February 22, 2008

Office of the Chief Information Officer (HFA–080)
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Re: Docket No. 2007D–0481; Draft Prescription Drug User Fee Act IV Information Technology Plan; 72 Federal Register 73851 (December 28, 2007)

Dear Sir or Madam:

The Pharmaceutical Research and Manufacturers of America (PhRMA) and the Biotechnology Industry Organization (BIO) are pleased to provide the following comments in support of the Draft PDUFA IV Information Technology (IT) Plan published on December 28, 2007. PhRMA and BIO represent the country's leading research-based pharmaceutical and biotechnology companies, which are devoted to inventing medicines and biotechnology products that allow patients to lead longer, healthier and more productive lives. In addition, both organizations have demonstrated a desire to work with the Agency to enable regulatory process efficiency through effective use of information technology.

PhRMA and BIO member companies have supported the creation of the IT Plan since its first inception during the PDUFA IV IT discussions. We would like to take this opportunity to congratulate you on your successful completion of the draft, and we praise the Agency's commitment to developing this plan and soliciting public comment.

The attached document contains comments that were compiled by member companies over the past several weeks. The document is organized into two sections: The first section contains general comments pertaining to the overall IT Plan; the second contains a table with comments pertaining to particular sections of the document. These comments are organized in the order in which the referenced sections appear in the IT Plan.

PhRMA and BIO trust that these comments are useful to the Agency as it further refines and finalizes the PDUFA IV Information Technology Plan. We thank the Agency for this opportunity to provide you with our views on this important topic.

Sincerely,

/S/

Alan Goldhammer
Deputy Vice President
Regulatory Affairs
PhRMA

/S/

Andrew J. Emmett
Director
Science and Regulatory Affairs
BIO

1. GENERAL COMMENTS

PhRMA and BIO appreciate the opportunity to review FDA's draft PDUFA IV Information Technology Plan, so that FDA constituents have the opportunity to plan for aligning resources and timelines according to the business process changes being introduced by FDA. Because the IT plan will allow sponsors to better plan ahead, it is an important benefit of the plan, and would be valuable to include in the Purpose section of the document.

Timelines and Technical Communication:

The development and implementation of new information technology standards and systems for the exchange of regulatory information requires substantial technical coordination between the agency, industry, and other relevant stakeholders. A clear understanding of the methods of communication and the timing of key milestones will help to facilitate the adoption of new technologies on the part of both FDA and industry.

- This plan provides milestones for many projects within the first 18 months of the PDUFA timeframe, but needs to evolve to include FDA's vision beyond the first 1-2 years. Industry recognizes that circumstances will likely impact project scopes and timelines, but it is important for FDA to include items in the 3 to 5 year range that may have less certain scope or timeline, and not limit the Plan to include only those projects that have more definitive milestones and timelines established. Sharing this vision will greatly increase the value of this plan.

- Industry strongly supports the PDUFA IV commitment to periodically publish updates to the Plan that would update the timelines and milestones for each specific IT project/program. FDA constituents will align resources and timelines to ensure proper compliance, but costs and efficiencies vary greatly with the degree of upfront planning we are afforded. We understand that project milestones and timelines often change due to a variety of circumstances, but if we have timely access to the actual timeline the FDA is working from then we can adjust our resources accordingly. This will add value to the IT Plan in terms of ensuring greater accuracy and therefore credibility to sway our internal decision-makers.

  It will be more helpful to external constituents if FDA can provide updates, particularly the table in section 6.1 IT Architecture (page 20-22), more closely to the timeframe that we begin making business plans for the next year. This assumes that the immediate 1-2 yrs of the Plan will realistically contain greater detail and accuracy of FDA's IT projects than the subsequent years. We welcome an opportunity to discuss the actual timing and the benefit of receiving these updates immediately before committing our resources to initiatives for the next year.

Additionally, we note that there is no explicit mention that this will be a rolling plan except in the Appendix. We suggest adding a description of the nature of this plan as a rolling 5-year plan.

- The Plan indicates that stakeholders will be notified or consulted through public meetings, pilots, etc., but does not include a specific commitment to engaging stakeholders before project plans are finalized. It should speed industry adoption if there are effective opportunities for stakeholder feedback to influence FDA plans. We recommend that the Plan more clearly indicate that FDA will engage stakeholders that might be affected by or able to leverage changes FDA at appropriate stages in a project such as requirements gathering, testing and piloting. We recognize that it is not reasonable to engage all affected stakeholders early in development and request FDA clarify how they intend to assemble appropriately representative stakeholder groups for this purpose. Better understanding this potential impact should help FDA improve US healthcare systemically.

- We recommend that the descriptions of individual initiatives more consistently convey the underlying business goal for each initiative and how they intersect with key components, such as the future of the eCTD backbone and the e-gateway. We also recommend the overall strategy indicate, or individual initiatives specify, the plan for harmonized deployment of these e-initiatives across the various FDA review divisions.

- All major IT projects should be presented as well as to identify relationships or dependencies between projects. We recommend adding milestones and timelines for each major project that would include timeframes for: project design, stakeholder feedback, technical design, technical development, testing, stakeholder testing, guidances, pilots, implementation, and timeframe for compliance requirement.

- We recommend the Plan describe the consistent mechanisms that FDA will implement to distribute technical specifications in order to assure that Sponsors can consistently access authoritative technical specifications.

Standards and Interoperability:

PhRMA and BIO and FDA share an appreciation of the importance of global standards for the exchange of documents and data. We regard global standards as a critical aspect of our ability to exchange information with regulatory authorities, co-development partners, and third party providers in an end-to-end manner across the full lifecycle of a marketed medical product.

- The most common industry concern was that the Plan does not reflect sufficient commitment to encourage, develop and adopt globally harmonized standards. The

plan should acknowledge the role of internationally harmonized healthcare standards as reflected in the PDUFA IV commitment letter. We suggest this commitment be stated somewhere in the overall description of the Plan, similar to the following sentence. “FDA continues to be committed to participating in the development of international IT standards and controlled vocabularies for drug development wherever such standards will support the overall advancement of effective electronic healthcare.”

- Throughout the document FDA refers to "standards-based information systems". In keeping with the previous comment promoting effective healthcare systems, we recommend use of the term “standards” should at a minimum impart meaning of "open” or “accredited” standards. We suggest that FDA add these qualifications to the term “standards” (perhaps by addressing this in Section 5.4, “Data Standards”).

- We recognize the importance of controlled terminologies as a critical component of many open, accredited standards. We recommend FDA clarify how they plan to approach standardized terminology development to assure semantic interoperability for controlled terminologies.

- The electronic submission and review of promotional materials (i.e. via DDMAC) could provide substantial business benefit to both industry and FDA, and is clearly an opportunity to leverage information technology. In the Plan there is no mention of a project to introduce electronic submissions capabilities for DDMAC submissions. Yet these submissions are a component of final approval negotiations for Fast Track products and are key to ongoing post marketing compliance for all PDUFA products. We suggest the Plan address FDA’s vision for end-to-end electronic product submissions including those to support all phases of drug development including the commercial phase. Perhaps the idea could be presented in the Plan for further exploration in a Public Meeting forum.

FDA Bioinformatics Board:

PhRMA and BIO are supportive of the development of FDA’s Bioinformatics Board (BiB) to help to coordinate the agency’s business process analysis and information technology management, and offer the following comments:

- The Bioinformatics Board appears to have no input from stakeholders. Noting that FDA actions affect multiple stakeholder communities, we recommend a conduit to the BiB be established to allow the BiB to solicit and receive direct feedback from external constituents. The FDA might also consider establishing a small group for each major external constituency to serve as consultants for initiatives that are expected to have potential major impact. These groups could serve multiple purposes, including feasibility and impact analysis of new initiatives, technologies, and standards.

- Can FDA make the Business Review Boards' strategic roadmaps available as appendices to this Plan? We believe they may help frame the business vision for many IT initiatives in terms that our business leaders will more quickly understand.

- The document notes: "The FDA adopted a consistent methodology for modelling business processes for Agency-wide initiatives. " Can FDA describe this methodology within the plan or by reference to other publicly available material?

Other General Comments:

- We request that FDA clarify the relationship of the FDA Strategic Action Plan and FDA Science and Mission at Risk Report to this document. Perhaps FDA can include an explanation of the relationships of these initiatives in the Introduction of the Plan.

- The IT Plan utilizes tables throughout the document to provide critical information. We recommend that the FDA label and number these tables for better clarity and for ease of reference.

2. COMMENTS WITH SPECIFIC REFERENCES

#	Citation Location Section/Page	Proposed Change	Rationale
S1	2.0 Purpose, first paragraph (page 4)	Add text (bold italics): Improve the FDA's ability to ***receive***, communicate, share, and disseminate information more clearly within the Agency and with other government organizations, the regulated industry, and the American Public; and..	*Reference is made to strengthening the product review process. However, no reference is made to the submission aspect (either data or documents) of the overall process.*
S2	3.0 Vision – Page 5	Add a sentence after the first to suggest that in addition to support of the process for review, the vision also supports FDA's four strategic goals – 1) Strengthen FDA for Today and Tomorrow, 2) Improve Patient and Consumer Safety. 3) Increase Access to New Medical and Food Products, and 4) Improve the Quality and Safety of Manufactured Products and the Supply Chain.	*It helps to align business and IT vision and strategies.*
S3	5.2 Target Architecture, page 9	Add text (bold italics): The primary purpose of the Target EA is to effectively plan a course for achieving the FDA's strategic vision and goals***, while reducing the costs of semantic interoperability across the IT systems portfolio***.	*This could drastically reduce the costs of FDA's systems to work with each other. The same applies to systems working across Divisions and Centers.*
S4	4.2.2 Information Management/Information Technology Strategy **–** Page 6	Change text (bold italics): 4.2.2 Information Management/Information Technology ***Goals***	*This subsection comes under the section entitled "Goals and Objectives". The term "Goals" seems more suitable that "Strategy"*
S5	Section 5.0 PDUFA IV IT Strategy, Page 6, paragraph 1, 5th sentence:	Add text (bold italics:) To realize this goal, the Agency's strategy is to evaluate current business processes, IT Applications, data exchange standards and the overall FDA IT data architecture to define a target enterprise architecture that will achieve the IT goals defined in the PDUFA IV Commitment Letter.	*Data exchange standards are a critical component, and we suggest it be explicitly included in the context of FDA's strategy.*

#	Citation Location Section/Page	Proposed Change	Rationale
S6	Section 5.0 PDUFA IV IT Strategy page 6	Add text (bold italics:) To realize this goal, the Agency's strategy is to evaluate current business processes, IT Applications, and the overall IT architecture to define a target enterprise architecture that will achieve the IT goals defined in the PDUFA IV Commitment Letter. ***This target enterprise architecture will be drafted to include a timeline of milestones by month/year.***	*There appears to be no defined timeline or description of how FDA will measure the effectiveness of the target enterprise architecture. This should be somehow measurable; adding a timeline with key milestones should provide a reasonable measure.*
S7	Page 8, last paragraph	The reference to the BRB 5-year goals (Appendix 7.4) more appropriately belongs in Section 4 where goals are discussed. Suggest including the text directly in the document rather than in an attached appendix.	
S8	Section 5.2 Target Architecture – page 9	In this section, the FDA states that the Agency's primary focus will be on pre-market activities. Suggest including a statement of how FDA will incorporate post-marketing product information management.	*Such a focus would potentially overlook significant opportunity is in the area of post-marketed product information management that is or could be supported by electronic processes. This is particularly the case for legacy products.*
S9	Section 5.2 Target Architecture – page 10	Within the IT assessment, suggest including a strategy for how FDA will take into account the lifecycle of a system	*We recognize the impact of legacy systems on overall IT costs, and believe sharing system retirement plans will assist industry with its long-term planning*
S10	Section 5.2 Target Architecture, E-Platform Initiatives – page 10	Suggest adding dates to milestones (e.g. harmonized requirements, data extraction, etc.).	
S11	Section 5.2 Target Architecture	When citing "business needs, do these needs pertain solely to FDA or do they extend to its constituent community? Please clarify.	
S12	Page 10 E-Platform Initiatives	The E-Platform initiative implementation timeline should be timed to leverage the benefits of the Target Enterprise Architecture.	*Without a TEA being defined, implementation of these initiatives may be premature and potentially waste resources and dollars.*
S13	E-Platform Initiatives table page 11	Request clarification on FDA expectations of sponsors to adopt the SPL Collaborative Portal and E-List on the FDA timeline (2Q-08).	*This will assist industry with its internal IT planning.*

#	Citation Location Section/Page	Proposed Change	Rationale
S14	*Section 5.2 Target Architecture, Collaborative Portal (Page 11)*	The time frames listed in the IT Plan for prototype testing and production of Release 1.0 appear to be unattainable given the amount of time required to pilot, develop, implement and train users of this new technology. Specifically, the table references Jan 2008 for prototype testing by FDA and industry users. We note that the software vendor recently contacted industry users (as of mid-Jan) and is targeting February for the first round of prototype testing); the first round of prototype testing is with a very limited pool of participants. Implementation of this technology will require process changes for both agency review divisions and sponsors. The FDA should include stakeholders in assessing the Collaborative Portal. We believe sponsors and agency review divisions working together would be especially beneficial. A pilot with a much broader scope of sponsor participation, as well as agency review division participation, is essential for development of a collaborative portal that will be used by stakeholders. We strongly recommend a pilot program utilizing the SPL Working Group and agency review divisions to ensure stakeholder needs are identified and addressed prior to use of the tool becoming a requirement.	*The FDA should include stakeholders in the assessment of the Collaborative Portal. We strongly recommend a pilot program utilizing SPL WG and agency reviewers to ensure sponsor needs are met before becoming a requirement.* *Given the need for an expanded pilot program, the FDA should consider revising its 2nd Quarter 2008 timeframe for the production of Release 1.0.* *We request further clarification on the status of use of the collaborative portal be included in the IT plan.*
S15	Section 5.3 Guidance, Policy and Regulation (page 12)	Section 5.3 seems unnecessary... FDA might acknowledge there are different audiences for this document, but a better option would be to include a hyperlink to existing content elsewhere on FDA's web site rather than to detail how they make regs/guidances here...	

#	Citation Location Section/Page	Proposed Change	Rationale
S16	Section 5.3 Guidance, Policy and Regulation	Please add text to describe how regulation for paper-based processes will be revised. ***The FDA will develop and implement a long-term plan to revise and/or withdraw regulations that are based upon paper-based processes.***	*Promulgation and implementation of regulations supporting electronic processing of clinical and safety data is unnecessarily slow. FDA's vision is "the elimination of future paper-based submissions."*
S17	Section 5.3 (page 12), third paragraph	Please add text (*bold italics*): FDA will continue to work with "our stakeholders" regarding format and data standards. ***Our Stakeholders include Reviewers, Sponsors, Vendors, Investigators***, …	*It would be useful to those reading the plan to understand those groups the FDA considers stakeholders in the development and implementation of standards so that those groups can plan to participate and provide feedback on that development.*
S18	Section 5.4 Data Standards page 14	Please add text (*bold italics*): The FDA recognizes the importance of, and is committed to, ***global harmonization of data standards through open, structured processes*** and using / implementing ***such*** data standards for regulatory submissions wherever possible.	*The Agency's approach should be international in scope so that this work can be implemented, consistently, worldwide as reflected in the PDUFA IV Commitment Letter. Suggest utilizing language from the PDUFA IV commitment letter.*
S19	Section 5.4 Data Standards page 14	Please add text: ***When developing plans, in order to encourage rapid standard update, FDA will consider change management needs.***	*Change management associated with standards needs to be considered and clearly communicated to encourage rapid uptake. Consider the addition of text in this regard.*
S20	Section 5.4 (page 14)	Please add text: ***In understanding the business needs a process map will be developed defining the current and future business process. A gap assessment will be developed to identify the future process gaps that will be addressed by proposed standard(s).***	*The needs assessment should include a business process evaluation and gap analysis as part of a needs assessment. Suggest addition of text to describe this*

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S21	Section 5.4 Needs Assessment and Requirements Gathering (page 14)	Please add text: ***Where standards involve the receipt of data or messages from stakeholders outside the agency the agency will engage those stakeholders to identify any additional requirements specific to the needs and processes of the stakeholders***.	*There is no mention of processes to gather requirements outside the Agency. Where messages from external parties are involved it is critical to successful development of a usable standard to engage those on both sides of the message. This will speed adoption by ensuring both Agency requirements and the other parties' requirements are met.*
S22	Section 5.4 Data Standards, Needs Assessment and Requirements Gathering: Page 14 – 15,	Please add text (*bold italics*): The appropriate Business Review Board reviews the need ***and the impact (economic or other) associated with the adoption of a given standard*** if it concurs, raises it to the Bioinformatics Board for review.	*The impact of adoption of a given standard should be a key component of the decision to proceed with the development of a standard. So that the total cost/benefit can be assessed.*
S23	Section 5.4 Data Standards	Diagram 6 portrays a data exchange process. (Suggest adding a process step - the development of an implementation plan.)	*There are multiple ways to develop and deliver a standard that have impact on the cost of implementation. These costs should be considered in the development phase to help keep healthcare costs from escalating. Adding a process step to develop an implementation plan will help assure that these costs are considered in the implementation.*
S24	Section 5.4 Data Standards, Needs Assessment and Requirements Gathering, last sentence	Please add text: **The Data Standards Council will identify if similar needs exist in the global health care community in an effort to encourage global harmonization of data standards.**	*Within the context of the plan, FDA states it supports global standards this language helps assure global harmonization is considered.*

#	Citation Location Section/Page	Proposed Change	Rationale
S25	Section 5.4 Data Standards, 2nd paragraph Page 14	Please add text (*bold italics*): This section describes the FDA's strategy for managing ***the use*** *of* data standards throughout their life-cycle	*FDA is a user of standards, whereas a SDO would more appropriately manage the actual life-cycle of a standard.*
S26	Section 5.4 Data Standards, Development, Adoption and Maintenance, Paragraph following bullets, Page 15,	Please add text (bold italics): In instances where work with these organizations is inconsistent with applicable FDA processes or otherwise impractical or inappropriate, then the DSC may develop the standard. ***In such instances the approach will be reviewed by the BiB prior to proceeding with the project, including a review of the impact (economic or other) associated with the development of an FDA-exclusive standard.***	*This should be an infrequently used exception and it is recommended that an additional BiB review and approval be required before proceeding with independent standards development. The downstream cost to both the agency and the Health Care industry operating to an FDA exclusive standard should be thoroughly assessed and considered prior to taking this approach to help keep healthcare costs from escalating.*
S27	5.4 Data Standards; Pages 14 thru 18	We recommend that the role of external stakeholders be recognized in each step of the Data Standards development process described in section 5.4.	*Engagement of external stakeholders in all phases of data standard development helps to assure end to end business process understanding and increases the quality of submitted data.*
S28	5.4 Data Standards; Development, Adoption, and Maintenance; Page 15	We recommend changing the bullet heading to "***Accredited and/or open consensus SDO***"	*Technically, ISO is not accredited by any organization.*
S29	5.4 Data Standards; Implementation; Page 16	We recommend that the phrase "Business Community" should be more precisely defined (to include industry, Standards Development Organizations, and any other relevant external stakeholders.	*Multiple external parties are keenly interested in data exchange and play a role in the adoption and implementation of these standards.*

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S30	5.4 Data Standards; Implementation; Page 17	We request that the FDA improve the readability of Figures 6 and 7 (including the font size)	*The font in Figures 6 and 7 is very difficult to read, impeding the ability to properly review the document.*
S31	5.4, Data Standards; Development, Adoption, and Maintenance; Page 15	We recommend that the FDA clearly identify how the Data Standards Council will communicate progress on data standards initiatives to external stakeholders.	*It is important to external stakeholders to understand when and how progress on data standards initiatives will be communicated.*
S32	5.4 Data Standards; Data Standards Investment Strategy; Page 18	We recommend that the Data Standards Council consider including fully functional examples for each proposed capability as an activity under the "Exchange Standards Development" topic.	*Conformance specifications do not traditionally include process-based scenarios. Implementers are impacted at the business/regulatory process level and benefit from inclusion of this perspective.*
S33	5.4 Data Standards; Data Standards Investment Strategy; Page 18	We suggest that Impact Analyses would better serve projects if they are performed prior to the implementation phase.	*Impact Analyses provide greater benefit when assessments of process and technology change are done on the front end of projects and not as an activity of the implementation phase.*
S34	6.0 Programs; Pre-market Activities; Page 19	We suggest adding a description of the historical differences in requirements between FDA Centers (e.g., guidance documents, unwritten submission requirements).	*This section speaks to the historical differences in the development and use of systems by different FDA Centers.*
S35	6.0 Programs; Pre-market Activities; Page 20	We note that the timeline for RPS indicates very aggressive milestones in 2008. We suggest further clarification or revision of these milestones, as they appear to be contrast with recent discussions at HL7 for developing RPS Release 2.	*RPS Timeline appears inconsistent with current discussions within Health Level 7.*
S36	6.0 Programs; Pre-market Activities; Page 20, RPS	We recommend a broader description of the strategy and timeline for requiring RPS in US submissions and considerations for international submissions.	*Understanding the transition process from the current eCTD format to RPS is important to Sponsors.*

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S37	Section 6.1 Premarket Activities (Page 20)-RPS	The plan should include a timeline for FDA implementation of RPS (and phasing out eCTD), including plans to coordinate ICH requirements into RPS (with the ultimate goal of using RPS to replace eCTD)	*Many industry stakeholders have worked hard to establish eCTD capability. Understanding FDA's plan/timeline for evolving to RPS will be important to stakeholders for their long-term planning. Equally important will be knowing that FDA will support efforts to evolve RPS to accommodate other non-US regional interests and ultimately shape RPS towards becoming a global standard.*
S38	Section 6.1, Page 21:-ESG	Describe the plan and timeline for ESG expansion, including plans for establishing 2-way communications capability.	*This will help to ensure that industry capability to use the ESG aligns with FDA capability accordingly.*
S39	Page 21 (ESG)	Describe plans and target dates for use of the ESG by DDMAC.	*As DDMAC represents a significant percentage of industry submissions to FDA, use of the ESG for DDMAC submissions represents a significant opportunity to increase efficiency and reduce cost.*
S40	On page 21, eCTD Review system	Please provide a timeline for sharing the eCTD validation criteria with sponsors. Also please include plans for communicating compliance statistics with sponsors.	*It is difficult for sponsors to ensure they meet validation criteria without knowing the criteria. Additionally it will be very helpful for sponsors to understand how well we are achieving compliance as an industry.*
S41	On page 21 ICT21	Recommend moving ICT21 to section 5.2 Target Architecture	*This project seems to better align with the Targeted Enterprise Architecture and perhaps should be discussed in that section.*
S42	On page 21,EDR Strategy/Milestone, 3rd bullet	Kindly clarify which Divisions/Centers are included in "Full Implementation – 3rd qtr 2009"	*This will help stakeholders to plan their own strategy for keeping pace with this capability at FDA.*

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S43	*Section 6.1 Premarket Activities (Page 22)- Electronic Listing*	Please clarify whether use of Release 1.0 (if approved by business stakeholders) will be a requirement, or on a voluntary usage basis. Also, please clarify the proposed timeline for SPL Release 4 to become an approved HL7 or ANSI standard, as this cannot occur prior to the end of Q2 at the earliest,	*A Q2 in-production" timeline will be difficult for stakeholders to meet. The requirements for electronic listing information to be submitted via SPL will constitute a significant process change for sponsors, involving new stakeholders with little or no SPL experience and knowledge.*
S44	*Section 6.1 Premarket Activities (Page 22)- Electronic Listing*	Please provide an explanation and/or example of "other electronic means" for making listing data available to the public.	*It is important to understand how FDA will be providing this information to the public, as well to understand how this information may be potentially reused by other (non-FDA) entities.*
S45	*Section 6.1 Premarket Activities (Page 22)- Electronic Listing*	Please include plans for implementation of DFRM (Drug Facility Registration Module), if still valid, particularly in the context of SPL Release 4, which may provide the same information originally intended to be entered manually via DFRM. Conversely if DFRM is no longer planned to be implemented, please include a more detailed proposal of how establishment information will be shared between sponsor and FDA.	*DFRM was not included in the list of current IT projects, yet (if implemented_ could have a significant impact on industry stakeholders. If DFRM is no longer to be implemented, the plan provides no description of how establishment information will be submitted.*
S46	On page 22 , - Electronic Listing, Strategy/Milestones	Please clarify who are the "business stakeholders" who will approve the Electronic Listing Prototype and the rationale for their representation?	*All stakeholders have a vested interest in knowing that FDA is using a representative, well rounded consistency.*
S47	*Section 6.1 Premarket Activities (Pages 23-24)-CDISC – HL7*	Please provide a more detailed description on the HL7 implementation of SDTM and AdaM datasets.	*It is unclear from the IT Plan whether the HL7 messaging implementation will be simply a transport mechanism or "wrapper" around SDTM and ADaM datasets or a new transformation model, of both.*

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S48	*Section 6.1 Premarket Activities (Pages 23-24) CDISC – HL7*	Describe strategy to provide for a consistent view of study tabulation and analysis datasets by FDA and sponsors.	*It is imperative that sponsors and the FDA see the exact same study tabulation and analysis datasets in order to communicate effectively. We are concerned that the introduction of HL7 output files into the submission data flow might reduce this ability.*
S49	*Section 6.1 Premarket Activities (Pages 23-24)- Clinical Data Flow*	Please describe how a link between analysis and tabulation datasets will be maintained with the new clinical data flow scheme.	*Analysis dataset metadata and data are based on a known study tabulation metadata and data structure and content. Therefore, ADaM metadata and data are either created by the sponsor based on the sponsor's SDTM files, or at least harmonized if SDTM and ADaM are generated in parallel. This is an important connection that allows trace-back from the derived analysis datasets to the tabulation data sets. It is unclear whether the proposed clinical data flow scheme (Figure 10; page 23) will break this essential link between tabulation and analysis datasets that is crucial for FDA reviewers and sponsors alike.*
S50	*Section 6.1 Premarket Activities (Pages 23-24) Clinical Data Flow*	Describe how information from ADaM datasets will be stored in Janus Data Warehouse.	*In Figure 10, ADaM datasets are submitted to FDA via HL7 output file and stored in a Janus Analytical data Warehouse. Janus is not currently able to accept or store ADaM datasets. It is unclear from the IT Plan whether the FDA is proposing to modify Janus to be able to store ADaM datasets.*
S51	On page 24, *CDISC – HL7, Strategy/Milestones*	Please Clarify why an ICSR message will be developed in the context of the CDISC Content to Message Project.	*It is not clear why ICSR would be developed under this project, where there already exists an ICSR project under the Joint Initiative by HL7/ISO/CEN.*

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S52	On page 24 - *CDISC – HL7*	Recommend deleting all content in the description of the CDISC-HL7 Project after the first sentence. Recommend moving the first bullet under Milestones to the project description column. Recommend deleting the remaining bullet under Milestones and replace it with the anticipated timeline for requirements gathering, testing of the draft standard and anticipated pilot/implementation timeframes, especially probable overlap with existing formats.	*References to the historical HL7 Exploratory project add no value to this prospective plan.* *Comments about modelling in BRIDG could repeat often in this plan and are better addressed once in the appropriate section describing adherence to SDO development processes when developing standards through an established SDO.* *Relevant timelines for this project have already been publicly communicated and should be included in this plan as they are critical for stakeholder business planning (either for involvement in the dev/testing or for production implementation).*
S53	On page 24- BRIDG Model	Recommend removing BRIDG from the list of projects. A brief acknowledgement of FDA's involvement in building the BRIDG model might be appropriate in the section of the document where FDA describes HL7 as a preferred SDO and commits to following HL7 processes for standards developed in that forum.	*We believe FDA's involvement in building the BRIDG model stems from participation in HL7 RCRIM and RCRIM's requirement that content be modelled in BRIDG. Thus, it is a means to an end and not a specific capability FDA intends to implement. At least, we know of no commitment from FDA to use BRIDG for anything other than HL7 RCRIM project work.*
S54	On page 24- JANUS data warehouse	Recommend the project description be amended to clarify if NCI or FDA intend for other parties to be able to use or be impacted by the capabilities described. If so, then the timelines for engaging or impacting those parties should be included in the milestones.	*Unless one has additional information, it is not apparent how this project will impact other parties and how or when they should plan to be ready.*
S55	6.1 Pre-market activities – Clinical/Preclinical Data Standards	Recommend the strategy/milestones be amended to include effort to test SEND by other Centers/Divisions so that when implemented by CDER, it is also effective for use more broadly across FDA.	*Promotes the use of common standards across Centers/Divisions.*

#	Citation Location Section/Page	Proposed Change	Rationale
S56	6.1 Pre-market activities – Clinical/Preclinical Data Standards	Recommend figure 10 on page 23 be enhanced with shading to indicate which components are envisioned, experimental or complete (proven robust) and when they anticipated to be completed.	*This would be a very effective representation of the current status or anticipated completion of the target environment for management to understand at a glance.*
S57	On page 25- SEND	Recommend deleting content under Current Status that describes activity from 2003-2005 and include a description of activity currently in progress. Recommend the Milestones frame timelines for Phase 2 pilot start/end and probable next steps following the Phase 2 pilot.	*To encourage participation in the current pilot or plans to implement SEND nearer the end of PDUFA IV PhRMA and BIO members request more transparency on FDA's current/prospective plans.*
S58	On page 25- eCRF	Recommend that FDA revise the plan to take the ODM content already developed by CDISC and work through HL7 RCRIM to develop an HL7 exchange message. If not acceptable to the Agency, then clarify the rational for not using an HL7 exchange message for this content when that has been the Agency's stated architectural strategy.	*ODM is not an HL7 exchange message. All other exchange messages discussed have been HL7 messages. It seems inconsistent with FDA's stated architectural decision re:HL7 not to take the content already completed by CDISC and develop it into a semantically interoperable HL7 message. Also, considering the more prevalent adoption of HL7 standards in the healthcare setting, an HL7 clinical research standard for CRFs would likely be more interoperable with other clinicians systems than ODM ever will be.*
S59	On page 25- eCRF	Recommend that Milestones specify the timeframe anticipated for developing, testing and implementing a new, standard electronic format that can replace the PDF-based CRF for CDER and CBER.	*PhRMA and BIO members request additional detail on the timeframe of initiatives to plan to participate in the development and testing or to be ready to comply.*

#	Citation Location Section/Page	Proposed Change	Rationale
S60	Page 25 – eCRF	Recommend most of the content in the Milestones column be moved to the Description column (with the exception of the final statements about the intended pilot activity which should be expanded to include desired timeframes for the pilot activity and potential subsequent steps). Recommend that the language pattern not associate legacy practices (submitting CRFs in paper or PDF format) with new practices (submitting data/metadata/audit trail in computable format). Recommend further justification for including audit trail data be included as it will be particularly difficult to render meaningful audit trail data in the format used to submit data to FDA that are not necessarily the formats used to conduct clinical trials. Recommend expanding on the interactions between the eCRF project and the CDISC-HL7 project.	*It is confusing to say that CRFs will be submitted in ODM format. It would be clearer to state that if the appropriate data, metadata and audit trail data from clinical trials are submitted in a computable, standardized format then there is no need to submit CRFs. FDA reviewers will be able to render appropriate views from the datasets to conduct their review.*
S61	On Page 26 - ADaM	This project description appears to be a component of the broader CDISC-HL7 initiative. Recommend it be framed in the context of that initiative or more clearly differentiate the two efforts. In either case, further insight into next steps/milestones is needed.	*Lack of milestones/timeframes may hinder stakeholders in planning resources to participate in next steps or plan internal process changes to better align with FDA changes/expectations.*
S62	6.2 Post-Market Activities	While not limited to post-marketing surveillance or Sentinel specifically, it is obvious that public private partnerships will be key to advancing some Agency goals. Can this plan frame the Agency's expectations and expected next steps for such processes? They are envisioned by some in industry as key to advancing multiple PDUFA goals or represent the most valuable possible solution for all affected parties – specifically for driving faster adoption of change (new processes/systems/standards) and doing so economically.	

#	Citation Location Section/Page	Proposed Change	Rationale
S63	7.1 PDUFA IV Metrics	Recommend that FDA augment the metrics reporting to include a reasonable measure of the Agency's internal progress for staff, processes and systems to be ready to handle new electronic submission formats. Also, recommend both pre-market and post-market submissions be included in the measure tracking numbers of electronic submissions. Recommend that FDA use their website to report metrics and indicate how often they plan to be updated.	*The cited metrics will indicate the rate of adoption of e-submissions by sponsors. The Agency can promote faster adoption by more clearly conveying when the internal FDA transition from experimentation and pilot activity transcends to full readiness, support and training.*
S64	7.1 PDUFA IV Metrics –	Recommend that the statement describing reporting of failed submissions be amended to reflect "anonymously reported".	*This change should assure that sponsors value the feedback on errors FDA observes rather than fear it.*
S65	7.2 PDUFA Information Management/IT Goals and Objectives -- Within Drug Safety Goals (Section VIII), bullet A.	We look forward to the time when FDA's analysis and planning have progressed further and additional insight into the strategy and milestones expected to deliver on the drug safety goals VIII.A.1.C and VIII.A.1.E can be added to this plan.	
S66	Section 7.2 A.1.f PDUFA IM/IT goals objectives (Page 30)	We recommend the strategy/milestones developed to fulfill goal VIII.A.1.f include the business process changes associated with eliminating the supplemental formats (Word/PDF) currently required to effectively support label negotiations. We also recommend the strategy explicitly indicate utilizing the diversely represented SPL Working Group to evaluate and refine the proposed business process changes to assure they offer value to all parties while still meeting all of FDA's requirements.	*This specific milestone of eliminating the supplemental formats conveys to sponsors that this change represents a valuable transition and not merely an added burden.* *In order to meet FDA's objectives with stakeholders, we recommend opening early discussions on desired process change and supporting tools.*
S67	Section 7.3 Page 33 Table	Recommend the table be amended to show that the Electronic Labelling Review System and Electronic Listing is linked to goal A.1.f. Also recommend the ICSR is linked to goal A.1.g.	

#	Citation Location Section/Page	Proposed Change	Rationale
S68	Section 7.4, Page 35:	We are interested to understand more about the remit of the SC/CS BRB and whether their priorities will likely impact business processes directly affecting Sponsors.	
S69	Page 35, Summary Schedule	We applaud the attempt to summarize graphically the progression of projects. However, not all projects are listed nor is there a consistent use of milestones. We suggest that all projects be listed. This likely cannot be done effectively with a single timeline so subgrouping related initiatives might be an effective way to communicate this information. Recommend that the DARRTS acronym be explained elsewhere in the IT Plan as it is listed in the summary schedule but is not described anywhere else in this draft plan.	