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

RE: [Docket No. FDA-2013-D-1543] Draft Guidance for Industry on Nonproprietary Naming of Biological Products

Merck & Co., Inc. (Merck) is a global healthcare leader in pharmaceutical and biologics development. Through a combination of the best science and state-of-the-art medicine, Merck has produced many important medicines and vaccines. Today the company is continuing to actively develop a broad portfolio of small molecules, vaccines and biologic products—including biosimilars—to significantly improve worldwide patient access to important/life-saving therapies.

Merck Research Laboratories (MRL), Merck's research division, is one of the leading biomedical research organizations. MRL tests many compounds as potential drug candidates through comprehensive, leading edge R & D programs. Merck supports regulatory oversight of product development that is based on sound scientific principles and good medical judgment. In the course of bringing Merck drug and biological product candidates through preclinical and clinical testing, Merck scientific teams have acquired extensive experience in this field.

Our comments included below are in response to the recently issued Draft Guidance on Nonproprietary Naming of Biological Products ("Guidance"), and the accompanying Federal Register notice issued on August 27, 2015 (Docket No. FDA-2013-D-1543). In compiling our comments, Merck Regulatory Affairs consulted and incorporated the perspectives of our clinical safety, regulatory policy, regulatory affairs, public policy, commercial and legal divisions. Importantly, our perspectives have been collected from internal stakeholders representing both our originator biologics and biosimilars business divisions.

We commend the Food and Drug Administration ("FDA" or "Agency") on its continued leadership in drug development, approval, and in its support of scientifically-sound regulatory policy.

If you have any questions or comments, please feel free to contact me directly via the information provided below.

Sincerely,

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General Comments

We commend the Food and Drug Administration ("FDA" or "Agency") for drafting the recently issued Draft Guidance on Nonproprietary Naming of Biological Products ("Guidance") to clarify the Agency's current thinking about nonproprietary naming of biological products.

Merck has publically supported distinguishable naming policies for biologics and biosimilars, and believes that such approaches will promote stakeholder confidence while allowing companies to closely monitor the safety of their respective products. The proposed FDA Guidance on nonproprietary naming of biological products meets Merck's fundamental principles regarding the tracking and tracing of all biological products. FDA is asking for additional stakeholder input regarding the design and implementation of a suffix for biological products

With regard to the below FDA questions, our position on meaningful, company-associated suffixes can be summarized as follows:

1. For the purpose of pharmacovigilance and product tracking, we believe that either a "meaningful" or "non-meaningful" suffix would be sufficient.
2. For the purpose of policy implementation, suffix acceptance and suffix use by healthcare stakeholders, we believe that "meaningful" or "memorable" suffixes would hold significant advantage.
3. For the purpose of permitting companies to select or nominate meaningful suffixes of their own design, we believe that this approach raises several legal issues that the FDA should address prior to implementation of the nonproprietary naming position.

Further detail is provided below.

Question 1a. Potential benefits and challenges of designating a suffix in the proper name of a biological product that is devoid of meaning versus meaningful.

As a fundamental issue, it is important to recognize that the concept of "meaningful" is subjective, and any random suffix assigned by the FDA has the potential to become meaningful through use over time. For the purpose of this question, however, we interpret the term "meaning" to refer to any four-letter suffix that is assigned through interaction and cooperation with a sponsor company, where that company can propose or select a suffix believed to have some advantages in memorability among stakeholders and users.

Merck believes that, either a "meaningful" suffix or a "random" suffix (i.e., a suffix devoid of meaning) would be sufficient for the purpose of pharmacovigilance. Either approach provides an additional tool to sponsors, prescribers and pharmacists to appropriately track and trace biological products to their source. Intuitively, a meaningful suffix specific to a company would have advantages in preventing accidental switching between medicines. Further, the use of a meaningful suffix might be more easily communicated by a company and recalled by a healthcare worker; if true, this would help support associations with, and trust within, a particular product or product-line.

However, meaningful suffixes can carry several legal complexities associated with suffix use. These complexities might create an additional burden on both the FDA and sponsors, and Merck believes these issues must be addressed by FDA.

Merck supports the use of a meaningful suffix on condition that the below concerns are first addressed. Meaningful suffixes proposed by companies add to the likelihood that such suffixes would invoke trademark concerns. Importantly, company selection of meaningful suffixes risks deliberate or inadvertent confusion with an unrelated product, company, or brand; such risk of confusion could negate any added advantage in pharmacovigilance or traceability that a meaningful suffix could bring. Accordingly, this approach raises the following additional issues:

- Although the suffix is intended to be nonproprietary, it will nevertheless have proprietary aspects, e.g., a suffix can only be used by the company producing the particular biosimilar bearing that suffix. Nevertheless, a company will have no mechanism to "protect" its suffix from confusion with other suffixes, and there is no legal precedent within the FDA to address such a situation.
- Further, if the FDA permits use of a suffix that is derived from a company's corporate name:
    - companies that operate under different names globally may not be able to use such a suffix outside the US;
    - such suffixes may suggest or resemble more than one company and cause confusion or lead to errors in medication selection; or
    - another sponsor company may choose a corporate name that could resemble the existing suffix or name of another company and thereby cause confusion or lead to errors in medication selection, etc.
- Accordingly, FDA should establish a mechanism by which companies or individuals may object to a suffix that would cause confusion with their company names, proprietary names, or other corporate or product indicia that call to mind the company name or associated proprietary names. Such safeguards are

particularly important to prevent companies from selecting suffixes that either inadvertently or deliberately cause confusion with a third-party company or product.

It is possible that the FDA could design and implement strategies to safeguard against these concerns, such as effective opportunity to challenge a proposed suffix or a public comment period for new suffixes. In any event, it is critical that such strategies be thoughtfully constructed through additional conversation with stakeholders prior to implementation, to minimize unintended consequences, such as unintentional filing delays. Such steps must be taken prior to the implementation of any policy involving company nomination or selection of a suffix, as with the approach described above.

If the FDA pursues an approach allowing meaningful suffixes, the Agency should consider additional forums to discuss and design practical solutions for implementation, such as pilot trials, or workshops with industry, regulatory, and intellectual property experts. Merck supports the FDA pursuing these avenues even if it delays the adoption of a final nonproprietary naming process for biologicals.

Question 1b. Potential benefits and challenges of designating a suffix in the proper name of a biological product that is unique to each biological product versus unique to each license holder and shared by each biological product manufactured by that license holder.

Assigning suffixes on a company-wide basis is another strategy for attaching meaning to a particular suffix. Such company-wide suffixes can potentially improve its memorability among prescribers and pharmacies, and would likely have advantages in preventing accidental switching between medicines as well as accelerating the use and implementation of the suffixes among healthcare providers. Further, we see no particular advantage from a pharmacovigilance perspective to assigning suffixes on a product-by-product basis, and in fact believe this approach may result in a greater administrative burden to the FDA.

In pursuing a policy that allows for company-wide suffixes, we believe the FDA must take the following practical considerations into account:

First, the **FDA should allow flexibility** in whether the proposed suffix is assigned to the license holder, or to a company associated with the safety and/or distribution of the product. This approach would provide sponsor discretion in instances where the license holder in the US is not readily recognized by

prescribers (e.g., is not the product distributor), or is not responsible for global safety of the product.

Second, the suffix **must be changeable** under certain conditions. Ownership and pharmacovigilance responsibilities can change several times during the lifecycle of an approved product. Company mergers, acquisitions, as well as product licensure and divestitures would undermine any advantage of a single-company suffix, unless that suffix can also be changed.

Third, a safeguard must be in place **to promote global alignment.** In many instances, a company might use a name that differs between the U.S. and ex-U.S. territories. In the interest of global alignment, any consideration of a nonproprietary naming strategy that utilizes company names as the suffix must take into account the global context. Systems might be considered that parallel the small-molecule approach that favors a global name with the opportunity for public comment.

Question 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?

Sharing a suffix between an interchangeable biologic and a reference product would significantly interfere with the ability to trace back adverse events to the underlying drug product. The pharmacovigilance goals around biologics and biosimilars include both drug substance and drug product. Product-related safety issues can arise regardless of whether the underlying drug substance is found to be interchangeable with a reference product, and can have an impact long after a regulatory approval has been made. The status of a product being interchangeable does not affect this risk. As such, it is important that rapid tracing of a product is always possible, regardless of whether that product is interchangeable with a reference biologic. In addition, if the FDA permits a sponsor to adopt a suffix that is derived from its company name, an interchangeable biologic should not carry a suffix identified with the company sponsoring the reference product.

Question 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?

As with Question #2, we see no advantage to an interchangeable biologic sharing a suffix with a reference product, and believe that sharing suffixes would carry significant disadvantages in being able to readily attribute adverse events to a particular drug product.

Question 4. How could FDA and/or other Federal partners improve active pharmacovigilance systems for purposes of monitoring the safety of biological products?

[Not Addressed]

Question 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?

See our answer to Question 6 below.

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

We believe that the FDA should accommodate any company that asks to implement the proposed FDA policy on nonproprietary naming of biologics before the expiration of any relevant exclusivity period.

Aside from this, the FDA should first prioritize biologics that will, or have already, gone off patent and have no current FDA data or market exclusivity. These biologics are (or will soon be) eligible to be used as a reference product for the entrance of a biosimilar product. By contrast, the FDA should deprioritize the use of suffixes for products that are at the beginning of their 12 year data exclusivity period, and where biosimilar entry is not likely in the near future.

Further prioritization could be based on medical criteria, such as the nature of the biologic and the condition being treated. For example, analogous of endogenous glycosylated proteins should be prioritized due to the significant potential impact on safety associated with heightened immunogenicity.

Question 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?

We believe that a period of at least one-year would be necessary to fully implement a suffix in association with a previously licensed product. The use of the suffix will need to be integrated into all aspects of the business, including marketing/promotion, clinical safety databases, labeling and PI, reimbursement schedules, among others. This process is resource intensive and extensive; in order to be sure that companies can comply with the adoption of a suffix, a minimum one-year time period is required.

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

One strategy could be to include an FDA-authored general description of what are biosimilars, including the related nomenclature, with prescribing information. This would provide means to communicate with all who take the product.

Question 9. 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?

Global alignment is preferable, and could serve as an important component in designing and implementing a truly global drug surveillance strategy. Such alignment would assist with database searches, cross-border pharmacovigilance, and retrospective data mining. However, we believe that the necessary pharmacovigilance activities are still possible even without global implementation of a uniform policy for the naming of biological therapeutics.