Guidance title	CFR cite referenced in guidance	Another guidance referenced in guidance	OMB control No(s).	New collection covered by PHE PRA waiver
Policy for Monkeypox Tests to Address the Public Health Emergency.	.....	Emergency Use Authorization of Medical Products and Related Authorities; Guidance for Industry and Other Stakeholders.	0910–0595	
		Administrative Procedures for Clinical Laboratory Improvement Amendments of 1988 Categorization.	0910–0607	
	803	.....	0910–0437	
	806	.....	0910–0359	
	807, subpart E	.....	0910–0120	
				FDA Notification of Laboratory Development and Validation of Monkeypox Test (including notification template).
				Statements on patient test reports.
				Commercial Manufacturer Test for Monkeypox—EUA Test Summary Information.
				EUA templates for monkeypox tests.

Dated: September 7, 2022.

Lauren K. Roth,

Associate Commissioner for Policy.

[FR Doc. 2022–19709 Filed 9–12–22; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2018–N–2065]

Alternative or Streamlined Mechanisms for Complying With the Current Good Manufacturing Practice Requirements for Combination Products; List Under the 21st Century Cures Act

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: As required by the 21st Century Cures Act (Cures Act), the Food and Drug Administration (FDA, Agency, or we) is finalizing a list of alternative or streamlined mechanisms for complying with the current good manufacturing practice (CGMP) requirements for combination products. A combination product is a product composed of any combination of a drug, a device, and/or a biological product.

DATES: This notice is published in the **Federal Register** on September 13, 2022.

ADDRESSES: For access to the docket, go to *https://www.regulations.gov* and insert the docket number, found in brackets in the heading of this document, into the ''Search'' box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, between 9 a.m. and 4 p.m., Monday through Friday, 240–402–7500. Publicly available submissions may be seen in the docket.

FOR FURTHER INFORMATION CONTACT: John Barlow Weiner, Office of Combination Products, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 32, Rm. 5130, Silver Spring, MD 20993, 301–796–8930, *john.weiner@fda.hhs.gov* or *combination@fda.hhs.gov.*

SUPPLEMENTARY INFORMATION:

I. Background

On January 22, 2013, FDA issued a final rule on CGMP requirements for combination products (see 78 FR 4307 and part 4, subpart A (21 CFR part 4, subpart A)) (CGMP Rule). The drugs, devices, and biological products included in combination products are referred to as ''constituent parts'' of the combination product. Combination products include ''single-entity'' combination products, the constituent parts of which are physically, chemically, or otherwise combined or mixed and produced as a single entity (see § 3.2(e)(1) (21 CFR 3.2(e)(1))) (*e.g.,* prefilled syringes and drug-eluting stents), and ''co-packaged'' combination products where the constituent parts are packaged together in a single package or as a unit (see § 3.2(e)(2)) (*e.g.,* a surgical or first-aid kit).[1] Section 4.4 (21 CFR 4.4) outlines how manufacturers of single-entity and co-packaged combination products (hereafter ''CP manufacturers'') can demonstrate compliance with applicable CGMP requirements, including through implementation of a streamlined approach to meet the requirements of both the drug CGMP and the device quality system (QS) regulations.

In December 2016, the Cures Act (Pub. L. 114–255) was signed into law. Section 3038(c) of the Cures Act mandated that FDA publish in the **Federal Register** a list identifying types of combination products and manufacturing processes for which ''good manufacturing processes'' may be adopted that vary from the requirements set forth in § 4.4, or that FDA proposes can satisfy the requirements in § 4.4 through ''alternative or streamlined mechanisms,'' and to review this list periodically. In accordance with this statutory mandate, FDA published a proposed list on June 13, 2018 (83 FR 27609).

FDA received six comments on this proposed list, has considered them, and is now publishing a list after such consideration (see section II of this document). In response to the comments, FDA added and refined examples and provided additional clarity regarding FDA's expectations for CP manufacturers when applying mechanisms presented in this list. FDA also added reference to a guidance on how to request FDA feedback on combination products, which provides additional detail on interacting with

[1] There are also ''cross-labeled'' combination products (§ 3.2(e)(3) and (4)). See Ref. 1 for additional information regarding CGMP requirements for them, as well as use of the ''streamlined approach'' if a device and drug or biological product constituent part of a cross-labeled combination product are manufactured at the same facility.

FDA, including with respect to CGMP issues addressed in this list.

While FDA has provided examples in this notice of the types of mechanisms that may be appropriate, CP manufacturers should consider the suitability of an approach in the context of their product and manufacturing process. For these examples, we have recommended engaging the Agency before adoption of some, whereas others may be evaluated on inspection as appropriate. Additional approaches may be permissible as well for evaluation on a case-by-case basis for a particular product and CP manufacturer. FDA continues to apply a risk-based approach to evaluating alternative or streamlined mechanisms for ensuring the quality of combination products, and as FDA and CP manufacturers develop additional data and rationales, this list may be expanded, including to provide additional examples or to identify types of combination products for which alternative or streamlined mechanisms may be applicable.

II. List of Mechanisms for Complying With § 4.4 CGMP Requirements for Combination Products

A. Introduction

Sections II.B and II.C present mechanisms for demonstrating compliance with relevant combination product CGMP requirements. Where applicable, reference is made to sections of the ''Guidance for Industry and FDA Staff: Current Good Manufacturing Practice Requirements for Combination Products'' for additional information (Ref. 1). FDA will continue to evaluate this list in light of Agency experience and stakeholder input. CP manufacturers are welcome to propose other approaches not described, including approaches to other requirements set forth in § 4.4 for which FDA is not currently describing mechanisms for demonstrating compliance in the sections below.

For each mechanism described below, CP manufacturers should consider what documentation would be sufficient to support that the mechanism, including the specific approach for implementing it, assures appropriate control of the manufacture of the combination product to ensure safety and effectiveness of the product. Appropriate evidence and an explanation of the rationale to support the approach should be accessible at the manufacturing facility for review during facility inspections regardless of whether the approach has been discussed with FDA.

In some cases, CP manufacturers may need to interact with FDA to gain approval or otherwise notify FDA of a manufacturing change (see section III.A). For example, if a CP manufacturer utilizes a bracketing/matrixing design for stability studies, this approach should be submitted to FDA either as a proposal at the time of premarket review or as a postmarket change.

For additional discussion on how to interact with FDA regarding the mechanisms described below, see section III.

B. Mechanisms for Complying With Drug CGMP Requirements (Part 211) Specified in § 4.4[2]

FDA interprets the mechanisms identified in the sections below as means to demonstrate compliance with the following part 211 (21 CFR part 211) requirements specified in § 4.4:

1. Section 211.165 Testing and Release for Distribution

Use of samples that are not finished combination products, but that are representative of the finished combination product with respect to the characteristics and attributes being tested, when performing testing required by § 211.165 (21 CFR 211.165) to determine whether the drug constituent part, and thus the combination product, meets relevant final specifications. To meet the requirements of § 211.165, the CP manufacturer using this mechanism would need to establish, including where appropriate through bridging studies and other quantitative means, that any differences in the manufacturing process for the representative samples as compared to the finished combination product do not affect the drug constituent part (*i.e.,* to establish that there is no difference in the quality attributes related to the drug constituent part in the representative sample as compared to the attributes related to the drug constituent part in the finished combination product). For example, as part of product release testing, drug-eluting lead CP manufacturers could perform release testing for identity, potency, or other quality attributes on a representative lead tip assembly that contains the drug constituent part, rather than on the finished combination product containing the full electronic and mechanical assembly, so long as they can establish that the representative lead tip assemblies meet the relevant acceptance criteria and there are no statistically significant differences in the test results for the representative lead tip assemblies compared to the finished combination product.

(See also section IV.B.5 of Ref. 1 for additional information on testing and release for combination products.)

2. Section 211.166 Stability Testing

Use of bracketing and matrixing approaches to stability studies for combination products. Principles for bracketing and matrixing approaches to meet the requirements of § 211.166 (21 CFR 211.166) have already been addressed by the Agency, including in The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) guidelines with regard to drug products (Refs. 2 and 3), and such principles can also be applied to combination products. CP manufacturers could utilize a bracketing/matrixing design, if appropriate, for stability studies. For example, when assessing stability for a prefilled syringe that is marketed in various fill volumes, one of the approaches that a CP manufacturer could utilize, if appropriate, is bracketing based on the smallest and the largest fill volume of product configurations. In determining the extremes for a bracketing approach and/or when justifying the use of a matrix design for single-entity combination products, it is important that the drug-device interactions and variations in the manufacturing processes are considered. For co-packaged combination products, such approaches can only be applied to the drug constituent part of the product.

Leveraging stability data for an already marketed combination product. Mechanisms that use prior stability knowledge, data, or information for an existing product to support stability assessment for a modification to that product may be appropriate when a new combination product is a modification of an already marketed product and the modification does not have the potential to impact the stability of the drug constituent part. For example, when developing new lengths of a drug-coated catheter product for which the catheter materials, drug coating, manufacturing process, and packaging configurations are largely unchanged from existing marketed sizes, the CP manufacturer would generally be able to leverage existing stability data to establish initial product shelf life or to support reduced stability data requirements, so long as characteristics of the product that could impact stability (*e.g.,* materials, packaging configuration) remain the same. However, if the device constituent

[2] Several drug CGMP mechanisms included in this list depend upon use of a more broadly defined batch. FDA notes that approaches that depend upon broadly defined batches may increase the number of distributed products implicated when corrective actions are necessary to address postmarket issues.

part of a drug-coated catheter includes a new material that is in contact with the drug coating or is a new design with a different drug-coated area or geometry, for example, new stability studies would generally be needed under § 211.166.

(See also section IV.B.6 of Ref. 1 for additional information on stability requirements for combination products.)

3. Section 211.167 Special Testing Requirements

Defining ''batch'' based on the drug constituent part rather than the finished combination product for purposes of special testing requirements for pyrogens and endotoxins. For example, a CP manufacturer of a combination product consisting of a device that is coated with a drug, where a larger batch of coating is used to manufacture several ''batches'' or ''lots'' of the overall combination product, may be able to define a batch for purposes of pyrogen and endotoxin testing as a set of combination products that were all manufactured using the same coating batch for purposes of meeting the requirements of § 211.167 (21 CFR 211.167). As with the other mechanisms described in this list, this mechanism would only potentially be available if there would be no impact on the endotoxin or pyrogen levels for the finished combination product from subsequent manufacturing processes, including when the constituent parts are combined to produce the final combination product (*e.g.,* there are no statistically significant differences in pyrogen or endotoxin test results for the combination product immediately following the coating process step as compared to the finished combination product). When defining the batch, CP manufacturers should consider whether such risks may be introduced later in the production process.

(See also section IV.B.7 of Ref. 1 for additional information on special testing requirements for combination products.)

4. Section 211.170 Reserve Samples

Keeping reserve samples that are representative of the finished combination product. CP manufacturers may use validated surrogates as representative samples to meet the requirements of § 211.170 (21 CFR 211.170), provided the surrogate is appropriate, both in terms of the manufacturing process and the characteristics of the container closure. For example, it may be permissible to maintain as a reserve sample only the drug-containing subassembly of a single-entity combination product, such as only the distal tip subassembly (with drug-containing collar) of a pacemaker lead without the associated internal electronic components, or the drug constituent part of a co-packaged combination product, such as the prefilled cartridge of a combination product that is distributed as a prefilled cartridge with an injector system. Such approaches would generally be permissible under the regulation when: (1) all subsequent manufacturing process steps to produce the final combination product are shown not to affect the drug constituent part, (2) the immediate container closure has essentially the same characteristics as that for the drug constituent part as packaged in the combination product for distribution, and (3) the representative samples are suitable for all required testing of the drug constituent part for which the reserve samples are being kept.

Using samples from representative lots of a larger batch for retention of reserve samples. To meet the requirements of § 211.170, CP manufacturers may be able to use bracketing and matrixing approaches to retain reserve samples from certain lots to adequately represent the broadly defined batch of the combination product. For example, where relevant lot-release tests, analytical procedures, and acceptance criteria are the same for the product matrix and the relevant aspects of the manufacturing process are the same, CP manufacturers might be able to retain reserve samples of appropriately varied sizes of a drug-coated combination product from across that matrix.

(See also section IV.B.8 of Ref. 1 for additional information on reserve sample requirements for combination products.)

C. Mechanisms for Complying With Device Quality System Requirements (Part 820) Specified in § 4.4

FDA interprets the mechanisms identified in the sections below as means to demonstrate compliance with the following part 820 (21 CFR part 820) requirements specified in § 4.4:

1. Section 820.30 Design Controls

Using existing pharmaceutical development practices and documentation that align with the design control principles and requirements of § 820.30 (21 CFR 820.30). Robust pharmaceutical development practices would address many design control requirements to assure compliance with § 820.30 where applicable (Ref. 4). CP manufacturers need to demonstrate how development processes, procedures, and terminology align with design control principles and requirements in § 820.30, when applicable, including developing additional design control elements, if necessary. When evaluating the adequacy of existing pharmaceutical development processes and related documentation, particular attention should be given to postmarket management of design changes to the combination product and the alignment of change control practices with the principles and requirements of § 820.30, as applicable.

(See also section IV.A.2 of Ref. 1 for additional information on the requirements of § 820.30 as they apply to combination products.)

2. Exemption of Combination Products From Device QS Regulation

Exemption of the combination product from provisions of the device QS regulation (part 820) if the device constituent part of the combination product is itself exempt from the device QS requirements specified in § 4.4(b)(1) (i.e., the intended use of the device as a constituent part falls within the scope of the relevant exemption). Some devices are exempt from certain provisions of the device QS regulation (see, for example, liquid medication dispensers such as cups and droppers that fall within the scope of § 880.6430 (21 CFR 880.6430); see also, for example, limitations to device exemptions under 21 CFR 880.9). Accordingly, a combination product is exempt from the associated provisions of the device QS regulation specified in § 4.4(b)(1) if the device constituent part falls within the scope of the relevant exemption; *i.e.,* if the intended use of the device in the combination product is not a new intended use and does not otherwise raise different safety and effectiveness questions for the device. This circumstance will most frequently apply to co-packaged combination products. For example, an oral dosing syringe (a liquid medication dispenser under § 880.6430) that is co-packaged with a drug may be exempt from all provisions of the device QS regulation except for 21 CFR 820.180 (general requirements concerning records) and 21 CFR 820.198 (requirements concerning complaint files) when marketed as a stand-alone device (and hence the combination product may also be exempt from such provisions). Accordingly, if the CP manufacturer for the co-packaged combination product is using a streamlined approach based on drug CGMP requirements (see § 4.4(b)(1)), the CP manufacturer does not need to demonstrate compliance

with the device QS requirements because the product is exempt from all device QS requirements specified in § 4.4(b)(1) and, therefore, must only be compliant with the drug CGMP requirements. However, incorporating such a dispenser into a primary container closure system or co-packaging of such a dispenser with a drug with a narrow therapeutic index, for example, each may constitute a new intended use for the dispenser or raise different safety and effectiveness questions related to performance of the dispenser, such that the relevant exemption would not apply.

(See also section III.C.3 of Ref. 1 for additional information on the exemption from provisions of the device QS regulation for combination products.)

III. Interacting With FDA on Mechanisms for Complying With CGMP for Combination Products

A. Process for Interacting With FDA

In some cases, CP manufacturers may need to interact with FDA to gain approval or otherwise notify FDA of a manufacturing change. In other cases, although a submission or notification is not required, CP manufacturers may want to discuss potential use of CGMP mechanisms with FDA. CP manufacturers are encouraged to interact early with FDA on any such contemplated use of alternative or streamlined CGMP mechanisms for combination products (see also Ref. 5 regarding interactions with FDA on combination products).

- *Pre-Submissions and Meeting Requests.* CP manufacturers who want to obtain FDA feedback prior to making a premarket submission or submitting a postmarket supplement or who otherwise want to obtain feedback on their CGMP approach, may interact with FDA via the processes available for such questions at the lead Center [3] for the combination product (see Ref. 5). For combination products reviewed under a new drug application (NDA) or a biologics license application (BLA), such interactions will generally be through Type C meetings (Ref. 6). For combination products reviewed under an abbreviated new drug application (ANDA), such interactions will generally be through the pre-ANDA program or controlled correspondence for a premarket application (Refs. 7 and 8). For combination products reviewed under a device premarket submission (*e.g.,* a premarket approval application (PMA), de novo classification, or premarket notification (510(k)), these interactions will generally be via the pre-submission process (Ref. 9). Regardless of the type of submission or meeting, such interactions should be focused on a general discussion of the CGMP approach the CP manufacturer wishes to pursue and associated justification to support the approach.[4] Only representative data is typically appropriate in these interactions; complete data should be included in the subsequent premarket submission or postmarket supplement and/or be maintained at the manufacturing facility, as appropriate.
- *Premarket Review.* CP manufacturers should include in their original submission for NDAs, BLAs, ANDAs, and PMAs information on any alternative or streamlined mechanisms for complying with combination product CGMP requirements. For PMAs, this information should be included in the manufacturing section of the PMA. For information regarding where to place information in NDAs, BLAs, or ANDAs, refer to ''eCTD Technical Conformance Guide'' (Ref. 10).
- *Postmarket Supplements or Notifications to FDA.* Postmarket changes to implement a combination product CGMP mechanism for NDAs, ANDAs, BLAs, and PMAs may require submission of a supplement or notification to FDA.[5] CP manufacturers should consult related guidances relevant to the type of constituent part(s) included in the combination product (*e.g.,* Refs. 11 to 13, as appropriate). If a CP manufacturer has questions on the appropriate submission type or the need for a submission, they can contact the lead Center for assistance.

B. Submission Content

When submitting information on a CGMP mechanism, CP manufacturers should refer to applicable guidance (see section V below) as the primary reference regarding what information to provide. Along with other information indicated in relevant guidance (see section V), the following content should be included:

- *Applicable CGMP Regulation.* Identify the applicable CGMP regulation to which the described mechanism relates. For example, if a submission includes a mechanism related to stability testing, indicate that § 211.166 is the applicable CGMP requirement.
- *Applicable Products.* If the mechanism is to be applied to multiple products and/or product configurations, list all related sizes, strengths, etc., as well as all related application numbers.
- *Prior, Related Interactions with FDA.* If the CP manufacturer has had previous interactions with FDA relevant to the proposed mechanism, either for the product addressed in the submission or for related products, the CP manufacturer should provide reference to those interactions. Where applicable, the CP manufacturer may cross-reference previously submitted information.
- *Justification and Scientific Data.* Include a justification to support that the proposed mechanism assures adequate manufacturing control to ensure product safety and effectiveness. When describing a CGMP alternative or streamlined mechanism in a premarket or postmarket submission, the description should be accompanied by such data as may be necessary to support the approach. When proposing a change from a CGMP approach that was reviewed previously by FDA, such justification should include analysis of how the proposed approach compares to the previously reviewed approach as an effective manufacturing control, including representative data, as appropriate, to substantiate the analysis.
- *Exemption from Part 820.* For interactions with FDA regarding whether a combination product is exempt from the provisions of part 820 specified in § 4.4(b)(1), the submission should include a description of the device constituent part and justification

[3] A combination product is assigned to an Agency center (Center for Biologics Evaluation and Research, Center for Drug Evaluation and Research, or Center for Devices and Radiological Health) that will have primary jurisdiction (*i.e.,* be the ''lead Center'') for that combination product's review and regulation. Assignment of a combination product to a lead Center is based on a determination of which constituent part provides the primary mode of action of the combination product (21 U.S.C. 353(g)). Manufacturers who are unsure of the lead Center for their combination product or of whether their product is a combination product, should contact the Office of Combination Products.

[4] Note that to discuss a mechanism for complying with CGMP requirements for which the CP manufacturer is referencing information in a master file, the CP manufacturer must have the appropriate authorization from the master file holder (see, *e.g.,* 21 CFR 314.420 and 814.20(c)). The authorization should clearly identify the specific information within the master file that is being made available to reference. For more information on biologics, device, and drug master files, see CBER's master files for CBER-Regulated Products web page (available at *https://www.fda.gov/vaccines-blood-biologics/development-approval-process-cber/master-files-cber-regulated-products*), CDRH's master files web page (available at *https://www.fda.gov/medical-devices/premarket-approval-pma/master-files*), and CDER's drug master files web page (available at *https://www.fda.gov/drugs/forms-submission-requirements/drug-master-files-dmfs*), respectively.

[5] Requirements for postmarket supplements are contained, for example, in 21 CFR 314.70 and 314.97 (NDAs and ANDAs), 21 CFR 601.12 (BLAs), and 21 CFR 814.39 (PMAs). Any questions on whether FDA review is required for a postmarket CGMP mechanism should generally be directed to the lead Center.

that: (1) the intended use of the device in the combination product is consistent with the intended use of a separately marketed device that has been exempted from the requirements of part 820 specified in § 4.4(b)(1), and (2) the use of the device constituent part in the combination product does not raise any different device performance-related safety and effectiveness questions as compared to a separately marketed device.

C. FDA Engagement

CP manufacturers are encouraged to discuss combination product CGMP mechanisms with FDA. In some cases, CP manufacturers may need to interact with FDA to gain approval or otherwise notify FDA of a manufacturing change (see III.A above). Any questions on how to engage FDA in such discussions should generally be directed to the lead Center for the product (see Ref. 5). The lead Center will engage appropriate expertise from within the lead Center and from other FDA Centers and the Office of Combination Products, as needed, to support review (see Ref. 14), and FDA will provide appropriate feedback (see section III.D below).

D. FDA Review

FDA may review information from a CP manufacturer related to alternative or streamlined mechanisms in pre-submissions and meetings, premarket applications, postmarket supplements or notifications, and during facility inspections. FDA may determine whether the data and rationale presented by a CP manufacturer for a particular mechanism are sufficient to demonstrate that the mechanism, as proposed or implemented, is acceptable. In such cases, FDA generally will notify the CP manufacturer and/or applicant regarding acceptability of the mechanism, consistent with existing policies and practices for the submission type and, if the Agency finds the approach insufficient, FDA intends to provide the scientific and/or regulatory basis for this determination.

IV. Paperwork Reduction Act

This notice refers to previously approved collections of information found in FDA regulations. These collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3521). We note that the information collected under the underlying CGMP regulations for drugs, devices, and biological products, including current good tissue practices for human cells, tissues, and cellular and tissue-based products, found in parts 211, 820, 600 through 680, and 1271 (21 CFR parts 211, 820, 600 through 680, and 1271), have already been approved and are in effect. The provisions of part 211 are approved under the OMB control number 0910–0139. The provisions of part 820 are approved under OMB control number 0910–0073. The provisions of parts 606 and 640 are approved under OMB control number 0910–0116. The provisions of part 610 are approved under OMB control number 0910–0116 and OMB control number 0910–0338 (also for part 680). The provisions of part 1271, subparts C and D, are approved under OMB control number 0910–0543.

We note that the information collected under the related submission types have already been approved and are in effect. The collections of information regarding formal meetings with sponsors and applicants are approved under OMB control number 0910–0429. The collections of information regarding NDA and ANDA are approved under OMB control number 0910–0001. The collections of information regarding the pre-ANDA program and controlled correspondence are approved under OMB control number 0910–0797. The collections of information regarding pre-submissions are approved under OMB control number 0910–0756. The collections of information regarding PMAs are approved under OMB control number 0910–0231. The collections of information for premarket notification (510(k)) are approved under OMB control number 0910–0120. The collections of information for the de novo classification process are approved under OMB control number 0910–0844. The collections of information regarding BLAs are approved under OMB control number 0910–0338. The collections of information regarding combination product agreement meetings are approved under OMB control number 0910–0523.

V. References

The following references are on display in the Dockets Management Staff (see **ADDRESSES**) and are available for viewing by interested persons between 9 a.m. and 4 p.m., Monday through Friday; they are also available electronically at *https://www.regulations.gov.* FDA has verified the website addresses, as of the date this document publishes in the **Federal Register**, but websites are subject to change over time.

1. ''Guidance for Industry and FDA Staff: Current Good Manufacturing Practice Requirements for Combination Products,'' January 2017. *https://www.fda.gov/media/90425/download.*
2. ''Guidance for Industry Q1D Bracketing and Matrixing Designs for Stability Testing of New Drug Substances and Products,'' January 2003. *https://www.fda.gov/media/71720/download.*
3. ''Guidance for Industry Quality of Biotechnological Products: Stability Testing of Biotechnological/Biological Products'' Q5C, July 1996. *https://www.fda.gov/media/71441/download.*
4. ''Guidance for Industry Q8(R2) Pharmaceutical Development,'' November 2009. *https://www.fda.gov/media/71535/download.*
5. ''Guidance for Industry and FDA Staff: Requesting FDA Feedback on Combination Products,'' December 2020. *https://www.fda.gov/media/133768/download.*
6. ''Draft Guidance for Industry Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products,'' December 2017. *https://www.fda.gov/media/109951/download.*
7. ''Guidance for Industry Formal Meetings Between FDA and ANDA Applicants of Complex Products Under GDUFA,'' November 2020. *https://www.fda.gov/media/107626/download.*
8. ''Guidance for Industry Controlled Correspondence Related to Generic Drug Development,'' December 2020. *https://www.fda.gov/media/109232/download.*
9. ''Guidance for Industry and FDA Staff Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program,'' January 2021. *https://www.fda.gov/media/114034/download.*
10. ''eCTD Technical Conformance Guide,'' March 2022. *https://www.fda.gov/media/93818/download.*
11. ''Guidance for Industry Changes to an Approved NDA or ANDA,'' April 2004. *https://www.fda.gov/media/71846/download.*
12. ''Guidance for Industry Chemistry, Manufacturing, and Controls Changes to an Approved Application: Certain Biological Products,'' June 2021. *https://www.fda.gov/media/109615/download.*
13. ''Guidance for Industry and FDA Staff: 30-Day Notices, 135-Day Premarket Approval (PMA) Supplements and 75-Day Humanitarian Device Exemption (HDE) Supplements for Manufacturing Method or Process Changes,'' December 2019. *https://www.fda.gov/media/72663/download.*
14. FDA Staff Manual Guide SMG 4101 ''Inter-Center Consult Request Process,'' June 2018. *https://www.fda.gov/media/81927/download.*

Dated: September 7, 2022.

Lauren K. Roth,

Associate Commissioner for Policy.

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