SafeBiologics
ALLIANCE for SAFE BIOLOGIC MEDICINES

May 7, 2019

Commissioner Norman E. Sharpless, M.D.
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Re: Comments to March 2019: "Nonproprietary Naming of Biological Products: Update" (Docket No. FDA-2013-D-1543)

Dear Acting Commissioner Sharpless:

The Alliance for Safe Biologic Medicines (ASBM) appreciates the opportunity to comment on the United States Food and Drug Administration's draft "Nonproprietary Naming of Biological Products: Update - Guidance for Industry." We support the revised guidance and FDA's decision to apply unique suffixes to biologics at the time of approval.

A 2019 survey of 202 US prescribers of biologics conducted after the FDA announced its recent policy update shows that there is overwhelming physician support for the FDA's suffix-based distinct naming approach. Respondents were drawn in equal proportion from specialties in which biologics are routinely prescribed, including rheumatology, gastroenterology, endocrinology, oncology, dermatology, neurology, immunology, nephrology, and ophthalmology. The full survey is attached as an addendum to this comment letter.

85% of physicians surveyed said they "strongly agree" or "somewhat agree" with the FDA's policy of adding 4-letter suffixes to distinguish biosimilars from the originator product on which they are based, and from other biosimilars to that product. Only 7% strongly or somewhat disagree with the policy, while 8% were "unsure".

The FDA has taken a sound, practical approach to ensuring the safety of patients and the nation's supply of biologic medicines in its plan to:

- Designate for interchangeable products, as it does for originator and biosimilar products, a proper name that is a combination of the core name and a distinguishing suffix.
- Refrain from modifying the proper names of biological products that have already been licensed or approved under the Public Health Service Act without an FDA-designated suffix in their proper names.
- Refrain from applying the naming convention to the proper names of transition biological products.

Here again, the survey data show overwhelming support among US prescribers for these FDA decisions:

- **71% strongly or somewhat agree with the FDA's decision** not to rename previously-approved biologics with suffixes, while 25% strongly or somewhat disagreed and 5% were unsure.

- **67% strongly or somewhat agreed with the FDA's decision** not to rename insulin, desirudin, and somatropin products previously approved under the Food Drug and Cosmetics Act. 23% strongly or somewhat disagreed, while 9% were unsure.

Even interchangeable biosimilars- those that can be substituted without physician involvement- should have distinct suffixes, according to physicians:

- **82% of respondents strongly or somewhat agreed with the FDA's decision to assign suffixes to interchangeable biosimilars**, 9% strongly or somewhat disagreed, and 9% were unsure.

- **67% of respondents strongly or somewhat agreed with the FDA's decision** not to rename biosimilars that are subsequently designated as interchangeable; 24% strongly or somewhat disagreed, and 9% were unsure.

Biologics have transformed the treatment of many serious diseases and biosimilars are helping to make these important medicines more affordable. However, access to medicine is only valuable when those medicines remain safe and are used as intended by the prescriber. We commend FDA's ongoing commitment to and leadership in ensuring effective pharmacovigilance and prevention of inadvertent substitution of biologic medicines.

The scientific properties of biologic medicines present distinct regulatory challenges. The naming policy is effectively tailored to address these challenges. We agree with FDA's comments in the 2017 guidance,

> Although safety of biological products is rigorously assessed before approval, safety issues that are specific to a manufacturer may arise after approval with any marketed product. To help ensure patient safety and allow the Agency and the manufacturer to swiftly identify and address a problem, FDA aims to track adverse events to a specific manufacturer (and as appropriate, to a lot or manufacturing site for a particular biological product) and allow surveillance systems to detect safety signals throughout the life cycle of a product. Identifying a biological product's manufacturer can help target remedial action (including recall) to avoid implicating a broader set of products for which no such problem exists.[1]

Applying suffixes to products at the time of approval is essential to the safety of patients and the integrity of the U.S. biologic drug supply. Changes can and do occur in biologic products over time due to the nature of biology. This aspect of biotechnology is well known and must be managed. Efforts on the part of regulators and manufacturers to ensure product consistency and safety are reinforced and rewarded by effective pharmacovigilance. Any problem with a product – which can occur despite best

[1] https://www.fda.gov/downloads/drugs/guidances/ucm459987.pdf (at page 4)

efforts and intentions – is likely to be detected more quickly and accurately attributed with the presence of robust pharmacovigilance.

ASBM supports the decision to apply distinguishable suffixes to products deemed interchangeable. The need for effective pharmacovigilance applies regardless of whether a product is an originator, biosimilar or interchangeable product. The robust pharmacovigilance is of particular interest in the context of interchangeable products given the expectation that they will be substituted at the pharmacy during a course of treatment, a practice that is not presumed for noninterchangeable biosimilars.

Another benefit of clear product identification as a result of the FDA's naming policy is the opportunity to learn more about patients and biotechnology products. In this era of big data, important insights are discerned over time and in ways that are not anticipated before or at the time of approval. Those insights are only available if data is recorded with sufficient specificity. This specificity is facilitated by a shared cored name amongst originator, biosimilar and interchangeable biosimilar products that will consistently and readily associate newly gathered information with a specific set of products, while not detracting from the effective pharmacovigilance supported by the distinguishing suffix.

The agency has implemented a policy that will stand the test of time and make the future safer. It is easy to aggregate granular data, but in the absence of granularity, data cannot be disaggregated. You cannot unscramble the egg. Nonproprietary names are the common element utilized across prescribing, claims, billing and PV databases, and identical nonproprietary names will essentially serve to "scramble the egg". It is the job of the FDA to make sure that the necessary data does not get scrambled on the front end, and the suffix policy facilitates clear product identification and helps to prevent the issue of uninterpretable data.

FDA's decision to refrain from changing the nonproprietary names of biologics approved without suffixes is prudent. In a perfect world, the suffix policy would have been in place when biologics first entered the marketplace and every biologic would have a distinct suffix. However, when the first biologics were approved, the regulatory pathway to approve biosimilar products did not exist, and neither did the problem of unique product identification for biologics.

It is necessary to make the best policy decision for the circumstances as they exist – rather than as we would prefer them to be. The assignment and use of suffixes increase accountability and traceability; they are enormously valuable for pharmacovigilance and safe use, as discussed above, even in the absence of suffixes on a subset of originator biologics. Few of the approved biologics lacking a suffix will have biosimilar products and thus there will be little confusion about product identity, so these products can still be tracked and traced appropriately.

FDA's policy is forward looking, preparing for when the market place will be even more complex; the vast majority of biologics – originator, biosimilar, and interchangeable – will have suffixes. FDA has assigned a unique suffix at the time of approval to more than forty biologics approved since adoption of the policy, including more than two dozen originator biologics. There is every reason to continue doing so. Arguments to the contrary lack veracity and data.

The presence or absence of a suffix plays no role in uptake of the product. This is demonstrated by data; the 36-month uptake rate of a biosimilar named "filgrastim" in Europe and "filgrastim-sndz" in the United States is 41 percent in both jurisdictions. The tracks with data presented to FDA in 2015:

> In Japan, for instance, epoetin alfa biosimilar 1 – a biosimilar epoetin product – has 94% market share despite the requirements that it have a different [nonproprietary name] (NPN) and that it specifically be identified as a biosimilar. In four of the five largest European markets, Germany, Italy, Spain, and the UK, a biosimilar with a distinguishable NPN has a greater market share than a biosimilar with the same NPN (where both products reference the same originator biologic). In Australia, the NPN of the biosimilar short-acting erythropoiesis-stimulating agent (ESA) is distinguishable from the reference product, but biosimilar G- CSFs do not have distinguishable names; the biosimilar ESA and G-CSFs respectively have 47% and 57% of unit shares of their accessible markets, suggesting no strong correlation between the naming convention and uptake. The factors that will ultimately drive uptake of a biosimilar are myriad and more complicated than the NPN.[2]

Arguments with regard to the presence or absence of a suffix influencing perception around a product also fall short. More originator products than biosimilars have received suffixes to date. Over time, most products will have suffixes. As then-FDA Commissioner Gottlieb noted in his comments announcing the Guidance Update,

> In advancing consistency in the convention for naming all newly licensed biologicals – be it originator, biosimilar or interchangeable products – we aim to mitigate the risk of false perceptions from health care providers and patients that there's a difference in the relative safety and effectiveness of these biological products based on their name. [3]

With regard to the question of assigning suffixes to vaccines, we believe the considerations are very different and therefore suffixes may not be essential to effective pharmacovigilance for vaccines as they are for other biologics. For example, many robust vaccine safety monitoring systems already are in place in the US to help ensure appropriate pharmacovigilance without requiring an additional suffix. These programs include the Immunization Safety Office: Vaccine Adverse Event Reporting System (VAERS), Vaccine Safety Datalink (VSD), and Clinical Immunization Safety Assessment (CISA). In addition to robust global pharmacovigilance surveillance programs by vaccine manufacturers, healthcare professionals also understand very well how and when to file suspected adverse events for vaccines. These tools have proven a workable approach to pharmacovigilance for vaccines in large part because vaccines are administered infrequently – e.g. seasonally for the flu vaccine or far less frequently for vaccines such as chicken pox and measles. This is the second reason vaccines are distinct from other biological products for which suffixes are necessary. Many, if not most, biologics are administered multiple times; many are administered repeatedly over long periods of time. Under those circumstances, the data to be recorded is substantial and the potential to receive different versions of the product is quite high. Finally, vaccines are intended to induce an immune response. For other biologics, an unwanted immune response is exactly what we are guarding against and may result when something goes wrong. Given the molecular size of biologic medicines, it is easier to trigger an immune response than to avoid triggering an unwanted response which could have dire consequences for patients.

In summary, we support FDA's decision to continue providing suffixes to all new biologics – both originator and biosimilar – and to forgo assigning suffixes to the limited number of already marketed

[2] Comment from Amgen, Inc. Posted to regulations.gov October 27, 2015. Available at https://www.regulations.gov/document?D=FDA-2013-D-1543-0166 at page 4

[3] https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm632870.htm

products that lack a suffix. This policy is future focused and facilitates accurate prescribing, dispensing and adverse event reporting for biologics without additional cost or confusion for patients or prescribers. Finally, the sensibility of the FDA's policy is borne out by the data, which show strong support for it from the very specialists who regularly and routinely prescribe biologic medicines.

Sincerely,

Michael Reilly
Executive Director,
Alliance for Safe Biologic Medicines

Madelaine Feldman, MD, FACR
Executive Director,
Alliance for Safe Biologic Medicines

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ASBM US
Prescribers Survey

Industry Standard Research

Kevin Olson, CEO | KevinO@ISRreports.com | 919-301-0106

May, 2019

Survey Methodology

- 202 Prescribers were recruited from specified practice areas in the United States
- 10 practice areas: Dermatology, Endocrinology, Gastrointestinal, Immunology, Nephrology, Neurology, Oncology, Ophthalmology, Rheumatology
- All N-size targets (country/practice area combinations) were reached
- 5 minute web-based survey
- Data were collected in May 2019

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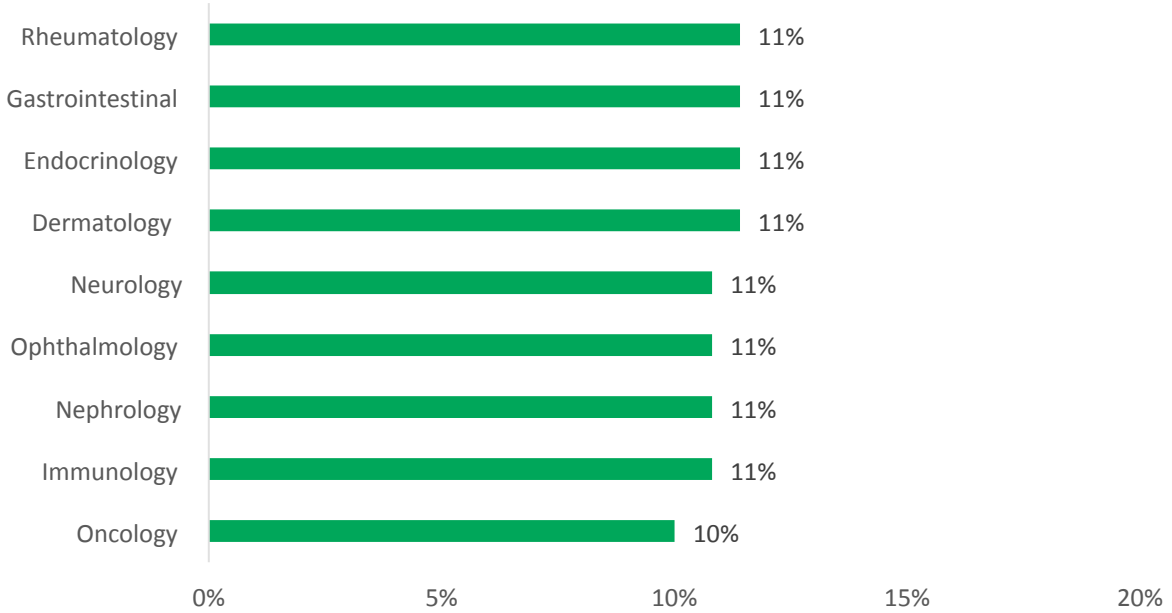
DEMOGRAPHIC DATA/ SAMPLE CHARACTERISTICS

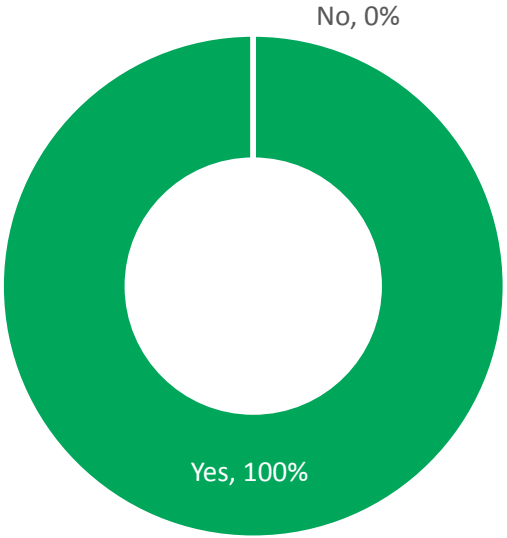
Primary Therapeutic Area

S1. Please indicate your primary practice area or therapeutic area in which you practice. (n=202)



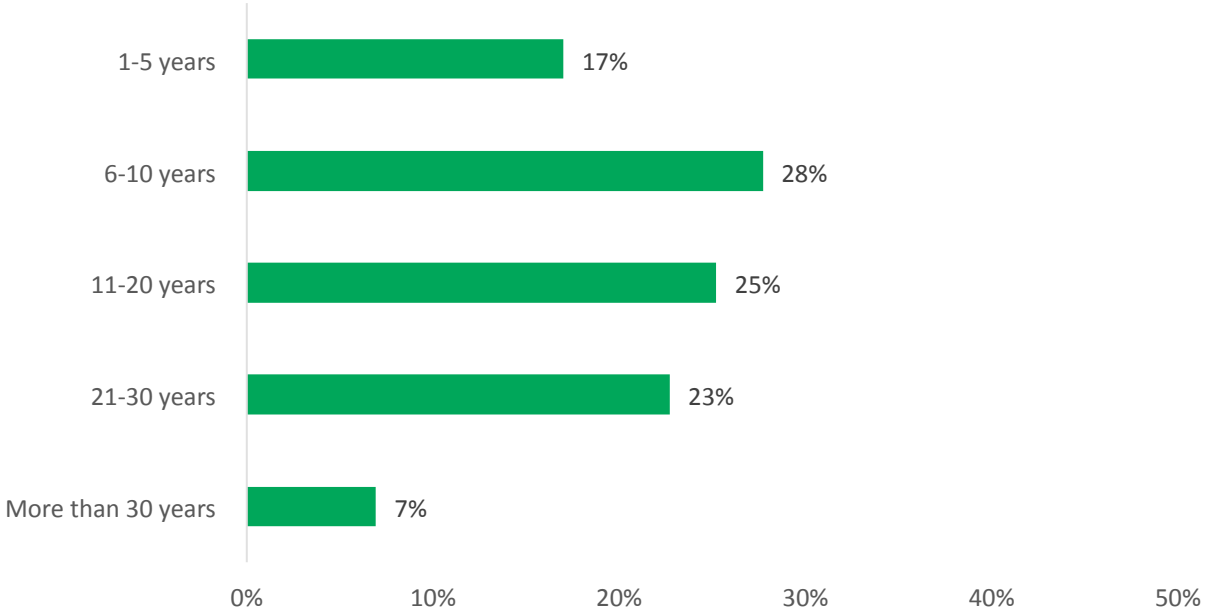
Biosimilar Approval Awareness

S2. Are you aware that a biosimilar may be approved for several or all indications of the reference product on the basis of clinical trials in only one of those indications? (n=202)



Length of Time Practicing Medicine

S3. For how many years post-residency have you been practicing medicine? (n=202)



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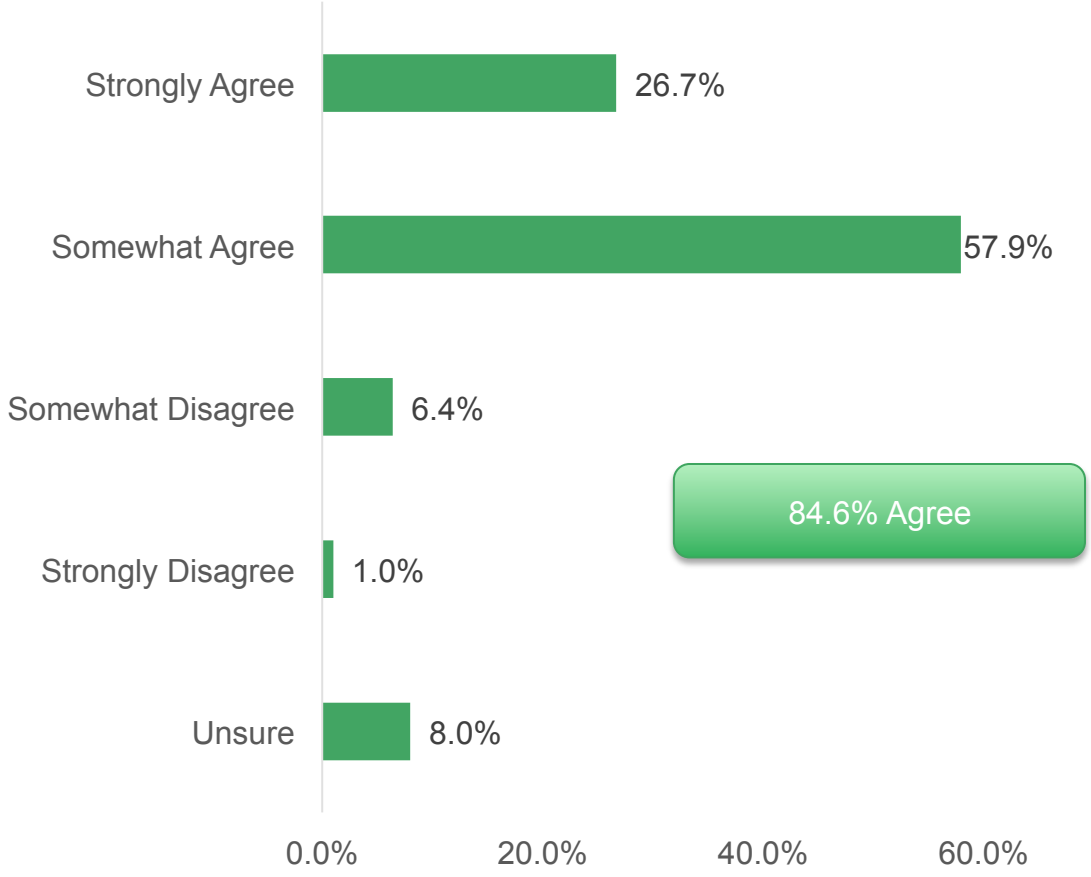
FINDINGS

Participant Introduction

- On March 8, FDA released updated draft guidance regarding their policy on the naming of biologic and biosimilar products: Proposed Suffix for the Proper Name of a Biological Product (Docket No. FDA-2013-D-1543). The Draft Guidance is intended to reflect FDA's current thinking on nonproprietary names of certain biological products. According to the guidance:
  - Originator biologics previously approved without a suffix as part of the name would not be renamed to incorporate a suffix;
  - Biological products previously approved without a suffix under the Food, Drug and Cosmetic Act (e.g., insulin products, desirudin products, somatropin products) that will transition to be regulated under the Public Health Service Act in 2020, would not be renamed to incorporate a suffix
  - Biosimilars subsequently designated as interchangeable would not be renamed; each product would retain the unique suffix it was given at the time of biosimilar approval
  - Biologics approved as interchangeable would receive a unique 4 letter suffix, consistent with the naming practice for biosimilars and newly approved originator biologics

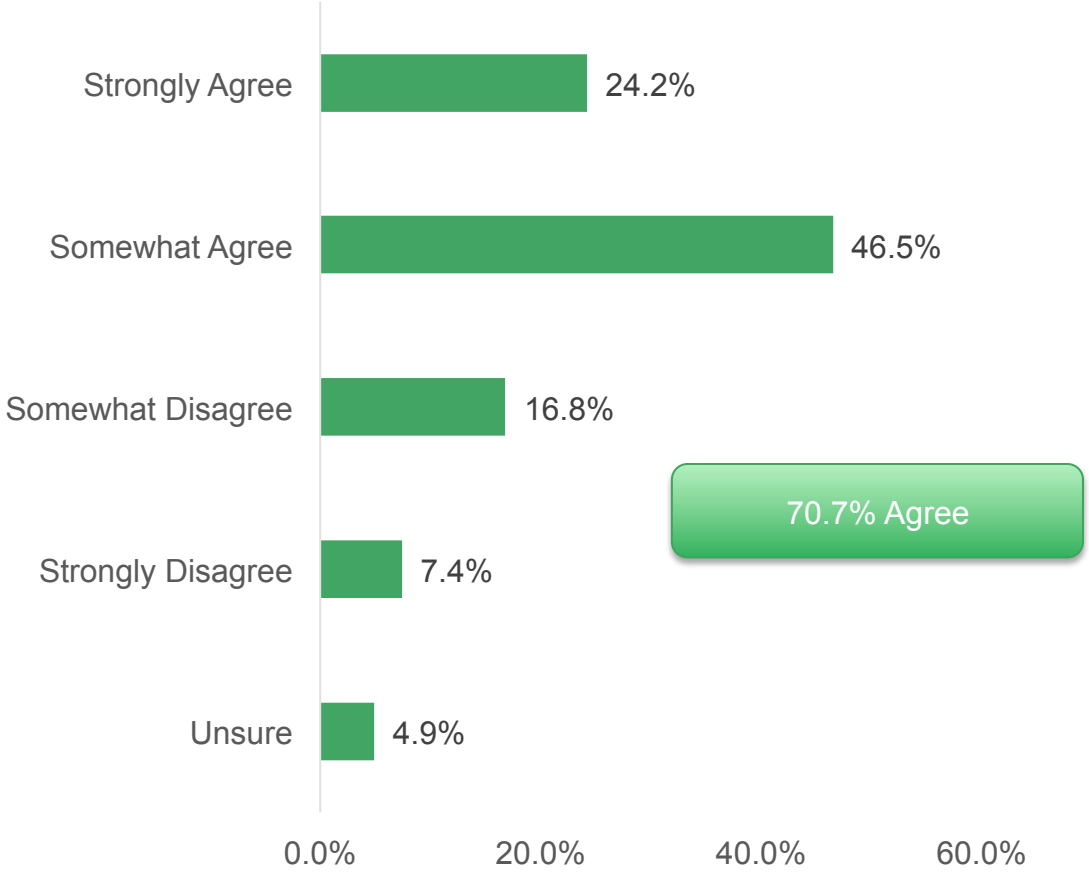
Use of Suffixes

Please rate your level of agreement with the FDA's decision to use 4-letter suffixes to clearly distinguish biosimilars from the originator product on which they are based, and from other biosimilars to that product? (n=202)



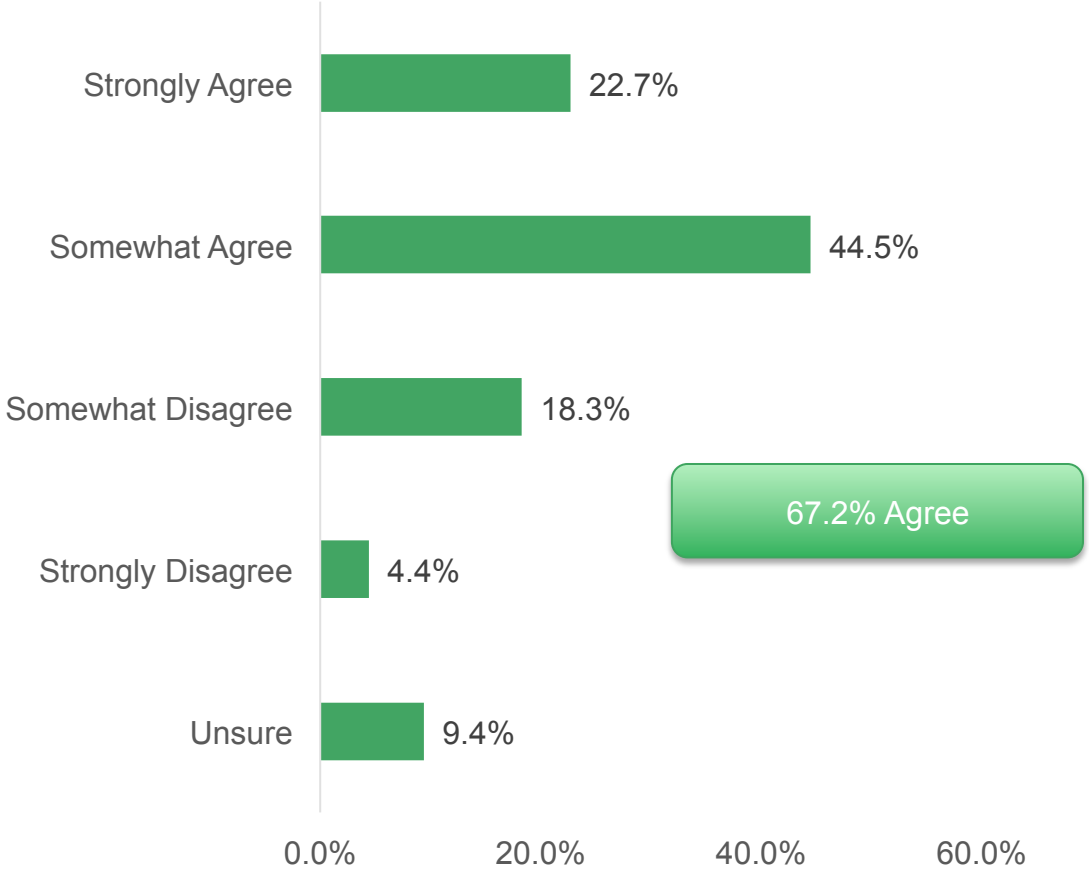
Retrospective Renaming

Please rate your level of agreement with FDA's decision not to rename previously approved biologics to incorporate a suffix? (n=202)



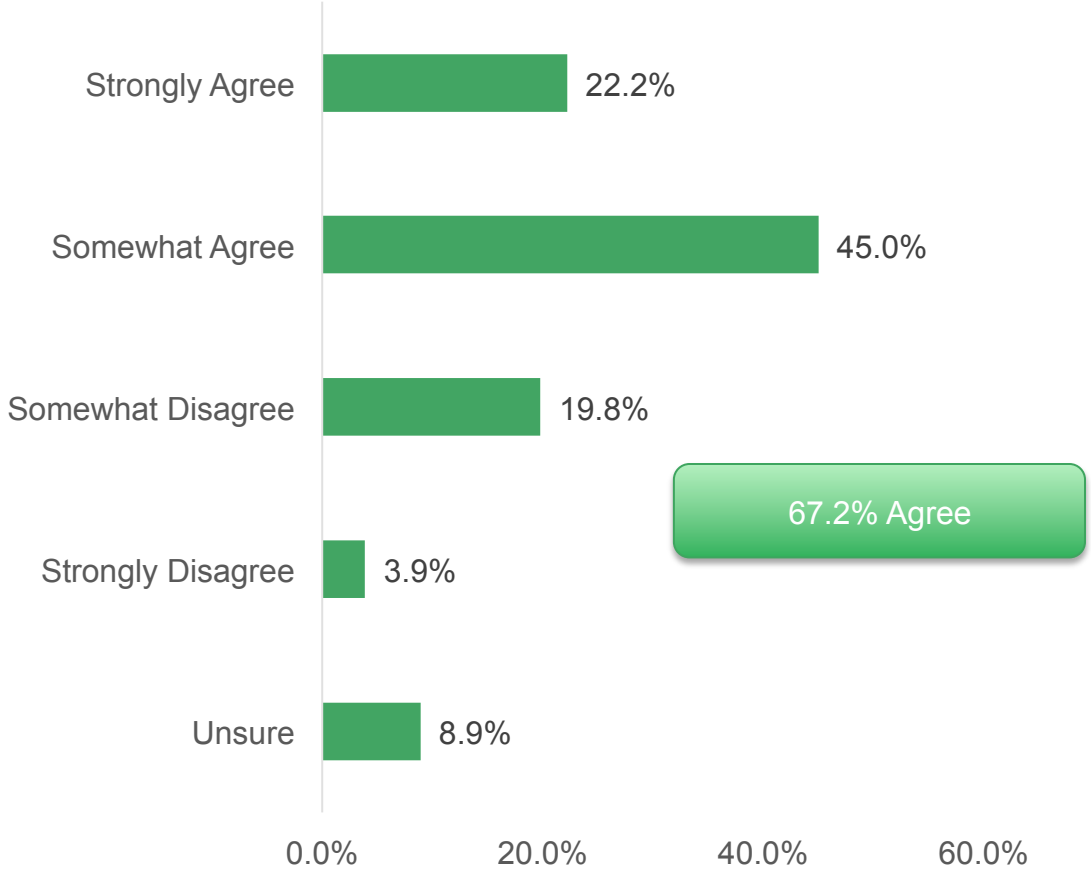
Retrospective Renaming

Please rate your level of agreement with FDA's decision not to rename biologics previously approved under the Food, Drug and Cosmetic Act (e.g., insulin products, desirudin products, somatropin products) that will transition to be regulated under the Public Health Service Act in 2020 to incorporate a suffix? (n=202)



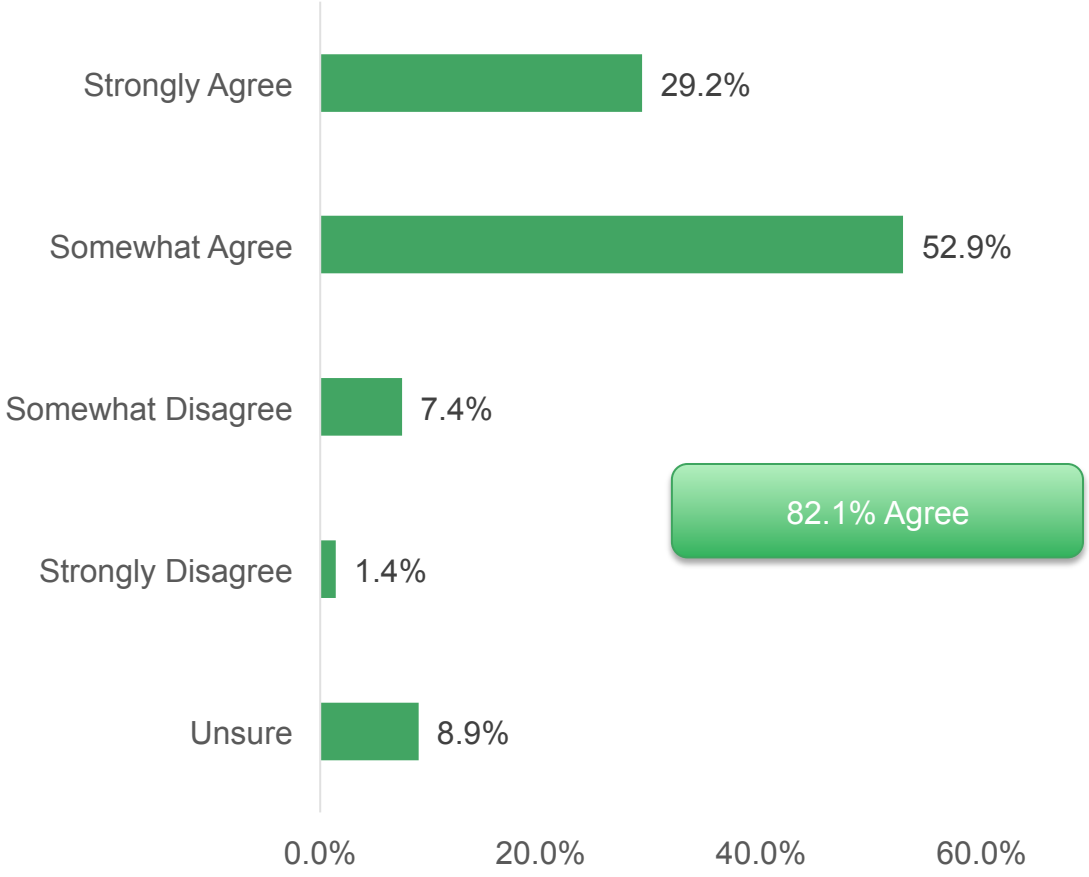
Renaming Post-Interchangeability Designation

Please rate your level of agreement with FDA's decision not to rename biosimilars subsequently designated as interchangeable; instead each product would retain the unique suffix it was given at the time of biosimilar approval? (n=202)



Use of Suffixes

Please rate your level of agreement with FDA's decision to give a biologic approved as interchangeable a unique 4 letter suffix, as it does for biosimilars and newly approved originator products? (n=202)



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