Food and Drug Administration

Report and Plan on Best Practices for Guidance

2024

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I. Executive Summary

Clear, concise, and timely communication through guidance documents is essential to the public health mission of the U.S. Food and Drug Administration (FDA, the Agency, or we). Since 2011, when FDA issued its "Food and Drug Administration Report on Good Guidance Practices: Improving Efficiency and Transparency" ("2011 GGP Report"),[1] FDA has made significant strides to implement the recommendations in the 2011 GGP Report and to modernize and enhance our best practices for the efficient initiation, prioritization, development, review, clearance, and issuance of our guidance documents. As a result of these and other Agency improvement efforts, FDA has significantly increased the number of guidance documents it publishes annually.[2] During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency (PHE), determined under section 319 of the Public Health Services Act, FDA considered innovative approaches to expedite the development of guidance documents for a broad audience and streamline the processes for regulatory submissions. The facts and circumstances surrounding COVID-19 and the COVID-19 PHE enabled FDA to more rapidly disseminate Agency recommendations and policies related to COVID-19 to industry and other interested parties, FDA staff, and the public, including patients and consumers. Specifically, the Agency relied upon waivers of Paperwork Reduction Act (PRA) requirements by the Secretary of the Department of Health and Human Services for certain voluntary collections of information, FDA's statutory authority to issue guidance documents "for immediate implementation" when prior public participation is not feasible or appropriate, and expedited external review of guidance documents, which resulted in more rapid issuance of COVID-19-related guidance documents. These tools were critical to the significant work FDA accomplished during the COVID-19 pandemic. Now that the COVID-19 PHE is over, FDA has considered the lessons learned from that experience and reassessed our current best practices for guidance to explore additional areas for improvement and efficiency consistent with our statutory and regulatory framework.

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[1] FDA, "Food and Drug Administration Report on Good Guidance Practices: Improving Efficiency and Transparency", available at https://www.fda.gov/media/82644/download.

[2] The 2011 GGP report noted that FDA published 103 Level 1 guidance documents in 2010. Between 2005 and 2010, FDA annually published between 89 and 121 (average 101 per year) guidance documents with an accompanying Notice of Availability (NOA). However, FDA annually published between 112 and 231 (average 173 per year) guidance documents with an accompanying NOA between 2011 and 2019. In Fiscal Year (FY) 2022, FDA published 187 guidance documents with an accompanying NOA, and in FY 2023, FDA issued more than 190 guidance documents with an accompanying NOA. This is actually an underestimate of the annual number of guidance documents that FDA publishes, as it is based on a count of guidance documents issued with an accompanying NOA. FDA sometimes "bundles" multiple related guidance documents under a single NOA, as appropriate and also issues most "Level 2" guidance documents (described in section III.A., below) without an accompanying NOA, in accordance with our GGP regulation (21 CFR 10.115). FDA also notes additional limitations of a comparison of the total number of guidance documents issued year-to-year, including that these totals cannot account for factors such as the complexity of issues addressed in a guidance, the length of the document, and competing Agency priorities.

As part of FDA's reassessment of our best practices for guidance and in accordance with section 2505(a) of the Consolidated Appropriations Act, 2023, FDA published a "Draft Report and Plan on Best Practices for Guidance" (Draft Report and Plan) on our website on December 28, 2023.[3] Pursuant to section 2505(c) of the Consolidated Appropriations Act, in a *Federal Register* Notice announcing the availability of the Draft Report and Plan, FDA solicited public comment from a broad range of interested parties.[4] The 60-day public comment period closed on March 4, 2024. FDA received over 30 sets of comments. After carefully considering all submitted feedback, FDA is now issuing this Report and Plan on Best Practices for Guidance (Report and Plan).

[3] FDA, "Draft Report and Plan on Best Practices for Guidance", available at https://www.fda.gov/media/175121/download?attachment. As explained in the Draft Report and Plan, FDA will issue a separate Report and Plan in accordance with Section 2505(b) of the Consolidated Appropriations Act, 2023.

[4] 89 FR 380 (Jan. 3, 2024).

II. Table of Acronyms

Acronym	What it Means
CBER	FDA's Center for Biologics Evaluation and Research
CDER	FDA's Center for Drug Evaluation and Research
CDRH	FDA's Center for Devices and Radiological Health
CFR	Code of Federal Regulations
COVID-19	Coronavirus Disease 2019
CTP	FDA's Center for Tobacco Products
CVM	FDA's Center for Veterinary Medicine
FDA	Food and Drug Administration
FD&C Act	Federal Food, Drug, and Cosmetic Act
FR	*Federal Register*
FY	Fiscal Year
GGP	Good Guidance Practices
HFP	Human Foods Program
ICH	International Council for Harmonisation
IND	Investigational New Drug Application
NOA	Notice of Availability
OII	Office of Inspections and Investigations
OCP	Office of Combination Products
OCE	Oncology Center of Excellence
PDF	Portable Document Format
PHE	Public Health Emergency
PRA	Paperwork Reduction Act
U.S.C.	United States Code

III. Background

A. Statutory and Regulatory Requirements for FDA Guidance

Guidance documents are documents prepared for FDA staff, regulated industry, applicants/sponsors, and the public that describe the Agency's interpretation of, or policy on, a regulatory issue.[5] The development and issuance of guidance documents is governed by FDA's Good Guidance Practices (GGP) regulation,[6] which implements section 701(h) of the Federal Food, Drug, and Cosmetic Act (FD&C Act).[7] The GGP Regulation establishes two types of guidance documents (Level 1 and Level 2) and describes the procedures for issuing both types of guidance documents. Specifically, pursuant to the GGP Regulation, Level 1 guidances include those that: (1) set forth initial interpretations of statutory and regulatory requirements, (2) set forth changes in interpretation or policy that are of more than a minor nature, (3) include complex scientific issues, or (4) cover highly controversial issues.[8] In contrast, Level 2 guidances "set forth existing practices or minor changes in interpretation or policy."[9] Typically, FDA solicits input on Level 1 guidances prior to implementation, and in preparing the final guidances, we review and consider all comments we receive.[10] Both draft and final Level 1 guidance documents are posted on FDA's website, and Notices of Availability (NOAs) announcing these guidances are published in the *Federal Register*. Consistent with our statutory and regulatory requirements, FDA does not solicit public input prior to the issuance of: (1) final Level 1 guidances for which "prior public participation is not feasible or appropriate,"[11] or (2) final Level 2 guidances.[12] However, FDA posts all guidance documents, including Level 1 guidance documents "for immediate implementation" and Level 2 guidance documents, on our

[5] See 21 CFR 10.115(b)(1).

[6] 21 CFR 10.115.

[7] 21 U.S.C. 371(h).

[8] 21 CFR 10.115(c)(1).

[9] 21 CFR 10.115(c)(2).

[10] 21 CFR 10.115(g)(1)(ii)(C) and (g)(1)(iv)(A).

[11] 21 U.S.C. 371(h)(1)(C); 21 CFR 10.115(g)(2).

[12] 21 CFR 10.115(g)(4).

website[13] and interested parties may comment on them at any time after they have been issued. FDA periodically reviews all comments and revises its guidance documents as appropriate.[14]

B. Value of FDA Guidance Documents

FDA guidance documents greatly benefit the Agency, regulated industry, and the public as a whole by providing consistency, transparency, and valuable insight into approaches that may assist industry and other interested parties in complying with applicable statutes and regulations, ensuring consumer and patient safety, and developing new and innovative products to improve public health. Specifically, FDA uses guidance documents to assist regulated industry, FDA staff, and the public in understanding the Agency's current thinking on policy, scientific, medical, and regulatory issues, such as: the design, manufacturing, and testing of regulated products; scientific issues; content and evaluation of applications for product approvals; and inspection and enforcement policies. While most regulations are legally enforceable and are thus binding, a guidance document typically does not establish any rights for any person and generally is not binding on FDA or the public.[15] Consequently, pursuant to our GGP Regulation and as stated on all non-binding FDA guidance documents, an alternative approach may be used as long as such approach satisfies the requirements of the applicable statutes and regulations.[16] Additionally, while regulations often take longer to develop than guidances and thus are less frequently amended, guidance documents are intended to be developed on a faster timeframe and, ideally, more quickly revised to keep pace with rapidly evolving science and technology and to reflect current scientific, medical, and public health recommendations. Issuing guidance documents makes FDA's recommendations accessible and transparent, facilitates consistency, and prevents unnecessary expense and delay in product development. Guidance documents, therefore, may be especially important to newer or smaller entities that may have less experience interacting with FDA and fewer resources to hire outside counsel or consultants. To meet our mission, FDA continues to seek mechanisms to optimize the quality and efficiency of its guidance processes.

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[13] "Search for FDA Guidance Documents", available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

[14] 21 CFR 10.115(g)(5).

[15] 21 CFR 10.115(d). In some instances, for example section 745A(a) of the FD&C Act, 21 U.S.C. 379k-1, Congress granted FDA the authority to implement the statutory requirements in guidance; however, the vast majority of FDA guidance documents are not binding.

[16] 21 CFR 10.115(d).

C. FDA's Draft Report and Plan on Best Practices for Guidance and Overview of Public Comments

In accordance with section 2505(a) of the Consolidated Appropriations Act, 2023, FDA published a Draft Report and Plan identifying FDA's current best practices for the efficient prioritization, development, review, clearance, issuance, and use of guidance documents. Additionally, the Draft Report and Plan summarized FDA's implementation of certain best practices set forth in its 2011 GGP Report and described FDA's proposals to further improve efficient development, issuance, and use of guidance and to continue to use guidance to streamline processes for regulatory submissions.

In the NOA for the Draft Report and Plan, FDA solicited feedback on the Draft Report and Plan from a broad range of commenters, including regulated industry; researchers; academic organizations; pharmaceutical, biotechnology, and medical device developers; clinical research organizations; clinical laboratories; healthcare providers; food manufacturers; and consumer and patient groups. In the NOA, we specifically requested input on the following areas:

- Suggestions for additional or revised best practices, consistent with our statutory and regulatory framework;
- The circumstances, categories of guidance documents, or topics for guidance for which it may be appropriate and consistent with the FD&C Act and the GGP Regulation for FDA to consider issuance as a Level 1 guidance document "for immediate implementation" without prior public comment or for which FDA should consider issuance as Level 2 guidance documents;
- Identification of any specific innovative or novel guidance document formats that would be of particular utility;
- The utility of guidances in streamlining regulatory submissions and any additional categories or types of guidance that would be helpful to streamline processes for regulatory submissions to the Agency;
- Whether the currently available mechanisms for submitting suggested areas for guidance development and proposed guidance documents are useful and sufficient or whether additional mechanisms would ease the process for such submissions; and
- The utility of FDA's guidance agendas and what, if any, modifications to these agendas would be helpful for the Agency to consider.[17]

FDA received over 30 sets of comments on the Draft Report and Plan from interested parties, including industry and trade groups; healthcare providers and entities; patient and

[17] 89 FR 380 (Jan. 3, 2024).

consumer advocacy groups; researchers, scientific, and academic experts; and private citizens. The majority of comments focused on the following topics: (1) general best practices for guidance documents, (2) suggestions for improving FDA's current "Search for FDA Guidance Documents" web page, (3) FDA's guidance agendas, and (4) FDA's proposal to publish additional guidance documents as Level 1 "for immediate implementation" and Level 2 guidance, consistent with applicable statutes and regulations. FDA also received comments encouraging FDA's continued use of guidance to streamline the process for regulatory submissions and providing support for further Agency use of novel and innovative guidance formats. A few comments proposed specific topic areas for consideration of future guidance development. FDA convened a cross-Agency workgroup to carefully review, discuss, and consider all comments received as it prepared this Report and Plan.

IV. FDA's Report and Plan on Best Practices for Guidance

Pursuant to section 2505 of the Consolidated Appropriations Act, 2023, FDA has developed this Report and Plan, which responds to the comments received on our Draft Report and Plan and describes FDA's plans to: (A) develop and implement new and revised best practices for the guidance document lifecycle, including improving the consistency of our guidance templates and formats, improving the guidance comment process, assessing comments and finalizing guidance, and improving access to withdrawn guidance documents; (B) enhance FDA guidance communication and outreach, including improving the functionality and utility of the FDA Guidance web page, building more consistency into FDA guidance agendas, and creating more transparent and accessible mechanisms for public input on guidance topics and suggestions; (C) update FDA's GGP Regulation to better reflect current technology and provide more transparency, access, and public engagement into FDA's guidance agendas and procedures for suggesting topics for future guidance development; and (D) promote continued use of guidance to augment, announce, and supplement FDA efforts to help streamline the process for regulatory submissions, as appropriate.[18]

A. FDA's Best Practices for the Guidance Document Lifecycle (Drafting, Commenting, Finalizing, and Withdrawing Guidance Documents)

1. Best Practices for Drafting FDA Guidance Documents (Format and Templates for FDA Guidance Documents)

As described in the Draft Report and Plan, FDA currently uses templates for development of guidance documents and their accompanying NOAs, which provide for the organization of guidance content and presentation of information in a logical sequence and ensure inclusion of

[18] Full implementation of this plan may be contingent on factors outside of FDA's control.

standard elements and statements and information required by FDA's GGP Regulation and relevant PRA mandates. FDA received multiple comments requesting that FDA consider further standardizing its guidance templates to provide a more consistent visual format across Centers and Offices for FDA guidance documents. FDA notes that our Centers and Offices issue guidance documents addressing a broad range of topics and intended for a variety of audiences. As such, a single template for all FDA guidance documents would not be appropriate. However, FDA agrees that having more consistency in the format of our guidance documents is a best practice for drafting guidance documents. FDA intends to review the templates currently used to determine whether and how existing templates might be revised to provide some additional consistency in the visual format of our guidance documents across FDA Centers and Offices.

Commenters on the Draft Report and Plan suggested continued, or in some cases expanded, use of templates, Q&A guidance, and bulleted guidance, with some commenters noting that such formats are more accessible to the lay public and easier to revise. FDA also received multiple comments requesting that FDA consider additional use of visuals (e.g., flowcharts), real-life examples and hypotheticals to clarify key concepts, information to clarify roles and responsibilities, references with links to applicable laws and other relevant guidance documents, and glossaries of technical terms. FDA agrees that use of such features in appropriate circumstances is a best practice to improve the readability and utility of guidance documents; FDA currently uses many of these suggested tools and intends to continue to seek opportunities for their use, as appropriate for the intended audience and subject matter of the guidance. FDA intends to also continue to provide citations to relevant statutes, regulations, and related guidance in its guidance documents. With regard to providing references with links to applicable laws and other relevant guidance documents, FDA notes many of our Centers and Offices already provide these resources on their web pages. As FDA undertakes a review of its guidance templates and internal procedures, FDA intends to incorporate these suggestions to encourage use by each Center or Office if appropriate to the particular guidance being developed.

Some commenters also suggested that FDA strive to reduce inconsistencies and redundancies in FDA guidance documents across its Centers and Offices and to increase harmonization with international standards to the extent possible. With regard to ensuring consistency across FDA Centers and Offices to reduce inconsistencies and redundancies, guidance documents that address issues relevant to multiple FDA Centers or Offices are commonly jointly drafted and cleared by all affected FDA Centers and Offices. Further, all Level 1 and certain Level 2 guidance documents are reviewed and cleared by the policy leadership of the issuing Center and FDA's Office of Policy. An example of this cross-Center coordination is described in the paper entitled, "Artificial Intelligence & Medical Products: How CBER, CDER,

CDRH, and OCP Are Working Together,"[19] which explains how these FDA Centers and Offices are actively working together on guidance regarding the use of artificial intelligence in medical product development and in medical products to help ensure consistency across FDA Centers and Offices. FDA's Centers and Offices also have procedures in place for collaboration with its international counterparts on certain topics and, as feasible and appropriate, consider harmonization with international standards in drafting FDA guidance documents. For example, in 2021, FDA began an ongoing collaboration with Health Canada and the United Kingdom's Medicines and Healthcare products Regulatory Agency. This international collaboration resulted in the joint identification of 10 guiding principles for Good Machine Learning Practice, which supports the development of safe, effective, and high-quality artificial intelligence/machine learning technologies that can learn from real-world use and, in some cases, improve device performance.[20] In June 2024, this international collaboration built upon its Good Machine Learning Practice principles by adding guiding principles for transparency for machine learning-enabled medical devices.[21] Additionally, FDA participates in international standards development and considers international standards, as appropriate, when developing guidance. For example, in collaboration with the International Council for Harmonisation (ICH), in June 2023, FDA published a draft guidance titled, "E6(R3) Good Clinical Practice (GCP),"[22] which, when finalized, will revise a 2018 guidance[23] to "provide a unified standard to facilitate the mutual acceptance of clinical trial data for ICH member countries and regions" and to provide clarity on FDA's expectations around clinical trials in order to help encourage more innovative and efficient trial design.[24] FDA has published over 140 ICH guidance documents. Collaboration within FDA and with its international counterparts is already an ongoing best practice.

2. Use of Communications to Accompany Guidance

[19] FDA, Artificial Intelligence & Medical Products: How CBER, CDER, CDRH, and OCP are Working Together (Mar. 2024), available at https://www.fda.gov/media/177030/download.

[20] Good Machine Learning Practice for Medical Device Development: Guiding Principles, available at https://www.fda.gov/medical-devices/software-medical-device-samd/good-machine-learning-practice-medical-device-development-guiding-principles.

[21] See www.fda.gov/medical-devices/medical-devices-news-and-events/cdrh-issues-guiding-principles-transparency-machine-learning-enabled-medical-devices.

[22] E6(R3) Good Clinical Practice, available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/e6r3-good-clinical-practice-gcp.

[23] E6(R2) Good Clinical Practice: Integrated Addendum to ICH E6(R1), available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/e6r2-good-clinical-practice-integrated-addendum-ich-e6r1.

[24] E6(R3) Good Clinical Practice (GCP) at 1.

Comments on the Draft Report and Plan supported continued use of town hall meetings with questions and answers and publicly available transcripts. In response to these comments, FDA intends to continue to consider, as appropriate to the topic of the guidance document and as resources permit, when a webinar, town hall, or other public meeting or communication should accompany a guidance document. For example, Centers and Offices might consider whether a webinar or town hall meeting would be appropriate when the topic of the guidance is especially complex or the science is evolving or in circumstances where more data or input on the particular draft guidance or guidance topic would be helpful. Each Center and Office will continue to consider whether to make transcripts available depending upon the nature of the meeting and as resources permit.

3. Best Practices for the Comment Process and Finalization of Guidance Documents

FDA received multiple comments regarding the comment process for draft guidances and the accessibility of public comments. Specifically, comments suggested that FDA improve the process for commenting on guidance documents by including line numbers on all draft guidance documents and providing tips for commenting on guidance documents. Some comments also suggested easier access to public comments on a particular guidance, including provision of a folder or "zip file" of comments received. Comments further requested additional transparency into changes from draft to final guidances, with a variety of suggested approaches, including that FDA provide a detailed comment summary and response, a line-by-line summary of changes made, a chart of changes in the NOA for the final guidance, and an explanation as to why FDA declined to make certain changes. Some comments also sought greater transparency regarding revisions to guidances, access to prior versions of guidance documents, and improved timely finalization of draft guidance documents. Finally, a few comments requested that FDA consider providing for longer comment periods for some or all guidance documents or tailoring the comment periods to the length and complexity of the guidance document.

With regard to the suggestions to include line numbers on all draft guidance documents and provide tips for commenting on guidance documents, FDA agrees that facilitating the process for public comment on guidance documents by using line numbers and providing tips for commenting is a best practice. Many FDA draft guidance documents currently contain line numbers; going forward, FDA will strive to ensure that draft guidance documents generally include line numbers, to the extent feasible. FDA also agrees that it is a best practice to provide tips for commenting and intends to develop and make such tips available on FDA's website along with comment tables. In addition to facilitating the process for public comments, these resources may streamline the Agency's review of comments and may help support timely finalization of guidance documents.

FDA agrees that providing public access to comments on guidance documents is a best practice. Comments received on guidance documents that are not marked as confidential when

submitted to the Agency are included in the docket for that guidance document, which is directly accessible via the "Search for FDA Guidance Documents" web page and regulations.gov.[25] FDA considered the suggestion that we further compile comments in a zip file or other folder; however, because the public may comment on any guidance at any time, FDA concluded that a zip file or folder would not necessarily be comprehensive and, therefore, the docket is the appropriate location for the public to reliably access comments.

With regard to providing additional transparency of changes from draft to final guidance documents, FDA carefully balanced the recommendations for a more detailed comment summary and response with the overall purpose and nature of FDA guidance documents. FDA guidance documents and the process for guidance issuance are distinguishable from regulations in multiple key respects, including guidances' non-binding nature, the fact that the process for issuing guidance is under section 701(h) of the FD&C Act, as opposed to the requirements for rulemaking in the Administrative Procedure Act,[26] and the benefits of having guidance keep pace with evolving scientific, technological, and medical advancements and provide the Agency's current recommendations to interested parties in a timely fashion. As a result, FDA issues significantly more guidance documents than rules. Providing detailed comment summaries and responses for guidance documents akin to rulemaking, including the rationale for every comment that was rejected, would require more resources and could slow the finalization of FDA guidance and thus delay issuance of important information. Although FDA declines to provide detailed comment responses for guidance documents of the degree we provide for rulemaking, FDA agrees that it is a best practice to provide a brief general description of changes made to a guidance in response to comments. Therefore, FDA generally intends to briefly describe any overarching themes in comments received and any noteworthy changes to the final guidance made related to those themes in the NOA for the final guidance. In addition, FDA intends to update its guidance templates to include a summary table providing a brief chronological history of revisions to that guidance.

With regard to access to earlier versions of guidance documents, prior versions of a guidance generally remain available in the docket for that guidance document. The docket can be accessed from the "Search for FDA Guidance Documents" web page and regulations.gov so that interested parties can access the draft guidance in the docket even after the final guidance has published and posted on the "Search for FDA Guidance Documents" web page.

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[25] Information on FDA's policy regarding public availability of comments is available at https://www.fda.gov/regulatory-information/dockets-management/posting-comments#:~:text=The%20commenter%20is%20solely%20responsible,number%2C%20or%20confidential%20business%20information%2C.

[26] 21 U.S.C. 371(h).

FDA agrees that timely finalization of guidance is a best practice. As described in FDA's Draft Report and Plan, since 2011, FDA Centers and Offices have implemented strategies to support the finalization of draft guidance documents. As discussed in the Draft Report and Plan, FDA continues to make progress in finalizing guidance and has finalized a greater number of its guidance documents in recent years.[27] However, recognizing the number of guidance documents issued each year as well as the varied other demands on FDA's finite resources, FDA believes that each Center and Office is best equipped to determine how to allocate its resources with respect to prioritizing finalization of a particular draft guidance document versus prioritizing other critical work (e.g., preparing new draft guidance to address novel technologies and other issues for which FDA guidance is lacking; addressing urgent public health issues; and facilitating review of medical product applications that are subject to user fee performance goals and which may make new treatments available to patients). As discussed above, FDA also intends to facilitate the process for commenting on guidance and plans to amend its internal procedures to encourage FDA Centers and Offices to consider whether use of a shorter Q&A and/or bulleted guidance document format is appropriate, which may help FDA finalize guidance documents in a more efficient manner.

In terms of setting the lengths of comment periods for guidance documents, FDA believes that, generally, a 60-to-90-day comment period is appropriate for most Level 1 guidance documents, depending on, for example, complexity, length, and planned timelines for finalizing. However, we recognize that a longer comment period may be appropriate for a small subset of our guidance documents; as a result, we intend to amend our internal procedures to assist Centers and Offices in determining when a longer comment period may be warranted for a particular guidance document.

4. Best Practices for Periodic Guidance Review and Access to Withdrawn Guidance

As discussed in the Draft Report and Plan, since 2011, FDA Centers and Offices have periodically reviewed guidance documents, with the aim of determining whether each guidance should be (1) withdrawn because it is obsolete (i.e., in conflict with, or no longer reflective of FDA's current thinking) or has been replaced by another guidance document that better reflects the Agency's current policies or recommendations on an issue or (2) revised and reissued to ensure that it reflects the Agency's current thinking. Several comments requested that FDA provide a clear mechanism to receive public input on which guidance documents FDA should consider either revising or withdrawing. FDA agrees that this is a best practice and, as described in the discussion of guidance agendas below, each Center and Office that routinely issues guidance intends to provide an email address or public docket for such feedback.

[27] 2023 Draft Report and Plan at 11.

Numerous comments also requested easier access to withdrawn guidance documents. Although the 2011 GGP Report recommended that FDA build a centralized web page that links to a list of withdrawn guidance documents, FDA currently makes information about withdrawn guidance documents available on Center- and Office-specific web pages. Further, comments to the Draft Report and Plan requested that guidance documents be grouped on the website by topic/product area. As such, FDA believes that the public can best locate these withdrawn guidance documents by product area. Therefore, FDA will continue to utilize the Center- and Office-specific web pages to list withdrawn guidance documents.[28] In response to comments requesting that FDA provide links to the withdrawn guidance documents themselves, FDA understands the desire to access withdrawn guidance documents on occasion to understand the history of a regulatory issue and how the Agency's thinking has evolved over time. However, we note that withdrawn guidance documents no longer reflect the Agency's current thinking or policy on a matter. As such, the public should not rely upon a withdrawn guidance document as reflecting FDA's current policy. Withdrawn guidance documents generally remain available in the docket for that guidance. To facilitate access to withdrawn guidance documents, going forward, FDA Centers and Offices will provide either information needed to access the docket or links to the archived webpage with the withdrawn guidance document so that interested parties who wish to understand a previous policy or how FDA's thinking has evolved over time may more easily access copies of withdrawn guidance documents.

B. Best Practices for FDA Guidance Communication/Outreach

1. Best Practices for FDA Guidance Communication on FDA.gov and the "Search for FDA Guidance Documents" Web Page

As discussed in the Draft Report and Plan, in 2014, FDA launched the "Search for FDA Guidance Documents" web page, an Agency-wide, guidance web page that provides centralized access to all current FDA guidance documents.[29] This web page links to over 2,700 draft and final FDA guidance documents. The "Search for FDA Guidance Documents" web page allows users to filter their search by a number of parameters, including product type, FDA organization, topic, document type (e.g., Guidance, Compliance Policy Guidance, Small Entity Compliance

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[28] CBER (https://www.fda.gov/regulatory-information/search-fda-guidance-documents/withdrawn-guidances-biologics); CDER (https://www.fda.gov/drugs/guidances-drugs/withdrawnexpired-guidances-drugs); CDRH (https://www.fda.gov/medical-devices/guidance-documents-medical-devices-and-radiation-emitting-products/withdrawn-or-expired-guidance); CTP (https://www.fda.gov/tobacco-products/rules-regulations-and-guidance/withdrawnreplaced-guidances); CVM (https://www.fda.gov/animal-veterinary/guidance-industry/withdrawnreplaced-guidances); Office of the Chief Medical Officer (https://www.fda.gov/science-research/clinical-trials-and-human-subject-protection/withdrawn-or-expired-clinical-trial-guidance-documents).

[29] FDA, "Search for FDA Guidance Documents", available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

Guide), issue date, and comment closing date. Additionally, searchers may sort the table of guidance documents by issuing Center or Office, issue date, topic, whether the guidance document is draft or final, whether the comment period on a draft guidance document is still open, and comment period closing date on a draft guidance document. The public may access the docket for each guidance document from the "Search for FDA Guidance Documents" web page and via the landing page for that guidance, which is accessible by clicking on the "Summary" column for a particular guidance. The "Search for FDA Guidance Documents" web page is promptly updated as new guidance documents are issued and is accessible via a link from the Regulatory Information web page.[30] As described in the Draft Report and Plan, in 2019-2020, FDA undertook a review of the "Search for FDA Guidance Documents" web page. This review confirmed that all current FDA guidances were posted and that guidance documents that no longer reflected current policy had been removed. FDA also reviewed the accuracy of the metadata that support the functionality of the filters and search tools on the "Search for FDA Guidance Documents" web page and made updates as needed.

Comments to the Draft Report and Plan offered additional suggestions to improve the format and functionality of the "Search for FDA Guidance Documents" web page, including improved categorization of guidances by subject/topic; better searchability of guidances, including requests for the ability to search for FDA guidance documents by searching the content of the guidance document Portable Document Formats (PDF) files themselves; and better communication on when FDA issues new guidance or revises existing guidance, such as a "What's New" section. FDA believes that it is a best practice to make information about its guidance documents clear and easily accessible. As such, in response to these comments, FDA plans to make the following improvements to its website:

- **Creation of an updated FDA Guidance web page.** FDA's plan is to use the updated FDA Guidance web page to house general background information about FDA guidance, provide links to other FDA guidance-related web pages (e.g., the "Search for FDA Guidance Documents" web page, all FDA Center and Office guidance agendas, and Center web pages listing withdrawn guidance documents), and provide clear information to the public on how to subscribe to an email to receive notifications of newly-issued FDA guidance documents.
- **Improvements to organization and descriptions of the functionality of the "Search for FDA Guidance Documents" web page to assist stakeholders in identifying all relevant guidance on given topics.** In response to a comment requesting that FDA provide a list of newly issued guidance, FDA revised the "Search for FDA Guidance Documents" web page to clarify that the search results table defaults to a reverse-chronological list of guidance documents, with the most recently issued guidances appearing at the top of the list. Additionally, FDA more prominently highlighted the

[30] FDA, Regulatory Information, available at https://www.fda.gov/regulatory-information.

existing option available on the "Search for FDA Guidance Documents" page to subscribe to receive periodic email notifications about recently issued guidance documents.

- **Improvements to accessibility and functionality of searches for guidance documents by topic.** The "Search for FDA Guidance Documents" web page currently allows for browsing guidance documents by providing links to web pages covering broad topics from which users may access guidance documents on those topics. The "Search for FDA Guidance Documents" web page also offers users the ability to filter all guidance documents by "topic" with over 70 discrete topics to choose from (e.g., labeling, rare diseases, etc.). In response to comments, FDA updated the "Search for FDA Guidance Documents" web page to make the links to the topical web pages more visible to users. Additionally, FDA recently expanded the list of topics in the "topic" filter to allow searches for guidance documents related to pediatric product development and intends to continue to add new topics to these search filters, as appropriate and as resources allow.

Several comments requested that FDA provide an alternate format for its guidance documents, such as HyperText Markup Language or other digitally enabled format and that FDA enhance its capabilities to allow users to identify FDA guidance documents of potential interest through searches of key words or phrases in the guidance documents themselves, in addition to the filters available on the "Search for FDA Guidance Documents" web page. A few comments requested that FDA provide hyperlinks to related documents within guidance documents. Currently, FDA plans to continue to support making its guidance documents available in PDF format and to support searches using the filters and metadata available via the "Search for FDA Guidance Documents" web page. Additionally, the advanced search function on FDA.gov supports searches of FDA guidance documents. FDA will also continue to provide references and citations to laws, regulations, and related guidances in its guidance documents, as relevant and appropriate, so that interested persons may review these references.

2. Best Practices for Input on Topics for Guidance Development and Guidance Agendas

In addition to the opportunity to comment on guidance documents themselves, interested persons may provide input on topics for future guidance development. Such input may be provided to FDA in a variety of forums, including at advisory committee meetings, industry meetings, roundtables, and listening sessions; during user fee negotiations; or by contacting the applicable FDA Center or Office. Although not required by statute, FDA on its own initiative formalized in its GGP regulation the standard practice of publishing guidance agendas listing topics anticipated for upcoming guidance development or revision. These guidance agendas provide the public with information on possible new topics for guidance documents or revisions to existing guidance documents that each Center or Office is currently intending to issue in the

coming year. The Centers and Offices are not bound by these agendas; they are not required to issue every guidance document on the agenda, nor are they precluded from issuing guidance documents on topics not on the agenda.[31] Nonetheless, FDA provides these guidance agendas so that interested persons may obtain general information regarding FDA's guidance plans, as well as offer comments and suggest other topics that would benefit from guidance. Making these agendas available on the internet provides transparency and thus access to all interested parties, including those who may not be directly involved in user fee negotiations or otherwise do not have direct contact with the Agency. Additionally, FDA currently provides a docket where the public may submit proposed drafts of guidance documents: Docket No. FDA-2013-S-0610.[32] FDA reviews and takes into consideration all submitted comments on FDA guidance agendas, guidance topic suggestions, and proposed draft guidance documents.

Comments on the Draft Report and Plan offered several suggestions on ways to improve the Agency's guidance agendas and the current methods for public input into guidance development. Specifically, comments requested more consistency across FDA Centers and Offices regarding guidance agenda location, format, publication timing, and public input mechanisms. Comments also supported adding a guidance agenda for Office of the Commissioner offices that do not currently provide a guidance agenda and that are not currently represented by the Center guidance agendas, providing easier access to these agendas, maintaining access to the prior year's agenda, and offering more transparent and accessible mechanisms for submitting comments to FDA on guidance topics. FDA agrees that it is a best practice to provide for additional consistency and transparency across the Centers and Offices regarding the availability of their guidance agendas and opportunities for public input into topics for guidance development.

With regard to the content and location of the guidance agendas, while many comments expressed support for FDA's proposal to post its guidance agendas on the internet only, a few comments expressed concern with FDA eliminating the annual *Federal Register* publication of these agendas. Others requested that FDA include more details in the guidance agendas, such as whether a guidance is required by statute or is an Agency priority and the stage of development of the guidance. In response to these comments, FDA carefully weighed a number of factors, including the potential benefits of increasing the level of detail of FDA's guidance agendas, the varied constituencies that may have an interest in the agendas, the purpose and non-binding nature of FDA guidance, the fact that such agendas are not mandated by statute, the time and resources involved in preparing more detailed agendas, and the reality that Agency priorities frequently change significantly over a 12-month period. Considering all of these factors, FDA

[31] Several factors may impact FDA's ability to issue the listed guidances, including, for example, new Administration priorities and emerging public health issues.

[32] 21 CFR 10.115(f)(3).

believes that posting these guidance agendas on the FDA Center or Office web pages with links from the central FDA Guidance web page is the optimal approach. To provide interested parties with reliable access to the most current guidance agendas and to provide an efficient process for revising these agendas during the year, as appropriate, FDA believes that the Center- or Office-specific guidance web pages are the optimal location to house these agendas.

Specifically, in response to the comments regarding announcing the agendas, the availability of agendas, and mechanisms for input into topics for guidance development, FDA intends to implement the following best practices:

- Publish an NOA in the *Federal Register* in January of each calendar year announcing the availability of all FDA guidance agendas (with the exception of the Center for Devices and Radiological Health (CDRH), which will continue to publish its NOA and agenda on a Fiscal Year (FY) schedule). The NOA will include links to the web pages on which each Center/Office guidance agenda is posted and provide clear information on how interested parties may submit comments to each Center/Office.
- Provide links to the current Center and Office guidance agendas and the most recent previous agenda on the FDA Guidance web page.
- Provide a clear mechanism, either a docket or email address, for each Center/Office that issues a guidance agenda to receive public input on guidance agendas, topics, and suggestions for guidance development and suggestions that FDA revise or withdraw a particular guidance. Each Center or Office will periodically review and consider the comments and suggestions received.
- Consistent with our GGP regulation, FDA will continue to make Docket No. FDA-2013-S-0610 available for the public to submit drafts of proposed guidance documents for FDA to consider.[33]

Regarding comments supporting agendas for Office of the Commissioner offices, going forward, the Office of the Chief Medical Officer and the Oncology Center of Excellence (OCE) intend to publish an annual guidance agenda.[34] Other comments requested that FDA provide additional opportunities for input into guidance content and development via, for example,

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[33] 21 CFR 10.115(f)(3).

[34] As part of an approved reorganization effective October 1, 2024, an Office of the Chief Medical Officer was established in the Office of the Commissioner to strengthen central coordination of activities that promote safe, effective, and innovative medical products for patients through agency-wide collaboration. At that time, the Office of Clinical Policy and Programs was renamed and functions were realigned as part of the new Office of the Chief Medical Officer. The reorganization also established the Human Foods Program (HFP) by realigning the functions of the Center for Food Safety and Applied Nutrition and the Office of Food Policy and Response, as well as key functions from the former Office of Regulatory Affairs (now the Office of Inspections and Investigations or OII). See 89 FR 47567 (Jun. 3, 2024). For more information, see: https://www.fda.gov/about-fda/fda-organization/fda-modernization-efforts-establishing-unified-human-foods-program-new-model-field-operations-and.

Requests for Information, public meetings, and/or "Advanced Notice of Guidance Development" akin to an Advanced Notice of Proposed Rulemaking. FDA intends to consider using such tools if appropriate, while also considering that doing so may require additional resources and delay the issuance of important recommendations to industry and the public.[35] FDA agrees with comments that, in some instances and as described in the Draft Report and Plan, it may be appropriate for FDA to receive additional public input into guidance development through mechanisms such as public meetings, Requests For Information, or other means. FDA intends to review its internal procedures to ensure that they encourage each Center and Office to consider when the development of a particular guidance document would benefit from additional mechanisms for input and to pursue those opportunities as resources allow.

3. Best Practices for Guidance Outreach

Some comments suggested that FDA continue to explore opportunities to improve outreach for guidance documents. FDA agrees that it is a best practice to use multiple means of communication to announce the availability of guidance documents. Currently, FDA publishes NOAs in the *Federal Register* when it publishes Level 1 and certain Level 2 guidance documents. The Federal Register website is updated twice every business day with the current issue of the *Federal Register* as well as documents for public inspection. In addition, new guidance documents are promptly uploaded to the "Search for FDA Guidance Documents" webpage, which defaults to displaying most recent guidance documents at the top of the list. FDA intends to continue to use, as appropriate, communications tools such as email updates, social media, trade press announcements, Constituent Updates, and other communication methods to announce new guidance documents and significant revisions to existing guidance documents. FDA appreciates that the use of such communications is especially important to clarify any changes made to existing guidance documents and in circumstances where there may not be an accompanying NOA, such as the issuance of most Level 2 guidance documents and Level 2 updates to existing guidance documents. As another example of transparent communication and dissemination of Center for Drug Evaluation and Research (CDER) guidance documents, CDER also offers its Guidance Snapshot Pilot[36] for a subset of cross-cutting guidance documents on topics that seek to modernize drug clinical trials and accelerate drug development. Guidance Snapshots are a communication tool providing highlights from guidance documents using visuals and plain language and are intended to increase public awareness of, and engagement with, FDA guidance documents on innovative topics in order to support the efficient dissemination of the guidance documents' recommendations.

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[35] This would also run counter to another comment requesting that FDA guidance documents have fewer layers of external review and that FDA seek statutory authority to revise the GGP regulation to allow guidance to function more like living, continually evolving documents and less like formal rulemaking.

[36] https://www.fda.gov/drugs/guidances-drugs/guidance-snapshot-pilot.

C. Updates to FDA GGP Regulation

As noted in the Draft Report and Plan, FDA believes it should update its GGP Regulation, which is now more than 20 years old. FDA intends to consider amendments to better reflect current technology, to optimize use of the internet to make guidance documents and agendas readily accessible, and to provide more transparency into how the public can comment on guidance agendas and provide input into topics for future guidance development.

D. Best Practices Regarding Use of Level 1 Guidance "for Immediate Implementation" and Level 2 Guidance

Under section 701(h)(1)(C) of the FD&C Act, FDA must ensure public participation prior to the implementation of a Level 1 guidance unless FDA determines that such prior public participation is not feasible or appropriate. In the preamble to FDA's GGP regulation, we articulated three circumstances in which we expected the exception might generally be used such that FDA would issue guidance for immediate implementation: (1) there are public health reasons for the immediate implementation of the guidance document; (2) there is a statutory requirement, executive order, or court order that requires immediate implementation; or (3) the guidance document presents a less burdensome policy that is consistent with public health.[37] Under these circumstances, stakeholders still may comment on the guidance any time. FDA reviews the comments and revises the guidances, as appropriate.[38]

In general, FDA has issued a small proportion of Level 1 guidance "for immediate implementation," and the 2011 GGP Report recommended that FDA use innovative forms of guidance that comply with the GGP requirements, such as Level 1 guidance "for immediate implementation," to help make the issuance of final guidance more efficient and expeditious. Subsequently, in the 2023 Draft Report and Plan, we observed that use of these procedures during the COVID-19 pandemic enabled FDA to rapidly disseminate Agency recommendations and policies, including updates in response to comments as appropriate. These streamlined processes were critical to FDA's ability to address the pandemic.

Based on this history, in the Draft Report and Plan, FDA signaled our intent to consider whether, consistent with the FD&C Act and the GGP regulation, there might be additional categories of Level 1 guidance documents that would be appropriate "for immediate implementation." We likewise signaled our intent to consider whether, consistent with the FD&C Act, there are additional categories of guidance that would be appropriate for issuance using the

[37] 65 FR 56468, 56472 (Sept. 19, 2000).

[38] 21 CFR 10.115(g)(3), (4).

procedures for Level 2 guidance documents. We sought public comment specifically on these issues in the NOA for the Draft Report and Plan.

Commenters expressed a desire for FDA to retain the practice of seeking public comment prior to issuance of its Level 1 guidance documents, with only rare exceptions. Likewise, some commenters expressed concern with FDA's intent to consider whether, consistent with the FD&C Act and the GGP regulation, there are additional categories of guidance that would be appropriate for issuance using the procedures for Level 2 guidance documents.

FDA values public participation in the development of its guidance documents and intends to provide for prior public participation for Draft Level 1 guidance documents unless such prior public participation is not feasible or appropriate. As noted in the preamble to our GGP regulation, we anticipate that prior public participation will generally not be feasible or appropriate when: (1) there are public health reasons for the immediate implementation of the guidance document; (2) there is a statutory requirement, executive order, or court order that requires immediate implementation; or (3) the guidance document presents a less burdensome policy that is consistent with public health.[39] FDA also intends to issue Level 2 guidance, consistent with the FD&C Act and our GGP regulation, when the guidance sets forth existing practices or minor changes in interpretation or policy.

E. Best Practices for Using Guidance to Streamline the Process for Regulatory Submissions

As discussed in the Draft Report and Plan, it has been longstanding FDA practice to use guidance documents to help streamline the process for regulatory submissions. FDA has issued hundreds of guidance documents that directly and indirectly assist industry in making regulatory submissions to FDA, including those that are intended to help streamline the process for such regulatory submissions. These guidance documents generally assist in the development of FDA-regulated products and/or preparation of regulatory submissions for these products or describe and clarify processes for interacting with and/or submitting information to FDA. These guidance documents help expedite and create efficiencies in product development, manufacturing, and review.

Guidance documents designed to assist in the development of FDA-regulated products describe FDA's current thinking regarding the overall development program and (where applicable) clinical study design to support legal marketing of FDA-regulated products. For example, to help facilitate approval of medical products to treat a specific disease or condition, a guidance may contain recommendations on issues related to that disease or condition such as

[39] 65 FR 56468, 56472 (Sept. 19, 2000).

clinical trial population, trial design, dose selection, efficacy endpoints, and statistical considerations. By giving these types of recommendations about clinical trial design, these guidances assist industry as they plan and conduct trials to support future regulatory submissions for marketing approval. As another example, such guidances may support the submission of a modified risk tobacco product application, a premarket tobacco product application, or a substantial equivalence report to the Center for Tobacco Products (CTP). The content of these guidance documents may be informed by discussions the Agency has had with individual sponsors or applicants and other interested parties, e.g., during meetings prior to submission of a marketing application or via deficiency letters. Providing this information in a guidance document allows FDA's recommendations and current thinking to consistently reach all interested parties.

A few examples of such guidance documents that FDA has issued in recent years include:

- Rare Diseases: Considerations for the Development of Drugs and Biological Products (December 2023)
- Real-Time Oncology Review (RTOR) (November 2023)
- Demonstrating Substantial Evidence of Effectiveness Based on One Adequate and Well-Controlled Clinical Investigation and Confirmatory Evidence (September 2023)
- Migraine: Developing Drugs for Preventive Treatment (June 2023)
- Soft (Hydrophilic) Daily Wear Contact Lenses - Performance Criteria for Safety and Performance Based Pathway (March 2023)
- Studying Multiple Versions of a Cellular or Gene Therapy Product in an Early-Phase Clinical Trial (November 2022)
- Acute Myeloid Leukemia: Developing Drugs and Biological Products for Treatment (October 2022)
- Tobacco Products: Principles for Designing and Conducting Tobacco Product Perception and Intention Studies (August 2022)

As another example, FDA actively pursues opportunities to streamline the process for regulatory submissions through issuance of guidance documents that provide recommendations, templates, and examples to help industry more efficiently and accurately make regulatory submissions to the Agency. For instance, these guidances might provide detailed information for the submission of files that meet Structured Product Labeling standards and for submissions related to marketing applications or post-marketing adverse event reports, such as submissions to the FDA's Adverse Event Reporting Systems and Drug Registration and Listing System. These "procedural" guidances might also provide recommendations to industry on how to utilize electronic systems to obtain export certificates, provide electronic document signatures, or identify any forms applicable to a submission.

Examples of such guidance documents that FDA has issued in recent years include:

- Predetermined Change Control Plans for Medical Devices (Draft Guidance August 2024)
- Electronic Submission Template for Medical Device De Novo Requests (August 2024)
- Standardized Format for Electronic Submission for Marketing Applications Content for the Planning of Bioresearch Monitoring (BIMO) Inspections for Center for Biologics Evaluation and Research Submissions (Draft Guidance June 2024)
- REMS Logic Model: A Framework to Link Program Design with Assessment (Draft Guidance May 2024)
- Providing Regulatory Submissions in Electronic Format: IND Safety Reports (April 2024)
- Registration and Listing of Cosmetic Product Facilities and Products (December 2023)
- Electronic Submission Template for Medical Device 510(k) Submissions (October 2023)
- Center for Veterinary Medicine (CVM) GFI #108 Registering with CVM's Electronic Submission System (April 2023)
- Revision to Draft GFI #227 – Chemistry, Manufacturing, and Control (CMC) Technical Section Filing Strategies (September 2024)

Comments to the Draft Report and Plan overwhelmingly supported FDA use of templates, technical conformance guides, and submission checklists to assist with, and help streamline, regulatory submissions. As appropriate to the subject matter of the guidance, guidance documents related to the development of FDA-regulated products and guidances that describe processes for submitting information to FDA may incorporate tools such as templates or submission checklists or may be accompanied by a technical conformance guide to assist with related regulatory submissions. FDA notes that some of these tools may constitute collections of information under the Paperwork Reduction Act, which require additional time and resources to implement. Nonetheless, FDA agrees that making these tools available in conjunction with guidance is a best practice to help streamline the process for regulatory submissions and FDA intends to continue to consider, as resources permit, whether use of such tools in conjunction with development of a particular guidance document would be appropriate.

While FDA believes it is a best practice to use guidance documents when appropriate to help streamline the process for regulatory submissions to FDA, the Center or Office with regulatory responsibility for the particular product or type of submission possesses the

appropriate subject matter expertise to determine when such guidance is warranted for a particular product or program. Because these subject matter experts have the greatest familiarity with factors that may indicate when a guidance related to a particular regulatory submission may be beneficial (e.g., the types of questions and frequency of questions they receive from industry on a given topic or issue, any observed patterns of submitters omitting necessary information from regulatory submissions, suggestions for topics for guidance development received from interested parties, as well as knowledge of available resources), they are best positioned to determine when a guidance will help to streamline the process for, or improve the quality and efficiency of, specific regulatory submissions. Each Center or Office with responsibility for a particular regulatory submission will continue to develop guidance documents to help clarify, augment, and streamline the process for regulatory submissions, as appropriate.