July 29, 2015

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

Re: Docket No. FDA-2015-P-2000–Citizen Petition Filed by AbbVie, Inc.
(June 2, 2015)("AbbVie Citizen Petition")

Dear Sir/Madam:

INTRODUCTION

Momenta Pharmaceuticals, Inc. ("Momenta") submits these comments in response to the AbbVie Citizen Petition dated June 2, 2015, Docket No. FDA-2015-P-2000 ("AbbVie Citizen Petition"). Momenta is a leader in the analysis, characterization, and design of complex pharmaceutical products. Our scientific foundation is a set of tools and methods that enable one to develop a deep understanding of the links between a compound's chemical structure, its manufacturing process and its biological function. We are applying our innovative technology to the development of generic versions of complex drugs, biosimilar and potentially interchangeable biologics, and to the discovery and development of novel therapeutics for oncology and autoimmune indications. Momenta is deeply interested in supporting the U.S. Food and Drug Administration (the "FDA") regulatory policy that promotes innovation and investment in biosimilars and interchangeable biologics. The AbbVie Citizen Petition seeks to promote policy that would undermine such innovation and we urge that it be denied.

Specifically, AbbVie is seeking to create barriers to the development and commercialization of biosimilars and interchangeable biologics. It does so by arguing that Section 351(k) of the Biologics Price Competition and Innovation Act of 2009 (the "BPCIA") was enacted and signed into law to label and promote biosimilars as "different" from their reference product counterparts. They ask the FDA to *mandate* that biosimilars be labeled differently so that such products can be promoted differently and thus considered as "different" by physicians. This argument turns the BPCIA on its head. The BPCIA was enacted to recognize that biosimilars, as well as interchangeable biologics, are scientifically achievable and that these products can be carefully and thoughtfully reviewed, evaluated and approved for marketing by expert scientists at the FDA based on innovation.

Under Section 351(k) of the BPCIA, Congress found that a biosimilar can only be approved if the applicant demonstrates, among other requirements, that there are *"no clinically meaningful*

differences" (emphasis added) between the reference biologic product and the biosimilar product, and that an interchangeable biologic can, when approved as interchangeable, be substituted for a reference brand biologic at the pharmacy without the intervention of a physician. *See* Section 351(i). This is contrary to AbbVie's argument that BPCIA was enacted to promote biosimilars as different. If a product is different, i.e., not biosimilar, it is not highly similar and should be reviewed and approved under the Section 351(a) regulatory pathway. A different product would require independent establishment of its own clinical safety and efficacy profile through clinical studies, as well as its own label, save for class labelling sections of the label for products determined to be in the same product class.

The purpose of the BPCIA was to make possible more affordable, competitive alternatives to biologic products after patent rights end. The BPCIA contemplates significant advances in science that allow for increasingly more precise capabilities to characterize and demonstrate similarity between biosimilars and their reference biologic products and more rigorous control of biologics manufacturing. AbbVie attempts to weave a storyline that because biologics, in general, are different from drugs, that their labeling must necessarily be different from generic drug labeling. This is an over-simplified political message; not science. There is nothing in the BPCIA that supports the message that biosimilars are clinically different from the reference biologic. Rather, AbbVie's position, would contravene several major goals of the BPCIA, namely:

- Innovation in biosimilar science to enhance biologic safety and facilitate use of the pathway;
- Targeted clinical development resulting from enhanced capability to show biosimilarity to reduce development costs and accelerate approvals; and
- Affordability from competitive biosimilar pricing and additional savings from substitution of interchangeable biologics that that could be substituted at the pharmacy without a significant need for sales and marketing activities.

We urge the FDA to continue to rely on scientific expertise and recognize the evolving state of the art in the science of biologics. Policy should make possible, rather than inhibit, the continuous innovation of the highest quality biosimilars and interchangeable biologics. If barriers to biosimilar development and commercialization are promulgated in policy, innovation will be deterred.

If the FDA were to accept AbbVie's principal premise, that biosimilars and, implicitly, interchangeable biologics *must always* have different labeling from the reference product, then the FDA would be undermining its expert determination that *"there are no clinically meaningful differences"* between a biosimilar and its reference biologic. The only rationale for a different label is a clinically meaningful difference in the product from the reference biologic. Moreover, FDA would be aligning itself in AbbVie's commercial campaign to assert, as it does in its petition, that biosimilars are different, not biosimilar, and thus *must always* be labelled differently.

Momenta believes that Congress intended a different outcome; one in which biosimilar applicants are encouraged to invest in the development of technology to assure biosimilarity and interchangeability and to provide physicians and patients with the highest level of confidence to use competitive biologics that offer *the same clinical profile*. Congress also sought to inject affordable competition into the biologics marketplace to create room in payor budgets from biosimilar savings to pay for new medicines for unmet medical needs. To achieve this end, should the FDA adopt labeling

guidance or continue its current policy, Momenta encourages the FDA to use a flexible, pro-competitive approach to ensure physicians are properly informed about biosimilars, and not confused by *mandatory* differential labeling.

Specifically, Momenta recommends the FDA:

- Allow biosimilar applicants to propose labeling, as it did with Zarxio® (filgrastim-sndz) based on the evidence in the regulatory file. Some applicants may seek to include additional information in a label where the science used to demonstrate biosimilarity or interchangeability could in the applicant's view be useful to physicians, patients or formulary committees. By leaving it optional, it allows for competition to drive innovation, as well as affordability. At the same time it does not mandate the inclusion of information that the applicant determines is unnecessary for a product and could be used by the reference biologic sponsor to assert that a biosimilar or interchangeable biologic is "different."

- Make available for use the non-confidential summary basis of approval of each product, as has been done at the time of approval for complex generics and other products to provide a scientific basis for the biosimilarity and/or interchangeability decision. This creates a balanced record for discussing the science of biosimilarity and interchangeability for each product. For example, at the time enoxaparin was approved, the FDA issued a clear communication of the basis of approval, the factors considered and the scientific rationale. While the generic label was the same as the reference drug product, this additional information was made available to physicians to assure that there was a high level of confidence in the "sameness" determination at the time of approval of the generic drug.

DISCUSSION

AbbVie raises a series of claims in its petition in support of its position that biosimilars are meaningfully different than their reference biologic product and *must* have differential labeling. A careful examination of each argument will demonstrate, however, the commercial motivation of the claims and that many of the "concerns" raised by AbbVie can be more effectively addressed by the FDA and biosimilar companies in a more innovative and competitive manner, as contemplated by the BPCIA. A fair reading of the AbbVie Citizen Petition leads to the conclusion that its objective intent may in fact be to deter biosimilar development and competition by confusing physicians and patients and by raising so called "concerns" about biosimilar safety.[1]

[1] AbbVie Citizen Petition at 1 (special labeling is required "to avoid potentially unsafe substitution" and "to combat widespread misconceptions among prescribers", etc.). It is important to note that the AbbVie Citizen Petition follows a prior attempt to forestall biosimilar development and commercialization by AbbVie. *See e.g. Abbott Laboratories (Covington & Burling)-Citizen Petition* (May 8, 2012), Docket ID: FDA-2012-P037- 0001 *available with attachments at* www.regulations.gov/#!documentDetail: D=FDA-2012-P-037-0001 (August 1, 2012). The use of citizen petitions has been a frequent tactic to delay competitive generic and biosimilar product development. *See* Avery et al., Antitrust Implications of Filing "Sham" Citizen Petitions with the FDA, 65 Hastings L.J. 113 (2013-14).

1. The BPCIA Contains *No* Language Requiring the FDA to use the *Same or Different* Labeling for a Biosimilar and/or Interchangeable Biologic Product as its Reference Biologic.

The BPCIA contains no language requiring the FDA to use the same or different labeling for a biosimilar and/or interchangeable biologic product as its reference biologic. Yet, AbbVie attempts to argue that the FDA must require differential labeling for *every* biosimilar.

AbbVie makes its argument, by assuming that the FDA has applied a "mandatory" same labeling requirement to Zarxio, and thus has set a policy requiring that *all* biosimilars and/or interchangeable biologics must, as a matter of policy, have the same labeling. In our view, the FDA has done no such thing. Using this manufactured premise, AbbVie then asserts, by citing the generic drug law and its supporting regulations[2] that the presence of a *same* labeling *requirement* in the generic drug law and the absence of the *same* labeling *requirement* in the BPCIA means that the BPCIA has a mandatory differential labelling requirement for biosimilars and/or interchangeable biologics. Because of AbbVie's false premise, the articulated logic does not support AbbVie's conclusion that the absence of language in the BPCIA means instead that there *must* be a differential labeling requirement.

AbbVie's position is a carefully crafted rhetorical argument that misses the more salient point; that the absence of a provision in the BPCIA does not legislatively dictate a labeling approach. Rather, it creates an intentional gap leaving it to the FDA's expert scientific discretion to resolve.[3] If anything can be read from the law, Congress decided not to mandate differential labeling and left the labeling decision to the discretion of the FDA, as it does for other biologics, based on proposed labeling submitted by each applicant.

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[2] 21 C.F.R. §314.94(a)(8)(iv) and 21 U.S.C. § 355(j)(2)(A).

[3] As the Supreme Court taught in Chevron USA, Inc. v. Natural Resources Defense Council, Inc., 467 U.S. 837, 842-44 (1984):

> When a court reviews an agency's construction of the statute which it administers, it is confronted with two questions. First, always, is the question whether Congress has directly spoken to the precise question at issue. If the intent of Congress is clear, that is the end of the matter; for the court, as well as the agency, must give effect to the unambiguously expressed intent of Congress. If, however, the court determines Congress has not directly addressed the precise question at issue, the court does not simply impose its own construction on the statute, as would be necessary in the absence of an administrative interpretation. Rather, if the statute is silent or ambiguous with respect to the specific issue, the question for the court is whether the agency's answer is based on a permissible construction of the statute.
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> "The power of an administrative agency to administer a congressionally created . . . program necessarily requires the formulation of policy and the making of rules to fill any gap left, implicitly or explicitly, by Congress." *Morton* v. *Ruiz*, 415 U. S. 199, 231 (1974). If Congress has explicitly left a gap for the agency to fill, there is an express delegation of authority to the agency to elucidate a specific provision of the statute by regulation. Such legislative regulations are given controlling weight unless they are arbitrary, capricious, or manifestly contrary to the statute. Sometimes the legislative delegation to an agency on a particular question is implicit rather than explicit. In such a case, a court may not substitute its own construction of a statutory provision for a reasonable interpretation made by the administrator of an agency.

In an attempt to bolster its argument, AbbVie mixes "apples" and "oranges." It looks to Section 505(b)(2), which is irrelevant, because it both does not pertain to biologics but to drugs that sponsors have not shown to be the "same" as a reference drug product under a Section 505(j) ANDA. Biosimilars are shown instead to be biosimilar and/or interchangeable to their reference biologic. AbbVie argues that when *FDA exercised its discretion and found* that Section 505(b)(2) did not have a *mandatory* same labeling requirement for drugs, that the FDA could no longer determine in some instances based on appropriate scientific data, that another Section 505(b)(2) drug might, based on substantial evidence, be eligible to have substantially the same labeling. That decision though, unlike labeling for a 505(j) ANDA, was not mandated by the statutory language and requires FDA scientific judgment. Conversely, the same labeling is mandated for a Section 505(j) drug and there is no FDA discretion. Consequently, it does not even serve as binding precedent for FDA policy for all future Section 505(b)(2) approvals where an exercise of judgment is permitted by the law to allow product by product decision-making. Moreover, because the policy for labeling of biosimilars is an entirely different scientific matter, the FDA has additional authority to decide the scope of each biosimilar product labeling on its own merits.

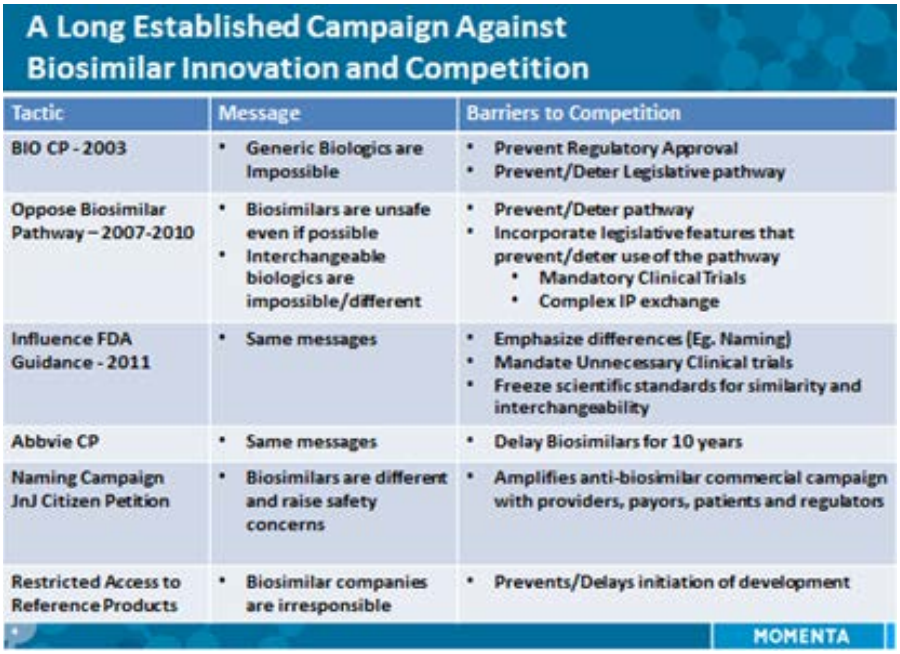
The rational approach, we believe, is for the FDA to do what Congress intended – review the science in each application, ask the applicant to propose labeling based on the science in its application, and depending on the application and the product in question, consider whether the product should or should not have the same labeling as the reference product. It is conceivable that for some products, an applicant may seek to include additional data that demonstrates the quality of its biosimilarity or interchangeability testing and that it may be appropriate to include this information. Whether it should be mandatory, one way or the other, should be left to the applicant to propose and the FDA to review.[4] It should not be a vehicle for deterring biosimilar development and competition. If Congress had created a *mandatory* labeling difference, biosimilar manufacturers might have less incentive to invest in biosimilars and even less of an incentive to invest in interchangeable biologics that were meant to be substituted at the pharmacy without the intervention of a physician.

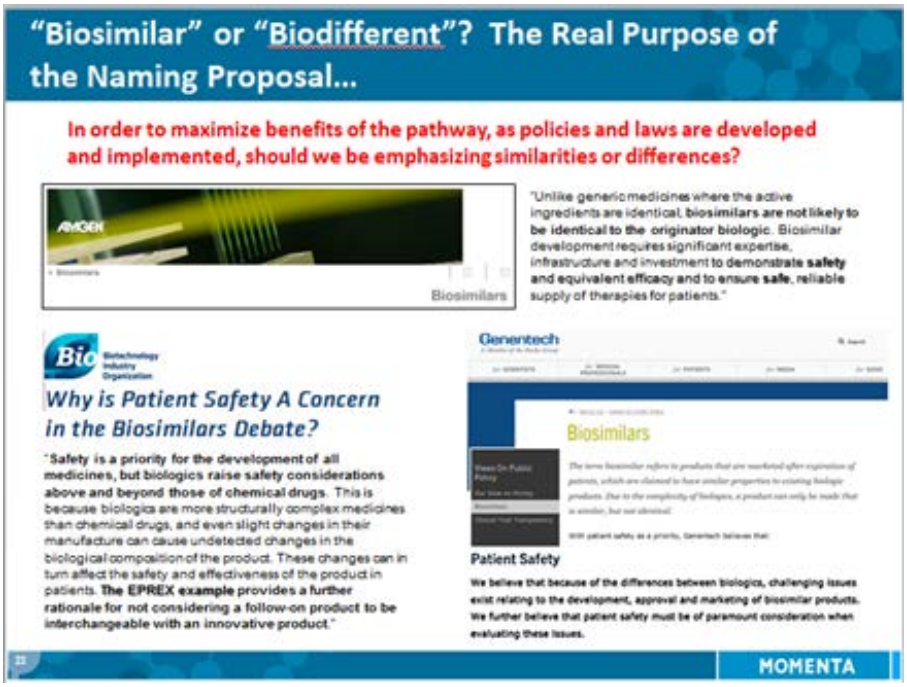
2. <u>Biosimilar Labeling Should Include Scientifically Relevant Information to Inform Physicians and Should Not Create or Reinforce Common Misconceptions about Biosimilars.</u>

All biologics manufacturers seek to ensure that physicians and patients have access to the information in labeling that is needed to make informed prescribing decisions and choices, respectively. Informed choices, and good prescribing decisions, however, are not facilitated by repeated

[4] The AbbVie Citizen Petition correctly cites Momenta's comments in response to the FDA draft guidance. Momenta stated that it may be scientifically warranted and desirable for a sponsor obtaining an interchangeability approval to include that information in its labeling. Momenta supports the authority to do so, but that is different from AbbVie who asserts it must be done or it would be misleading. *See* Draft Guidance for Industry: Scientific Considerations in Demonstrating Biosimilarity to a Reference Product (February 2012) ("Draft 2012 Scientific Guidance") and Momenta comments to Docket No. FDA-2010-N-0477 (December 22, 2010).[5] Testimony of Bruce Leicher, Momenta Pharmaceuticals, Inc., Federal Trade Commission, February 4, 2014.

disparagement and misleading communications about biosimilars by companies promoting reference biologic products. The use of phrases like "biosimilars are different" or charged phrases like "potentially unsafe substitution" by AbbVie presume that the FDA will not follow sound science and require all biologics manufacturers to meet the legal and regulatory standards of the BPCIA. It also ignores the quality enhancing role biosimilar innovation brings to biologics manufacturing. Unlike historic biologic practice, a biologic is increasingly not defined by its manufacturing process, but by thorough characterization and product quality attributes making it possible to detect product quality concerns prior to use in humans. A biosimilar manufacturer may have a deeper understanding of its product, and a greater ability to avoid defects than a manufacturer that relies on its "process" alone.





If there are common misconceptions about the safety and efficacy of biosimilars and their use, AbbVie could offer more constructive help to dispel any common biosimilar misconceptions with balanced, scientific and credible discourse that informs physicians about the state of the art in biologics process development, characterization, manufacturing and quality control. Too often, out-of-date knowledge about the capability to manufacture highly similar and interchangeable biologics is cited to disparage biosimilars and thwart physician acceptance. Much of this dated science precedes the enactment of the BPCIA, and through repeated usage is a primary cause of misinformation about biosimilars. Examples of common misleading commercial claims about the safety issues surrounding biosimilars are in the slides on this page that were included in Momenta's testimony to the Federal

Trade Commission in 2014.[5] A common source of misinformation cited during the debates by industry trade organizations representing AbbVie involved the patient safety issues related to EPREX, a biologic reference product, and its manufacturing change. In that case the manufacturer changed a stopper in the delivery device which apparently reacted with the biologic leading to fatal, serious adverse events. Because the biologic manufacturer may not have had release specifications and product quality attributes in place that detected the structural change in the product, clinical events were the means available to detect the safety event. The incentive to thoroughly characterize and understand biologics is inherent in the development of biosimilars and interchangeable biologics. Thus, biosimilars offer the opportunity to enhance the ability to detect and prevent these types of risks before a product is dispensed to patients. The EPREX case has been cited repeatedly over the years in political forums to attempt to argue why biosimilars were "unsafe," but the facts of the example, in fact, demonstrate why biosimilar development should help reduce this safety risk. Should the EPREX example continue to be used in a commercial campaign with physicians to disparage a biosimilar, it would not be based on substantial evidence, and would consitute off-label, comparative advertising that deserves FDA scrutiny.

AbbVie also cites the Alliance for Safe Biologic Medicine ("ASBM") to create a veneer of social science for its advocacy. ASBM is by its own account was formed and is largely supported by the reference biologic industry. Its primary objective appears to be to challenge biosimilar safety and posit a risk of non-interchangeable biosimilar substitution, and perhaps even interchangeable biologic substitution. It is not surprising that AbbVie cites survey data from the ASBM survey[6] as indicative of physician confusion and a fear that physicians will substitute biosimilars that are not interchangeable. Because of the apparent conflict of interest, their survey deserves a closer look including a careful examination of the form of the questions asked. We believe that a seasoned survey expert would find that the questions used were leading questions which resulted in answers that supported the ASBM objectives. For example, in testing whether physicians were familiar with biosimilars, they asked:

> How familiar are you with biosimilar medicines?

ASBM received a response of 80% as very familiar or familiar; even though no biosimilars had been approved yet. This form of this question would require a highly educated professional to acknowledge implicitly they are not educated on the subject. Questions like this could potentially measure familiarity inaccurately among a professional group that prides itself on its continuing education responsibilities.

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[5] Testimony of Bruce Leicher, Momenta Pharmaceuticals, Inc., Federal Trade Commission, February 4, 2014. https://www.ftc.gov/system/files/documents/public_events/Follow-On%20Biologics%20Workshop%3A%20Impact%20of%20Recent%20Legislative%20and%20Regulatory%20Naming%20Proposals%20on%20Competition/leicher.pdf

[6] ASBM Labeling Survey (2015) at http://safebiologics.org/resources/wp-content/uploads/2012/09/ASBM-Survey-1.pdf .

Or to test the impact of having the same name, ASBM asked:

> If two medicines have the same non-proprietary scientific name, does this suggest to you or imply that the medicines are structurally identical?

Again, this answer led to a nearly 75% yes because that is true for generic medicines today and education about biosimilars and naming is only just beginning. It reinforces any misconceptions about biosimilars rather than educates about what "no clinically meaningful differences" means and the science for demonstrating biosimilarity. It might have said, for example, "If two medicines have the same non-proprietary scientific name, does this suggest to you they do not have clinically meaningful differences?

The next question injects a safety concern about biosimilars by asking:

> If two medicines have the same non-proprietary scientific name, does this suggest to you or imply that a patient could safely receive either product and expect the same result?

This question does not state that the FDA determined the biosimilar to be safe and effective precisely because it does not have clinically meaningful differences or might even be interchangeable. Given the noted exclusion of information, it seems doubtful that the survey answer has utility.

Other questions about whether doctors desire to be informed of substitution could also be expected to lead to an affirmative response. When a question directed to a professional asks if they want to be informed, it can be expected to be biased in that direction. Each question appears to have been designed or if not designed, was written in a manner that elicited the desired results.[7]

Momenta fully supports engagement with physicians and furnishing of balanced information that provides education about the science that supports biosimilar development and commercialization. It would be unfortunate, though, if the politics and competitive commercial objectives of reference biologic companies surrounding the creation of the biosimilar pathway were used as scientific data in this endeavor.

3. <u>While not Mandatory, Inclusion of Biosimilar Research and Development Data could be Informative for some Products based on Review and Discussion between the Applicant and the FDA.</u>

The FDA has a duty and the discretion to determine with each applicant the contents of labeling for each biologic – brand or biosimilar. AbbVie selectively cites a portion of Section 201(n) of the Act and conveniently leaves out the statutory reference to the determination to be made by the FDA in reviewing product labeling. In pertinent part, Section 201(n) explicitly provides that:

[7] Notably, as support for our shared view that education is needed, AbbVie also cites (at page 9) data from several surveys that a majority of physicians had not heard of the biosimilar pathway in 2010 or that it existed. This is not surprising in that the pathway was new and no products had been developed or commercialized. Yet, when ASBM asked its version of the question, they found 80% of physicians were familiar with biosimilars.

> If an article is alleged to be misbranded because the labeling or advertising is misleading, *then [the FDA] in determining* whether the labeling or advertising is misleading, there shall be taken into account (among other things) not only representations made or suggested by statement, word or design, device or *any* combination thereof, but also *to the extent* to which the labeling or advertising fails to reveal facts *material* in light of such representations or material with respect to consequences which may result from the use of the article to which the labeling or advertising relates under the conditions of use prescribed in the labeling or advertising thereof or under such conditions of use as are customary or usual.[8] (Emphasis added).

AbbVie seeks to strip the FDA of its authority to make scientific, evidence based determinations. The statutory text makes it clear that when the FDA approves labeling at the time of marketing approval for any product, it determines based on substantial evidence in the administrative record what facts or information are explicitly needed in the label so that the product is not misbranded. The statute does not mandate that particular scientific data be included in the label. Given that the approval of a biosimilar means that the applicant has demonstrated to the satisfaction of the FDA that it does not have "any clinically meaningful differences" from the reference biologic product, it is rational for the FDA to conclude that it would be misleading to spotlight data that could be improperly interpreted to undermine the FDA's finding of biosimilarity. AbbVie's position assumes that the additional data is necessary for every product, but there is no basis for AbbVie's position based on BPCIA and thus AbbVie cites none. Many products such as Zarxio, may be sufficiently characterized, and be so highly similar to the reference brand biologic, that additional labeling information would have no useful or meaningful purpose to a physician. Other products, may have important non-clinical or clinical data supporting biosimilarity or interchangeability that the applicant might propose its inclusion in the labeling in support of the use of the product. The basis for inclusion or exclusion should not be the result of theoretical, non-clinically meaningful arguments.

Applicants should have the opportunity to provide scientific data demonstrating that labeling should or should not include data on a product-by-product basis. The FDA may consider such data, as part of the labeling review, and exercise discretion in whether to include any additional information based on sound scientific principles, not on commercial interests or legal positioning. For example, where all indications are not approved that are licensed for the reference product, the approved indications may not be the same for the biosimilar and the reference biologic product. Or, if a biosimilar is approved as interchangeable, the interchangeability could be noted on the labeling. As noted above,[9] Congress left it to the FDA to make this determination based on sound scientific principles, not on commercial interests or legal positioning. We believe that AbbVie has misinterpreted the Zarxio review. The FDA had the responsibility to carefully review the Sandoz 351(k) application for Zarxio, and concluded that the proposed labeling was informative and not misleading. We assume the FDA also concluded that differential labeling might in fact be misleading and could lead to confusion among physicians about the use of Zarxio as an alternative for Neupogen® (filgrastim).

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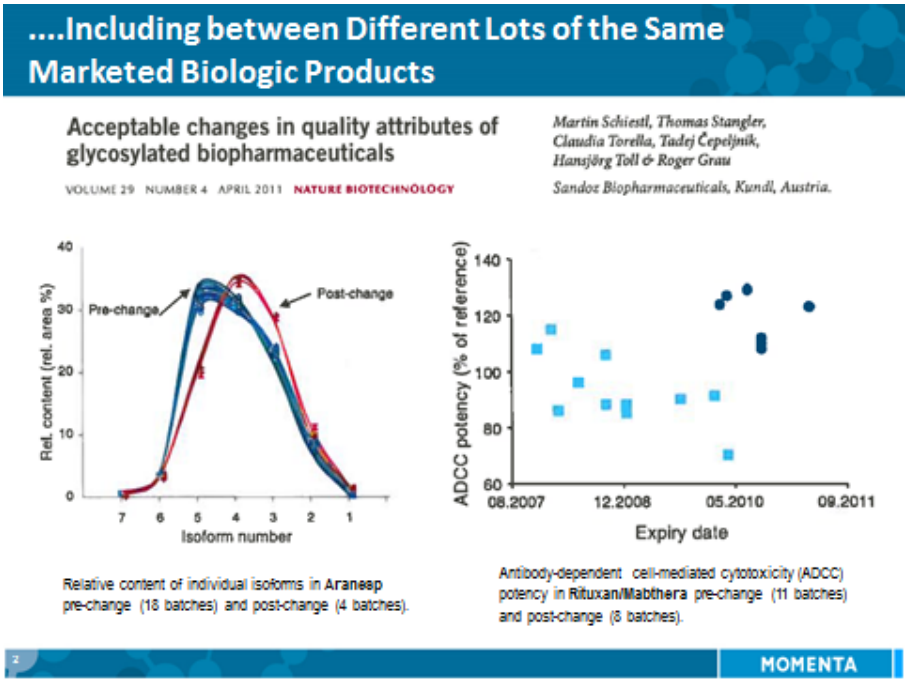
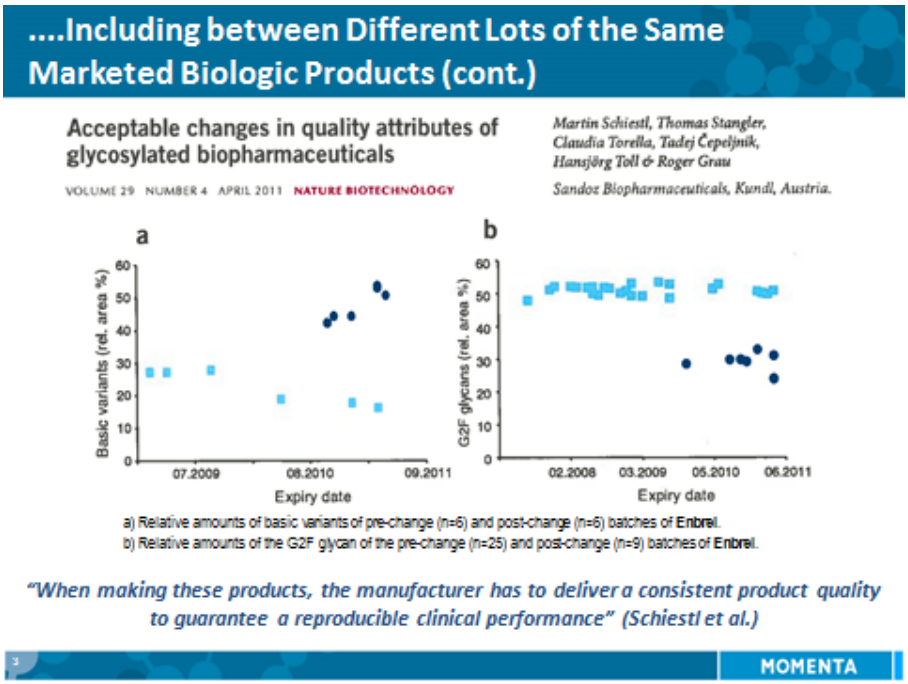
[8] Section201(n), 21 U.S.C. § 321(n).

[9] See note 3, supra.

[10] Labeling or advertising is "false, lacking in fair balance, or otherwise misleading, or otherwise violative of section 502(n) of the act, among other reasons, if it:

The flaw in AbbVie's argument is further revealed by the discriminatory nature of its position; one designed to create a commercial competitive advantage for the reference biologic. If, as AbbVie posits, the absence of data about product variability and structural/functional changes is *always* misleading, then why does the AbbVie Citizen Petition fail to request non-discriminatory treatment for all biologics? As noted in the accompanying slides, biologics often undergo substantial structural/functional changes, yet AbbVie does not propose that all biologic labeling is misleading when comparability data is excluded from reference product labelling; nor does it propose unique naming for changes in these biologics or notification to physicians when these changes are implemented. This is so regardless of whether the changes are more significant structurally or functionally in some cases than might be considered acceptable for a biosimilar or an interchangeable biologic. The reason is that unless the applicant and the FDA determines such data is important to physicians, it is ordinarily not included in labeling and the same principles should apply to biosimilars and interchangeable biologics.





Finally, AbbVie asserts a view on labeling that is inconsistent with well-established FDA practice for regulating comparative claims. For good reason, FDA advises that in order to claim differences among products, one ordinarily is required to furnish substantial evidence documented by two well-controlled studies to assure that a comparative claim is not misleading.[10]

[10] Labeling or advertising is "false, lacking in fair balance, or otherwise misleading, or otherwise violative of section 502(n) of the act, among other reasons, if it:

When a biosimilar is approved, the FDA is determining, based on substantial evidence, that the biosimilar has no "clinically meaningful differences." The inclusion of differences in the labeling would suggest to physicians that there are clinically meaningful differences in the biosimilar or interchangeable biologic. This would, in the absence of appropriate comparative data, be misleading and entirely inconsistent with many years of FDA regulatory precedent.

It is worth noting that the same principle applies to the policy for non-proprietary naming. By requiring a biosimilar to adopt a unique non-proprietary name, one is creating a distinction from the brand that would suggest to physicians and patients that there are "clinically meaningful differences" that would require the distinguishing name when the package insert and the packaging will already identify the product with a manufacturer name and manufacturer specific NDC number for pharmacovigilance purposes.

4. <u>The FDA Fully Complied with the Administrative Procedure Act when it Considered Comments Solicited on a Non-Binding Draft and Adopted a Final Guidance Document.</u>

The FDA issued *draft* guidance in February 2012 prior to the receipt of any biosimilar applications, and prior to significant review activities that were conducted in connection with biosimilar user fee meetings on many products in the past 3 years.[11] The Draft 2012 Scientific Guidance is just that, a draft, and contained express language in a "Block Box" warning stating[12]:

> This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the page of this guidance.

AbbVie reads the word "draft" out of the title and never even mentions this important disclaimer that explicitly states that current thinking is not current thinking until it is "finalized". Could the Agency be any clearer? The purpose of the draft guidance was to solicit comment, and consider those comments as the FDA began to implement its statutory requirements.[13] The FDA decision to drop language from a

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…(ii) Contains a drug comparison that represents or suggests that a drug is safer or more effective than another drug in some particular when it has not been demonstrated to be safer or more effective in such particular by substantial evidence or substantial clinical experience." 21 CFR 202.1(e)(6)(ii).

[11] FDA, Draft Guidance for Industry: Scientific Considerations in Demonstrating Biosimilarity to a Reference Product (February 2012) ("Draft 2012 Scientific Guidance").

[12] *Id. at 1.*

[13] Several FDA staff statements are referenced in the AbbVie Citizen Petition. AbbVie Citizen Petition at page 18-19, notes 109-111. Staff statements are useful for understanding the direction and evolution of FDA thinking

the Draft 2012 Scientific Guidance based on its regulatory and scientific experience suggests that it has been thoughtful and responsive to comments regarding from relevant stakeholders.[14] Consequently, there was and is no cognizable abandonment of policy by the FDA under the Administrative Procedure Act or any basis for such a claim.

CONCLUSION

Momenta urges the FDA to read the AbbVie's Citizen Petition with awareness of the context in which it was submitted. AbbVie has not reported that it is developing any biosimilars. AbbVie currently markets Humira® (adalimumab) among other biologics that generates, without biosimilar competition, in excess of $12 billion in revenues worldwide. AbbVie is highly incented to promote FDA policy that raises the barriers to entry of biosimilars and interchangeable biologic competition and increases the cost of commercialization of biosimilar and interchangeable biologic products. Safety concerns, without substantial evidence, more often than not are the means used to challenge the legitimacy of biosimilars and interchangeable biologics in public forums as a means for creating competitive advantage. Labeling that creates *non-clinically meaningful distinctions* between a reference biologic product and a biosimilar and/or an interchangeable biologic product would not only be misleading and potentially violate the Section 201(n) rules against misbranding, they would discourage the use of the 351(k) approval pathway, reduce the incentives for investment in biosimilar and interchangeable biologic development and innovation, and be contrary to the BPCIA.

Momenta believes that the decision to include biosimilar specific information in a label should be proposed by the applicant in circumstances where substantial evidence from the biosimilar development warrants inclusion of that information. The applicant ordinarily is in the best position to furnish such data and the BPCIA does not mandate inclusion or exclusion of such data. Rather, the BPCIA delegates to the FDA the responsibility to exercise case-by-case scientific judgment as it approves labeling for each product. In circumstances where biosimilarity testing provides useful information for physicians and patients there are less restrictive, pro-competitive means available to the FDA and biosimilar applicants to achieve those purposes. These include inclusion of useful information proposed by the biosimilar applicant, or the publication of the non-confidential biosimilarity or interchangeability determination by the FDA at the time of approval that contains that information. The

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but are well understood to not constitute FDA rulemaking or guidance. Like the Draft 2012 Scientific Guidance individual statements were made to promote discussion and input as the FDA evaluated its position during the implementation of the new regulatory pathway and are not intended to bind the FDA in any manner.

[14] Recent research suggests that industry seeking to protect a marketing advantage will engage in regulatory policy making to create barriers to innovation and enhancement of quality. The effort to make biosimilars appear different and embed such differences in regulatory policy are just another means for doing so. W. Nicholson Price II, Academic Fellow, Petrie-Flom Center for Health Law Policy, Biotechnology and Bioethics, Harvard Law School, has studied pharmaceutical CMC innovation and found that regulatory barriers and calcification may be the principal cause of the absence of innovation in quality by design in pharmaceutical manufacturing; the area where biosimilar and interchangeable biologics companies are most innovative. Price, Making Do in Making Drugs: Innovation Policy and Pharmaceutical Manufacturing (2013); http://ssrn.com/abstract=2311682 . It is not surprising that industry seeks to enact into law and regulation limits benefitting commercially from biosimilar innovation as a "legal" means to impede competition, particularly in the biosimilars field.

latter was more than sufficient to address analogous sameness questions by physicians at the time of the approval of the enoxaparin and glatiramer acetate ANDAs and the labeling remained identical.

Momenta appreciates the opportunity to submit these comments and urges the FDA to deny the petition.

Sincerely Yours,

Bruce A. Leicher
Senior Vice President and General Counsel

cc: Elizabeth Jex, Office of Policy Planning, U.S. Federal Trade Commission