PDA Global Headquarters
Bethesda Towers,
Suite 600
4350 East West Highway
Bethesda, MD 20814 USA
TEL: +1 (301) 656-5900
FAX: +1 (301) 986-0296

PDA Europe gGmbH
Am Borsigturm 60
13507 Berlin
Germany

4 March 2024

Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Reference: Docket No. FDA-2023-N-5653 for “FDA Draft Report and Plan on the Best Practices for Guidance, Request for Comments

Dear Madam or Sir,

PDA appreciates the opportunity to provide feedback to the FDA as the agency develops and establishes best practices for the efficient prioritization, development, issuance, and use of guidance documents. In our attached comments, PDA offers specific comments and feedback that we believe will be helpful in the further development of this program.

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, device manufacturing, and quality. Our comments have been prepared by a committee of PDA members with expertise in quality systems, quality management, quality culture, and quality metrics on behalf of PDA’s Regulatory Affairs and Quality Advisory Board.

If you have any questions, please do not hesitate to contact me via email at wright@pda.org.

Sincerely,

Glenn Wright
President and CEO

cc. Josh Eaton, PDA; Carrie Horton, PDA

PDA Member response to: FDA Draft Report and Plan on the Best Practices for Guidance, Request for Comments (Docket No. 2023 N-5653)

Responses to "FDA Draft Report and Plan on the Best Practices for Guidance, Request for Comments."

FDA Summary: This draft report responds to the Consolidated Appropriations Act of 2023, which directs the FDA to issue a report identifying best practices for the efficient prioritization, development, issuance, and use of guidance documents and a plan for implementation of such best practices. It also directs the FDA to publish a draft report and plan no later than 1 year after enactment of the Consolidated Appropriations Act and to consult with stakeholders in developing the report and implementation plan.

---

1) FDA regularly considers its processes for the development, clearance, and issuance of guidance documents, with a goal of streamlining these processes and making the best use of Agency resources. The draft report summarizes FDA's current best practices for the initiation, prioritization, development, review, clearance, and issuance of guidance documents that FDA has implemented in response to the 2011 report and other continual improvement efforts not described in the 2011 report. The draft report also proposes additional initiatives that FDA could consider to further improve its processes for the issuance of guidance documents. FDA solicits input on whether there are additional or revised practices, consistent with our statutory and regulatory framework, for the Agency to consider.

   PDA Comment: The current "Draft Report and Plan on Best Practices for Guidance" does not provide an overview and metrics regarding the initiatives in the 2011 GGP report. PDA suggests that the FDA include a section in this draft report with this information or publish this data on their website.

---

2) Level 1 guidance documents are guidance documents that include initial interpretations of a statute or regulation, changes in interpretation or policy that are of more than a minor nature, complex scientific issues, or highly controversial issues. Level 2 guidance documents describe existing practices or minor changes in interpretation or policy. Pursuant to FDA's statutory and regulatory requirements, while the public may comment on a guidance document at any time, public participation is directly solicited prior to the implementation of Level 1 guidance documents unless we determine that such prior public participation is not feasible or appropriate. In the preamble to the final GGP rule, we noted that we anticipated that this exception would generally be applicable when there are public health reasons for the immediate implementation of the guidance document; there is a statutory requirement, executive order, or court order that requires immediate implementation; or the guidance document presents a less burdensome policy that is consistent with public health.[1] Issuing more guidance documents either as Level 1 guidance documents for immediate implementation, as FDA did during the COVID–19 PHE, or as Level 2 guidance documents would allow FDA to allocate its limited resources more efficiently, which would help FDA

keep pace with rapid scientific developments and better serve the public health. In addition, FDA's GGP regulation provides that the public may comment on any guidance at any time, including Level 1 guidance documents for immediate implementation and Level 2 guidance documents, and FDA may delay implementation of any guidance document.

a. In light of the above, we seek input on whether there are any additional circumstances, categories of guidance documents, or topics for guidance for which it may be appropriate and consistent with the FD&C Act and FDA's GGP regulation for FDA to consider issuance as a Level 1 guidance document for immediate implementation without prior public comment.

PDA Comment:

PDA suggests that only guidance documents that imminently and critically affect patient safety or have substantial life-threatening implications for public health are designated as Level 1 guidance with immediate implementation. This approach should be reserved for genuine emergencies. Prompt distribution of information—whether in draft or final form—is essential when stakeholders require urgent access to crucial data.

PDA suggests that if a Level 1 guidance is designated as “for immediate release”, the FDA either forecasts this with their guidance agenda or publishes their intention in advance on the FDA website to reflect this designation.

FDA should not use the “for immediate release” process to circumvent OMB's good document management practices. Guidance that requires significant new or additional effort from the industry should not be considered for Level 1 “Immediate Release” guidance but should be evaluated through formal processes to ensure the reporting burden does not exceed legally allowable limits. Examples are additional reporting requirements or significant changes in how information should be formatted or prepared for submission.

In addition, PDA recommends that the FDA formalize a process to address, communicate, and eliminate the status of long-standing guidance documents that are in the “draft” stage, some of which have been referenced during FDA inspections. We also suggest standardizing this process across the FDA Centers, especially since numerous guidance documents are issued from multiple Centers.

b. We also seek comment on whether there are additional categories or types of guidance documents that FDA should consider issuing as Level 2 guidance documents to streamline the guidance process and allow the Agency to better leverage its resources for the timely development of more guidance documents.

PDA Comment: PDA agrees that for adjustments to existing guidance documents that have a minor impact, the Level 2 guidance document process should be utilized to alleviate the operational challenges faced by the Agency. Nonetheless, there may be instances when a minor modification issued via a Level 2 guidance – such as a small textual edit, image update, or clarification—may carry the risk of provoking controversy, introducing ambiguity, or leading to significant repercussions. PDA suggests FDA consider an impact assessment process to avoid unforeseen ambiguity or overly burdensome or unintended consequences

as a result of issuing the guidance as Level 2. Recognizing stakeholders can still comment after the publication of Level 2 guidance, PDA suggests FDA establish an internal process, such as a 60-day docket review, to understand and respond to signals from stakeholders indicating the impact may be greater than originally intended. This process should allow for FDA to use enforcement discretion for any Level 2 guidance documents where industry has raised concerns which would be indicated with a revision or comment by the FDA to the docket. Additionally, FDA should fully publicize Level 2 guidance documents when released to ensure industry awareness.

---

3) FDA requests comment on any novel guidance document formats that would be of particular utility, such as use of templates to accompany a guidance document, Q&A formats, flowcharts, etc., that are used in FDA guidance documents or that were used in guidance documents issued in response to the COVID–19 PHE.

PDA Comment:

PDA has identified a number of tools and suggestions to support the general understanding and implementation of FDA guidance. Drawing upon standard document control practices, PDA suggests the following:

- Adopting standardized templates, where appropriate, to facilitate a uniform reading experience across various documents by presenting information in a consistent manner.
- Including relevant examples to clarify key concepts and interpretations within FDA guidance.
- Including a summary of changes between the new and old documents to capture the change history of the guidance. FDA could utilize the line numbers from the draft guidance to make clear where changes between the draft and final guidance have occurred. Additionally, providing red-lined versions so that stakeholders can see the changes between the old and new documents can facilitate industry review and assessment of guidances.
- Implementing a version control system for each document to facilitate cross-referencing among related guidance documents and documents that are suspended/withdrawn, thereby improving the coherence and traceability of updates and revisions.
- Developing a Traceability Matrix for each guidance to eliminate redundancies and inconsistencies between guidances, as well as an applicability matrix for principles and concepts contained in Level 1 guidances that might impact stakeholders outside of the direct oversight of the issuing center such as data integrity principles.
- Incorporating a dedicated section within each document that cross-references relevant guidance documents, statutes, or regulations that are pertinent to the content. The inclusion of hyperlinks to these references would further enhance the utility of the document by allowing readers to swiftly access related information.

- Developing a matrix or providing a statement of topology to relevant third-party documents such as those coming from ICH or PIC/S, which are aligned with the concepts and principles reflected in the FDA guidance.
- Increasing the use of the Q&A format for guidances, especially in the areas of personalized medicine, Cell & Gene Therapy, Biologics, and other highly specialized areas.

---

4) FDA makes robust use of guidance documents to assist industry in making regulatory submissions. As described in the report, examples of such guidances include device-specific guidance documents, disease or indication specific guidance documents that include recommendations on developing drugs intended to treat a specific disease or for a specific indication to support submissions of New Drug Applications (NDAs) or Supplemental NDAs, product specific guidances for generic drug development to support submission of Abbreviated New Drug Applications (ANDAs), Data Technical Conformance Guides to accompany guidance documents, and guidance documents that provide assistance with registration and listing requirements. FDA requests comments on the utility of guidances in streamlining regulatory submissions and whether there are additional categories or types of guidance that would be helpful to streamline processes for regulatory submissions to the Agency.

PDA Comment: PDA believes it would be helpful if the FDA considers harmonizing requirements across the centers and potentially consolidating guidance for similar product types, for example, adding other relevant CDRH or CDER (combination product) guidance to the device-specific guidance.

---

5) Currently, FDA's GGP regulation (§ 10.115) provides that interested persons can suggest areas for guidance document development and that such suggestions should address why a guidance document is necessary. (§ 10.115(f)(2)). In addition, proposed guidance documents can be submitted to a specified docket for FDA consideration. (§ 10.115(f)(3)). FDA requests comments on whether the currently available mechanisms for submitting suggested areas for guidance development and proposed guidance documents are useful and sufficient or whether additional mechanisms, for example, a Center-specific or Office-specific mailbox for such suggestions would ease the process for such submissions.

PDA Comment: PDA recognizes there is an open docket process for suggesting areas for guidance document development but believes there is a lack of awareness of this process. To improve awareness, FDA may consider renaming the actual docket for clarity. Additionally, when FDA publishes a guidance agenda, PDA suggests that FDA provide information on the availability of this process allowing stakeholders to suggest areas for guidance document development via the open docket.

6) FDA Centers publish guidance agendas on their web pages to give interested parties and the public notice of the areas in which FDA is considering upcoming guidance**.** We request comments on the utility of these guidance agendas and what, if any, modifications to these agendas would be helpful for the Agency to consider.

PDA Comment: The publication of guidance agendas on the FDA website is useful for stakeholders to understand the current focus of the FDA and potential documents to expect. It would be of greater utility if the FDA would make regular and frequent updates to the agenda to include where the guidance is in the GGP lifecycle, when documents are withdrawn/added, or if designations (such as immediate release) are assigned. It would be beneficial for the industry if, within these guidance agendas, the FDA identified those guidances that are required to be issued by law/statute (ex: FDORA, PDUFA), the associated section/page reference, and the target issue date. This would better prepare stakeholders for commenting and/or implementation activities.

The FDA may also consider providing agenda updates through subscription-based email notifications, similar to email notifications of the Weekly Enforcement Reports.