I. Background

FDA is announcing the availability of a draft guidance for industry entitled ''Bispecific Antibody Development Programs.'' This draft guidance provides recommendations to assist those involved in the bispecific antibody drug development process. This draft guidance discusses general considerations and recommendations, as well as regulatory, quality, nonclinical, and clinical considerations in the context of bispecific antibody development programs. This draft guidance does not discuss development considerations for other multitarget therapies that are combinations of monoclonal antibodies, antibody cocktails, or polyclonal antibodies.

Since the first therapeutic monoclonal antibody was commercialized in 1986, monoclonal antibodies have become a vital component of therapy for various diseases and conditions including cancer, autoimmune and infectious diseases, and inflammatory conditions. The regulatory pathway for evaluation of monoclonal antibodies is well established, but additional draft guidance is needed about antibody-based products that target more than one antigen. Advances in technology and an interest in novel therapies that combine targets have led to the development of bispecific antibodies, which are genetically engineered, recombinant antibodies that consist of two distinct binding domains capable of binding two different antigens or two different epitopes of the same antigen.

There are a number of challenges in developing bispecific antibodies, one of which may be significant immunogenicity caused by novel epitopes. This draft guidance addresses these considerations and provides recommendations regarding the type of data necessary to support the approval of bispecific antibodies.

This draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the current thinking of FDA on ''Bispecific Antibody Development Programs.'' It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. This guidance is not subject to Executive Order 12866.

II. Paperwork Reduction Act of 1995

This draft guidance refers to previously approved collections of information found in FDA regulations.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. 3501–3520). The collections of information in 21 CFR part 312 have been approved under 0910–0014.

III. Electronic Access

Persons with access to the internet may obtain the draft guidance at *https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm, https://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm,* or *https://www.regulations.gov.*

Dated: April 16, 2019.

Lowell J. Schiller,

Principal Associate Commissioner for Policy.

[FR Doc. 2019–07930 Filed 4–18–19; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2019–N–1265]

Agency Information Collection Activities; Proposed Collection; Comment Request; Food Labeling: Nutrition Facts Label and Supplement Facts Label

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing an opportunity for public comment on the proposed collection of certain information by the Agency. Under the Paperwork Reduction Act of 1995 (PRA), Federal Agencies are required to publish notice in the **Federal Register** concerning each proposed collection of information, including each proposed extension of an existing collection of information, and to allow 60 days for public comment in response to the notice. This notice solicits comments on the collection of information for the nutrition facts label and supplement facts label, which the Agency believes will serve to promote and protect public health.

DATES: Submit either electronic or written comments on the collection of information by June 18, 2019.

ADDRESSES: You may submit comments as follows. Please note that late, untimely filed comments will not be considered. Electronic comments must be submitted on or before June 18, 2019. The *https://www.regulations.gov* electronic filing system will accept comments until 11:59 p.m. Eastern Time at the end of June 18, 2019. Comments received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are postmarked or the delivery service acceptance receipt is on or before that date.

Electronic Submissions

Submit electronic comments in the following way:

- *Federal eRulemaking Portal: https://www.regulations.gov.* Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to *https://www.regulations.gov* will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on *https://www.regulations.gov.*
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see ''Written/Paper Submissions'' and ''Instructions'').

Written/Paper Submissions

Submit written/paper submissions as follows:

- *Mail/Hand Delivery/Courier (for written/paper submissions):* Dockets Management Staff (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in ''Instructions.''

Instructions: All submissions received must include the Docket No. FDA–2019–N–1265 for ''Agency Information Collection Activities; Proposed Collection; Comment Request; Food Labeling: Nutrition Facts Label and Supplement Facts Label.'' Received comments, those filed in a timely manner (see **ADDRESSES**), will be placed in the docket and, except for those submitted as ''Confidential

Submissions,'' publicly viewable at *https://www.regulations.gov* or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday.

• Confidential Submissions—To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states ''THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.'' The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on *https://www.regulations.gov.* Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as ''confidential.'' Any information marked as ''confidential'' will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: *https://www.gpo.gov/fdsys/pkg/FR-2015-09-18/pdf/2015-23389.pdf.*

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, 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.

FOR FURTHER INFORMATION CONTACT: Domini Bean, Office of Operations, Food and Drug Administration, Three White Flint North, 10A–12M, 11601 Landsdown St., North Bethesda, MD 20852, 301–796–5733, *PRAStaff@fda.hhs.gov.*

SUPPLEMENTARY INFORMATION: Under the PRA (44 U.S.C. 3501–3520), Federal Agencies must obtain approval from the Office of Management and Budget (OMB) for each collection of information they conduct or sponsor. ''Collection of information'' is defined in 44 U.S.C. 3502(3) and 5 CFR 1320.3(c) and includes Agency requests or requirements that members of the public submit reports, keep records, or provide information to a third party. Section 3506(c)(2)(A) of the PRA (44 U.S.C. 3506(c)(2)(A)) requires Federal Agencies to provide a 60-day notice in the **Federal Register** concerning each proposed collection of information, including each proposed extension of an existing collection of information, before submitting the collection to OMB for approval. To comply with this requirement, FDA is publishing notice of the proposed collection of information set forth in this document.

With respect to the following collection of information, FDA invites comments on these topics: (1) Whether the proposed collection of information is necessary for the proper performance of FDA's functions, including whether the information will have practical utility; (2) the accuracy of FDA's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) ways to minimize the burden of the collection of information on respondents, including through the use of automated collection techniques, when appropriate, and other forms of information technology.

Food Labeling: The Nutrition Facts Label and Supplement Facts Label—21 CFR 101.9 OMB Control Number 0910–0813—Extension

This information collection supports requirements for the Nutrition Facts and Supplemental Facts labels. Section 403(q) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 343(q)) specifies certain nutrients to be declared in nutrition labeling and authorizes the Secretary of Health and Human Services (Secretary) to require other nutrients to be declared if the Secretary determines that a nutrient will provide information regarding the nutritional value of such food that will assist consumers in maintaining healthy dietary practices. The Secretary also has discretion under section 403(q) of the FD&C Act to remove, by regulation and under certain circumstances, nutrient information that is otherwise explicitly required in food labeling under this section. Accordingly, we promulgated regulations in § 101.9 (21 CFR 101.9) setting forth how nutrition information is presented to consumers. The regulations also establish standards to define serving size and require that certain products provide additional information within the Nutrition Facts label that conveys that information to consumers.

Specifically, §§ 101.9 and 101.36 list nutrients that are required or permitted to be declared; provide Daily Reference Values and Reference Daily Intake values that are based on current dietary recommendations from consensus reports; provide requirements for foods represented or purported to be specifically for children under the age of 4 years and pregnant and lactating women and establish nutrient reference values specifically for these population subgroups; and provide the format and appearance of the Nutrition Facts label. Section 101.12 (21 CFR 101.12) defines a single-serving container; requires dual-column labeling for certain containers; updates, modifies, and provides several reference amounts customarily consumed (RACCs); provides the label serving size for breath mints; and provides various aspects of the serving size regulations.

The regulations also require that, under certain circumstances, manufacturers make and keep certain records to verify the amount of added sugars when a food product contains both naturally occurring sugars and added sugars, isolated or synthetic non-digestible carbohydrates that do not meet the definition of dietary fiber, different forms of vitamin E, and folate/folic acid declared on the Nutrition Facts or Supplement Facts label, which is the amount in the finished food product.

Firms make and keep certain records necessary to verify the amount of the nutrients in the finished food product. This collection of information does not specify what records are to be used to verify the amounts of these nutrients but does specify the information that the records must contain. The collection requires manufacturers to provide FDA, upon request during an inspection, with the records that contain the required information for each of these nutrients to verify the amount of the nutrient declared on the label. These records may include analyses of nutrient databases, recipes or formulations, information from recipes or formulations, batch records, or any other records that contain the required information to verify the nutrient content in the final product.

Description of Respondents: Respondents to this collection of information are manufacturers of food products sold in the United States. Respondents are from the private sector (for-profit businesses).

We estimate the burden of this collection of information as follows:

TABLE 1—ESTIMATED ANNUAL RECORDKEEPING BURDEN [1]

Type of declaration; 21 CFR section	Number of recordkeepers	Number of records per recordkeeper	Total annual records	Average burden per recordkeeping	Total hours
Added Sugars; 101.9(c)(6)(iii) [2]	31,283	1	31,283	1	31,283
Dietary Fiber; 101.9(c)(6)(i) [2]	31,283	1	31,283	1	31,283
Soluble Fiber; 101.9(c)(6)(i)(A) [2]	31,283	1	31,283	1	31,283
Insoluble Fiber; 101.9(c)(6)(i)(B) [2]	31,283	1	31,283	1	31,283
Vitamin E; 101.9(c)(8) [3]	31,283	1	31,283	1	31,283
Folate/Folic Acid; 101.9(c)(8) [3]	31,283	1	31,283	1	31,283
New Products	216	1	216	1	216
Total					187,914

[1] There are no capital costs or operating and maintenance costs associated with this collection of information.

[2] These estimates are likely to be large overestimates, as not all manufacturers will need to keep records for added sugars, dietary fiber, and soluble and insoluble fiber. Manufacturers will only need to keep records for products with both added and naturally occurring sugars, added sugars that undergo fermentation in certain fermented foods, and products with non-digestible carbohydrates (soluble or insoluble) that do and do not meet the definition of dietary fiber.

[3] These estimates are likely to be large overestimates, as not all manufacturers will need to keep records for vitamin E and folate/folic acid. The declaration of vitamin E and folate/folic acid is not mandatory unless a health or nutrient content claim is being made or these nutrients are directly added to the food for enrichment purposes.

Based on our experience with food labeling regulations, records that are required to be retained are records that a prudent and responsible manufacturer uses and retains as a normal part of doing business, *e.g.,* analyses of nutrient databases, recipes or formulations, batch records, or other records. Thus, the recordkeeping burden of this collection of information consists of the time required to identify and assemble the records for copying and retention. Based on our previous experience with similar information collections, we estimate the recordkeeping burden to be 1 hour per product as estimated in table 1.

The declarations for added sugars, dietary fiber, soluble fiber, and insoluble fiber are mandatory, and we conservatively estimate all of the roughly 31,283 food manufacturers would incur this recordkeeping burden and the required recordkeeping would be 1 hour per manufacturer. These calculations are reflected in table 1, rows 1 to 4. The declaration of vitamin E and folate/folic acid is not mandatory unless a health or nutrient content claim is being made or these nutrients are directly added to the food for enrichment purposes. However, we conservatively estimate that all 31,283 respondents would incur this recordkeeping burden and that the required recordkeeping would be 1 hour per manufacturer. These calculations are reflected in table 1, rows 5 and 6.

We estimate that the number of newly introduced products that are covered under this collection of information is 216. We assume the required recordkeeping is 1 hour per product, for an annual recurring recordkeeping burden of 216 hours, as reflected in table 1, row 7. Adding the burden from new products to the burden for existing products results in a total of 187,914 annual recordkeeping burden hours.

TABLE 2—ESTIMATED ANNUAL REPORTING BURDEN [1]

Filing of citizen petition regarding a particular isolated or synthetic non-digestible carbohydrate	Number of respondents	Number of responses per respondent	Total annual responses	Average burden per response	Total hours
Dietary Fiber; 101.9(c)(6)(i)	28	1	28	1	28

[1] There are no capital costs or operating and maintenance costs associated with this collection of information.

Manufacturers of food products that contain an isolated or synthetic non-digestible carbohydrate that is not listed in the definition of dietary fiber have the option of submitting a citizen petition to FDA requesting us to amend the definition of ''dietary fiber'' to include the carbohydrate as a listed dietary fiber, by demonstrating the physiological benefits of the isolated or synthetic non-digestible carbohydrate to human health.

We estimate that there are approximately 28 isolated or synthetic non-digestible carbohydrates that do not meet the definition of dietary fiber. Once a citizen petition filed by a manufacturer related to a particular isolated or synthetic non-digestible carbohydrate is granted or denied, or the carbohydrate is the subject of an authorized health claim, and the dietary fiber is listed in the definition of dietary fiber, the use of the dietary fiber as an ingredient in any food product must be included in the total amount of dietary fiber declared in nutrition labeling for such product.

Thus, we estimate that 28 manufacturers would incur burden associated with filing a citizen petition to amend the listing of dietary fiber related to an isolated and synthetic non-digestible carbohydrate that is not currently listed in the definition of dietary fiber and that the required recordkeeping would be 1 hour per manufacturer. This calculation is shown in table 2.

TABLE 3—ESTIMATED ANNUAL THIRD-PARTY DISCLOSURE BURDEN

21 CFR 101.9	Number of respondents	Number of disclosures per respondent	Total annual disclosures	Average burden per disclosure	Total hours
Nutritional labeling for new products	500	1	500	2	1,000

[1] There are no capital costs or operating and maintenance costs associated with this collection of information.

Under §§ 101.9 and 101.12, some manufacturers of retail food products make labeling changes to modify the serving sizes and other nutrition information based on changes to what products may be or are required to be labeled as a single serving, or based on updated, modified, or established RACCs. We estimate that about 500 new products will be affected by these requirements each year and that the associated disclosure burden is 2 hours per product, for an annual burden of 1,000 hours.

Dated: April 15, 2019.

Lowell J. Schiller,

Principal Associate Commissioner for Policy.

[FR Doc. 2019–07929 Filed 4–18–19; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2019–D–1261]

Technical Considerations for Non-Clinical Assessment of Medical Devices Containing Nitinol; Draft Guidance for Industry and Food and Drug Administration Staff; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of the draft guidance entitled ''Technical Considerations for Non-Clinical Assessment of Medical Devices containing Nitinol.'' Due to the unique properties of nitinol, the Agency has developed this draft guidance to provide FDA's current thinking on technical considerations specific to devices using nitinol. This draft guidance document is intended to provide clarity and consistency in recommended non-clinical assessments across a variety of medical devices that contain nitinol. This draft guidance is not final nor is it in effect at this time.

DATES: Submit either electronic or written comments on the draft guidance by June 18, 2019 to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance.

ADDRESSES: You may submit comments on any guidance at any time as follows:

Electronic Submissions

Submit electronic comments in the following way:

- *Federal eRulemaking Portal: https://www.regulations.gov.* Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to *https://www.regulations.gov* will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on *https://www.regulations.gov.*
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see ''Written/Paper Submissions'' and ''Instructions'').

Written/Paper Submissions

Submit written/paper submissions as follows:

- *Mail/Hand Delivery/Courier (for written/paper submissions):* Dockets Management Staff (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in ''Instructions.''

Instructions: All submissions received must include the Docket No. FDA–2019–D–1261 for ''Technical Considerations for Non-Clinical Assessment of Medical Devices containing Nitinol.'' Received comments will be placed in the docket and, except for those submitted as ''Confidential Submissions,'' publicly viewable at *https://www.regulations.gov* or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday.

- Confidential Submissions—To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states ''THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.'' The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on *https://www.regulations.gov.* Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as ''confidential.'' Any information marked as ''confidential'' will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: *https://www.gpo.gov/fdsys/pkg/FR-2015-09-18/pdf/2015-23389.pdf.*

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, 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.

You may submit comments on any guidance at any time (see 21 CFR 10.115(g)(5)).