Generic Pharmaceutical Association

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Division of Dockets Management
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane
Room 1061
Rockville, MD 20852

CITIZEN PETITION

The Generic Pharmaceutical Association (GPhA) submits this petition under 21 C.F.R. § 10.30 to request that the Commissioner of Food and Drugs take the action requested below.

A. Action Requested

GPhA respectfully requests:

- that FDA implement its INN naming policy equally to all biologics; and
- that because all biologics approved under the Section 351(k) pathway are "highly similar"; and thus, have no clinically meaningful differences from the reference protein product (RPP) that they *share the same INN name as the RPP*, just as comparable originator products produced by a change in a manufacturing process or facility (post-change product) share the same INN as the original RPP (pre-change product).

B. Statement of Grounds

Background and Overview of the Naming of Biosimilars

The World Health Organization (WHO) administers the international naming convention known as the International Non-proprietary Naming (INN) system. An INN names the active ingredient, such that products that share the same INN can be readily identified as sharing the same active ingredient[1]. Conversely, different INNs denote products with different active ingredients. The INN has never been the name of the final, formulated product itself. In addition to the INN, a product (including biosimilars) will have other names and identifiers; for example, a brand name and in the US a national drug code number (NDC), that readily distinguish it from other products that share the same INN.

In the US, local non-proprietary names can be assigned by the United States Adopted Name (USAN) Council, which is co-sponsored by the American Medical Association (AMA), the United

States Pharmacopeial Convention (USP), and the American Pharmacists Association (APhA) and includes FDA representation. The USAN program aims to select simple and informative non-proprietary names[2] (also called generic names) for drugs and biologics by establishing logical nomenclature classifications based on pharmacological and/or chemical relationships. The USAN Council works in conjunction with the WHO INN Expert Committee and other national nomenclature groups to standardize drug nomenclature and establish rules governing the classification of new substances. Usually the USAN and the INN match each other.

The Biologics Price Competition and Innovation Act (BPCIA), enacted March 23rd, 2010, specifically authorized the approval of biosimilars and interchangeable biologics. The legal and regulatory approval standards allow FDA to approve a biosimilar upon a showing that it is highly similar to its RPP and the Agency conclusion that the biosimilar does not have clinically meaningful differences from its RPP.[3] After approval by FDA, a biosimilar would share one, some, or all of the labeled indications of its RPP. An interchangeable biologic is a biosimilar that must be supported by additional data to FDA to allow a conclusion that it can be switched with its RPP during treatment, and they are by law substitutable at the pharmacy without the need to inform the original prescriber of the switch (that prescriber can, as with any other product, preclude such a switch by checking the do not substitute box on the prescription).

No provision of the BPCIA addresses the naming of biosimilars.[4] The absence of such provisions in the law does not reflect an oversight by Congress. In fact, during drafting of the bill, legislators discussed in detail whether unique INNs should be required for biosimilars, and then chose not to include language that would have provided for separate INNs. Without new statutory authority, FDA lacks specific authority to require separate INNs for biosimilars, and existing conventions for biologics should be expected to prevail.

FDA outlined its naming position for biosimilars in a policy paper sent to the WHO in 2006, in support of the current WHO naming conventions.[5] In this paper, FDA clearly supports the original purpose of the INN (to identify the active ingredient of a product), rejects the use of non-proprietary names to communicate interchangeability, and states that concerns about pharmacovigilance "transcend a naming convention," explaining that "[i]t would be the FDA's preference that INNs continue to be granted based only on molecular characteristics and pharmacological class of the active ingredient(s)."[6] In this paper FDA agrees that there should be no change in global policy and rejects distinctive INN designations for biosimilars. The 2006 FDA policy is widely supported by multiple stakeholders. For example, Congresswoman Anna Eshoo, in her April 16, 2012 letter to the FDA biosimilar guidance docket stated that a unique proprietary name for biosimilars is needed, but a unique non-proprietary name is not.[7] Multiple pharmacy groups have expressed their support in letters to Commissioner Hamburg.[8] While BPCIA was enacted subsequent to this policy position being presented to WHO, nothing in the new statute is incompatible with the 2006 FDA position on biosimilar naming.

Given that FDA is a scientific, data-driven agency, the Agency is obligated to apply its standards equally to all applicants and products. Requiring unique INNs for biosimilars while allowing sharing of INNs for other biologics in comparable situations would run contrary to this tenet. FDA routinely allows originator biologic products in the same class approved under separate 351(a) or 505(b) applications and using different manufacturing methods implemented by different sponsors to share the same INN. For example, a number of Anti-hemophilic Factor (Recombinant) products, some of the most complex biologics licensed in the US, share the same INN. Attached, as Appendix A, is a list of products which share INNs, most of which have never been compared and several of which have known differences but still share the same

INN.[1] Further, FDA has for many years without question authorized originator manufacturers to modify biologics' manufacturing processes and develop biologics that have minor changes and differences that are not clinically meaningful without requiring a change in non-proprietary name. This authorization is contingent on a sponsor submitting data that the post-change product is "comparable" to the pre-change product. If the sponsor demonstrates such comparability FDA deems the (pre- and post-change) products interchangeable for all indications irrespective of the mechanism of action being understood. The standard for both comparability and biosimilarity is "highly similar" quality attributes.[9]

As FDA itself articulated in its 2006 Policy Paper:

> "Considering the inherent difficulties in additional INN product distinctions (e.g. retroactive and lifecycle changes in naming, additional INN responsibility and liability), if the world community decides to proceed with a change in the policies regarding the assigning of INNs, it should be preceded by (a) appropriate exploration of alternatives (e.g. improvements in education and/or labeling), (b) assuring the such changes fall within the scope, competence, and expertise of the INN program, and (c) the performance and independent validation of a formal risk assessment and/or documentation of events with appropriate statistical treatment."[10]

GPhA concurs that any concerns with pharmacovigilance call for tailored solutions capable of fixing the actual problem without creating additional confusion. Unsupported pronouncements of inadequate tracking capabilities for biosimilars with the same INN as their RPPs represents, at best, a hypothetical problem given that no biosimilars have yet been approved in the US and Europe has been successful at tracking biosimilars which share INNs with their RPPs. Rather than using inadequacies with pharmacovigilance systems as a whole to assert that biosimilars alone will have tracking and tracing issues and suggesting unique INNs will remedy the stated but unspecified concerns, patients would be better served if we focused on practitioner education and system enhancements to address any problems in the pharmacovigilance system for all pharmaceutical products. Currently, a well-established process exists to track product quality problems that does not rely primarily on INNs, but instead uses a product's brand name, manufacturer, lot number and NDC to track quality and safety events. GPhA does not believe requiring unique INNs for biosimilars could remedy the poorly defined concerns and, instead would cause confusion and potential harm to patients by interfering with the present system. In contrast, we fully support vigorous enhancement of track and trace and education of physicians and pharmacists to include NDCs, manufacturer names and other relevant identifiers on all safety reports. This applies equally to all biologics, and must not be used as a wedge to create an anticompetitive barrier to biosimilar development and commercialization.

In summary, a major goal of the BPCIA is to create competition in the marketplace for biologics, thereby expanding access to, and increasing the affordability of, these critical medicines. Adoption of unique names for each biosimilar could frustrate this goal as well as jeopardize patient safety, inhibit market competition and innovation, and disrupt the current global naming system. GPhA proposes that the same scientific principles that underlie the 60-year-old policy of INNs, as applied throughout the world to drugs and biologics, also must apply to biosimilars. This means that as a fundamental element of its licensure, each biosimilar product should have the same INN as the single RPP to which it has been demonstrated to be highly similar and to have no clinically meaningful differences.[11] FDA will not approve any biosimilar product that does not achieve these standards. Moreover, it is beyond any reasonable reading of the BPCIA

that interchangeable biologics would not share the same INN as the RPP, because FDA would have concurred that they had been shown to be fully substitutable without the need for physician intervention. While sharing an INN, each biologic and biosimilar will have a unique manufacturer name, NDC, lot number and brand/trade name and therefore will be readily distinguishable in the same manner as originator products are today. Biosimilars have already been given the same INNs as their RPPs in other highly regulated regions throughout the world and have not been confused[12]. As explained below, maintaining consistency in applying scientific principles to regulatory matters requires that if FDA were to require new INNs for biosimilars, all existing products that share INNs would need to be renamed, and new INNs would be needed in every instance of a manufacturing change to a currently licensed product. This would require a significant and immediate regulatory review and renaming effort by sponsors and FDA for virtually every licensed biologic on the market in the US today.
We expect that FDA's existing policy on naming will continue to be consistently applied to all biologics, biosimilars included. FDA should implement a policy that promotes biologic safety by allowing biosimilar products to share INNs with their RPPs.[13] It is also very important to consider the negative impact on utilization and uptake of the 351(k) pathway that different INNs would create, and therefore the barrier to meet the overall access and competition objectives of the BPCIA that would be being created by any such requirement.

Biosimilars, as Highly Similar to their RPPs, Should Share INNs with their RPPs just as Post-Manufacturing Change Biologics Share INNs with their Pre-Change Versions

FDA uses state-of-the-art science to review and approve biologics. The Agency has in-depth understanding of all the biologics that it has reviewed and licensed for the US market, and by definition these will comprise the entirety of the RPPs for biosimilars in the US[14]. GPhA's goal is to see FDA's experience and expertise with biologics consistently and fairly applied to all sponsors based on the Agency's current application of the same scientific principles for changes made to biologics submitted pursuant to Section 351(a) as for approving biologics submitted under Section 351(k). Specifically, regulatory authorities oversee manufacturing changes with comparability approaches by using many of the same "highly similar" analytical standards as have been written into the biosimilar legislation enacted by Congress. This has been coordinated among regulatory authorities across the highly regulated markets and gone through full notice and comment rulemaking in the US[15]. It is the highly similar standard with which FDA has extensive experience and enables full extrapolation of indications and interchangeability of the resulting biologics on the US market today.

The highly similar biosimilar standard is conceptually the same regulatory standard that FDA currently applies to originator products undergoing manufacturing changes – a showing of similarity between batches of active ingredient before and after the manufacturing change enables FDA to conclude that the batches have no clinically meaningful differences. With this evidence, a comparable post-change product is permitted to use the same established non-proprietary name, and is even viewed as interchangeable with the pre-change product. A comparable biologic product must have all of the pre-change product's indications and be interchangeable for every single one of them (even without an understanding of the product's mechanism of action). Such is the confidence in the "sameness" of the resulting products that neither health care providers nor their patients are informed about the change (nor are the data that form the basis of these supplemental applications made publically available. This standard is already being successfully used for biosimilar approval (as well as manufacturing changes to biosimilars) in other highly regulated markets[16]. In scenarios, manufacturing changes and biosimilar approval, the demonstration of highly similar analytical and functional characterization

is an essential component for the regulatory authorities', including FDA's, expectation that the clinical outcomes of the products will be the same. Further, in contrast to manufacturing changes which do not routinely require thorough characterization involving animal and clinical studies[17], biosimilar approval will likely require a higher level of characterization using a stepwise development approach where *in vivo* studies for immunogenicity are routinely expected. This approach, along with FDA's authority to request any information that it deems essential for approval of a biosimilar product, assures there are no meaningful clinical differences between a biosimilar and its RPP.

We recognize the biologic variability inherent in manufacturing changes and that comparability analysis is critical to the supply and availability of these products to the patients that need them. Data published in peer-reviewed scientific literature demonstrates that while originator products do change over time, they are generally well-controlled between manufacturing changes, and, even after manufacturing changes, the clinical attributes of the products are acceptable[18]. GPhA does not believe that FDA should vary from their own current practice and assign unique INNs for those approved biologics that undergo post-approval changes that are deemed acceptable based on comparability testing. However, because the post-change product bears the same name and it's label is unaltered after a manufacturing change, patients and their providers are not informed that a change has occurred even though the post-change product is only similar to (i.e., not the same as) the pre-change product. In the interests of transparency and further regulatory consistency, all use of comparability for U.S. biologics should be made public, just as it is for biologics in Europe and just as it will be for biosimilars. A recent paper from a European regulator shows the extent of the use of comparability – one instance being 37 manufacturing changes post-approval for Remicade® (infliximab) [19]. This information could also be indicated in labeling so that patients and their health care providers can readily access this information. Likewise, having the manufacturer name on the label alerts providers and patients to a biosimilar.

In sum, because of the robust science used for both biosimilars and comparability assessments, GPhA believes that all products that are found to be highly similar should be assigned the same INN. Should FDA believe that biosimilars require different INNs than their RPPs, there will be consequences for all biologics because regulatory parity and consistent scientific reasoning dictates that if biosimilars require unique INNs then:

(1) all current products sharing INNs must be re-examined;

(2) in the future FDA must require new INNs for any product, originator or biosimilar, which undergoes a manufacturing change using comparability.

Consequently, a significant and immediate regulatory review and renaming effort by sponsors and FDA would be triggered for virtually every licensed biologic on the market in the US today. This would then be the immediate priority for FDA as these are the products currently available on the US market today, whereas no biosimilar application has yet been filed with the FDA. There is simply no reasonable distinction between biosimilars (as highly similar to their RPPs) and post-manufacturing change biologics (as highly similar/comparable to their pre-change counterparts) that warrants a unique INN for biosimilars and not for post-manufacturing change biologics.

Pharmacovigilance

A. The Global Pharmacovigilance System Works, Products Sharing INNs in the US and European Biosimilars Sharing INNs with their RPPs Are Successfully Tracked and Tracked

In the current global system used for drugs and biologics, the INN is the name of the active ingredient, not the name of the product, nor the sole basis of prescribing[20]. FDA has already endorsed this system for biosimilars as well (discussed above, and attached[21]). To keep with the intent of the INN, which is to allow immediate identification of a product's active ingredient, all biosimilar products should share an INN with their RPP because they must contain, as a fundamental requirement of their licensure, the same active ingredient. Some have asserted that biosimilars sharing an INN with their RPP can or will interfere with successful tracking of specific products leading to safety concerns. However, we are not aware of any evidence of a problem unique to products sharing INNs or even potentially unique to biosimilars alone. Nor do we believe that this will be the case given that (1) no biosimilars are currently marketed in the US, therefore any current problems in the US pharmacovigilance system cannot be attributed to biosimilars, (2) we know of no tracking issues with currently marketed originator products sharing INNs and (3) experience with marketed biosimilars in highly regulated markets outside the US has identified no safety issues resulting from biosimilars sharing INNs, and their use is now sufficiently extensive that even unusual events would be expected to be caught[22]. Thus, there is no safety reason to give a unique INN to a biosimilar in the US, especially since the biosimilar will have been found, by virtue of its FDA approval, to be highly similar and to not have any clinically meaningful differences from the RPP.

To elaborate, because biosimilars have not yet entered the US market, any problems with the current US pharmacovigilance system cannot be attributed uniquely to biosimilars and, therefore, a remedy specific to biosimilars alone is not appropriate if the goal is to optimize patient safety. Second, GPhA is unaware of pharmacovigilance issues that have arisen as a result of products sharing the same INN. For example, as expressed in our September 4, 2012 letter to FDA Commissioner Hamburg[23], FDA currently allows different recombinant and naturally-derived products from different manufacturers to share INNs. These examples include ones in which multiple products, *which have never been compared*, share the same INN. No demonstration of "sameness" was required by FDA for the approval of such products and indeed if they were to be compared, differences would be expected.[24] As further evidence that an INN is not meant to convey the "sameness" of the product itself, FDA routinely supports the same name for biologics even after comparability testing demonstrating that highly similar quality attributes have *not* been shown (see Myozyme® and Lumizyme® in the table attached as Appendix A). Similarly, with regard to comparability testing of pre- and post-manufacturing changes, FDA allows the same INN to remain with the product based on the pre- and post-change products having been shown to be "highly similar"/comparable (recognizing that they are not the same but only similar[25]). And comparability has been used multiple times on the same originator products since their licenses were first issued – as mentioned above with 37 published in Europe for Remicade® (infliximab).[26] Importantly, these products are currently being marketed and made available to patients in the US today. If there are any concerns, at FDA or from other stakeholders, about possible confusion through shared nonproprietary names then these are the products that must be addressed first.

In fact, we believe that experience with manufacturing changes to originator products in the US demonstrates that track and trace mechanisms are more than adequate to assure patient safety among highly similar products (i.e., in this case post and pre-manufacturing changed originator

products) as well as standalone independently approved products (see Appendix A). Current regulations require the manufacturer's name on the product label, and GPhA member companies are committed to labeling biosimilar products with their corporate names and/or product proprietary (brand) names. Each container label will prominently display a brand name in addition to the INN (the same information as is required for an originator product), even on the smallest dispensed unit of a biosimilar (as a parenteral). Therefore, even if problems are specific to a particular product, the label information including the biosimilar proprietary name, manufacturer, lot number and NDC will allow for specificity in tracking and tracing of biosimilars. In practice, when an adverse event is reported to FDA that triggers a need to investigate, the Agency typically contacts the physician and then checks with the pharmacist to determine the product's manufacturer and precise batch information. This specific information, not the product's INN, enables FDA and the actual manufacturer to investigate possible causes of the adverse event. Unique INNs do not provide any additional information to enhance the current system of tracking and tracing products.

To better understand adverse event (ADE) reporting practices, GPhA commissioned an independent research group (Drug Safety Institute, a division of Brand Institute, Inc.) to evaluate health care practitioner preferences and recommendations related to ADE reporting.[27] This practitioner survey identified which reporting elements health professionals reported as most critical and thus which elements are most likely to be reported.[28] Health professionals typically report multiple elements whenever possible and include only the INN as the sole data point less than 30% of the time.[29] This data supports GPhA's view that the INN is only one of several identifiers of a product that is important to capture for purposes of pharmacovigilance, and further demonstrates that creating a unique or differentiated INN is not likely, in and of itself, to result in a substantive improvement in pharmacovigilance practices. Likewise, FDA's own Guidance for Industry "Contents of a Complete Submission for the Evaluation of Proprietary Names" [30] notes that:

> "In the U.S. medication-use system, health care providers rely on the proprietary name as the critical identifier of the appropriate therapy in a market of thousands of products."

If a concern exists that the US track and trace system is inadequate for biosimilar products, then that same concern applies equally to post-manufacturing change products and arguably even more so to products that share the same non-proprietary name but have not been compared or have failed comparability. Moreover, if the problem perceived is precision reporting of pharmacovigilance information, then we should fix the actual problem for *all biologics and products.* Fortunately, emerging technology can contribute to improved reporting and record keeping using the current systems. For example, FDA in collaboration with Boston Children's Hospital and Harvard Medical School has developed a smartphone and computer APP, Medwatcher,[31] which allows a physician, patient or pharmacist, with the click of a button, to submit a photograph of the label within an adverse event report from their mobile phone or personal computer. The photograph can clearly identify more than the INN name. For example, the following photograph could accompany the report and be sent in real time using the APP, leaving no doubt as to the manufacturer or the batch and lot number.

This is just one example of an APP that provides an opportunity to improve adverse event reporting by making it quicker and easier to be more complete. These technologies continue to emerge as valuable tools for physicians and pharmacists that ameliorate any additional burdens that might otherwise be being seen to be imposed.

Finally, in Europe, where biosimilars have been on the market since 2006, biosimilars and their corresponding RPPs share the same INN. In each case, the individual biosimilar product is identified by a brand name. A recent study of the identification of biosimilars in the European Union pharmacovigilance system found that the naming convention for biosimilars has a successful product identification rate of 96.2% across all three marketed biosimilar classes currently on the market (somatropin, filgrastim and epoetin).[32] There is no reason to expect that the US pharmacovigilance system cannot achieve similar or even higher product identification rates given that, unlike the European Union, the US has the advantage of a singular nationwide NDC product identification system for tracking.

B. Requiring That Each Biosimilar Have a Unique INN Could Jeopardize Patient Safety

Not only would requiring unique INNs for biosimilars not fix any purported problems with the current pharmacoviligance system, but it would in and of itself compromise patient safety.[33] Shared INNs between a biosimilar and its RPP accurately reflect the regulatory determination that there are no meaningful clinical differences between these products and thus indicate that both produce the same clinical outcome. Conversely, requiring a biosimilar and its RPP to use different INNs would, instead, inaccurately suggest that these products have meaningful clinical differences for patients. This would compromise patient safety in that: (1) clinician confusion may lead to prescribing errors, (2) access could be compromised and patients go untreated, and/or (3) safety data for these molecules would be disaggregated from the current system that allows for pooling of data, ensuring rapid identification and communication of class effects and lower frequency safety signals.

Specifically, a patient's health could be jeopardized if, for example, a physician inadvertently double dosed a patient by prescribing two highly similar products because he thought, based on their different INNs, that they contained different active ingredients. To avoid this, physicians and pharmacists would need to know the INN of every biosimilar and the INN for each RPP, and how they relate to each other (as well as the brand names since prescribing in the US is still largely by brand). Physicians also would need to be aware of the relationship between not only the biosimilar and its RPP, but also of potentially multiple biosimilars to the same RPP (that, likewise, would not be identifiable through the same shared INN). This would occur irrespective of whether FDA had designated some biosimilars as interchangeable with their RPP, while other sponsors had not sought the interchangeability designation.

As FDA explained in its 2006 policy paper:

> "The issue of interchangeability is not an issue of nomenclature but a scientific question that needs to be decided on its own merit. The question of nomenclature is more relevant to concerns about pharmacovigilance and the prevention of inappropriate substitution. However, the FDA believes that these issues transcend a naming convention. It would be the FDA's preference that INNs continue to be granted based only on molecular characteristics and pharmacological class of the active ingredient(s)."[34]

Currently, appropriate product sharing of INNs functions to instantly alert the physician to these relationships. This function would be destroyed if biosimilars and their RPPs could not share INNs. It would be similarly disruptive to currently approved products, and products pre- and post-manufacturing changes, as those products would similarly need different INNs in order to maintain regulatory consistency.

Furthermore, assigning unique biosimilar INNs may cause the INN to replace brand names as the primary means of identification and prescribing, increasing the potential for medication errors, given that unlike brand names[35], INNs are not specifically reviewed by FDA for the potential of creating medication errors (a process whereby confusion with other products through similar sounding names is minimized).

Unique biosimilar non-proprietary naming may also imperil appropriate state pharmacy substitution of interchangeable biosimilars, as interchangeable biologics with different INNs could be incorrectly thought to have a different active ingredient. Each interchangeable biologic would then have to be detailed and marketed— an unnecessary cost that patients and payers

would bear. The BPCIA explicitly contemplates interchangeability of the RPP and biosimilar product and, as the products are deemed to be the same, they should share the same name. Interference with the substitutability of interchangeable products is legally questionable and would significantly reduce the savings from biosimilars that public and private payers as well as patients. This lack of competition will likely constrain access for patients and so limit the public health goals expected to be attained through the availability of biosimilars. This will undermine the intentions Congress had in enacting BPCIA.

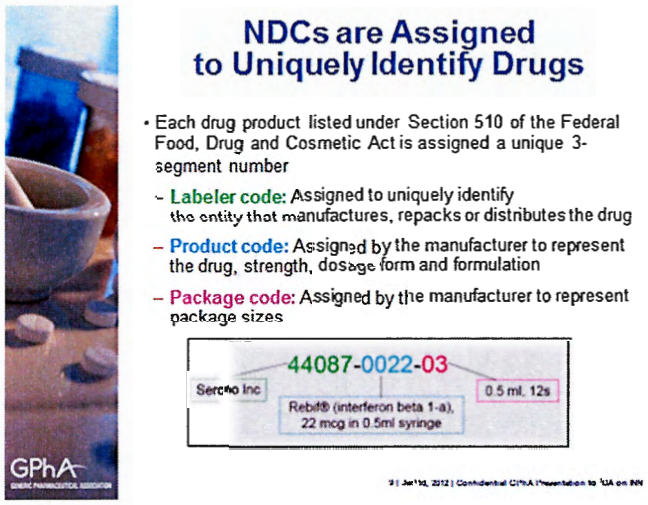
In addition, the use of unique biosimilar non-proprietary names would disrupt the current pharmacy systems (where the US established name[36] would not be the same as its INN, and may not even match its USAN[37]), and this poses its own safety risks by interfering with the existing safety alert functions used today to protect patients. GPhA believes there is a real danger to forcing a separation of pharmacovigilance data into separate silos specific to each biosimilar product(s) and the RPP - this may represent a greater safety risks than the theoretical risks of sharing the same INN[38]. Segregating relevant RPP and biosimilar pharmacovigilance data for their common active ingredient into two separate sets would obstruct appropriate pooling of data critical to patient safety[39]. Importantly, it also would dissociate the US biosimilar from "itself" in markets outside of the US where its INN already matches that of its RPP. In a world of global pharmacovigilance, this would have a significant negative impact on patient safety by preventing timely data associations and making identifying and communicating safety signals difficult, if not impossible. Many post-marketing adverse events are quite rare and if each product is analyzed separately, the risk that a product's safety signals would remain undetected would increase. As such, when an adverse event is first observed in the RPP or the RPP's biosimilar product, unique INNs will limit the investigation to a single manufacturer when all the biosimilar products need to be considered. This is precisely how class effects are captured today for RPPs which may be manufactured at different manufacturing facilities, as well as for products made by different companies which share the same active ingredient as represented by the INN.

In sum, the INN is not currently used to communicate information regarding comparability or interchangeability to physicians and pharmacists, nor is it the basis for prescribing in the US. GPhA endorses the more comprehensive and currently- established strategy of a biosimilar identification system relying on NDC number, manufacturer name, lot number and a trade name, just as is applied to currently marketed US biologics today. Additionally, this would go a step further in the prevention of medication errors as FDA reviews all trade names for the specific purpose of minimizing errors[40].

C. NDCs Are One of the Most Effective Methods for Tracking Products and Educational Efforts to Promote Reporting of NDCs Will be Far More Productive than Implementing Unique INNs

GPhA agrees that for pharmacovigilance purposes all drug products and biologics must be tracked; however, a tracking system does not require, and would not be helped by, assigning unique INNs to biosimilars. Brand names, manufacturer names, lot numbers and NDC numbers are currently used widely and successfully for tracking purposes, and facilitate the collection of more information than INNs. NDCs in fact may be the most precise method of tracking products.

The NDC contains considerably more information about the product than does the INN.[41] An NDC identifies the manufacturer and provides information on the drug strength, dosage form and formulation, as well as the package sizes. All pharmacy systems use NDCs to track drug products and biologics.[42] GPhA supports and would actively collaborate with FDA and other stakeholders in educational efforts to promote reporting of NDCs whenever possible.
Figure: *Placeholder for figure that makes clear how much more information the NDC# contains*



The FDA Sentinel System (Sentinel System), along with pharmacy and payer systems, uses NDCs to identify specific products. Some have raised the concern that the Sentinel System does not always draw from databases that capture NDCs. We note, however, that the Sentinel System has little utility (Positive Predictive Values of less than 50%) in identifying even the most clinically pronounced outcomes of an immunogenic reaction, anaphylaxis and other hypersensitivity reactions.[43] Thus, we believe it premature to point to the Sentinel System as a reason to change the current naming system, as development continues and the system can already accommodate NDCs.

Complete records with NDCs recorded at each transaction will be the most expeditious route to tracking and tracing each and every product in the most effective way possible. No system, however perfectly designed, can ever compensate for the failure to record the necessary data, and any new system requires significant investment and time for users to get up to speed. GPhA suggests that addressing any failure to include NDCs be addressed as the most immediate priority for those concerned with patient safety. GPhA also believes that approaches such as the current proposed federal legislation enhancing the track and trace system for all medicines will be better suited to assuring the quality of pharmacovigilance data than the introduction of different non-proprietary names for RPPs and biosimilars.

In sum, if problems exist with the current tracking system, assigning a unique INN to each biosimilar will not solve these problems, and indeed will distract from the real solution needed. Nonetheless, as stated by the FDA in their biosimilars naming statement to WHO in 2006:[44]

> "Considering the inherent difficulties in additional INN product distinctions (e.g. retroactive and lifecycle changes in naming, additional INN responsibility and liability), if the world community decides to proceed with a change in the policies regarding the assigning of INNs, it should be preceded by (a) appropriate exploration of alternatives (e.g. improvements in education and/or labeling), (b) assuring the such changes fall

within the scope, competence, and expertise of the INN program, and (c) the performance and independent validation of a formal risk assessment and/or documentation of events with appropriate statistical treatment."

Conclusion

A major goal of the BPCIA is to create competition in the marketplace for biologics, thereby expanding access to, and increasing the affordability of, these critical medicines. As its title suggests, the BPCIA also is intended to stimulate innovation and investment in the next generation of originator biologics and it is mutually beneficial if this happens alongside the availability of biosimilars. Patient access to affordable biologics should be of significant interest to FDA given the Agency's mission to protect and promote the public health. Biosimilar development provides a new opportunity to improve access to health care for many Americans to those products with which the FDA is already the most familiar. Adoption of unique non-proprietary names for each biosimilar could jeopardize patient safety, inhibit market competition and disrupt the current global naming system. Unsubstantiated concerns regarding biosimilar nomenclature must not be used as an anti-competitive barrier to biosimilar development and commercialization.

GPhA encourages the Agency and other stakeholders to begin a dialogue to explore how we can support our current pharmacovigilance system, and optimize complete and accurate data collection and analysis, rather than unilaterally assigning unique non-proprietary names to a specific subset of biologic products without any rationale or even preliminary data to suggest why this will improve outcomes for patients. We fully support vigorous enhancement of tracking systems and education of physicians, pharmacists and other healthcare practitioners to include the brand name, the INN, the NDC and the manufacturer name, as a minimum, on all safety reports whenever possible. These enhancements are of equal importance to all biologics, and most immediately to those already on the market in the US and available to patients today.

GPhA hopes that FDA will be consistent in applying the same scientific principles of nomenclature to biosimilars that it has applied successfully to all other products for 60 years. We look forward to a continued effort of working together with FDA to improve the lives of consumers by providing timely access to affordable pharmaceuticals.

C. Environmental Impact

The actions requested herein are subject to categorical exclusion under 21 C.F.R § 25.30.

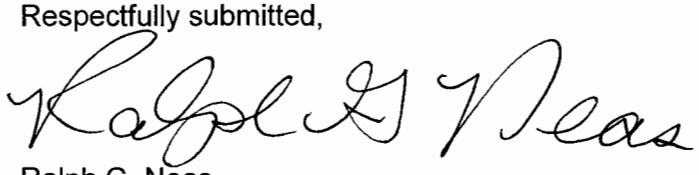
D. Economic Impact

Pursuant to 21 C.F.R. § 10.30(b), an economic impact statement will be submitted only at the request of the Commissioner.

E. Certification

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which is unfavorable to the petition.

Respectfully submitted,



Ralph G. Neas
President and CEO

Attachment

Table: Examples of FDA Approved/Licensed biologic products that share INNs

Brand/Trade Name	**Common Name (established, generic, INN, USAN)**	Sponsor	Original Approval Date	FDA Application Number
Myozyme®	**Alglucosidase Alfa**	Genzyme	April 28, 2006	BLA 125141
Lumizyme®		Genzyme	May 24, 2010	BLA 125291
Kogenate FS®	**Antihemophilic Factor (Recombinant)**	Bayer Corp	June 26, 2000	BL 103332
ReFacto®		Genetics Institute	March 6, 2000	BL 980137
Recombinate®		Baxter Healthcare Corporation	January 21, 2010	BL 103375
Advate®	**Antihemophilic Factor (Recombinant) - Plasma/Albumin Free**	Baxter Healthcare Corp	July 25, 2003	BL 125063
Xyntha®		Wyeth Pharmaceuticals, Inc.	February 21, 2008	BL 125264
Miacalcin®	**Calcitonin Salmon**	Novartis	August 17, 1995	NDA 020313
Calcimar®		Sanofi Aventis US	April 17, 1978	NDA 017760
Tripedia®	**Diphtheria & Tetanus Toxoids & Acellular Pertussis Vaccine Adsorbed**	Sanofi Pasteur, Inc	July 31, 1996	BL 103922
Infanrix®		GlaxoSmithKline Biologicals	January 29, 1997	BL 103647
Daptacel®		Sanofi Pasteur, Inc	May 14, 2002	BL 103666
VAQTA®	**Hepatitis A Vaccine, Inactivated**	Merck & Co, Inc	August 11, 2005	BL 103606
Havrix®		GlaxoSmithKline Biologicals	October 17, 2005	BL 103475
Engerix-B®	**Hepatitis B Vaccine (Recombinant)**	GlaxoSmithKline Biologicals	July 7, 1998	BL 103239
Recombivax HB®		Merck & Co, Inc	August 27, 1999	BL 101066

Wydase®	**Hyaluronidase**	Baxter	March 22, 1950	NDA 006343
Vitrase®		Ista Pharms	May 5, 2004	NDA 021640
Amphadase®		Amphastar Pharm	October 26, 2004	NDA 021665
Hydase®		Akorn Inc	October 25, 2005	NDA 021716
Fluzone®, Fluzone High-Dose and Fluzone Intradermal®	**Influenza Virus Vaccine**	Sanofi Pasteur, Inc	September 4, 2002	BL 103914
Fluarix®		GlaxoSmithKline Biologicals	August 31, 2005	BL 125127
Fluvirin®		Novartis Vaccines and Diagnostics Ltd	September 14, 2005	BL 103837
Flucelvax®		Novartis Vaccines and Diagnostics Ltd	November 20, 2012	BL 125408
FluLaval®		ID Biomedical Corp of Quebec	October 5, 2006	BL 125163
Afluria®		CSL Limited	September 28, 2007	BL 125254
Agriflu®		Novartis Vaccines and Diagnostics S.r.l.	November 27, 2009	BL 125297
Iletin® I	**Insulin Pork**	Eli Lilly	June 17, 1966	NDA 017931
Insulin and Regular Insulin		Novo Nordisk	Unknown	NDA 017926
Iletin® II and Regular Iletin® II	**Insulin Purified Pork**	Eli Lilly	December 5, 1979	NDA 018344
Regular Purified Pork Insulin		Novo Nordisk	March 17, 1980	NDA 018381
Velosulin®		Novo Nordisk	Unknown	NDA 018193

Exubera®	**Insulin Recombinant Human**	Pfizer	January 27, 2006	NDA 021868
Humulin® BR		Eli Lilly	April 28, 1986	NDA 019529
Humulin® R and Humulin® R Pen		Eli Lilly	October 28, 1982	NDA 018780
Novolin® R		Novo Nordisk	June 25, 1991	NDA 019938
Velosulin® BR		Novo Nordisk	July 19, 1999	NDA 021028
Humulin® 70/30 and Humulin® 70/30 Pen	**Insulin Recombinant Human; Insulin Suspension Isophane Recombinant Human**	Eli Lilly	April 25, 1989	NDA 019717
Novolin® 70/30		Novo Nordisk	June 25, 1991	NDA 019991
Mixtard® Human 70/30	**Insulin Recombinant Human; Insulin Suspension Isophane Semisynthetic Purified Human**	Bayer Pharms	March 11, 1988	NDA 019585
Novolin® 70/30		Novo Nordisk	Unknown	NDA 019441
Novolin® R	**Insulin Recombinant Purified Human**	Novo Nordisk	Unknown	NDA 018778
Velosulin® BR Human		Novo Nordisk	Unknown	NDA 019450
Insulin Insulatard NPH Nordisk	**Insulin Suspension Isophane Purified Pork**	Novo Nordisk	Unknown	NDA 018194
NPH Lietin® II (Pork)		Eli Lilly	December 5, 1979	NDA 018345
NPH Purified Pork Isophane Insulin		Novo Nordisk	July 30, 1981	NDA 018623
Humulin® N	**Insulin Suspension Isophane Recombinant Human**	Eli Lilly	October 28, 1982	NDA 018781
Novolin® N		Novo Nordisk	July 1, 1991	NDA 019959
Insulatard® NPH Human	**Insulin Suspension Isophane Semisynthetic Purified Human**	Novo Nordisk	Unknown	NDA 019449
Novolin® N		Novo Nordisk	Unknown	NDA 019065

Protamine Zinc and Iletin® II	**Insulin Suspension Protamine Zinc Purified Beef**	Eli Lilly	June 12, 1980	NDA 018476
Protamine Zinc Insulin		Bristol Myers Squibb	Unknown	NDA 017928
Lente®	**Insulin Zinc Suspension Purified Pork**	Novo Nordisk	March 17, 1980	NDA 018383
Lente Iletin® II		Eli Lilly	December 5, 1979	NDA 018347
Humulin® L	**Insulin Zinc Suspension Recombinant Human**	Eli Lilly	September 30, 1985	NDA 019377
Novolin® L		Novo Nordisk	June 25, 1991	NDA 019965
Avonex®	**Interferon Beta-1A**	Biogen	May 17, 1996	BLA 103628
Rebif®		Serono Inc	March 7, 2002	BLA 103780
Betaseron®	**Interferon Beta-1B**	Bayer Healthcare Pharms	July 23, 1993	BLA 103471
Extavia®		Novartis	August 14, 2009	BLA 125290
Asellacrin® 10, Asellarcrin® 2	**Somatropin**	EMD Serono	July 30, 1976	NDA 017726
Crescormon®		Genentech	April 6, 1979	NDA 017992

Accretropin®	**Somatropin Recombinant**	Cangene	January 23, 2008	NDA 021538
Bio-Tropin®		Ferring	May 25, 1995	NDA 019774
Genotropin® and Genotropin® Preservative Free		Pharmacia and Upjohn	August 24, 1995	NDA 020280
Humatrope®		Eli Lilly	March 8, 1987	NDA 019640
Norditropin® Flexpro and Norditropin® Nordiflex		Novo Nordisk	June 20, 2000	NDA 021148
Nutropin® and Nutropin® AQ		Genentech	Nov. 17, 1993 and Dec. 29, 1995	NDA 020168 and NDA 020522
Omnitrope®		Sandoz	May 30, 2006	NDA 021426
Saizen®		EMD Serono	October 8, 1996	NDA 019764
Serostim®		EMD Serono	August 23, 1996	NDA 020604
Tev-Tropin®		Ferring	May 25, 1995	NDA 019774
Valtropin®		LG Life	April 19, 2007	NDA 021905
Zorbtive®		EMD Serono	December 1, 2003	NDA 021597
Brand Name®	The blue background means the product has been withdrawn but not for safety or efficacy reasons, and so the product is still available as a reference product			

[1] WHO INN Home Page, available at: http://www.who.int/medicines/services/inn/en/ (accessed August 23, 2013).

[2] For example, both Recombinate (Antihemophilic Factor (Recombinant)) and Kogenate (Antihemophilic Factor (Recombinant)) are full-length factor VIII products made by different manufacturing processes but from the same genetic information. Refacto (Antihemophilic Factor (Recombinant)) is a substantially modified b-domain deleted factor VIII product and also shares the same INN.

[3] We recognize that some regions of the world do not use standards of highly similar/no clinically meaningful differences for marketed biosimilars and they may consider unique INNs due to lack of scientific support for comparability. However, for highly regulated regions that

adhere to scientifically sound approaches for assessing biosimilars, there is no justification for departing from FDA's long-held naming policy. In fact, with the expansion of highly sophisticated analytical technologies there is even more support for continuing to assign the same INN to products deemed highly similar/no clinically relevant differences throughout the world.

[4] A search on the word "name" in the entirety of the BPCIA shows that the word is never used. The text of the BPCIA is available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/UCM216146.pdf (last accessed August 23, 2013).

[5] FDA, "US FDA Considerations: Discussion by National Regulatory Authorities with World Health Organization (WHO) On Possible International Non-proprietary Name (INN) Policies for Biosimilars" (submitted to WHO in Sept. 2006), attached to this submission.

[6] FDA, "US FDA Considerations: Discussion by National Regulatory Authorities with World Health Organization (WHO) On Possible International Non-proprietary Name (INN) Policies for Biosimilars" (submitted to WHO in Sept. 2006), attached to this submission.

[7] Letter from Rep. Anna Eshoo to FDA Commissioner Hamburg (Apr. 16, 2012), available at: http://www.regulations.gov/#!documentDetail;D=FDA-2011-D-0611-0043 (accessed August 23, 2013).

[8] The American Pharmacists Association (APhA), the National Association of Chain Drug Stores (NACDS) and the National Community Pharmacists Association (NCPA) letter to FDA, may 25, 2012, http://www.ncpanet.org/pdf/leg/may12/joint_biosimilar_letter.pdf

[9] ICH Q5E: Comparability of Biotechnological/Biological Products Subject to Changes in Their Manufacturing Process. EU: Adopted by CMPM, Dec. 1, 2004, CPMP/ICH/5721/03, date for coming into operation: June 2005; MHLW: Adopted April 26, 2005, PFSB/ELD Notification No. 0426001; FDA: Published in the Federal Register, Vol. 70, No. 125, June 30, 2005, p. 37861-37862, available at: http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Quality/Q5E/Step4/Q5E_Guideline.pdf (accessed August 23, 2013).

[10] FDA, "US FDA Considerations: Discussion by National Regulatory Authorities with World Health Organization (WHO) On Possible International Non-proprietary Name (INN) Policies for Biosimilars" (submitted to WHO in Sept. 2006), attached to this submission.

[11] Section 7002 of the BPCIA defines the term reference product as "the single biologic product licensed under subsection (a) against which a biological product is evaluated in an application submitted under subsection (k)", and with this relationship essential to the approval of a biosimilar, that relationship must be readily apparent to all stakeholders, especially patients and their health care providers.

[12] Niels Vermeer (UU/MEB) presentation to the EMA "Traceability of biopharmaceuticals in spontaneous reporting systems" (May 25, 2012), available at:

http://www.ema.europa.eu/docs/en_GB/document_library/Presentation/2012/05/WC500127934 (accessed August 23, 2013).

[13] For a description of the debate, see e.g., Senior, Melanie, The Name Game: Will Innovators' Latest Battlefront Kill Biosimilars?, The RPM Report, September 2013, posted July 8, 2013, Available at: http://www.elsevierbi.com/publications/rpm-report/9/8/the-name-game-will-innovators-latest-battlefront-kill-biosimilars (accessed August 23, 2013).

[14] Section 7002 of the BPCIA notes that the statute requires a single 351(a) reference product for each biosimilar and this section also provides a 12-year exclusivity provision, both of which is evidence of the experience that FDA has with that reference product.

[15] ICH Q5E: Comparability of Biotechnological/Biological Products Subject to Changes in Their Manufacturing Process. EU: Adopted by CMPM, Dec. 1, 2004, CPMP/ICH/5721/03, date for coming into operation: June 2005; MHLW: Adopted April 26, 2005, PFSB/ELD Notification No. 0426001; FDA: Published in the Federal Register, Vol. 70, No. 125, June 30, 2005, p. 37861-37862, available at: http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Quality/Q5E/Step4/Q5E_Guideline.pdf (accessed August 23, 2013).

[16] Weise et al. Biosimilars: what clinicians should know. *Blood* (October 26, 2012 online pre-publication) 10.1182/blood-2012-04-425744.

[17] Janet Woodcock, Deputy Commissioner, Chief Medical Officer, FDA, testimony before the House Committee on Oversight and Government Reform, March 26, 2007, available at http://www.fda.gov/NewsEvents/Testimony/ucm154070.htm (accessed August 23, 2013).

[18] Schiestl, M et al. "Acceptable Changes in Quality Attributes of Glycosylated Biopharmaceuticals", Nature Biotechnology, (Apr. 2011); **29**, 4, 310-312.

[19] Christian Schneider, "Biosimilars in rheumatology: the wind of change", Ann Rheum March 2013 Volume 72, No 3. Available at http://ard.bmj.com/content/72/3/315.full.pdf+html?sid=1198ecf7-6e8f-4cda-8a8c-f343d0e7917b (accessed August 23, 2013).

[20] WHO, Guidance on INN, available at http://www.who.int/medicines/services/inn/innguidance/en/index.html (accessed August 23, 2013).

[21] FDA, "US FDA Considerations: Discussion by National Regulatory Authorities with World Health Organization (WHO) On Possible International Non-proprietary Name (INN) Policies for Biosimilars" (submitted to WHO in Sept. 2006), attached to this submission.

[22] Presentation by Mark McCamish at FDA/DIA Biosimilars Conference Washington DC (Sept. 12, 2012): "Sandoz biosimilars are **sold in over 50 countries** and have accumulated **more**

than 50 million patient days drug exposure", and this is just one sponsor of biosimilars in highly regulated markets.

[23] Complete Reference with hyperlink to GPhA website

[24] Mark McCamish, Agnieszka Moskal Gallagher, John Orloff, "Biosimilar By Name and Biosimilar By Nature", July 2013 Feature Article RPM Report: June 28 2013. Available at: http://www.elsevierbi.com/publications/rpm-report/9/7/biosimilar-by-name-and-biosimilar-by-nature (accessed August 23, 2013).

[25] In their letter to Dr. Hamburg, dated June 25, 2012, PhRMA and BIO state: "Because a biosimilar or interchangeable biological product is highly similar to, but not the same as, its respective reference product, it would be inappropriate, from a patient safety perspective, to permit use of the same name for biological products that are not the same. Unique names will be necessary to ensure appropriate pharmacovigilance. Thus, it is essential that each biological product have a unique non-proprietary name." Since the same name is maintained after a manufacturing change using the highly similar standard, GPhA reaches a different conclusion, but the one used by FDA and individual product sponsors, namely, that the same non-proprietary name is appropriate when the highly similar standard has been achieved. Nonetheless, we would agree with PhRMA and BIO that consistency is important and that the same rules should apply to all biologics.

[26] Christian Schneider, "Biosimilars in rheumatology: the wind of change", Ann Rheum March 2013 Volume 72, No 3. Available at http://ard.bmj.com/content/72/3/315.full.pdf+html?sid=1198ecf7-6e8f-4cda-8a8c-f343d0e7917b (accessed August 23, 2013).

[27] Brand Institute/Drug Safety Institute Survey conducted among 270 healthcare professionals on behalf of GPhA, February 28, 2103.

[28] Ibid.

[29] Ibid.

[30] Guidance for Industry Contents of a Complete Submission for the Evaluation of Proprietary Names U.S. Department of Health and Human Services, FDA February 2010. Available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM075068.pdf (accessed August 23, 2013).

[31] About MedWatcher, available at https://www.medwatcher.org/about.php (accessed August 23, 2013).

> "MedWatcher is a project out of Boston Children's Hospital and Harvard Medical School. It was created in collaboration with the Food and Drug Administration (FDA) Center for Devices and Radiologic Health. The system is run by Epidemico, a Boston Children's spin-out company. Questions? Contact us at info@medwatcher.org."

[32] Presentation by Niels Vermeer "Traceability of biopharmaceuticals in spontaneous reporting systems," (May 25 2012), at the Fifth stakeholder forum on the implementation of the new pharmacovigilance legislation, available at: http://www.ema.europa.eu/docs/en_GB/document_library/Presentation/2012/05/WC500127934.pdf (accessed August 23, 2013), and also presentations available at: http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/events/2012/05/event_detail_000582.jsp&mid=WC0b01ac058004d5c3 (accessed August 23, 2013).

[33] In its 2006 position, FDA demanded this be considered before any changes are made: "Considering the inherent difficulties in additional INN product distinctions (e.g. retroactive and lifecycle changes in naming, additional INN responsibility and liability), if the world community decides to proceed with a change in the policies regarding the assigning of INNs, it should be preceded by (a) appropriate exploration of alternatives (e.g. improvements in education and/or labeling), (b) assuring the such changes fall within the scope, competence, and expertise of the INN program, and (c) the performance and independent validation of a formal risk assessment and/or documentation of events with appropriate statistical treatment." FDA, "US FDA Considerations: Discussion by National Regulatory Authorities with World Health Organization (WHO) On Possible International Non-proprietary Name (INN) Policies for Biosimilars" (submitted to WHO in Sept. 2006), attached to this submission.

[34] FDA, "US FDA Considerations: Discussion by National Regulatory Authorities with World Health Organization (WHO) On Possible International Non-proprietary Name (INN) Policies for Biosimilars" (submitted to WHO in Sept. 2006), attached to this submission.

[35] Guidance for Industry Contents of a Complete Submission for the Evaluation of Proprietary Names U.S. Department of Health and Human Services, FDA February 2010. Available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM075068.pdf (accessed August 23, 2013).

[36] "Established name" is the historical term given to a FDA issued non-proprietary name. This becomes the United States Adopted Name when endorsed by the USAN Committee. Generally, the USAN committee tries to make the USAN match the INN, but this may not be possible for a biosimilar when an INN already exists that matches that of the reference product, if FDA decides to adopt a different approach.

[37] Comments of USP on "Draft Guidances Relating to the Development of Biosimilar Products; Public Hearing" (May 24, 2012), available at http://www.regulations.gov/#!documentDetail;D=FDA-2011-D-0618-0053 (accessed August 23, 2013).

[38] FDA, "US FDA Considerations: Discussion by National Regulatory Authorities with World Health Organization (WHO) On Possible International Non-proprietary Name (INN) Policies for Biosimilars" (submitted to WHO in Sept. 2006), attached to this submission.

[39] Statement of Janet Woodcock, M.D., Deputy Commissioner, Chief Medical Officer, FDA before the House Committee on Oversight and Government Reform, "Follow-on Protein Products" (March 26, 2007), available at: http://www.fda.gov/NewsEvents/Testimony/ucm154070.htm (accessed August 23, 2013).

[40] Guidance for Industry Contents of a Complete Submission for the Evaluation of Proprietary Names U.S. Department of Health and Human Services, FDA February 2010. Available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM075068.pdf (accessed August 23, 2013); MedERRS, available at http://www.med-errs.com/ (accessed August 23, 2013).

[41] Each drug product listed under Section 510 of the Federal Food, Drug and Cosmetic Act (21 USC. § 360) is assigned a unique 3-segment number called the NDC number – this comprises 5 digits that are known as the Labeler code, which are assigned to uniquely identify the entity that manufactures, repacks or distributes the drug; 4 digits which are known as the Product code, which are assigned by the manufacturer to represent the drug, strength, dosage form and formulation; and a final 2 digits, known as the Package code which are assigned by the manufacturer to represent package sizes.

[42] Discussed in the GPhA submission to docket FDA-2011-D-0618 inviting comments on the FDA draft biosimilars guidances, proposed future guidance, and the FDA Part 15 Hearing of May 11, 2012, available at: http://www.regulations.gov/#!documentDetail;D=FDA-2011-D-0618-0055 (accessed August 23, 2013).

[43] Platt, R et al. The US Food and Drug Administration's Mini-Sentinel Program: Status and Direction. Pharmacoepidemiology and Drug Safety 2012; 21(S1): 1–8.

[44] FDA, "US FDA Considerations: Discussion by National Regulatory Authorities with World Health Organization (WHO) On Possible International Non-proprietary Name (INN) Policies for Biosimilars" (submitted to WHO in Sept. 2006), attached to this submission.