Genentech
A Member of the Roche Group

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

Re: Docket No. FDA-2013-D-1543

Dear Sir or Madam:

Genentech, Inc. (Genentech) submits these comments on FDA Draft Guidance Nonproprietary Naming of Biological Products. In general, Genentech is supportive of FDA's proposed naming convention which is largely consistent with positions on naming that we have been advocating in public meetings and submissions to the docket.

- Product names must be easily recognizable and non-confusing to physicians, pharmacists, and patients. Further, product names should be clear and distinct, to minimize the potential for inadvertent or unintended substitution and to facilitate effective pharmacovigilance.

- We agree with the Agency's view that distinguishable non-proprietary names are in the best interest of patient safety, because they facilitate pharmacovigilance and mitigate inadvertent product substitution. This is important because the reference product and the biosimilar product are not identical, and because shifts in product attributes and manufacturing deviations can occur that need to be linked quickly to the responsible product.

Our comments on the questions FDA is seeking input are listed below:

Comments addressing FDA Questions

1a. What are the potential benefits and challenges of designating a suffix in the proper name of a biological product that is devoid of meaning versus meaningful?

Suffixes should be "memorable," convey some meaning

- Memorable suffixes will increase transparency and result in more well-informed and safe use of medicines. Also, having a meaningful suffix will make it easier for people to remember it. The latter has several advantages, including
    - reduction of prescribing errors;
    - improved traceability (ADR reporters are more likely to recall a memorable suffix) and;

  - may also decrease the chance of multiple switches from one product to another (for example if only INN is given, because suffix was forgotten, this could lead to unnecessary switches).

- Suffixes devoid of meaning: Random "suffix" (such as "jpts") could potentially result in medical errors or prescriber "mix ups" because health care providers may not remember a random suffix, and could inaccurately link AEs to the wrong product. Thus, market acceptance could be potentially reduced since they may not recall the appropriate product name.

- For suffixes consisting of random letters, there is a greater potential for transposing random letters than for memorable suffixes

- Random suffixes raise several concerns, related to practicality of use, and potential copyright and trademark infringement issues with other companies.

- Meaningful suffixes associated with the company – such as "gene" or "amgn" – could be easier to remember, and reduce potential errors for prescribing, enhance quality of safety reporting, and market acceptance.

- Using a suffix associated with the manufacturer's name on the license, is unlikely to convey an advantage to innovator companies vs biosimilar companies, because many biosimilar companies also manufacture innovator drugs.

- Using a suffix associated with the manufacturer's name on the license will also reduce time needed by manufacturers to select a random code and for FDA to review them, thereby increasing efficiencies and reducing costs.

- Each product already has a meaningful proper name, and adding 4 random letters could likely lead to errors when referencing the product by the new proper name, thereby miss-representing the product. However, using letters that have some meaning or that serves as an identifier, perhaps for the manufacturer, will significantly reduce the risk of such errors.
  - An example of where such errors could be introduced is when a HCP is prescribing the product; it is easier to accurately use a suffix that has meaning, than one that has random letters and that could cause confusion when the product is dispensed or at the point of use.
  - Another example is numerous systems utilized both by the manufacturer, as well as by distributors where an incorrect transcription of the proper name could potentially create further challenges in fulfilling orders, etc.

- It would also be more convenient to reference a product that has a meaningful suffix that serves as an identifier (in correspondence), than having to continually consult a directory/listing to confirm the product in question.

- In order to facilitate effective pharmacovigilance practices, suffixes need to be "memorable."
    - The need for distinguishability goes beyond electronic databases; "memorability" is important in helping health care practitioners to understand the distinct identity of each product and enable pharmacovigilance.

- Suffixes should convey meaning
    - Suffixes, if unique to a BLA holder or manufacturer (rather than to each individual biological product), could acquire meaning through use

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?

Interchangeable products should have unique distinguishable suffixes from their reference products, not bear the same suffix as their reference product

- Each interchangeable biological product should have a unique suffix to facilitate pharmacovigilance and recognize that interchangeable biologics are not identical.

- Quality/Manufacturing issues always can happen. Having the same suffix will make it very difficult to track back potential adverse events to quality/manufacturing problems associated with a particular product.

- Interchangeable biological products may not be interchangeable for all indications, and may develop unique safety and indication profiles after reaching the market.

- Concerns about pharmacovigilance and the ability to trace adverse events to an individual manufacturer are still relevant to interchangeable biological products.

- When considering adverse event reporting, whether or not a product is interchangeable, the manufacturer/applicant would certainly need to know whether any events are related to their product vs that of another manufacturer, especially if any relabeling occurs during dispensing/administration. Without the use of a different suffix, additional systems and processes at both the manufacturer as well as within the healthcare system would be needed in order to further confirm and distinguish whether an event applies to one product or its interchangeable alternate.

It should be a distinct suffix, also for interchangeable products for two key reasons:

- First of all, interchangeability will likely be granted sometime after approval of the product as a biosimilar. If the suffix of an interchangeable product is the same as the

reference medicine, the suffix of such a biosimilar (which initially was approved as biosimilar, and later as interchangeable) would change over time. This would be a burdensome procedure and could lead to confusion because the exact same product would have a change in suffix over time.

- Secondly, the overall aim with the suffix is to have product specific traceability. When having the same codes for interchangeable biosimilars, this product specific traceability is not possible. Therefore, important differences in the safety profile from the originator to its biosimilar (possibly due to manufacturing changes of either the originator or the biosimilar) cannot be linked to the appropriate product. This could lead to a situation where safety issues result in unnecessary suspensions of safe drugs, due to false attribution of ADRs associated with a manufacturing change or quality issue for one product impacting other products having the same suffix.

3a. 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?

The suffix of a biosimilar should not change upon a determination of interchangeability

- The label should indicate, among other things, whether a biological product has or has not been determined to be interchangeable with the reference product. A determination of interchangeability should therefore be reflected with a labeling change.

- Additionally, most interchangeable biological products will originally be biosimilar biological products and, therefore, already have a distinguishable suffix under the proposed naming convention.

- If a product is a biosimilar and becomes interchangeable, it should retain its unique identifier to distinguish it from the reference and other biosimilars for prescribing and pharmacovigilance/safety reporting purposes.
  - Label updates/revisions - Label updates may occur periodically (safety updates, clinical trial info, new indications etc). If a reference product has a label change to include a new indication – this should not automatically apply across the board to the biosimilar to expand its use/indication and safety considerations, etc.

3b. 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?

Allowing a manufacturer of a 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 would create greater confusion and uncertainty around whether the product is interchangeable or not, and potentially lead to inadvertent substitution and breakdown in effective pharmacovigilance.

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

- Enhance the education of Biologics vs Biosimilars vs Originator plus education to report AE in timely manner with the new suffix classification. Alternatively, as in the EMA, FDA could require that AEs be reported with brand name, generic name and lot number, requiring the MedWatch form to be revised in order to accommodate the mandatory inclusion of this information on every initial AE report.

- There is educational/training opportunity here for Physicians/Pharmacists/Nurses to learn about new requirements for biosimilars (CME/CE); send out FDA updates/emails and also include information on FDA website

- Enhanced training and education may require more stringent processes to be effective- such as shared REMS having medical and patient educational material to be monitored for effectiveness.

4b. 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?

- There are five product identifiers that could be included in AE reports. These are the brand name, nonproprietary name, National Drug Code (NDC), manufacturer name, and lot number. Other product identifiers, such as medical benefit reimbursement codes (Healthcare Common Procedure Coding System [HCPCS]), may be used for Active Surveillance (AS). Unfortunately, the utility of each of these identifiers may be limited in regard to their use in Spontaneous Reporting Systems (SRSs) and limited by the healthcare setting in which the AE reporting is performed. For example, Physician office and hospital outpatient claims for drug administration procedures commonly use HCPCS codes. Because this channel represents the majority of therapeutic biologic product prescriptions in the USA, such codes are particularly relevant to active surveillance of biologics. However, the CMS proposal to consolidate biosimilars that share the same reference product into the same HCPCS code would prevent AS of biosimilar products, allowing comparisons only between the experience with a reference product and the aggregate experience of its biosimilars. If the proposed rule is reversed and unique HCPCS codes are issued for biosimilars, it may be possible to perform product-specific active surveillance.

- It might be possible to include information on the manufacturer, lot number or NDC numbers in 2-D barcodes being considered for product serialization and tracking in the market.

- New identifiers would have to be established (e.g., tagging each product with a unique marker) and then requiring this information to be included on the MedWatch form

4c. 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?

- Require pharmacists to enter brand name and lot number information in a national registry at the time of prescription being filled

- Ensure that drug listing systems are able to accommodate the new format for proper names and validate their systems for the new software coding that will be needed

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?

- May consider the annual product review as a time to implement a suffix on the nonproprietary name of a previously licensed biological product.

- Request 1-2 years to deplete existing supply of packaged product, submit PAS to FDA, and allow time to implement process changes

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

- It makes sense to adopt the new naming combination first for those products where there is awareness of an application by another manufacturer for a biosimilar or interchangeable product. Other products not yet facing this scenario could be de-prioritized. For new product applications, if the suffix serves as a meaningful identifier, it would make sense to use the new naming convention at the time of initial IND or BLA stage.

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?

- Many factors could impact timing for introduction of product with a new nonproprietary name and sponsors will need to work with FDA on case by case basis to determine the appropriate time frame for each product.

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

- FDA updates, newsletters, website, Daily Med, CME, CE courses (online)

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?

The two proposals are conceptually similar, but with key technical and procedural differences.
WHO proposes randomly assigned, four random consonant BQs for all biological products.
FDA proposes meaningless applicant-provided four letter suffix, subject to FDA review. Alternatively FDA is proposing a meaningful code associated with name of manufacturer on the product license. WHO is also seeking comment regarding whether their BQ should be meaningful. The issue is whether it is preferable to have a single system with a random and meaningless suffix/BQ, or is it better to recommend that FDA adopt a more memorable suffix realizing that it may not match up with the WHO BQ.

- Harmonization between suffixes would be ideal, but harmonization to a disadvantageous suffix is not productive.

- Ideally both qualifiers should be aligned to facilitate global PV. Given that most biological products have global supply-chains, having different naming systems in different countries will generate a mess not only for industry but also for patients that are travelling and may require prescriptions valid across borders.

- If there is a means for FDA to collaborate with WHO to come up with an aligned naming convention, this would be ideal and beneficial when products are registered globally. Often documents are required from one HA approval to support licensure in other countries. Having different naming conventions certainly will pose challenges in being able to meet regulatory requirements when the proper name for a product is no longer recognized or accepted during the registration process in another country.

- During the licensure process, and lifecycle management of product applications, the use of a naming convention unique to the US, creates the need for generating unique license applications and amendments for the US reflecting the proper name (e.g. CTD sections where the proper name is used throughout), compared to taking a harmonized approach for registration of a product globally and using the same CTD sections - certainly an impact on efficiency and expediency.

- Each country has a separate license application, and as such, the naming convention adopted by FDA, if different to what WHO proposes, should not have an impact on being able to manufacture product at US approved sites for countries outside of the US. However, the questions below need to be considered by FDA for documentation issued in support of global licensure so that product export reflects the proper name accepted by the respective countries outside of the US.
    - How is FDA planning to approach the issuance of Certificates of Pharmaceutical Products either for export of product manufactured in the US, or to support licensure of a US approved product in other countries?
    - Similarly, what is FDAs plan for other types of licenses issued where the proper name for the product is stated and these documents are utilized by other HAs?
    - Alternatively, will FDA accept any documents, certificates, licenses issued by other HAs that do not utilize the proper name as adopted by FDA (without suffix).

10. FDA invites comment from all stakeholders on the application of this naming convention to biological products approved under the FD&C Act.

We believe for all the reasons stated above, the application of this naming convention to biological products approved under the FD&C Act is appropriate and should be implemented.

Respectfully submitted,

Eric Olson
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