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September 26, 2016

Division of Docket Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Reference: FDA Quality Metrics Technical Conformance Guide Technical Specifications Document
Docket ID: FDA-2016-D-1594

Dear Sir/Madam:

PDA appreciates the opportunity to comment on this Technical Conformance Guide and supports the FDA creating such a technical companion document to the Request for Quality Metrics draft guidance and recommends that both documents be finalized concurrently with special attention paid to ensure they are consistent. PDA notes that while the Metrics Draft Guidance allows for a comment field this is not mentioned in the Technical Conformance Guide and recommends this be added as a field for each data element.

To streamline implementation and maximize learning, PDA suggests FDA provide a pilot or "sandbox" where companies could make example submissions and receive FDA feedback on whether the response meets expectations. PDA further recommends FDA engage in collaborative dialogue on preparing the validation rules for these data sets rather than waiting to disclose the rules once finalized.

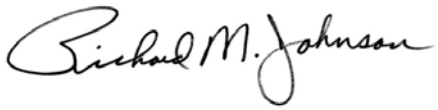
In order to have consistent data sets which are usable to both FDA and industry, PDA recommends FDA provide specific data formats and XML Schema definition which are applicable to cases of multiple product formulations and multiple manufacturing sites involved in production of a single drug product. One example of such level of detail is the ICH E2B EWG Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). PDA offers its assistance to help coordinate the drafting of data formats for various types of products and configurations. Additional detailed comments are attached.

PDA is a non-profit international professional association of more than 10,000 individual member scientists having an interest in the fields of pharmaceutical, biological, and device manufacturing and quality. Our

comments were prepared by a committee of experts with experience in pharmaceutical and biological manufacturing, including members representing the PDA Metrics Task Force, the Regulatory Affairs and Quality Advisory Board and Board of Directors.

If there are any questions, please do not hesitate to contact me.

Sincerely,



Richard Johnson

Cc: Denyse Baker, PDA; Richard Levy, PDA

**Food and Drug Administration Draft Guidance**
FDA Metrics Technical Conformance Guide
**26 September 2016**

General Comments

| General Comments | Rationale | Critical Comment? Y/N |
|---|---|---|
| PDA membership has concerns around data security and would like to understand mechanisms and provisions by which the agency will protect and ensure data integrity while under its control.. | PDA considers metrics data to be Confidential Commercial Information per 21 CFR 20.61(b) and would expect FDA to follow existing protections for this category of information as well as implement reasonable protections against electronic theft or unauthorized access (i.e. hacking). | No |
| PDA recommends FDA provide specific examples of data format and presentations including cases of multiple product formulations and multiple manufacturing sites involved in production of a single drug product. PDA also suggests including an example of how to organize data from multiple sites. or in cases when data is reported on multiple strengths of a product. One example of such level of detail is the ICH E2B EWG Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). | In order for FDA to receive metrics that are comparable and consistently reported over time, more specific examples of format and content would be valuable. PDA has attached one sample data file to illustrate the level of detail needed. PDA also recommends the FDA provide specific XML Schema Definition files. | Yes |
| PDA recommends that both documents Request for Metrics Guidance and Technical Conformance Guide be issued together to avoid confusion or inconsistency | If the documents are not closely linked there is concern that definitions in both documents may not be consistent. | No |
| PDA notes that the requirement for ASCII could be incompatible with some products names and suggests the FDA consider other formats. | Most products have a trademark or other symbol which is not recognized by ASCII. PDA recommends consideration of the UTF 8 (Unicode Transformation Format). The technical implementation of this requirement will need more information on number fields (floating point, integral, etc.) and for text (UTF, etc.) | No |
| The 2015 Draft Guidance Request for Metrics allowed for a comment field. PDA recommends a field under each metric with a limited size. | There are no technical requirements listed for the comment field in this technical document. If all industry comments are submitted in a separate section of the report,, then a link to each data element type or reference to specific data entry is needed | Yes |

| General Comments | Rationale | Critical Comment? Y/N |
|---|---|---|
| PDA suggests FDA create a "pilot on data submission" for companies to test in with sample requests to which industry could respond and receive FDA feedback on whether the response meets expectations. This is consistent with an FDA presentation made by Karthik Iyer at the 2015 PDA Metrics Conference | There does not seem to be a provision for beta testing of the system before companies submit live data. Having the means to test submissions would increase industry's confidence ensuring data is correctly transmitted. | Yes |
| PDA notes that CDRH has initiated a pilot metrics program. | PDA encourages CDER & CBER to engage with CDRH and consider aligning, preventing redundancy and to streamline data submissions for those companies who have a broad based product line including combination products. | Yes |
| Section 5.0 (Validation) While Data Validation rules are essential and paramount to ensure correct and useful data are available; data verification should also be part of the methodology to ensure consistent and reliable data. Conversion of XML data to other data formats requires this crucial to step ensures the conversation is done appropriately and there are no data loss and inconsistencies. | Disclosing the validation rules only when made final could cause delays during implementation. PDA recommends FDA engage in a collaborative dialogue on preparing validation rules so firms have time to prepare. | Yes |

Specific Comments to the Text

| Section No. | Current Text | Proposed Change | Rationale | Critical Comment? Y/N |
|---|---|---|---|---|
| 3 | **3. FILE FORMAT – ELECTRONIC SUBMISSIONS** | PDA requests that FDA augment the content in these sections with an actual XML Schema Definition and ensure that content of these sections are 100% matching the XML Schema Definition (i.e. no inconsistencies in the format or data types). | The purpose of including the XML Schema Definition is to express in technical terms and using a standard 'language' the format and data types of the actual data submission file(s). Having the XML Schema Definition will allow companies to program their software to: 1) format the data submission file correctly, 2) ensure the data submission file(s) are formatted properly and the data matches the expected data types (i.e. the submission file is 'valid').<br><br>PDA suggests either of two broadly accepted standards for expressing the schema of an XML file: XSD (XML Schema Definition – newer/modern) and DTD (Document Type Definition – older but still used). Either one would be fine to use in this context.<br><br>More details on XML Schema are available at: https://en.wikipedia.org/wiki/XML_Schema_(W3C), and<br>DTD: https://en.wikipedia.org/wiki/Document_type_definition | Yes |
| 3.5 | **Data Definition File** | As noted in the comments above to section 3, PDA requests further clarification and specifically recommends that FDA allow flexibility in submissions of one XML file per product, one per site, | Having a specific format defined in the guidance will allow companies to program their software to ensure data submitted matches the FDA expectations. Flexibility in submissions allows firms with different types | Yes |

| Section No. | Current Text | Proposed Change | Rationale | Critical Comment? Y/N |
|---|---|---|---|---|
| | | or one per company. | (e.g.API only, CMO, or FDF) to optimize resources in preparing, submitting and archiving data. | |
| 4.2.5 | **Applicant Name** The name of the application holder. | **Applicant Name** The name of the application holder **or other responsible party reporting the data**. | This section needs additional instructions for products not manufactured under an application. For example, it is not clear how to use this data element for monograph products. | No |
| 4.2.11 and 4.2.12 | **Time Period Start** The beginning of the time period within which the data being reported were collected. **Time Period End** The end of the time period within which the data being reported were collected. | **4.2.11 Time Period Start** The beginning of the time period within which the data being reported were collected **(dd/mm/yyyy).** **4.2.12 Time Period End** The end of the time period within which the data being reported were collected.**( dd/mm/yyyy)** | In order to standardize the electronic data reporting, PDA recommends that FDA explicitly state the date format to be used (e.g. dd/mm/yyyy) and specify that time is not required because different regions of the world have different standard practices. | No |
| 4.2.26 Activity type | Establishment Activity Classification | Keeping consistent with the registration terms – recommend "Establishment Operation". | Data Element Name: Activity – keeping consistent with the registration terms – recommend "Establishment Operation". In addition, an establishment may have multiple operation types: manufacturer, testing and packing etc. A clear distinction should determine if this single vs. multiple select field. | No |

| Section No. | Current Text | Proposed Change | Rationale | Critical Comment? Y/N |
|---|---|---|---|---|
| 4.3 Table 2 | Data Element Name: Dosage Forms | Data Element Name: Dosage Form~~s~~ | PDA recommends make the data element name singular, not plural, to be consistent with the definition in 4.2.24 and with the data element label. | No |
| 4.3 Table 2 | Data Element Name: Lots Attempted and Attempted Lots | APRWIDD ~~Attempted Lots~~ **Lots Attempted and Pending** | These data labels are too similar: Lots Attempted has a Data Label of "Lots Attempted" and Attempted Lots Pending Disposition has a Data Label of "Attempted Lots". PDA recommends terms that can be more easily distinguished. | No |
| 4.4.1 APR Approval | Indicate Yes/No to indicate whether each associated APR/PQR was reviewed and approved. | PDA recommends deleting this data element. | This question is redundant as written and should be removed. If the Data Element in 4.2.21 is "YES" for completion – then by default – it was approved. | No |
| 4.5 Table 3 Optional Data element Formats | Data Element Name APRAPPVDY | Data Element Name ~~APRAPPVDY~~ **APRQOPSB** | The data element name "APRAPPVDY" has 9 letters, when it should have 8, per table 1, section 3.1 Please re-propose a name consistent with the convention defined. PDA has made a suggestion based on the data element description | No |