additional comments

Informal Survey Results

Participants:

- 14 Responses
- Company either:
- Tier 1 (Large Pharma) = 5 (36%)
- Tier 3 (Small Pharma) = 9 (64%)

Revenue:

- Tier 1 = 1Billion and up
- Tier 3 = <500 Million

Informal Survey Results

Questions as they appeared in the survey:

1. How should FDA engage stakeholders while developing, testing and implementing these (elecronic submission and data stanadard) solutions?
2. What lead time is needed for stakeholders to respond to and be in alignment with FDA initiatives?
3. How should FDA coordinate with stakeholders on the adoption and implementation of data standards?
4. What data standards areas provide the greatest challenge?
5. What key areas require new or expanded electronic submission guidance?
6. Some companies are doing "end-of-pipe" remapping to SDTM and others are revamping thier entire process to integrate SDTM into their data collection systems. What factors are determining the chosen approach?
7. For each approach mentioned in question 6, what are the most important factors that affect the time required to adopt the standard?
8. For each approach in question 6, about how much personnel time is required, and for what types of personnel and skill levels?
9. For each approach mentioned in question 6, what kinds of benefits will companies get, and how long will it be before benefits are realized?

Additional Comments

Informal Survey Results

1. **How should FDA engage stakeholders while developing, testing and implementing these (elecronic submission and data standard) solutions?**

Tier 1:

- Use of Pilot submissions
- Publish information on FDA web site
- Meeting participation
- Involve industry groups

Informal Survey Results

Continued

- **How should FDA engage stakeholders while developing, testing and implementing these (elecronic submission and data standard) solutions?**

Tier 3:

- Include Tier 3 companies in testing
- Beta testing
- Use communication vehicles such as newsletters, on-line courses, electronic questionnaires, create information center on web site
- Set-up hotlines with FDA experts
- Use HL7 SPL team model for interactions with agency, but use FDA dictated team
- Focus groups with all sizes of pharma, biotech, device and include regulatory, clinical and IT (cross-functional)
- FDA should discuss any changes with industry experts to gain practical perspective

Informal Survey Results

2. What lead time is needed for stakeholders to respond to and be in alignment with FDA initiatives?

Tier 1:

- Requires integrated strategic plan, not spot solution
- Lead-time responses ranged from 3 months to 2 years

Tier 3:

- Most companies not ready for 1/1/2008
- Grandfather legacy studies for 2-3 years
- Lead-time responses ranged from minimum of 3 months to 7 years
- FDA equates all pharma with billion dollar companies
- Changes should be voluntary

Informal Survey Results

3. How should FDA coordinate with stakeholders on the adoption and implementation of data standards?

Tier 1:

- Through industry groups, meetings, opinion articles in key journals
- Notification to participate in meetings
- Through guidances

Tier 3:

- Simplify standards (CDISC too complex)
- Single point of contact at FDA for questions
- Focus groups
- Current communication is working fine
- In person/personal

Informal Survey Results

4. What data standards areas provide the greatest challenge?

Tier 1:

- Development and implementation of vocabularies and taxonomy, CDISC, SEND, domains not defined in SDTM model

Tier 3:

- ODM is impossible, SDTM is cumbersome but doable
- Changes to SDTM structure
- Standards applied to work already completed
- Adverse events and efficacy criteria that are not defined in SDTM
- Need more experienced FDA personnel with technical and regulatory experience

Informal Survey Results

5. What key areas require new or expanded electronic submission guidance?

Tier 1:

- Rule to require electronic submissions
- BLAs
- Additional detail on how study report data is provided
- SAS data submission and SAS programs submission

Tier 3:

- Therapeutic areas not currently supported (oncology)
- Any area that has FDA (or EMEA) guidances would eventually need CDISC models
- More training for medical officers reviewing data
- Rolling BLA/NDA using xml
- Data capture and electronic processing
- AE/SAE reporting
- eIND in eCTD format
- Hardware requirements

Informal Survey Results

6. Some companies are doing "end-of-pipe" remapping to SDTM and others are revamping their entire process to integrate SDTM into their data collection systems. What factors are determining the chosen approach?

Tier 1:

- End-to-end vs. reaction to change
- Efficiency and ease
- Revamp entire process rather than switch between old and new
- Project status at the time of CDISC standards implementation
- Cost to implement at early stage may not work for small companies

Informal Survey Results

Continued

6. Some companies are doing "end-of-pipe" remapping to SDTM and others are revamping their entire process to integrate SDTM into their data collection systems. What factors are determining the chosen approach?

Tier 3:

- New studies are not necessarily SDTM compliant (therapeutic variables do not fit)
- Few commercial systems that truly meet standards
- New systems should be “certified” compliant, easy to use, and reasonably priced
- Timing for SDTM integration, should be integrated into the operational database
- End-of-pipe too late, need to build in early
- CRO capability
- Phase of product development, size and resources of company
- Difficult process to transition from legacy paper file to comprehensive electronic environment

Informal Survey Results

7. For each approach mentioned in question 6, what are the most important factors that affect the time required to adopt the standard?

Tier 1:

- Company's commitment to change and understanding of impact and value vs. simply changing to meet FDA demands
- Time required to adopt depends on by-in by Senior Management and willingness to dedicate resources
- Industry needs to understand the need to change vs. FDA forcing change
- Understanding SDTM and impact/Training
- Development of internal processes to support SDTM/Training

Tier 3:

- Commercial availability of certified systems, easy to use and reasonably priced
- Implementing new standards causes delay in approval and increased costs
- Clinical operations and timing of product development in business market
- Reconfiguring information to the appropriate format

Informal Survey Results

8. For each approach in question 6, about how much personnel time is required, and for what types of personnel and skill levels?

Tier 1:

- Task force or project team devoted to process with director level to lower level involvement
- 4-8 hours/week per person over 3 months
- 8 weeks of SAS programmers, 3 months CRF designer, 6 months data manager

Tier 3:

- Do not have the capital to outsource or support
- Skill level depends on system
- Create dedicated team, include personnel from each functional area. All should have minimum of 5 years experience
- 1 FTE per year each for IT support and data management
- 10-30 hours per project for clinical and regulatory

Informal Survey Results

9. For each approach mentioned in question 6, what kinds of benefits will companies get, and how long will it be before benefits are realized?

Tier 1:

- Companies need to understand benefits
- Fully integrated processes from beginning to end and have entire staff understand SDTM and its impact
- Consistency across studies
- Easier to generate a pooled database of multiple studies
- Revamping of entire process allows for faster submission time to FDA
- Shorter review by FDA
- Companies can bring product to market earlier, increase revenue

Informal Survey Results

Continued

9. For each approach mentioned in question 6, what kinds of benefits will companies get, and how long will it be before benefits are realized?

Tier 3:

- Benefits will only be realized when standard is not just a set of criteria but true set of government defined blocks
- Worldwide submissions require fields that FDA does not
- Standard structure must be exhaustive to cover all therapeutic areas in all countries
- Running clinical trails would be much smoother
- Faster review time and stronger relationship with FDA reviewers

Informal Survey Results

Additional Comments

Tier 1: no additional comments

Tier 3:

- Studies conducted in other countries are often submitted to FDA. These meet ICH standards and GCP, but were not collected in a format that meets the new data standards. FDA requirements should be accommodating for those studies.
- Small companies should be “grandfathered”. They do not have the resources to support electronic and cannot afford outsouring
- The FDA should speak at more events
- FDA should ensure that there is an adequate amount of people on staff who are available who are trained and knowledgeable

Informal Survey Results

Summary

- Tier 1 and Tier 3 companies agree that mandated standards would shorten FDA review time, bring products to market faster and save money
- Tier 1 companies feel that a cross-functional approach, including all levels and departments is key to success
- Tier 3 companies are challenged by lack of resources and funding, which impacts their ability to respond to the need to implement new standards
- All respondents felt that communication with the FDA was very important and there should be an adequate number of skilled FDA reviewers available

IT Plans

Dockets Question #6:

What topics are most useful to include in IT plans?

- Maintain Enterprise Focus
- Standards-Based Development
- Component-Based, Distributed Computing Environment
- Planning for Change
- Architecture-Influenced Decisions

IT Plans

Dockets Question #12:

What lessons learned and best practices should FDA consider as we transition from program-specific to enterprise IT solutions using a reusable and modular model?

- Leverage industry experience
- Business requirements
- Functional requirements
- Centralize solution not point solution
- Not in the IT business – find a partner!

IT Plans

Dockets Question #13:

What specific concerns (i.e., security, confidentiality, etc.) exist for a third party entity or entities providing services related to electronic submissions and review and how can they be addressed?

- Protect against unauthorized access
- Authentication Techniques
- Limited Permission Levels
- Non-disclosure (or confidentiality) Agreement
- Computer viruses and other Malware
- Secure data transmission

Overall Summary/Conclusions

- Standards and formats are available
  - eCTD
  - CDISC SDTM
- Need to be mandated by Agency
- Needs to be implemented in a feasible and cost sensitive manner for all stakeholders
- Training and communication directly from agency would be critical to success