airspace divided by 100 (because the Oceanic rate is expressed per 100 nautical miles).

(b) Distance flown through each segment of Enroute or Oceanic airspace is based on the great circle distance (GCD) from the point of entry into U.S.-controlled airspace to the point of exit from U.S.-controlled airspace based on FAA flight data. Where actual entry and exit points are not available, the FAA will use the best available flight data to calculate the entry and exit points.

(c) The rate for each 100 nautical miles flown through Enroute or Oceanic airspace is:

Time period	Enroute rate	Oceanic rate
Through September 30, 2015	56.86	21.63
October 1, 2015 through September 30, 2016	58.45	23.15
October 1, 2016 through September 30, 2017	60.07	24.77
October 1, 2017 and beyond	61.75	26.51

(d) The formula for the total overflight fee is:

$R_{ij} = E*DE_{ij}/100 + O*DO_{ij}/100$

Where:

R_{ij} = the total fee charged to aircraft flying between entry point i and exit point j.

DE_{ij} = total distance flown through each segment of Enroute airspace between entry point i and exit point j.

DO_{ij} = total distance flown through each segment of Oceanic airspace between entry point i and exit point j.

E and O = the Enroute and Oceanic rates, respectively, set forth in paragraph (c) of this section.

(e) The FAA will review the rates described in this section at least once every 2 years and will adjust them to reflect the current costs and volume of the services provided.

§ 187.55 Overflight fees billing and payment procedures.

(a) The FAA will send an invoice to each user when fees are owed to the FAA. If the FAA cannot identify the user, then an invoice will be sent to the registered owner. Users will be billed at the address of record in the country where the aircraft is registered, unless a billing address is otherwise provided.

(b) The FAA will send an invoice if the monthly (based on Universal Coordinated Time) fees equal or exceed $250.

(c) Payment must be made by one of the methods described in § 187.15(d).

Appendix B to Part 187—[Removed and Reserved]

■ 5. Remove and reserve Appendix B to Part 187.

Issued under authority provided by 49 U.S.C. 106(f) and 45302, in Washington, DC, on August 24, 2015.

David Rickard,

Director, Office of Financial Analysis.

[FR Doc. 2015–21293 Filed 8–27–15; 8:45 am]

BILLING CODE 4910–13–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 299

[Docket No. FDA–2015–N–0648]

RIN 0910–AH25

Designation of Official Names and Proper Names for Certain Biological Products

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is proposing a regulation to designate official names and proper names for certain biological products. These products are filgrastim-sndz (Biologics License Application (BLA) 125553), filgrastim (BLA 103353), tbo-filgrastim (BLA 125294), pegfilgrastim (BLA 125031), epoetin alfa (BLA 103234), and infliximab (BLA 103772). The official names and proper names of these products would include distinguishing suffixes composed of four lowercase letters and would be designated as filgrastim-bflm (BLA 125553), filgrastim-jcwp (BLA 103353), filgrastim-vkzt (BLA 125294), pegfilgrastim-ljfd (BLA 125031), epoetin alfa-cgkn (BLA 103234), and infliximab-hjmt (BLA 103772). Although FDA is continuing to consider the appropriate naming convention for biological products, including how such a convention would be applied retrospectively to currently licensed products, FDA is proposing to take action with respect to these six products because of the need to encourage routine usage of designated suffixes in ordering, prescribing, dispensing, recordkeeping, and pharmacovigilance practices for the biological products subject to this rulemaking, and to avoid inaccurate perceptions of the safety and effectiveness of biological products based on their licensure pathway.

DATES: Submit either electronic or written comments on the proposed rule by November 12, 2015. See section IV of this document for the proposed effective date of any final rule that may publish based on this proposal.

ADDRESSES: You may submit comments by any of the following methods.

Electronic Submissions

Submit electronic comments in the following way:

- *Federal eRulemaking Portal: http://www.regulations.gov.* Follow the instructions for submitting comments.

Written Submissions

Submit written submissions in the following ways:

- *Mail/Hand delivery/Courier (for paper submissions):* Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

Instructions: All submissions received must include the Docket No. FDA–2015–N–0648 for this rulemaking. All comments received may be posted without change to *http://www.regulations.gov,* including any personal information provided. For additional information on submitting comments, see the ''Comments'' heading in section VIII of the **SUPPLEMENTARY INFORMATION** section of this document.

Docket: For access to the docket to read background documents or comments received, go to *http://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 Division of Dockets Management, 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, 301–796–2500.

SUPPLEMENTARY INFORMATION:

I. Background

With the passage of the Biologics Price Competition and Innovation Act of 2009 (BPCI Act), which established an abbreviated licensure pathway for products demonstrated to be biosimilar to or interchangeable with an FDA-licensed reference product, a growing number of biological products will be entering the marketplace.

Section 351(k) of the Public Health Service Act (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 or a supplement for a proposed interchangeable product. Section 351(i) of the PHS Act 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 (section 351(i)(2) of the PHS Act). To meet the additional standard of interchangeability, an applicant must provide sufficient information to demonstrate biosimilarity and also to demonstrate that the biological product can be expected to produce the same clinical result as the reference product in any given patient and, if the 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 biological product and the reference product is not greater than the risk of using the reference product without such alternation or switch (section 351(k)(4) of the PHS Act). Interchangeable products may be substituted for the reference product by a pharmacist without the intervention of the prescribing health care provider (section 351(i)(3) of the PHS Act).

During FDA's implementation of the BPCI Act, the Agency has opened several dockets to solicit comments on issues related to the naming of biological products licensed under section 351(k) of the PHS Act.[1]

FDA also has received several citizen petitions directed to the nonproprietary naming of biosimilar products. The citizen petition submitted by Johnson & Johnson requests that FDA require biosimilar products to bear nonproprietary names that are similar to, but not the same as, those of their reference products or of other biosimilars (see Docket No. FDA–2014–P–0077, available at *http://www.regulations.gov*). The citizen petitions submitted by the Generic Pharmaceutical Association and Novartis request that FDA require biosimilar products to be identified by the same nonproprietary name as their reference products (see Docket Nos. FDA–2013–P–1153 and FDA–2013–P–1398, respectively, available at *http://www.regulations.gov*). Novartis supplemented its petition to propose a unique name for all biologics and biosimilars, such that if a biosimilar sponsor elected not to use a unique proprietary name for its product, FDA should assign a unique nonproprietary name composed of the reference product nonproprietary name supplemented with a distinguishable suffix linked to the biosimilar sponsor so that it can be differentiated from the reference product. While FDA is proposing to designate distinguishable nonproprietary names for the six biological products that are the subject of this rulemaking for the reasons discussed in this document, FDA is continuing to consider the issues raised by these citizen petitions and the comments submitted to the corresponding public dockets with respect to establishing a general naming convention for biological products.

In a separate notice published elsewhere in this issue of the **Federal Register,** FDA announced the availability of a draft guidance document entitled ''Nonproprietary Naming of Biological Products'' (draft guidance). The draft guidance describes FDA's current thinking and requests additional public comment on the Agency's proposal to implement a naming convention of a proper name that will include a core name and a designated suffix for all biological products within the scope of the guidance. For originator products, FDA intends to use a core name that is the name adopted by the United States Adopted Names (USAN) Council for the drug substance when available. If the biological product is a related biological product,[2] a biosimilar product, or an interchangeable product, the core name will be the name of the drug substance contained in the relevant previously licensed product. As described in the draft guidance, a designated suffix composed of four lowercase letters will be added to the core name of each product and will be attached with a hyphen. Importantly, use of a shared core name would indicate a relationship among products. The placement of the identifier as a suffix should result in biological products with the same core name being grouped together in electronic databases to help health care providers identify these products. The draft guidance states that FDA intends to apply the naming convention described in the guidance to interchangeable products and is considering comment on two alternative approaches: A unique suffix that distinguishes an interchangeable product from other products sharing the same core name, or a suffix shared with the reference product.

While the draft guidance describes a naming convention in which the designated suffixes would be devoid of meaning, the notice of availability for the draft guidance invites comment not only on that naming convention but also on the benefits and challenges of alternate approaches, including meaningful suffixes such as a suffix derived from the name of the license holder.

The draft guidance describes FDA's rationale for the proposed naming convention and requests public comment on FDA's intention to apply this convention to biological products previously licensed and newly licensed under section 351(a) or section 351(k) of the PHS Act. The draft guidance explains that FDA is continuing to consider the most effective regulatory approach to implement the naming convention for previously licensed biological products, and FDA encourages interested parties to submit comments on biological product naming issues to the public docket established for the draft guidance (Docket No. FDA–2013–D–1543, available at *http://www.regulations.gov*).

For the reasons described in the following section, FDA believes it is necessary at this time to designate official names and proper names for the

[1] See, *e.g.,* notices that published in the **Federal Register** ''Approval Pathway for Biosimilar and Interchangeable Biological Products; Public Hearing; Request for Comments'' (75 FR 61497, October 5, 2010) and ''Draft Guidances Relating to the Development of Biosimilar Products; Public Hearing; Request for Comments'' (77 FR 12853, March 2, 2012) and other public dockets established by FDA.

[2] A ''related biological product'' is described in the guidance as a biological product submitted in a BLA under section 351(a) of the PHS Act (*i.e.,* a ''stand-alone'' BLA) for which there is a previously licensed biological product submitted in a different section 351(a) BLA that contains a drug substance for which certain nomenclature conventions (*e.g.,* USAN Guiding Principles) would be expected to provide for use of the same drug substance name. An ''originator biological product'' is defined as a biological product submitted in a BLA under section 351(a) of the PHS Act (*i.e.,* a ''stand-alone'' BLA) for which there is no previously licensed biological product submitted under section 351(a) that is a related biological product. FDA uses these definitions for purposes of this notice.

six biological products described in this proposed rule.

II. Description of the Proposed Rule

This proposed rule would designate the official names and the proper names of six biological products that fall under one of the following categories: (1) A reference product for an approved or publicly disclosed section 351(k) application (*i.e.,* filgrastim (BLA 103353), pegfilgrastim (BLA 125031), infliximab (BLA 103772), and epoetin alfa (BLA 103234)); (2) a related biological product to one of these reference products (*i.e.,* tbo-filgrastim (BLA 125294)); or (3) a biosimilar product (*i.e.,* filgrastim-sndz (BLA 125553)).[3]

Section 508 of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 358), which applies to biological products pursuant to section 351(j) of the PHS Act, provides FDA with authority to designate official names for drugs if it determines that such action is necessary or desirable in the interest of usefulness and simplicity. Section 508 further specifies that any official name designated under that section shall be the only official name of that drug used in any official compendium published after such name has been prescribed or for any other purpose of this chapter. Under § 299.4(e) (21 CFR 299.4(e)), FDA will publish official names under the provisions of section 508 of the FD&C Act when the Agency determines, among other bases, that the USAN or other official or common or usual name is unduly complex or is not useful for any other reason.

For biological products licensed under the PHS Act, FDA designates the proper name in the license for use upon each package of the biological product (see section 351(a)(1)(B)(i) of the PHS Act and 21 CFR 600.3(k)). The proper name of a biological product reflects certain scientific characteristics of the product, such as chemical structure and pharmacological properties. Among other things, the proper name of a biological product helps health care providers identify the product's drug substance and distinguish biological products from one another. Although FDA typically designates the proper name of a product upon its licensure, FDA also has the authority to designate proper names for biological products through regulation (see, *e.g.,* designation of proper names for various products in 21 CFR part 640).

A. Basis for the Designation of Distinguishable Names for Certain Biological Products

1. Safe Use

Biological products generally consist of large, complex molecules and can raise unique safety concerns related to immunogenicity. FDA believes that the nonproprietary naming convention for the biological products described in this proposed rule should help prevent inadvertent substitution, which may lead to unintended switching or alternating of biological products that have not been determined by FDA to be interchangeable with each other. FDA believes this naming convention will help to facilitate safe use and protect the safety of patients.

Inadvertent switching between biological products that have not been shown to be interchangeable may affect immune response. For example, in some instances, immune responses to therapeutic proteins may pose safety and efficacy issues (Ref. 1). For example, immune responses can lead to significant clinical consequences, such as pure red cell aplasia; inhibition of the efficacy of therapeutics; and reactions, including serum sickness and anaphylaxis (Ref. 1). Individual patients can vary in their immune responses to protein products, and these differences can be caused by the same genetic components that have an impact on sensitivity to small changes in structure (Ref. 2). Thus, switching or alternating of biological products not determined by FDA to be interchangeable may raise unique safety concerns related to immunogenicity.

If originator biological products, related biological products, and biosimilar products share the same proper name, a patient could receive a product different from what was intended to be prescribed, leading to medication errors. For example, this could occur if a biosimilar product were licensed for fewer than all of the indications and routes of administration for which its reference product is licensed, or is packaged in a different delivery system (*e.g.,* a pre-filled syringe instead of a vial) than approved for its reference product, which may lead to confusion and dosing errors. A related biological product also may be licensed for different indications than an originator biological product and may have different dosage forms or strengths than an originator biological product. Confusion may also arise among health care providers who, based on their experience with small-molecule drugs and generic versions of those drugs, may incorrectly assume the use of the same proper name to mean that the biological products are interchangeable.

Thus, FDA has determined that designation of a proper name containing a distinguishing identifier for these six biological products is the best mechanism to facilitate their safe use. FDA believes that incorporating a distinguishing suffix into the nonproprietary names of these six biological products will increase the likelihood that the intended biological product will be prescribed and will not be inadvertently substituted at the dispensing or product administration level. Specifically, FDA believes that incorporation of these suffixes into the nonproprietary product names listed in prescribing, ordering, and dispensing systems will assist prescribers in selecting the specific intended product, pharmacists in dispensing the correct product, and health care providers in administering the correct product.

Health care providers and information technology specialists who program electronic databases can consult the Purple Book (Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations), an online resource that lists all FDA-licensed biological products by their nonproprietary name and clearly identifies products that have been approved as biosimilar to or interchangeable with a particular reference product.

2. Pharmacovigilance

The Agency considers appropriate pharmacovigilance fundamentally important for all biological products. Although safety of drug and biological products is rigorously assessed prior to approval, safety issues that are specific to a manufacturer may arise after approval with any marketed product. Therefore, a robust pharmacovigilance program is essential to help ensure patient safety. To ensure continued safety of a biological product, appropriate pharmacovigilance necessitates that FDA be able to track adverse events to a specific manufacturer (and, as appropriate, site or lot for a particular biological product), and that surveillance systems be able to detect safety signals throughout the lifecycle of a product, so that the Agency and the manufacturer

[3] FDA recognizes that a limited number of previously licensed biological products share the same proper name. As described in the draft guidance, FDA intends to apply the naming convention to biological products previously licensed under section 351(a) of the PHS Act, and is continuing to consider the most effective regulatory approach. In the meantime, FDA is proposing to assign distinguishing identifiers to biological products that are referenced by approved or publicly disclosed section 351(k) applications and any related biological products to those reference products.

can act swiftly and in a targeted manner to identify and address a problem.

Pharmacovigilance systems, both active and passive, vary in their use of identifiers to differentiate among biological products; these identifiers may include the brand (proprietary) name, proper (nonproprietary) name, manufacturer, national drug code (NDC) number, lot number, and billing codes. Successful use of active pharmacovigilance systems (such as FDA's Sentinel system) for adverse event tracking relies on the standardized coding systems for capturing drug information in administrative and health care claims and billing records. These coding systems may vary based on the setting in which a drug is dispensed. Many therapeutic biological products are administered in settings, such as physician offices, clinics, or hospitals, where the administrative and billing data do not routinely include product identifiers such as brand name, manufacturer, NDC number, or lot number (Refs. 3 and 4). Thus, active pharmacovigilance systems that use administrative and billing data currently have limited ability to track biological products that share the same nonproprietary name to the manufacturer.

Similarly, in many passive pharmacovigilance systems, proprietary names and NDC numbers are often not included in adverse event reports (Refs. 5 and 6). FDA uses the FDA Adverse Event Reporting System, a ''passive'' surveillance system that compiles mandatory adverse event reports from manufacturers and voluntary reports submitted directly to FDA by health care professionals and patients. FDA requires manufacturers and others with mandatory reporting obligations to submit an adverse event report to FDA when a minimum of four elements (identifiable patient, identifiable reporter, suspect product, and an event or fatal outcome) are present, even if other required elements, such as NDC numbers, are not available. It is well known that many reports lack key information and that the information identifying products in spontaneous reports can be unreliable (Ref. 6). Proprietary names, even when included, may not reliably identify products in spontaneous adverse event reports since misattribution can occur with adverse event reporting. Furthermore, because national health care systems, health care professional organizations, and patient safety organizations recommend the use of nonproprietary names for prescribing and listing of drug products, the nonproprietary name may be the name used by some reporters to identify the drug products in the adverse event reports (Refs. 7 and 8). In addition, although NDC numbers can be used to identify manufacturer-specific information about a product, they are infrequently provided in spontaneous adverse event reports, and may not be available to the reporter at the time of reporting, or during followup with the reporter. As a result, the use of distinct proprietary names or NDC numbers is currently insufficient to address all concerns regarding pharmacovigilance. Distinguishable nonproprietary names for the biological products in this rulemaking would provide another critical tool in uniquely identifying these biological products. Use of such names for the biological products in this rulemaking would preserve the ability to detect both product-specific safety signals and class effects, and would facilitate prompt evaluation of safety signals in passive and active postmarketing surveillance systems.

Although FDA believes the use of distinguishable nonproprietary names for originator biological products, related biological products, and biosimilar products could improve pharmacovigilance, FDA is interested in comments addressing whether any potential alternative approaches such as increased use of NDC numbers and/or other tracking information would also improve pharmacovigilance of these products.

3. Additional Benefits of Consistent Naming Convention for These Biological Products

FDA believes that it is important to initiate and encourage routine usage of designated suffixes in ordering, prescribing, dispensing, recordkeeping, and pharmacovigilance practices for these six biological products. The designated suffix would provide a consistent, readily available, and recognizable mechanism for health care professionals (including providers and pharmacists) and patients to correctly identify these biological products, regardless of their licensure pathway. The consistent use of a designated suffix for these biological products would remove ambiguity about the identity of the intended biological product. If a core name was used without such identifier, it may be unclear whether the originator product, a related biological product, or a biosimilar product was intended to be ordered, prescribed, dispensed, administered, or reported.

This naming convention would have the added benefit of avoiding inaccurate perceptions of the safety and effectiveness of biological products based on their licensure pathway. The safety and effectiveness of biological products is rigorously assessed before approval. A number of comments have expressed concern that requiring distinguishable proper names only for biosimilar products would adversely affect health care provider and patient use of these new products (Ref. 9). FDA shares the concern that such an approach could lead to inaccurate and scientifically unfounded assertions of inferiority or clinically meaningful differences of an approved biosimilar product for its approved indications. FDA anticipates that use of proper names with designated suffixes for these originator biological products, related biological products, and biosimilar products, irrespective of their licensure pathway, would help avoid any inaccurate perceptions of the safety and effectiveness of biological products based on licensure pathway and thus address concerns raised by the comments.

B. Designation of Official Names and Proper Names for Certain Biological Products

We are proposing to add subpart B on Designated Names and proposed § 299.20 (21 CFR 299.20) to designate the official names and proper names of certain biological products. The six biological products included in proposed § 299.20 have been selected because they fall under one of the following categories: (1) Reference product for an approved or publicly disclosed section 351(k) application (*i.e.,* filgrastim (BLA 103353), epoetin alfa (BLA 103234), infliximab (BLA 103772), and pegfilgrastim (BLA 125031)); (2) related biological product to one of these reference products (*i.e.,* tbo-filgrastim (BLA 125294)); or (3) biosimilar product (*i.e.,* filgrastim-sndz (BLA 125553)).

We are proposing to designate the official name of ''filgrastim-jcwp'' for the biological product licensed under BLA 103353, held by Amgen, Inc. (Amgen) and to change the proper name designated in the license from ''filgrastim'' to ''filgrastim-jcwp.'' Filgrastim, marketed as NEUPOGEN, is the reference product for ZARXIO (filgrastim-sndz), a biosimilar product recently licensed under section 351(k) of the PHS Act.

We also are proposing to designate the official name of ''filgrastim-vkzt'' for the biological product licensed under BLA 125294, held by Sicor Biotech, UAB, and to change the proper name designated in the license from ''tbo-filgrastim'' to ''filgrastim-vkzt.'' Tbo-filgrastim, marketed as GRANIX, is a related biological product. FDA has

determined that the current names of filgrastim and tbo-filgrastim are not useful within the meaning of section 508 of the FD&C Act. Although these products are distinguished from each other and from filgrastim-sndz, FDA believes that the addition of a distinguishing suffix to both names, and the elimination of the prefix from tbo-filgrastim, would avoid confusion regarding these products' relationships to one another and to filgrastim-sndz. The placement of the identifier as a suffix should result in an originator product, a related biological product, and a biosimilar product being grouped together in electronic databases, yet remaining distinguishable, which should help health care providers identify these products. Also, assignment of suffixes to all filgrastim products would help avoid a potential inaccurate perception that filgrastim-sndz, or any other biosimilar product that may be licensed in the future, differs in a clinically meaningful way from its reference product or is inferior for its approved conditions of use.

In addition, we are proposing to designate the official name of ''filgrastim-bflm'' for the biological product licensed under BLA 125553, held by Sandoz, Inc., and to change the proper name designated in the license from ''filgrastim-sndz'' to ''filgrastim-bflm.'' Filgrastim-sndz, marketed as ZARXIO, is a biosimilar product recently licensed under section 351(k) of the PHS Act, and the distinguishing suffix designated at the time of licensure was derived from the name of the license holder. In light of FDA's current proposal to designate official names and proper names for five other biological products that would include distinguishing suffixes devoid of meaning, in the interest of usefulness and simplicity the name ''filgrastim-bflm'' should be designated as the official name and the proper name and codified with the names designated for filgrastim and tbo-filgrastim in proposed § 299.20.

We are proposing to designate the official names and change the proper names for three other reference products for section 351(k) applications that have been publicly disclosed. These reference products are epoetin alfa (BLA 103234), infliximab (BLA 103772), and pegfilgrastim (BLA 125031). We are proposing to designate the official name of ''epoetin alfa-cgkn'' for the biological product licensed under BLA 103234, held by Amgen and marketed as EPOGEN and PROCRIT, and to change the proper name designated in the license from ''epoetin alfa'' to ''epoetin alfa-cgkn.'' We also are proposing to designate the official name of ''infliximab-hjmt'' for the biological product licensed under BLA 103772, held by Janssen Biotech, Inc. and marketed as REMICADE, and to change the proper name designated in the license from ''infliximab'' to ''infliximab-hjmt.'' Finally, we are proposing to designate the official name of ''pegfilgrastim-ljfd'' for the biological product licensed under BLA 125031, held by Amgen and marketed as NEULASTA, and to change the proper name designated in the license from ''pegfilgrastim'' to ''pegfilgrastim-ljfd.''

FDA has determined that the current names of ''epoetin alfa,'' ''infliximab,'' and ''pegfilgrastim'' are not useful within the meaning of section 508 of the FD&C Act. Considerations similar to those described for filgrastim and tbo-filgrastim warrant the designation of official names and proper names that include distinguishing suffixes for pegfilgrastim, epoetin alfa, and infliximab. These products are the reference products for publicly disclosed applications under section 351(k) of the PHS Act (Ref. 10). FDA believes that it is important to initiate and encourage routine usage of designated suffixes in ordering, prescribing, dispensing, recordkeeping, and pharmacovigilance practices for these products. Also, in the event that a biosimilar product is approved that relies upon one of these products as a reference product, assignment of designated suffixes to the reference products would help avoid potential inaccurate perceptions that any biosimilar product with a proper name that features a distinguishing suffix differs in a clinically meaningful way or is inferior for its approved conditions of use. Accordingly, in the interest of usefulness and simplicity, FDA is proposing to designate official names with designated suffixes that would also be designated as the proper names for these products.

The official names and proper names in proposed § 299.20 include designated suffixes composed of four lowercase letters. The official names and proper names, if finalized, will appear on all labeling and marketing materials for these products where the product's proper name or drug substance name is provided.

In addition, FDA also has determined that the following alternative names that include distinguishing suffixes devoid of meaning may be acceptable for these products: epoetin alfa-mkdv, filgrastim-gknh, filgrastim-kbhj, filgrastim-zbdt, infliximab-djfg, and pegfilgrastim-vjbk.

FDA is also considering an alternative nonproprietary naming format for biological products in which the suffix attached to the core name would be derived from the name of the license holder listed on the license. Under this alternative naming format, the official names and proper names for the six products that are the subject of this proposed rule could be as follows:

BLA Number and holder	Official name and proper name
103234, Amgen, Inc.	epoetin alfa-amgn.
103353, Amgen, Inc.	filgrastim-amgn.
125553, Sandoz, Inc.	filgrastim-sndz.
125294, Sicor Biotech UAB	filgrastim-srbt.
103772, Janssen Biotech, Inc.	infliximab-jnsn.
125031, Amgen, Inc.	pegfilgrastim-amgn.

Each of the official names and proper names in proposed § 299.20 and each the alternative official names and proper names discussed previously was rigorously evaluated and determined unlikely to be a source of errors. Each of these official names and proper names (core name-suffix) would be sufficiently distinct from the nonproprietary names of other products. The designated suffixes are distinct from other drug substance names, do not look similar to the names of other currently marketed products, are sufficiently distinct from other suffix designations, and do not include any abbreviations commonly used in clinical practice in a manner that may lead the suffix to be misinterpreted as another element on the prescription or order.

While alternative official names and proper names are described in this preamble to the proposed rule, the final rule would designate a single official name that also would be designated as the proper name for each product.

FDA invites comment on the proposed official names and proper names for these products, including the alternative names listed previously and any other proposed names containing suffixes composed of four lowercase letters that would accomplish the objectives stated in this document. In particular, FDA invites comment on the benefits and challenges of designating a distinguishing suffix that is unique to each of these six biological products versus designating a distinguishing suffix that is shared by each product manufactured by a single license holder (*i.e.,* the three biological products manufactured by Amgen). FDA also invites comment on whether meaningful suffixes (*e.g.,* suffixes derived from the names of the license holders) would be expected to be more memorable or useful to health care providers or patients than suffixes devoid of meaning, and therefore be more useful for facilitating the safe use and appropriate pharmacovigilance of these products. FDA further requests comment on whether meaningful suffixes derived from the name of the license holder might create inappropriate market advantages that would impede biosimilar products' acceptance in the market.

Following approval of a BLA supplement to update product labeling with the official name and proper name designated in any final rule, FDA would take steps to ensure that its drug listings that interface with other databases and systems reflect the newly designated nonproprietary name. FDA also would work with other governmental organizations and external stakeholders that play a role in national drug naming or listings to help ensure that the official name and proper name for the product is displayed accurately in drug listing systems. We invite comment on the best means of coordinating with external stakeholders that play a role in drug naming and listing to achieve this objective considering, among other things, any transition period before market availability of products labeled with the newly designated nonproprietary names.

III. Legal Authority

Section 508 of the FD&C Act and section 351 of the PHS Act serve as the principal legal authorities for this proposed rule. Section 508 of the FD&C Act, which applies to biological products pursuant to section 351(j) of the PHS Act, provides FDA with authority to designate official names for drugs if it determines that such action is necessary or desirable in the interest of usefulness and simplicity. For the reasons described previously, FDA has determined that the interest of usefulness and simplicity warrants the designation of official names for the products included in this rulemaking. FDA also has authority under section 351(a) of the PHS Act to designate the proper name of a biological product and may do so through rulemaking. FDA is exercising this authority to designate matching proper names for these products.

Thus, section 508 of FD&C Act and section 351 of the PHS Act, in conjunction with FDA's general rulemaking authority in section 701(a) of the FD&C Act (21 U.S.C. 371(a)), provide legal authority for this proposed rule.

IV. Effective Date

FDA proposes that any final rule that may be issued based on this proposal become effective 90 days after the date of its publication in the **Federal Register**. During the 90-day period after publication of any final rule, FDA expects that BLA holders for these six products would submit a prior approval supplement to their BLA to update the labeling of their product. After approval of the supplement, FDA intends to work with sponsors to minimize any manufacturing and distribution disruptions related to the implementation of new labeling and any related marketing materials. FDA expects that manufacturers will implement the new labeling at the time of their next manufacturing run and does not intend to object to manufacturers exhausting existing inventories of finished product that is not labeled with the official names and proper names designated by this rule.

V. Environmental Impact

The Agency has determined under 21 CFR 25.30(h) and (k) and 25.31(a) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

VI. Economic Analysis of Impacts: Summary

FDA has examined the impacts of the proposed rule under Executive Order 12866, Executive Order 13563, the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act of 1995 (Pub. L. 104–4). Executive Orders 12866 and 13563 direct Agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). The Office of Management and Budget (OMB) has determined that this proposed rule is a significant regulatory action as defined by Executive Order 12866.

The Regulatory Flexibility Act requires Agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because the proposed rule imposes one-time relabeling costs on one small business, the Agency proposes to certify that the final rule will not have a significant economic impact on a substantial number of small entities.

Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that Agencies prepare a written statement, which includes an assessment of anticipated costs and benefits, before proposing ''any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted annually for inflation) in any one year.'' The current threshold after adjustment for inflation is $144 million, using the most current (2014) Implicit Price Deflator for the Gross Domestic Product. FDA does not expect this proposed rule to result in any 1-year expenditure that would meet or exceed this amount.

We estimate the one-time costs of learning about the rule; submitting labeling supplements, forms, and revised marketing materials to FDA; changing labeling on affected products; FDA review of labeling supplements, forms, and revised marketing materials; and activities to educate practitioners about name changes. The one-time costs range from $0.78 million to $3.04 million. Over 10 years, the annualized costs range from $0.10 million to $0.40 million with a 7 percent discount rate, and from $0.09 million to $0.35 million with a 3 percent discount rate.

We expect the rule would have other costs that are not yet included in these estimated costs. Additional costs to industry may include costs updating prescribing and reimbursement systems to reflect the new names and changing marketing materials to reflect the new names.

We lack data to quantify the benefits of the proposed rule. In the event of biosimilar entry, the name changes for certain products that would be required by this proposed rule may help mitigate a potential competitive disadvantage for

biosimilar products that receive a nonproprietary name that includes a distinguishing suffix. More competition between the biosimilar product and the reference product may reduce the price and increase the usage of those products. The proposed rule may also encourage the routine use of suffixes for these six biological products, which may facilitate more accurate prescribing and monitoring of these six biological products if biosimilar products enter the market.

TABLE 1—SUMMARY OF COSTS [1]

Total benefits	One-time costs ($ mil)		Total annualized costs over 10 years with 3 percent discount rate ($ mil)		Total annualized costs over 10 years with 7 percent discount rate ($ mil)	
	Low estimate	High estimate	Low estimate	High estimate	Low estimate	High estimate
Not estimated	0.78	3.04	0.09	0.35	0.10	0.40

[1] **Note:** Costs are rounded.

The Economic Analysis of Impacts of the proposed rule performed in accordance with Executive Order 12866, Executive Order 13563, the Regulatory Flexibility Act, and the Unfunded Mandates Reform Act is available at *http://www.regulations.gov* under Docket No. FDA–2015–N–0648 and at *http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/EconomicAnalyses/default.htm* (Ref. 11).

VII. Paperwork Reduction Act of 1995

FDA tentatively concludes that this proposed rule contains no new collection of information. The official names and proper names of each of these biological products, as designated by the proposed rule, would be information originally supplied by the Federal government to the recipient for the purpose of disclosure to the public, and the public disclosure of such information is not a ''collection of information'' within the meaning of the Paperwork Reduction Act of 1995 (the PRA). See 5 CFR 1320.3(c)(2). Therefore, clearance by the OMB under the PRA (44 U.S.C. 3501–3520) is not required.

The discussion of effective date in the preamble (section IV) to this proposed rule references certain actions that would be taken by manufacturers and applicants for the specific approved biological products for which this proposed rule would designate official names and proper names, in order to comply with existing FDA regulations that contain collections of information that are subject to review by OMB under the PRA.

Specifically, prior to the effective date of any final rule based on this proposal, a prior approval supplement would be submitted in accordance with § 601.12 (21 CFR 601.12) for each of six specific BLAs referenced in this rule, to update the labeling of the product (which includes the immediate container label and outer container or package) with the designated official name and proper name. The submission of supplements to approved license applications under § 601.12 is approved under OMB control number 0910–0338. We estimate that this rulemaking would result in the one-time submission of six supplements. In conjunction with our previously approved collection of information under § 601.12, we estimated that each such supplement would incur a burden of 40 hours.

The discussion of effective date also acknowledges that these applicants would revise their labeling, which includes the immediate container label and outer container or package, to reflect the newly designated official names and proper names. (As noted, disclosing the official names and proper names of each of these biological products to the public is not a ''collection of information'' within the meaning of the PRA. See 5 CFR 1320.3(c)(2).) The design and testing of prescription drug labeling required under §§ 201.56 and 201.57 (21 CFR 201.56 and 201.57) (including § 201.56(a)(2)) is approved under OMB control number 0910–0572. Concerning the immediate container label and outer container or package, in the **Federal Register** of December 18, 2014 (79 FR 75506), we published a proposed rule on the electronic distribution of prescribing information for human prescription drugs, including biological products. In section VII, ''Paperwork Reduction Act of 1995,'' we estimated the burden to design (including revisions), test, and produce the label for a drug's immediate container and outer container or package, as set forth in 21 CFR part 201 and other sections in subpart A and subpart B.

VIII. Comments

Interested persons may submit either electronic comments regarding this document to *http://www.regulations.gov* or written comments to the Division of Dockets Management (see **ADDRESSES**). It is only necessary to send one set of comments. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at *http://www.regulations.gov.*

IX. Federalism

FDA has analyzed this proposed rule in accordance with the principles set forth in Executive Order 13132. FDA has determined that the proposed rule, if finalized, would not contain policies that would have substantial direct effects on the States, on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of government. Accordingly, the Agency tentatively concludes that the proposed rule does not contain policies that have federalism implications as defined in the Executive order and, consequently, a federalism summary impact statement is not required.

X. References

The following references have been placed on display in the Division of Dockets Management (see **ADDRESSES**) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday. (FDA has verified all the Web site addresses in this reference section, but FDA is not responsible for any subsequent changes to the Web sites after this document publishes in the **Federal Register**.)

1. FDA, Guidance for Industry, ''Immunogenicity Assessment for Therapeutic Protein Products,'' August 2014, available at *http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm338856.pdf.*

2. Buck D., S. Cepok, S. Hoffmann, et al., ''Influence of the HLA–DRB1 Genotype on Antibody Development to Interferon Beta in Multiple Sclerosis.'' *Archives of Neurology,* 68(4):480–487, 2011.

3. Nease, R., S. Miller, and S. G. Frazee, ''2010 Specialty Drug Trend Report.'' Express Scripts Specialty Benefit Services (June 2011).
4. Vora, J. B., ''Evaluation of Medical Specialty Medications: Utilization and Management Opportunities,'' Commissioned by CVS Caremark (April 8, 2014), available at *http://info.cvscaremark.com/insights2014/Singh06-Medical-Specialty-Utilization-and-Management-Opportunities.pdf.*
5. Dal Pan, G. J., M. Lindquist, and K. Gelperin, ''Postmarketing Spontaneous Pharmacovigilance Reporting Systems,'' Chapter 10, in *Pharmacoepidemiology,* 5th ed., edited by B. L. Strom and S. Hennessy. Etobicoke (Canada): John Wiley & Sons; 2012.
6. Getz, K. A., S. Stergiopoulos, and K. I. Kaitin, ''Evaluating the Completeness and Accuracy of MedWatch Data,'' *American Journal of Therapeutics,* 21(6):442–446, 2014.
7. American Society of Health-System Pharmacists (ASHP), ''ASHP Guidelines on Preventing Medication Errors With Chemotherapy and Biotherapy,'' 2014, available at *http://www.ashp.org/DocLibrary/BestPractices/MedMisGdlAntineo.aspx.*
8. Institute for Safe Medication Practices (ISMP), ''ISMP's Guidelines for Standard Order Sets,'' available at *http://ismp.org/tools/guidelines/StandardOrderSets.asp.*
9. See, *e.g.,* Comments from AARP to Docket Nos. FDA–2011–D–0605, FDA–2011–D–0602, and FDA–2011–D–0611 on ''Draft Guidance Documents on Biosimilar Product Development,'' available at *http://www.regulations.gov.*
10. ''Apotex Announces FDA Has Accepted for Filing Its Biosimilar Application for Pegfilgrastim'' (December 17, 2014), available at *http://www.apotex.com/global/about/press/20141217.asp;* ''Hospira Submits New Biologics License Application to U.S. FDA for Proposed Epoetin Alfa Biosimilar,'' *PR Newswire* (January 12, 2015), available at *http://www.prnewswire.com/news-releases/hospira-submits-new-biologics-license-application-to-us-fda-for-proposed-epoetin-alfa-biosimilar-300018991.html;* ''Celltrion Files for US FDA Approval of Remsima®,'' (August 11, 2014), available at *http://www.celltrion.com/en/COMPANY/notice_view.asp?idx=456&code=ennews&intNowPage=1&menu_num=&align_year=all.*
11. ''Preliminary Regulatory Impact Analysis, Initial Regulatory Flexibility Analysis, and Unfunded Mandates Reform Act Analysis for Designation of Official Names and Proper Names for Certain Biological Products; Proposed Rule,'' available at *http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/EconomicAnalyses/default.htm.*

List of Subjects in 21 CFR Part 299

Drugs.

Therefore, under the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act, and under authority delegated to the Commissioner of Food and Drugs, FDA proposes to amend 21 CFR part 299 as follows:

PART 299—DRUGS; OFFICIAL NAMES AND ESTABLISHED NAMES

■ 1. The authority citation for 21 CFR part 299 is revised to read as follows:

Authority: 21 U.S.C. 331, 351, 352, 355, 358, 360b, 371; 42 U.S.C. 262.

■ 2. Add subpart B to Part 299 to read as follows:

Subpart B—Designated Names

§ 299.20 Official names and proper names of certain biological products.

(a) The Food and Drug Administration has designated official names under section 508 of the Federal Food, Drug, and Cosmetic Act for the biological products licensed under section 351 of the Public Health Service Act in the biologics license applications provided in the following list. The official name shall be the proper name designated in the license for use upon each package of the product.

Biologics license application (BLA) number	Official name and proper name
BLA 103234	epoetin alfa-cgkn.
BLA 103353	filgrastim-jcwp.
BLA 125553	filgrastim-bflm.
BLA 125294	filgrastim-vkzt.
BLA 103772	infliximab-hjmt.
BLA 125031	pegfilgrastim-ljfd.

(b) [Reserved]

Dated: August 25, 2015.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2015–21382 Filed 8–27–15; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF THE TREASURY

Internal Revenue Service

26 CFR Part 301

[REG–103033–11]

RIN 1545–BK62

Reportable Transactions Penalties Under Section 6707A

AGENCY: Internal Revenue Service (IRS), Treasury.

ACTION: Notice of proposed rulemaking.

SUMMARY: This document contains proposed regulations that provide guidance regarding the amount of the penalty under section 6707A of the Internal Revenue Code (Code) for failure to include on any return or statement any information required to be disclosed under section 6011 with respect to a reportable transaction. The proposed regulations are necessary to clarify the amount of the penalty under section 6707A, as amended by the Small Business Jobs Act of 2010. The proposed regulations would affect any taxpayer who fails to properly disclose participation in a reportable transaction.

DATES: Written or electronic comments and requests for a public hearing must be received by November 27, 2015.

ADDRESSES: Send submissions to: CC:PA:LPD:PR (REG–103033–11), Room 5205, Internal Revenue Service, P.O. Box 7604, Ben Franklin Station, Washington, DC 20044. Submissions may be hand delivered Monday through Friday between the hours of 8 a.m. and 4 p.m. to CC:PA:LPD:PR (REG–103033–11), Courier's Desk, Internal Revenue Service, 1111 Constitution Avenue NW., Washington, DC, or sent electronically via the Federal eRulemaking Portal at *http://www.regulations.gov* (indicate IRS and REG–103033–11).

FOR FURTHER INFORMATION CONTACT: Concerning the proposed regulations, Melissa Henkel, (202) 317–6844; concerning submissions of comments or requests for a public hearing, Oluwafunmilayo (Funmi) Taylor, (202) 317–6901 (not toll-free numbers).

SUPPLEMENTARY INFORMATION:

Background

This document contains proposed amendments to 26 CFR part 301 under section 6707A of the Internal Revenue Code. Section 6707A was added to the Code by section 811(a) of the American Jobs Creation Act of 2004 (Pub. L. 108–357, 118 Stat. 1418) and was amended