Biosimilar By Name and Biosimilar By Nature

The use of unique non-proprietary names for biosimilars has broad implications for brand biologics and FDA's established regulation in the area. Why would the agency want to go down that road?

By Mark McCamish, Agnieszka Moskal Gallagher, and John Orloff

The potential for biosimilars becoming available in the United States has generated a variety of policy recommendations, including that each biosimilar should have a unique non-proprietary name. Implementing such a policy recommendation would impact how FDA currently names all medicines. Therefore, prior to inviting such a measure we must explore the threshold question of why a change in FDA's current naming practice is necessary in the first place.

If a problem does exist with FDA's current naming practice, we must address whether assigning unique non-proprietary names to biosimilars would fix that problem. We must also carefully consider, as did the FDA in its naming policy submission to the World Health Organization in 2006, such a proposal's potential for any other secondary unintended consequences for patient safety. Equally importantly, we should not underestimate the disruption that a unilateral US decision to break from the global norm would have on adverse events reporting worldwide.

We have examined this issue in detail and find no evidence suggesting that FDA's current naming convention is broken or that it cannot accommodate biosimilars. Not only is a change in FDA's naming policy requiring biosimilars to have unique non-proprietary names unnecessary, it will neither protect nor promote the public health.

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The Current Naming System Works

The United States enacted the Biologics Price Competition and Innovation Act (BPCIA) in 2010 to establish a pathway for the Food and Drug Administration (FDA) to approve biologic products as biosimilar to already-approved biologics and to provide access to lower-cost versions of these critical medicines for patients.

Under the statute, a biosimilar must demonstrate to the satisfaction of FDA that it is "highly similar" to an originator reference product and, further, convince the agency that there are "no clinically meaningful differences" in terms of safety, purity and potency between it and its reference product.

The biosimilar will not be considered as interchangeable with its reference product unless the product sponsor provides additional information sufficient to show that the risk of alternating or switching between the biological product and the biosimilar is not greater than using the reference product without such switching. BPCIA is appropriately silent about the nomenclature FDA should apply to biosimilars as such nomenclature should be self-evident from BPCIA's stringent approval requirements: only products which demonstrate the absence of "clinically meaningful differences" from the originator reference products will be approved as biosimilars.

WHO administers the global naming convention, known as the International Non-proprietary Naming (INN) system. Non-proprietary names are intended to facilitate the identification of pharmaceutical substances, also known as active pharmaceutical ingredients, by health care professionals worldwide. INNs are therefore granted based only on the molecular characteristics and pharmacological class of proposed active ingredients, and WHO does not conduct a review of data on the actual product itself. In the United States, a sponsor may

obtain a United States Adopted Name (USAN) as the locally-assigned non-proprietary name.

In the past, USANs have been generally consistent with the INN, where already issued, but they can differ and a different USAN does not impact an already issued INN. INNs and USANs are by definition non-proprietary and therefore not designed to identify a specific product; indeed, once an INN is established, it identifies all products that share the same molecular characteristics (as recognized during the subsequent dossier review by the regulatory authority of the jurisdiction in which the product is to be marketed). WHO's role is not regulatory, the Organization does not conduct a technical review of any product and applying for an INN by a product sponsor is voluntary.

The debate surrounding whether biosimilars should share non-proprietary names with their reference products has confused the established role of the non-proprietary name to simply facilitate the identification of pharmaceutical substances, and instead created the incorrect and misleading impression that the non-proprietary name is intended to provide distinct identification of a specific product.

Lack of Evidence for Different Names

Despite the suggestions to the contrary, there is no indication that the current system will not work for biosimilars. As no product has been approved in the United States as a biosimilar under the BPCIA to date, we must look at existing products to extrapolate the current naming convention's application to biosimilars.

Interestingly, we have found that many existing biologics already share non-proprietary names. As can be seen in Table 1, FDA has approved numerous biologics which, based on their molecular characteristics, appropriately share non-proprietary names even though they were approved as independent applications (separate biologics license applications or new drug applications) and are manufactured by different sponsors. This sharing of non-proprietary names has not resulted in any safety or traceability issues.

Other highly regulated jurisdictions, where biosimilars are already on the market, provide more compelling data confirming that different non-proprietary names are not necessary for tracking and tracing of biosimilars. In Europe, where biosimilars have been on the market since 2006, they share the same INNs with their corresponding reference products, and 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 (somatropin, filgrastim and epoetin). This is the same rate as for originator biologics. There is no reason to expect that the United States' pharmacovigilance system cannot achieve similar or even higher product identification rates given that, unlike the European Union, the United States has the advantage of a singular, nationwide national drug code (NDC) product identification system for tracking.

Even assuming there is a legitimate and identifiable problem with the current naming system, the tracking system does not require, nor would it be helped by, unique non-proprietary names for biosimilars. Non-proprietary names are not, and cannot, be the primary tool relied on for tracking and tracing because they do not contain sufficient information by which they alone can achieve this. It is the proprietary, or trade name of a product that is more useful in that regard, and FDA agrees – "In the U.S. medication-use system, health care providers rely on the proprietary name as the critical identifier". And even trade names comprise only a part of the track and trace tool portfolio as products are also traced by NDCs, manufacturer names, and batch and lot numbers.

We believe that if there is a problem with traceability it appears to be an issue of accurate and complete reporting. As such, any problems with the current system cannot be rectified by assigning unique non-proprietary names to biosimilars – by definition *future* products cannot be considered relevant to any reporting failures for currently approved and marketed products. Further, if there are any weaknesses in the current system with regard to the traceability of a specific product to an adverse event, such weaknesses are not related to the non-proprietary name, given that it has never been a product specific identifier, and any weaknesses must be addressed for all currently approved products (See Table 1, at the end).

It is important to recognize that FDA does not have sole responsibility for oversight and tracking of the use of medical products in the US. Other systems implemented by states, payers and other government agencies, such as the Centers for Medicare & Medicaid Services (CMS), also provide means of product identification at the individual patient level. See Figure 1, for an overview of biologic identification in the current system.

Unique Naming Would Change Established FDA Practice

As FDA has clearly stated when it argued against unique non-proprietary names for biosimilars, "INNs should not be used to imply pharmacologic interchangeability of products with the same active ingredient(s) when no credible scientific data exist that demonstrate such. Likewise, INNs should not be used to differentiate products with the same active ingredient(s) when credible scientific data demonstrate that no pharmacologically relevant differences exist." If one accepts the arguments being proffered for separate non-proprietary names for biosimilars, one must also accept that new and separate non-proprietary names would be required for many biologics currently in the market, leading to inevitable confusion, doubt and prescribing mistakes.

Specifically, requiring unique non-proprietary names for biosimilars would put into question years of FDA's practice of using the well-established analytical standard of high similarity to approve even major manufacturing changes of originator biologic products without a parallel change in the originators' non-proprietary names, despite the fact that the manufacturing changes have altered, sometimes substantially, the originator biologics' molecular structures. Using the high similarity standard, FDA has in these cases satisfied itself that the altered originator biologic would produce the same clinical result in terms of safety, purity and potency as its pre-manufacturing change version. The label does not change and the product retains all indications (irrespective of an understanding of the mechanism of action) and is fully interchangeable with itself pre- and post- change.

FDA and other regulatory authorities worlwide review and approve manufacturing changes in biological products using comparability approaches that use the same highly similar standard that has been written into the biosimilar legislation enacted by Congress. Both similarity exercises are based on the "highly similar" concept as used in the BPCIA and described in FDA's draft guideline on the quality of biosimilars, as well as in the International Conference on Harmonization Q5E guideline (ICH Q5E).

ICH Q5E focuses on assessing quality of the altered molecule pre- and post-manufacturing change, and when the magnitude of the change so requires, on assessing preclinical and clinical data as well. This approach has been coordinated among regulatory authorities across the highly regulated markets, and also in the form of guidance by WHO for biosimilars in other emerging markets where patient access is also critically important.

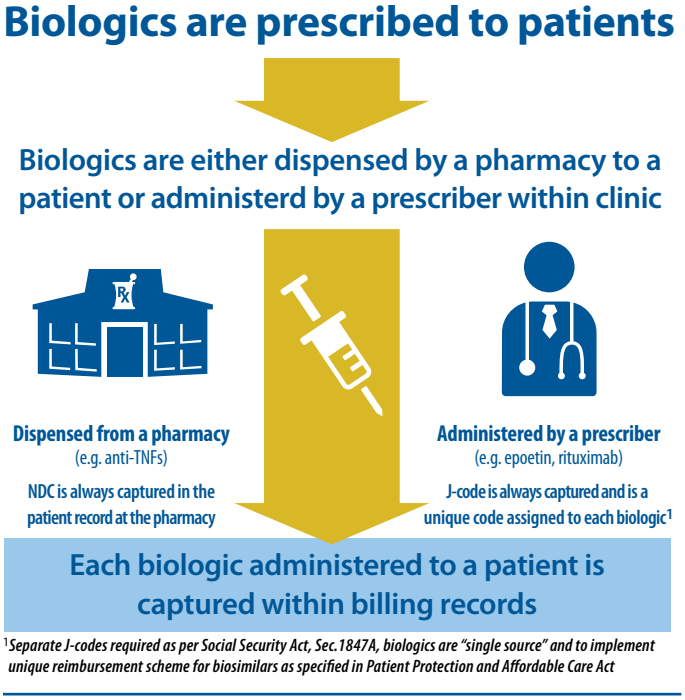
FDA has confirmed this approach. When discussing the biosimilar review process, FDA's Director of the Office of Biotechnology Products Steve Kozlowski commented that "[its] experience with biologics provides important relevant knowledge. Since the mid-1990s, for example, physicochemical and functional assays have been used to characterize changes in manufacturing processes for some biologics, and then animal or clinical studies are used to resolve any remaining uncertainties about the comparability of the products created before and after such changes and to provide sufficient confidence that safety and efficacy are not diminished."

Indeed, data published in peer-reviewed scientific literature demonstrate that, while originator products do change over time, they are well controlled between manufacturing changes, and, even after manufacturing changes, the clinical attributes of the products are acceptable.

FDA will use the same standards to satisfy itself that the biosimilar would produce the same clinical result as the reference product. But if a distinct non-proprietary name was imposed on a biosimilar to highlight, somewhat redundantly, that the product is similar but not the same as the reference product, one would have to question the continued use of the same non-proprietary name in post-manufacturing change originator biologics, and indeed, the absence of notification, on label or otherwise, of the potential change in molecular structures of the originator biologic.

Figure 1

BILLING SYSTEMS IDENTIFY THE SPECIFIC BIOLOGIC ADMINISTERED TO EACH PATIENT



[1]*Separate J-codes required as per Social Security Act, Sec.1847A, biologics are "single source" and to implement unique reimbursement scheme for biosimilars as specified in Patient Protection and Affordable Care Act*

Taken to its logical conclusion under this hypothetical scenario, FDA would require a new non-proprietary name for each post-manufacturing change biologic product. This may be no small feat given that a recent peer-reviewed article looking at the number of manufacturing changes for certain European biologics found that these products have undergone up to 37 manufacturing changes each since approval. Requiring separate non-proprietary names for biosimilars but not originator biologics would undermine FDA's own approval decisions, which in both cases require FDA's determination that the compared product (biosimilar or the post-manufacturing change originator biologic) produces the same clinical outcomes as its comparator (respectively, the reference product or the pre-manufacturing change biologic).

If an identical, consistent naming system is not adopted, patients and physicians may - and should - ask why they were not notified of the change in the originator biologic, which continued to be identified by the same non-proprietary name and brand name and whose label did not reflect the manufacturing change or the corresponding change in the product itself. The practice of maintaining the same non-proprietary names for post-manufacturing change originator biologics is well founded in law, health authority guidelines and science, and should apply equally to naming considerations for biosimilars. Any concern that somehow patients or physicians may be confused by biosimilars bearing the same non-proprietary name as the originator is addressed by the fact that biosimilars stakeholders will be on notice that they are dealing with a different product bearing a different brand name and having a different manufacturer than the reference product.

If FDA applies regulatory science consistently, such that the highly similar standard for manufacturing changes is the same as the highly similar standard for biosimilars, then patients can be confident that a biosimilar will be as similar to its reference as that reference is to itself over its lifetime, and more importantly, that in both cases any minor differences between them will be in clinically inactive components only.

Patient Safety a Major Issue in the Name Game

Far from advancing it, unique local non-proprietary names for biosimilars would be detrimental to patient safety. Assigning unique local non-proprietary names to biologics (especially, but not only, if different to the INN already issued for the same product and already in use in another jurisdiction), which were proved to be highly similar to their reference products, would send a signal that the non-proprietary names are intended to communicate more than the molecular characteristics and the pharmaceutical class of the active ingredient.

It would send a signal that, instead of simply being used as a global cataloguing mechanism for products with a related active ingredient, non-proprietary names are somehow intended to communicate an aspect of the regulatory review and approval itself, such as pharmacologic interchangeability, or indeed lack thereof, in products with the same active ingredient(s). This runs contrary to FDA's previously published position on naming of biosimilars.

A determination of pharmacologic interchangeability of products with the same active ingredient(s) must be made by regulatory agencies based on credible scientific data specific to that product.

For example, in the United States, FDA must make an affirmative determination that two products being compared and bearing the same non-proprietary name are therapeutically equivalent, i.e., that in FDA's judgment they are expected to have equivalent clinical effect. It is this determination by FDA and the subsequent listing of the products as therapeutically equivalent – and not the products' non-proprietary name – that informs physicians, pharmacies, state agencies and other stakeholders that the products can be substituted with the full expectation that they will produce the same clinical effect and safety profile.

Unlike for manufacturing changes, FDA will have to make a separate determination of interchangeability with respect to a biosimilar, and it will be that determination and its reflection on the biosimilar's label that will inform of the biosimilar's interchangeability with its reference product.

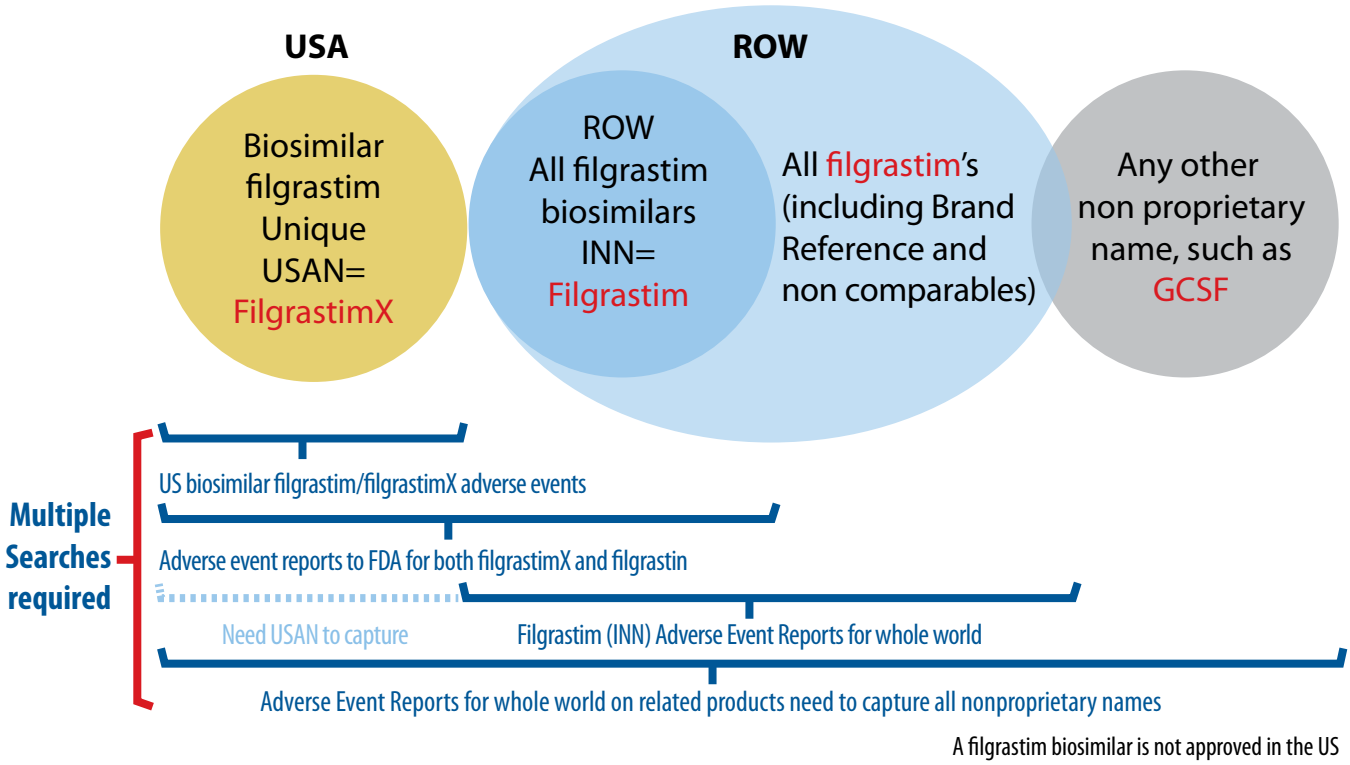
Indeed, FDA has, quite appropriately, expressed alarm at the potential confusion that would be created by the implication that assigning the same non-proprietary names to products was tantamount to a determination of pharmacological interchangeability. The determination of safety, efficacy, and in appropriate cases, interchangeability, is and should remain beyond the scope of any naming convention.

If FDA were to assign different non-proprietary names to products with the same active substance for the purpose of preventing inappropriate substitution, it would necessarily create an equally inappropriate implication that all products with the same non-proprietary names are by definition interchangeable.

This implication could have potentially negative effects on patient safety, especially if such an implication were to be applied to products which share non-proprietary names but which have never been compared with each other and which may even have different indications (again, see Table 1, below). We note that FDA already allows different recombinant and naturally-derived products from different manufacturers to share non-proprietary names, even though such products have been approved by FDA under separate BLAs or NDAs and have never demonstrated comparability (in fact, in one case, have explicitly failed comparability).

Figure 2

UNIQUE NON-PROPRIETARY NAMES CREATE THE POTENTIAL FOR INCREASED CONFUSION - HERE AN EXAMPLE IS CREATED FOR A BIOSIMILAR ALREADY APPROVED IN EUROPE AND WITH THE INN OF FILGRASTIM



Indeed, were a demonstration of "sameness" be required by FDA retrospectively today, many if not all of these products would fail to meet it. The fact that they share non-proprietary names has not resulted in any safety issues, but an implication that the same non-proprietary name indicates that those products are all interchangeable would indeed negatively impact the safe and rational use of these and other medicines which share non-proprietary names.

On the other hand, because non-proprietary names are assigned based on the molecular structure and pharmacological class of products, they have been utilized successfully in advancing pharmacovigilance monitoring. Non-proprietary names are used in national and regional pharmacovigilance systems to facilitate the detection of new safety information related to pharmaceutical substances on a global level. They support the aggregation of safety data, detection of class effects, and appropriate and timely response to safety alerts.

These significant safety benefits would be undermined if products with the same active ingredients were assigned different non-proprietary names, especially when such products have been shown to produce the same clinical result in terms of safety, purity and potency by credible scientific data. Different non-proprietary names (the locally assigned non-proprietary name in the US being the USAN) will necessarily decouple biosimilars approved in the United States from safety data of the same products elsewhere in the world, where consistent non-proprietary names are currently used, and vice versa (See Figure 2, above).

Inconsistencies with USP Naming

In addition, assigning different non-proprietary names to products which conform to an established compendia monograph in the US would be inconsistent with the current regulations governing United States Pharmacopeia (USP) names. The USP General Notices specify how the compendial standards,

including monographs for particular drug substances and drug products, are developed.

The current USP and National Formulary (NF) standards are then publically listed and referenced in the Federal Food, Drug, and Cosmetic Act (FDCA). USP is responsible, with FDA contributions, for publishing the compendial standards, and FDA is responsible for the enforcement of USP standards for all products marketed in the US.

The FDCA states that drugs, including biologics, will be deemed adulterated or misbranded if they do not conform to recognized compendial standards relating to non-proprietary naming and identity, and strength, quality and purity. Therefore, if USP has a monograph for a biologic product, which would be applicable to a biosimilar, such biosimilar will be deemed misbranded unless its label bears the official title recognized in USP-NF.

Of course, FDA has the authority to change a USP name in the interest of usefulness and simplicity, but first it must submit its act to public notice and comment and provide the opportunity for judicial review. We note that such a change would necessitate a parallel change to the USP name of the originator product used as a reference for that same biosimilar.

Unique Names Runs Counter to the BPCIA

The BPCIA was enacted to provide a pathway for approval of products that reference already-approved biological molecules. It is for FDA to determine whether a product sponsor under the BPCIA meets the demanding standards of high similarity to the reference biological molecule. If it does not demonstrate high similarity and a lack of clinically meaningful differences in terms of safety, purity and potency, it is for FDA to simply not approve the product as a biosimilar.

Approving it under a separate non-proprietary name would run counter to the very purpose of the BPCIA, a major goal of which is to create competition in the marketplace for biologics and expand access to, and increase the affordability of, these critical medicines. This goal of providing patients and providers with access to high quality, lower cost alternative products and incentivizing innovation in the field of medicine should never compromise patient safety.

It is the FDA review process, however, and not separate non-proprietary names, that will ensure patient safety is never compromised. Indeed, assigning separate non-proprietary names to biosimilars will undoubtedly undermine this objective by creating confusion in the healthcare system and unnecessarily casting doubt on FDA's robust and well-established practice of reviewing the relevance of differences in originator products after manufacturing changes. As unfortunate as such a result would be, it will only be compounded unnecessarily and equally tragically by thwarting the Congressional intent of increasing patient access to affordable biologics.

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Table 1

EXAMPLES OF FDA APPROVED/LICENSED BIOLOGIC PRODUCTS THAT SHARE INNS (LISTED ALPHABETICALLY BY INN; PRODUCTS SHADED IN BLUE ARE CURRENTLY DISCONTINUED, BUT NOT WITHDRAWN FOR SAFETY OR EFFICACY REASONS)

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 Corporation	July 25, 2003	BL 125063
Xyntha®		Wyeth Pharmaceuticals, Inc.	February 21, 2008	BL 125264
Miacalcin®	Calcitonin Salmon	Novartis	August 17, 1995	NDA 20313
Calcimar®		Sanofi Aventis US	April 17, 1978	NDA 17760
Calcitonin Salmon (Generic)		Apotex Inc	November 17, 2008	ANDA 076396
Calcitonin Salmon (Generic)		AstraZeneca	Unknown	ANDA 073690
Calcitonin Salmon (Generic)		Par Pharm	June 8, 2009	ANDA 076979
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

Brand/Trade Name	Common Name (established, generic, INN, USAN)	Sponsor	Original Approval Date	FDA Application Number
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 & 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