the special control for the automated blood cell separator device operating on a filtration separation principle intended for the routine collection of blood and blood components reclassified as class II (§ 864.9245 (21 CFR 864.9245)).

For currently marketed products not approved under the premarket approval process, the manufacturer should file with FDA for 3 consecutive years an annual report on the anniversary date of the device reclassification from class III to class II or, on the anniversary date of the 510(k) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 360) clearance. Any subsequent change to the device requiring the submission of a premarket notification in accordance with section 510(k) of the FD&C Act should be included in the annual report. Also, a manufacturer of a device determined to be substantially equivalent to the centrifugal or filtration-based automated cell separator device intended for the routine collection of blood and blood components, should comply with the same general and special controls.

The annual report should include, at a minimum, a summary of anticipated and unanticipated adverse events that have occurred and that are not required to be reported by manufacturers under Medical Device Reporting (MDR) (part 803 (21 CFR part 803)). The reporting of adverse device events summarized in an annual report will alert FDA to trends or clusters of events that might be a safety issue otherwise unreported under the MDR regulation.

Reclassification of this device from class III to class II for the intended use of routine collection of blood and blood components relieves manufacturers of the burden of complying with the premarket approval requirements of section 515 of the FD&C Act (21 U.S.C. 360e), and may permit small potential competitors to enter the marketplace by reducing the burden. Although the special control guidance recommends that manufacturers of these devices file with FDA an annual report for 3 consecutive years, this would be less burdensome than the current postapproval requirements under part 814, subpart E (21 CFR part 814, subpart E), including the submission of periodic reports under § 814.84.

Collecting or transfusing facilities, and manufacturers have certain responsibilities under the Federal regulations. For example, collecting or transfusing facilities are required to maintain records of any reports of complaints of adverse reactions (21 CFR 606.170), while the manufacturer is responsible for conducting an investigation of each event that is reasonably known to the manufacturer and evaluating the cause of the event (§ 803.50(b)). In addition, manufacturers of medical devices are required to submit to FDA individual adverse event reports of death, serious injury, and malfunctions (§ 803.50).

In the special control guidance document, FDA recommends that manufacturers include in their three annual reports a summary of adverse reactions maintained by the collecting or transfusing facility or similar reports of adverse events collected in addition to those required under the MDR regulation. The MedWatch medical device reporting code instructions (*http://www.fda.gov/cdrh/mdr/373.html*) contains a comprehensive list of adverse events associated with device use, including most of those events that we recommend summarizing in the annual report.

FDA estimates the burden of this collection of information as follows:

TABLE 1.—ESTIMATED ANNUAL REPORTING BURDEN[1]

Reporting activity	Number of respondents	Number of responses per respondent	Total annual responses	Average burden per response	Total hours
Annual Report	4	1	4	5	20

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

Based on FDA records, there are approximately four manufactures of automated blood cell separator devices. We estimate that the manufacturers will spend approximately 5 hours preparing and submitting the annual report.

Other burden hours required for § 864.9245 are reported and approved under OMB control number 0910–0120 (premarket notification submission 501(k), 21 CFR part 807, subpart E), and OMB control number 0910–0437 (MDR, 21 CFR part 803).

Dated: February 9, 2012.

Leslie Kux,

Acting Assistant Commissioner for Policy.

[FR Doc. 2012–3551 Filed 2–14–12; 8:45 am]

BILLING CODE 4160–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2012–N–1029]

Agency Information Collection Activities; Proposed Collection; Comment Request; General Licensing Provisions; Section 351(k) Biosimilar Applications

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing an opportunity for public comment on the proposed collection of certain information by the Agency. Under the Paperwork Reduction Act of 1995 (the PRA), Federal Agencies are required to publish notice in the concerning each proposed collection of information, and to allow 60 days for public comment in response to the notice. This notice solicits comments on the information collection for the requirements for an application for a proposed biosimilar product and an application for a supplement for a proposed interchangeable product.

DATES: Submit either electronic or written comments on the collection of information by April 16, 2012.

ADDRESSES: Submit electronic comments on the collection of information to *http://www.regulations.gov*. Submit written comments on the collection of information to the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane., Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT: Juanmanuel Vilela, Office of Information Management, Food and Drug Administration, 1350 Piccard Dr.,

PI50–400B, Rockville, MD 20850, 301–796–7651.

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 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.

General Licensing Provisions; Section 351(K) Biosimilar Applications

On March 23, 2010, the President signed into law the Patient Protection and Affordable Care Act (Affordable Care Act) (Pub. L. 111–148). The Affordable Care Act contains a subtitle called the Biologics Price Competition and Innovation Act of 2009 (BPCI Act) which amends the Public Health Service Act (PHS Act) and establishes an abbreviated licensure pathway for biological products shown to be biosimilar to, or interchangeable with, an FDA-licensed biological reference product. (See sections 7001 through 7003 of the Affordable Care Act.)

Section 351(k) of the PHS Act (42 U.S.C. 262(k)), added by the BPCI Act, sets forth the requirements for an application for a proposed biosimilar product and an application for a supplement for a proposed interchangeable product. Section 351(k) defines biosimilarity to mean ''that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components'' and that ''there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product''. (See section 351(i)(2) of the PHS Act.) A 351(k) application must contain, among other things, information demonstrating that the biological product is biosimilar to a reference product based upon data derived from analytical studies, animal studies, and clinical studies, unless FDA determines, in its discretion, that certain studies are unnecessary in a 351(k) application. (See section 351(k)(2).) To demonstrate interchangeability, an applicant must provide sufficient information to demonstrate biosimilarity, and that the biosimilar biological product can be expected to produce the same clinical result as the reference product in any given patient and, if the biosimilar biological product is administered more than once to an individual, the risk in terms of safety or diminished efficacy of alternating or switching between the use of the biosimilar biological product and the reference product is not greater than the risk of using the reference product without such alternation or switch. (See section 351(k)(4) of the PHS Act.) Interchangeable products may be substituted for the reference product without the intervention of the prescribing healthcare provider. (See section 351(i)(3) of the PHS Act.) This **Federal Register** information collection document begins the process of requesting public comment and obtaining OMB approval for the information collection regarding the burden on the submission of a 351(k) application not otherwise covered by existing OMB approvals.

In estimating the information collection burden for 351(k) applications, FDA has reviewed the collection of information regarding the general licensing provisions for biologics license applications (BLAs) under section 351(a) of the PHS Act to OMB (approved under OMB control number 0910–0338). For the information collection burden for 351(a) applications, FDA described § 601.2(a) (21 CFR 601.2(a)) as requiring a manufacturer of a biological product to submit an application on forms prescribed for such purpose with accompanying data and information including certain labeling information to FDA for approval to market a product in interstate commerce. FDA also added in the burden estimate the container and package labeling requirements provided under §§ 610.60 through 610.65 (21 CFR 610.60 through 610.65). The estimated hours per response for § 601.2, and §§ 610.60 through 610.65, were 860 hours.

In addition, in submitting a 351(a) application, an applicant completes the Form FDA 356h ''Application to Market a New Drug, Biologic, or an Antibiotic Drug for Human Use.'' The application form serves primarily as a checklist for firms to gather and submit certain information to FDA. The checklist helps to ensure that the application is complete and contains all the necessary information, so that delays due to lack of information may be eliminated. The form provides key information to FDA for efficient handling and distribution to the appropriate staff for review. The estimated burden hours for biological product submissions using FDA Form 356h are included under the applicable requirements approved under OMB control number 0910–0338.

FDA intends for an applicant to submit a 351(k) application following Form FDA 356h, modifying the information submitted to support the information required under section 351(k) of the BPCI Act. To submit an application seeking licensure of a proposed biosimilar product under section 351(k)(2)(A)(i) and (k)(2)(A)(iii), FDA believes that the estimated burden hours would be approximately the same as noted under OMB control number 0910–0338 for a 351(a) application—860 hours. The burden estimates for seeking licensure of a proposed biosimilar product that meets the standards for interchangeability under section 351(k)(2)(B) and (k)(4) would also be 860 hours. Until we gain more experience with biosimilar applications, FDA believes this estimate is appropriate for 351(k) applications because to determine biosimilarity or interchangeability of a proposed 351(k) product, the application and the information submitted is expected to be comparably complex and technically demanding as a proposed 351(a) application. FDA may determine, in its discretion, that an element required under a 351(k) application to be unnecessary to support licensure of a biosimilar or interchangeable product. In those cases, the number of hours per response may be less than the hours estimated.

A summary of the collection of information requirements in the submission of a 351(k) application as described under the BPCI Act follows:

Section 351(k)(2)(A)(i) requires manufactures of 351(k) products to

submit an application for FDA review and licensure before marketing a biosimilar product. An application submitted under this section shall include information demonstrating that:

- The biological product is biosimilar to a reference product based upon data derived from analytical studies, animal studies (including toxicity) and a clinical study or studies (including immunogenicity and pharmacokinetics or pharmacodynamics). The Secretary of Health and Human Services (the Secretary) may determine that any of these elements is unnecessary.
- The biological product and reference product utilize the same mechanism or mechanisms of action for the condition or conditions of use prescribed, recommended, or suggested in the proposed labeling, but only to the extent the mechanism or mechanisms of action are known for the reference product.
- The condition or conditions of use prescribed, recommended, or suggested in the labeling proposed for the biological product have been previously approved for the reference product.
- The route of administration, the dosage form, and the strength of the biological product are the same as those of the reference product.
- The facility in which the biological product is manufactured, processed, packed, or held meets standards designed to assure that the biological product continues to be safe, pure, and potent.

Section 351(k)(2)(A)(iii) requires the application to include publicly-available information regarding the Secretary's previous determination that the reference product is safe, pure, and potent. The application may include any additional information in support of the application, including publicly-available information with respect to the reference product or another biological product.

Under section 351(k)(2)(B) and (k)(4), a manufacturer may include information demonstrating that the biological product meets the standards for interchangeability either in the application described above to show biosimilarity, or in a supplement to such an application. The information submitted to meet the standard for interchangeability must show that: (1) The biological product is biosimilar to the reference product and can be expected to produce the same clinical result as the reference product in any given patient and (2) for a biological product that is administered more than once to an individual, the risk in terms of safety or diminished efficacy of alternating or switching between use of the biological product and the reference product is not greater than the risk of using the reference product without such alternation or switch.

In addition to the collection of information regarding the submission of a 351(k) application for a proposed biosimilar or interchangeable biological product, section 351(l) of the BPCI Act establishes procedures for identifying and resolving patent disputes involving applications submitted under section 351(k) of the PHS Act. The burden estimates for the patent provisions under section 351(l)(6)(C) of the BPCI Act are included in table 1 of this document and are based on the estimated number of 351(k) biosimilar respondents. Based on similar reporting requirements, FDA estimates this notification will take 2 hours. A summary of the collection of information requirements under 351(l)(6)(C) follows:

Not later than 30 days after a complaint from the reference product sponsor is served to a 351(k) applicant in an action for patent infringement described under 351(l)(6), section 351(l)(6)(C) requires that the 351(k) applicant provide the Secretary with notice and a copy of such complaint. The Secretary shall publish in the **Federal Register** notice any complaint received under 351(l)(6)(C)(i).

FDA has not received any 351(k) applications to date. Under table 1 of this document, the estimated number of respondents submitting 351(k) applications is based on the estimated annual number of manufacturers that would submit the required information to FDA and the estimated annual number of 351(k) submissions FDA would receive. In making this estimate, FDA has taken into account, among other things, the expiration dates of patents that relate to potential reference products, and general market interest in biological products that could be candidates for 351(k) applications.

On November 2 and 3, 2010, FDA held a public hearing and established a public docket to obtain input on specific issues and challenges associated with the implementation of the BPCI Act. (See Docket No. FDA–2010–N–0477.) Based in part on this input, FDA is announcing elsewhere in this issue of the **Federal Register**, the availability of three draft guidances describing FDA's current interpretation of certain statutory requirements added by the BPCI Act as well as quality and analytical issues, demonstrating biosimilarity, and implementation policy issues. These draft guidances are: ''Biosimilars: Questions and Answers Regarding Implementation of the Biologics Price Competition and Innovation Act of 2009,'' ''Quality Considerations in Demonstrating Biosimilarity to a Reference Protein Product,'' and ''Scientific Considerations in Demonstrating Biosimilarity to a Reference Product.'' The **Federal Register** documents for these guidances reference this **Federal Register** information collection document regarding the burden on the submission of a 351(k) application not otherwise covered by existing OMB approvals. In addition, we note that the draft guidance on ''Scientific Considerations in Demonstrating Biosimilarity to a Reference Product'' recommends that labeling for a product subject to approval under section 351(k) include statements that indicate that: (1) The product is approved as biosimilar to a reference product for stated indication(s) and (2) the product (has or has not) been determined to be interchangeable with the reference product. FDA has determined, under 5 CFR 1320.3(c)(2)), that these labeling recommendations are not ''collections of information'' for the purposes of the PRA because the statements will comprise solely information that FDA will supply to the applicant for the purpose of disclosing it to the public, i.e. FDA's determination upon review of the application submitted under section 351(k), that the product is biosimilar and/or interchangeable to its reference product.

FDA estimates the burden of this collection of information as follows:

TABLE 1—ESTIMATED ANNUAL REPORTING BURDEN [1]

351(k) Application for biosimilars (42 U.S.C. 262(k))	Number of respondents	Number of responses per respondent	Total annual responses	Average burden per response	Total hours
351(k)(2)(A)(i) and (k)(2)(A)(iii)	2	1	2	860	1720
351(k)(2)(B) and (k)(4)	1	1	1	860	860

TABLE 1—ESTIMATED ANNUAL REPORTING BURDEN [1]—Continued

351(k) Application for biosimilars (42 U.S.C. 262(k))	Number of respondents	Number of responses per respondent	Total annual responses	Average burden per response	Total hours
351(l)(6)(C)	2	1	2	2	4

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

Dated: February 9, 2012.

Leslie Kux,

Acting Assistant Commissioner for Policy.

[FR Doc. 2012–3548 Filed 2–14–12; 8:45 am]

BILLING CODE 4160–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2011–D–0605]

Draft Guidance for Industry on Scientific Considerations in Demonstrating Biosimilarity to a Reference Product; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry entitled ''Scientific Considerations in Demonstrating Biosimilarity to a Reference Product.'' This draft guidance is intended to assist sponsors in demonstrating that a proposed therapeutic protein product is biosimilar to a reference product for the purpose of submitting a marketing application through an abbreviated licensure pathway. This draft guidance gives an overview of FDA's approach to determining biosimilarity.

DATES: Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance, submit either electronic or written comments on the draft guidance by April 16, 2012.

ADDRESSES: Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 2201, Silver Spring, MD 20993–0002; or the Office of Communication, Outreach and Development (HFM–40), Center for Biologics Evaluation and Research, Food and Drug Administration, 1401 Rockville Pike, Suite 200N, Rockville, MD 20852–1448. Send one self-addressed adhesive label to assist that office in processing your requests. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the draft guidance document.

Submit electronic comments on the draft guidance to *http://www.regulations.gov*. Submit written comments to the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Sandra Benton, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 6340, Silver Spring, MD 20993–0002, 301–796–1042; or Stephen Ripley, Center for Biologics Evaluation and Research (HFM–17), Food and Drug Administration, 1401 Rockville Pike, Suite 200N, Rockville, MD 20852–1448, 301–827–6210.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled ''Scientific Considerations in Demonstrating Biosimilarity to a Reference Product.'' This draft guidance is intended to assist sponsors in demonstrating that a proposed therapeutic protein product is ''biosimilar'' [1] to a reference product for the purpose of submitting a marketing application through the abbreviated licensure pathway under section 351(k) of the Public Health Service Act (PHS Act) (42 U.S.C. 262(k)).

The Biologics Price Competition and Innovation Act of 2009, enacted as part of the Affordable Care Act (Pub. L. 111–148) on March 23, 2010, created an abbreviated licensure pathway under section 351(k) of the PHS Act for biological products demonstrated to be biosimilar to, or interchangeable with, a reference product. Under this abbreviated licensure pathway, FDA will license a proposed biological product submitted under section 351(k) of the PHS Act if FDA ''determines that the information submitted in the application * * * is sufficient to show that the biological product is biosimilar to the reference product * * *'' and the 351(k) applicant (or other appropriate person) consents to an inspection of the facility that is the subject of the application (i.e., a facility in which the proposed biological product is manufactured, processed, packed, or held).[2] The draft guidance gives an overview of FDA's approach to determining biosimilarity. FDA intends to consider the totality of the evidence submitted in a 351(k) application and is recommending that sponsors use a stepwise approach in their development of biosimilar products. The draft guidance discusses important scientific considerations in demonstrating biosimilarity, including:

- A stepwise approach to demonstrating biosimilarity, which can include a comparison of the proposed therapeutic protein product and the reference product with respect to structure, function, animal toxicity, human pharmacokinetics and pharmacodynamics, clinical immunogenicity, and clinical safety and effectiveness;
- The totality-of-the-evidence approach that FDA will use to review applications for biosimilar products; and
- General scientific principles in conducting comparative structural and functional analysis, animal testing, human pharmacokinetics and pharmacodynamics studies, clinical immunogenicity assessment, and clinical safety and effectiveness studies (including clinical study design issues).

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 Agency's current thinking on scientific considerations in demonstrating biosimilarity to a reference product. It does not create or confer any rights for or on any person

[1] In section 7002(b)(3) of the Patient Protection and Affordable Care Act (Affordable Care Act), Public Law 111–148, ''biosimilar'' or ''biosimilarity'' means ''that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components,'' and that ''there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product.''

[2] Section 7002(a)(2) of the Affordable Care Act, adding section 351(k)(3) of the PHS Act (citing section 351(a)(2)(C) of the PHS Act).