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October 26, 2015

By Electronic Submission

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville, MD 20852

Comments on Draft Guidance for Industry: Nonproprietary Naming of Biological Products [Docket No. FDA-2013-D-1543]

Dear Madam/Sir:

Pfizer Inc (Pfizer) is submitting these comments in response to the Federal Register notice of August 28, 2015 (80 FR 52296 - 52299) on the Draft Guidance for Industry: *Nonproprietary Naming of Biological Products (*Draft Guidance*).*

As a manufacturer of both innovator biologic and biosimilar products, Pfizer appreciates the Agency's proactive approach to resolving the many issues and challenges associated with the implementation of the Biologics Price Competition and Innovation Act of 2009 (BPCI Act). We look forward to future opportunities to provide input as the Agency implements its authorities over biosimilars and interchangeable biosimilars.

Pfizer's comments below include general feedback on the considerations posed in the Federal Register Notice related to approaches for designating and incorporating suffixes retrospectively and prospectively into the nonproprietary names of all biological products, and on ways to improve active pharmacovigilance systems for the purposes of monitoring the safety of biological products. Pfizer also has specific comments on the Draft Guidance.

I. GENERAL COMMENTS RELATED TO FEDERAL REGISTER NOTICE CONSIDERATIONS

1. What are the potential benefits and challenges of designating a suffix in the proper name of a biological product that is:

a) *Devoid of meaning versus meaningful (e.g., a suffix derived from the name of the license holder)*

b) *Unique to each biological product versus unique to each license holder and shared by each biological product manufactured by that license holder.*

In your comments, please address how each option would impact the following: Safe use of biological products; pharmacovigilance; and market acceptance and uptake for certain products.

Pfizer Comment

Pfizer considers it preferable that the four-letter suffix be meaningful and somehow derived from – or in some way related to – the name of the license holder [1]. In our view, a meaningful suffix that is related to the name of the responsible entity would be more easily recognizable to health care professionals and other adverse event (AE) reporters and aid them in appropriately identifying which entity should receive adverse event reports. It would also be helpful in reporting AEs to the FDA directly, as the reporter would be more likely to appropriately identify the manufacturer of the biosimilars if there is a clear and meaningful name.

Although a randomly assigned letter suffix would be better than no unique identifier, Pfizer does not believe a random suffix would achieve accurate and efficient reporting as easily as a meaningful suffix. A randomly assigned suffix would be difficult for patient and providers to remember/recall when reporting if the product was not in front of them. More importantly, it is likely more prone to errors in data collection. Without meaning, letters might be transposed by reporter or receiver. Incorrect entry would limit the usability of large databases to identify all cases related to a single producer of a biological product, which will be critical to perform necessary pharmacovigilance. If the Agency ultimately determines a randomly assigned letter suffix is preferential, Pfizer believes the suffix should be consistent across the company's biological products such that over time it will become associated with the company and make accurate reporting easier.

Pfizer recommends that the suffix for a biological product should be unique to each license holder (or the entity responsible for pharmacovigilance, if different from the license holder) and shared by each biological product in that license holder's portfolio. Importantly, having a single suffix that is used across all biological products manufactured by one company would be preferable for pharmacovigilance purposes. Again, using a single suffix per company would lend familiarity to providers, as well as those inputting data, making it more likely this suffix will be provided accurately and consistently. Further, having a single suffix linked across a company's products would allow for review of data across a portfolio (if

[1] Throughout the document, Pfizer considers license holder could also refer to the entity responsible for pharmacovigilance, if different from the license holder

perhaps there was concern about a process signal common to a portfolio), or for a company to rapidly evaluate the safety profile of its portfolio.

If the Agency opts for a suffix that is linked to the name of the responsible entity, Pfizer requests that the Agency develop a process whereby biologic products could have their suffix changed in certain exceptional situations where the long term benefit of transparency in prescribing and improved pharmacovigilance outweigh the need to manage potential short term issues associated with implementation of a change in suffix (see Table 1, Item 2 for specific examples). This process can be likened to significant labeling changes that occur for a product under similar circumstances.

Pfizer has considered various scenarios and potential hurdles to the implementation of this new naming. The table below (Table 1) highlights some of the complexities that may arise over time and will require consideration by the Agency as it considers the most appropriate approach and how best to implement the nonproprietary naming system for biologics. The first four considerations may arise if the Agency implements a system of designating a suffix in the proper name of a biological product that is meaningful in relation to the name of the license holder. The last two considerations are general comments that would be relevant regardless of the specific naming system the Agency ultimately implements.

Table 1: Complexities of Nonproprietary Naming			
	Consideration	**Discussion/Concern**	**Mitigation/Recommendation**
1.	Derivation of suffix associated with license holder may not always accurately reflect the company responsible for pharmacovigilance (PV)	In most cases the BLA holder is also the entity responsible for pharmacovigilance. However, there are situations where the BLA holder for biological products may not be the entity marketing the product or responsible for pharmacovigilance (PV). The system will only achieve the goals of enhanced PV if products can be accurately and efficiently traced. As such, familiarity to providers and those inputting data should be considered. In certain situations, the license holder and how the public sees the product may differ.	Pfizer suggests the Agency consider the patient / physician / PV perspective in determining the suffix on a case by case basis, rather than solely designating a suffix based on license holder. Consider the following scenario: Company A acquires Company B prior to FDA implementation of this nonproprietary naming proposal. Company A is responsible for the marketing and pharmacovigilance of Company B's biological products. Company A would prefer the suffix of such biological products to relate to the Company A name despite the fact that the BLA lists Company B as the license holder. Pfizer suggests that if the implemented process is to have meaningful suffixes that may in turn be somehow related to company names, then the suffix should reflect the entity responsible for pharmacovigilance, rather than strictly the license holder.

Table 1: Complexities of Nonproprietary Naming			
	Consideration	**Discussion/Concern**	**Mitigation/Recommendation**
2.	Complexities associated with mergers / acquisitions, and transfer of BLAs	There will be scenarios where the entity responsible for the manufacturing and pharmacovigilance of a biological product changes after a suffix has already been assigned to the product. Pfizer has considered whether it would be appropriate to change the suffix under these circumstances or if the suffix should remain unchanged though it would no longer be reflective of the company responsible for the product. The concern with not changing the suffix is that the original Sponsor is no longer in control of the quality of the product. For example, if there are quality issues following the transfer of the license and the original company's suffix is still attached to the product, the public may incorrectly associate the problems with the incorrect company. However, if the suffix were changed, you would potentially have AE reports for a product with different names (old and new suffix), even though the product itself would not have changed.	Pfizer considers this a very complex topic and highly relevant as it is a likely situation the Agency will encounter over time (for example due to a decision to out-license a product or as a result of company acquisitions after the suffix is assigned). Pfizer generally supports that the suffix should not change under most circumstances as changing the suffix could be disruptive, confusing, and has the potential to lead to an incorrect perception that the product has changed. That said Pfizer encourages the Agency to consider this situation carefully and ensure that the system allows for the suffix to be *changeable* on a case by case exceptional basis, following discussion between the Agency and parties of interest. The risk/benefit associated with a change in suffix, in terms of the overall goal of strengthening pharmacovigilance and ensuring safe use of the biological product, should be considered when determining whether or not it is appropriate to change the suffix in a given circumstance. It is also requested that the Agency develop a transparent change process for biologic products to change their suffix if deemed necessary.

Table 1: Complexities of Nonproprietary Naming			
	Consideration	**Discussion/Concern**	**Mitigation/Recommendation**
3.	Similarities in Company names	There could be situations where two companies have similar names and a four letter suffix related to or somehow derived from the company name could cause confusion.	FDA has indicated that the applicant should propose the suffix and has urged applicants to conduct due diligence and request review of proposed suffixes (draft Guidance Section V). Pfizer agrees that the company is best positioned to propose a suffix that is "meaningful." Pfizer also recommends that part of the review process of the proposed suffix should include a public comment period to ensure there is opportunity to raise concerns pertaining to potential for prescribing errors or other major concerns relating to the impact on the safe use of the product. This could be likened to the International Nonproprietary Names (INN) selection process, which includes publishing of newly selected, proposed INNs and a 4-month objection period.
4.	Trademark Considerations	Applicants may have considerations or concerns related to how the suffix might impact their trademark legal rights.	FDA has indicated that the applicant be the one to proposes the suffix. Pfizer supports this approach and considers it especially important if the suffix is to be meaningful in relation to the company name in order to ensure companies have opportunity to protect their company name and trademarks.

Table 1: Complexities of Nonproprietary Naming			
	Consideration	**Discussion/Concern**	**Mitigation/Recommendation**
5.	Labeling Considerations	The guidance notes that application of the naming convention both prospectively and retrospectively will help to encourage routine use of designated suffixes in ordering, prescribing, dispensing, and record keeping practices for these products. It is unclear how the Agency intends to utilize the naming convention in regard to labeling of biological products. For example, would the suffix be used throughout the labels and how would this appear in the label of biosimilar products?	Potential ramifications to labeling should be considered. The Agency should seek further comment on this topic before implementation and should request comment on this topic when the draft Guidance for Industry on Labeling of Biosimilars is released for comment.

Despite the fact that there may be some practical difficulties that will require additional consideration, there is likely no perfect system and Pfizer believes that the advantages of a meaningful suffix somehow derived from – or in some way related to – the name of the license holder, outweigh the potential difficulties. Further, Pfizer believes that a meaningful suffix that is related to the name of the responsible entity would be the best approach to ensure safe use of biological products and effective pharmacovigilance compared to a system relying on randomly derived suffixes per product.

2. What would be the potential benefits and challenges for an interchangeable product to share the same suffix as designated in the proper name of the reference product? Your response should consider that FDA's publicly available electronic resource, the Purple Book, will identify biological products determined by FDA to be biosimilar to or interchangeable with a reference product. If an interchangeable product does share the same suffix as the reference product, how would this impact your responses to question 1, including pharmacovigilance?

Pfizer Comment

The Draft Guidance states:

There is a need to clearly identify biological products to improve pharmacovigilance and, for the purposes of safe use, to clearly differentiate among biological products that have not been determined to be interchangeable (Lines 19-21).

A designation of interchangeability, either at initial licensure or subsequently via the filing of a supplement, does not negate the need to clearly identify biological products made by different manufacturers. For example, there could be product quality issues associated with either the reference product or the interchangeable biosimilar, and different suffixes would allow these to be handled more appropriately and efficiently. As such, it would not be advisable for an interchangeable product to carry the same suffix as designated in the proper name of the reference product.

3. Would there be additional benefits or challenges if the suffix designated in the proper name of a biosimilar product that is subsequently determined to be interchangeable were changed to that of the reference product upon a determination of interchangeability? Would there be benefits or challenges to allowing the manufacturer of the biosimilar product that is subsequently determined to be interchangeable to have the option of retaining its original suffix or adopting the same suffix as the reference product?

Pfizer Comment

As discussed in question two, it would not be advisable for an interchangeable product to carry the same suffix as the reference product. In most circumstances, it would be preferable to maintain the suffix throughout the lifecycle of the product. That said, Pfizer urges the Agency toestablish a consistent policy rather than allowing companies the choice of adopting the reference product suffix or not; inconsistencies in approach would be even less desirable and more impactful to pharmacovigilance.

4. How could FDA and/or other Federal partners improve active pharmacovigilance systems for purposes of monitoring the safety of biological products? For example, because NDC numbers are not routinely recorded in billing and patient records in many clinical settings in which biological products are dispensed and administered, are there other identifiers besides distinguishable nonproprietary names that are routinely accessible by active pharmacovigilance systems and could enable as good as or better pharmacovigilance? How can FDA and/or other Federal partners help ensure that a distinguishable identifier for each biological product would be captured at the point of dispensing or administration to the patient and be routinely accessible in systems used for pharmacovigilance?

Pfizer Comment

Pfizer considers that some form of meaningful suffix, as discussed above, would be helpful for the purposes of monitoring the safety of biological products. The Agency and/or other Federal partners can help ensure better pharmacovigilance by encouraging the use of the distinguishable identifier for each biological product at the point of dispensing or administration to the patient, or by encouraging reporters to consistently use the proper name (core name plus suffix). This can be accomplished through education and/or development of electronic reporting forms that automatically request this information. Given the variety of reporters, and reporting systems, consistent and automated requests to use the proper name (including the suffix), ensuring that the proper name is prominently displayed and used in common parlance (noted in all forms, required for dispensing, etc.), would provide the most assurance of its appropriate adoption over time. Beyond the recording of the distinguishable name, Pfizer also believes that recording of the batch/lot number would help to facilitate the most accurate recording of the specific product(s) used in the treatment of the patient. As such, the FDA, other Federal partners, license holders as well as healthcare professionals and systems should consider this the optimal standard to strive for.

5. What process and reasonable timeframe should FDA use to designate a suffix to include in the nonproprietary name of a previously licensed biological product?

6. What criteria should FDA use to prioritize retrospective application of this naming convention to previously licensed biological products?

7. What are the expected time frames for sponsors of previously licensed biological products to distribute products that conform to this naming convention after approval of a labeling supplement?

Pfizer Comment

Pfizer has consolidated our comments to questions five through seven, which pertain to retrospective application of the proposed naming convention to previously licensed biologics.

The topic of retrospective application has many complexities including, but not limited to, supply chain considerations, stock management, and potential effects on global trade. Pfizer acknowledges there may be unintended consequences of adding the suffix during the lifecycle of the product and that this should be carefully considered. For example, you would potentially have reports for a product with different names (pre and post suffix addition), even though the product itself would not have changed. This could lead to difficulties for pharmacovigilance in terms of potential impact to ease of signal detection and ability to quickly assess and address quality issues that may arise. Further, there could be a misconception that the product has changed. These potential issues will also need to be managed in the rare situation where the suffix must change (see Table 1). However, the long

term benefits of transparency in prescribing and improved pharmacovigilance outweigh the need to manage potential short term issues associated with implementation of the new naming system.

Implementation should be carefully planned to ensure there is no interruption of supply or impact to pharmacovigilance activities. Matters of practical application will need to be carefully thought out; this includes assessment of practicality of changing databases, impact to prescribing, the need to update systems, etc.

The timing of implementation should be considered carefully. Pfizer recommends a phased approach to implementation with measures implemented to ensure that ordering, prescribing, dispensing, and record keeping practices can accommodate a phased approach where some products will have a suffix and others will not.

The timing of retrospective application must also ensure that there is no perception of differences between biosimilars and reference products, or a perception of differences in the reference product over time, based on naming convention. For example, if a biosimilar product receives a suffix on approval and there has not been retrospective application of a suffix to the reference product the public perception may be that the biosimilar is inferior to the reference product. This could hamper the uptake and use of the biosimilar.

For these reasons Pfizer has the following recommendations:

- The Agency should provide some flexibility regarding retrospective application to ensure sponsors can manage internal processes and implement this new naming convention efficiently, and without interruption of supply or impact to pharmacovigilance.
    - Sponsors of previously licensed biological products should have an appropriate timeframe (Pfizer considers up to 2 years reasonable) to implement the requirement to add a new suffix to a nonproprietary name. After approval of a label supplement, new stock of the components will need to be ordered, tested and packaging scheduled. Using standard process times for long-lead time components, the first packaging activities would likely be performed approximately 4-6 months after label supplement approval. Introduction of these packs would be based on downstream market inventory, but would likely be 7-9 months after supplement approval assuming typical lead times and inventory levels.
- Retrospective application should be initiated *no later than* a reference product sponsor is notified of the filing of the first biosimilar or related biological product

application to the originator biological product, and provide for an adequate implementation period.

- The Agency has rightly applied this guidance to all biological products rather than only those licensed as biosimilars under section 351(k) of the PHS Act. Pfizer agrees with the concerns raised by others that requiring distinguishable proper names only for biosimilars "will adversely affect use of these new products by health care providers and patients" (Lines 237-240). This could be misinterpreted to suggest that biosimilar products are inferior. However, if there is a large time lag between the application of the suffix to a newly licensed biosimilar and the retrospective application of a suffix to the previously licensed reference product, this could result in the same unintended consequences. Therefore, the prioritization of retrospective application of suffixes to previously licensed biological products should take biosimilar applications into consideration.

- The Agency should ensure there is a transparent process for proposing, reviewing, and implementing a suffix for the proper name of a biological product

  - The Agency should provide additional guidance regarding the process for requesting feedback on proposed suffixes, and the timeline associated with the process in order to ensure there are not delays caused by implementation. The timeline for the process in particular should be transparent to permit internal planning.

  - Pfizer recommends that part of the review process of the proposed suffix should include a public comment period to ensure opportunity for public comment pertaining to potential for prescribing errors or other major concerns relating to the safe use of the product. This could be likened to the INN selection process, which includes publishing of newly selected, proposed INNs and a 4-month objection period.

  - The Agency should clearly outline the next steps and timing in situations where FDA rejects the suffixes proposed by the Sponsor, and ensure there is sufficient time for the company to respond or propose and implement an alternative suffix during launch planning. Due to the complexity of new product launches, 'last minute' changes to the suffix will unnecessarily delay biosimilar product launches and should be avoided.

- It should be noted that the process and time frames will be dependent on the Agency's policy surrounding the suffix. For example, a single suffix used across a company's portfolio of biological products may have different considerations for

implementation than a system where each biological product must have a new, unique suffix. Pfizer believes that a single suffix per company would be preferable, and easier to implement.

- The Agency should ensure resources for implementation of this process are assessed and considered in the user fee reauthorization processes.

8. What strategies could FDA use to enhance stakeholders' understanding of and education about this naming convention?

Pfizer Comment

Pfizer recommends the following strategies to enhance stakeholders' understanding of and education about this naming convention:

- Development of materials for health care professionals (physicians, nurses, pharmacists and other healthcare providers)
    - These materials should include details about the importance of naming conventions to pharmacovigilance, tracking, etc.
- Development of patient-centered materials to share with patient advocacy groups
    - These materials should include patient-friendly messages regarding the complexity of biologics and importance of naming conventions to patient safety.
- Development of supportive messaging for broad communication platforms
    - These materials would be public facing, to be added to media including Agency website, articles, interviews, webinars, and social media platforms.

9. FDA notes that this naming convention (i.e., use of a suffix) has some similarities to the World Health Organization (WHO) proposal, "Biological Qualifier—An INN Proposal." At the time of publication of this draft guidance, WHO was still evaluating the comments received on its proposal. If WHO adopts a Biological Qualifier proposal, how should the biological qualifiers generated by WHO be considered in the determination of FDA-designated proper names for the biological products within the scope of this guidance?

Pfizer Comment

Pfizer believes that it would be extremely helpful for all regulators and major governing bodies to adopt similar stances and naming conventions globally if at all possible. Pfizer urges the FDA to work with the WHO to find common ground in suffixes and naming conventions; Pfizer further urges FDA to encourage the European Medicines Agency (EMA) to partner with them to agree to a harmonized approach. Partial harmonization should be considered if there are certain aspects of the various proposals that prevent full harmonization. For example, harmonization on the nature of the suffix (random vs meaningful; per product vs per company) would be beneficial even if certain details (such as hyphenation or linkage to the INN) are difficult to globally align.

Global harmonization would be optimal from a pharmacovigilance perspective, by enabling timely signal detection if safety issues were to arise for a particular product or product class. That said, different systems do currently exist globally and the Industry has had experience managing this situation. From a practical/implementation perspective, inability to fully harmonize systems should not prevent implementation of a biological product naming convention system within the United States.

Although a randomly assigned letter suffix would be better than no unique identifier, Pfizer does not believe a random suffix would achieve accurate and efficient reporting as easily as a meaningful suffix. If the Agency ultimately determines a randomly assigned letter suffix is preferential, Pfizer believes the suffix should be consistent across the company's biological products such that over time it will become associated with the company and make accurate reporting easier. Pfizer reiterates that we consider it most preferable that the four-letter suffix be meaningful and somehow derived from – or in some way related to – the name of the license holder (or company responsible for pharmacovigilance, if other than the license holder). Having a single suffix that is used across all products manufactured by one company would also be preferable for pharmacovigilance purposes.

II. SPECIFIC COMMENTS

Line No.	Comment and Rationale	Proposed change (if applicable)
19-21	The Guidance states: *There is a need to clearly identify biological products to improve pharmacovigilance and, for the purposes of safe use, to clearly differentiate among biological products that have not been determined to be interchangeable.* Pfizer does not consider the determination of interchangeability to negate the need to clearly identify biological products.	*There is a need to clearly identify biological products to improve pharmacovigilance and, for the purposes of safe use, to clearly differentiate among biological products ~~that have not been determined to be interchangeable~~.*
64-69	The Agency has outlined the scope of the guidance and defined biological product broadly to mean: *..a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein (except any chemically synthesized polypeptide) or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a disease or condition of human beings...* Pfizer considers that some products listed within scope should be removed from the scope statement. The intent of designating a nonproprietary name that includes a suffix is to improve pharmacovigilance and clearly differentiate among biological products. Pfizer does not consider this applicable to vaccines, blood, blood components or derivatives, or allergenic products. We therefore believe that such product should be specifically omitted from the scope statement in the final guidance.	*Biological product means a virus, therapeutic serum, toxin, antitoxin, ~~vaccine, blood, blood component or derivative, allergenic product~~, protein (except any chemically synthesized polypeptide) or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a disease or condition of human beings.*
355-380	V. PROCESS FOR PROPOSING A SUFFIX FOR THE PROPER NAME OF A BIOLOGICAL PRODUCT This section of the guidance will require updating if the Agency determines the suffix should be meaningful in relation to the company name.	

Line No.	Comment and Rationale	Proposed change (if applicable)
388-395	The Agency encourages applicants to request FDA review of a proposed suffix for their products. Further guidance in regards to how to request this feedback and the timeline associated with the process would be helpful.	The Agency should ensure there is a transparent process for proposing, reviewing, and implementing a suffix for the proper name of a biological product • The Agency should provide additional guidance regarding the process for requesting feedback on proposed suffixes, and the timeline associated with the process in order to ensure there are not delays caused by implementation. The timeline for the process in particular should be transparent to permit internal planning. • Pfizer recommends that part of the review process of the proposed suffix should include a public comment period to ensure opportunity for public comment pertaining to potential for prescribing errors or other major concerns relating to the safe use of the product. This could be likened to the INN selection process, which includes publishing of newly selected, proposed INNs and a 4-month objection period. • The Agency should clearly outline the next steps and timing in situations where FDA rejects the suffixes proposed by the Sponsor, and ensure there is sufficient time for the company to respond or propose and implement an alternative suffix during launch planning. Due to the complexity of new product launches, 'last minute' changes to the suffix will unnecessarily delay biosimilar product launches and should be avoided.

The global policy landscape regarding the naming of biological products is dynamic, and the WHO recently held an open session (October 13, 2015) to discuss the INN Biological Qualifier proposal. Given the complexities outlined by the Agency in the Federal Register

Notice and the evolving regulatory landscape globally, Pfizer recommends the Agency hold a public stakeholder meeting to further discuss topics such as the timing of retrospective application, process for requesting feedback from the Agency on the proposed suffix, and global harmonization, among other topics that may arise as stakeholders have given more consideration to the complexities of a naming system for biological products.

We appreciate the opportunity to comment on this draft guidance. If you have any questions about these comments, please contact Carol Haley at 212-733-4787 or by email at carol.haley@pfizer.com.

Sincerely,

Laura McKinley

Laura McKinley, Ph.D.
Director
Worldwide Safety & Regulatory