May 13, 2016

BY ELECTRONIC SUBMISSION

Division of Dockets Management (HFA-305)
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. FDA-2015-D-4750; Implementation of the "Deemed to be a License" Provision of the Biologics Price Competition and Innovation Act of 2009; Comments of Mylan, Inc.

Dear Sir or Madam:

Mylan, Inc. ("Mylan") is pleased to submit comments to the Food and Drug Administration ("FDA" or "the Agency") on its recently-issued draft guidance[1] explaining how the Agency intends to interpret and implement the transition provisions in the Biologics Price Competition and Innovation Act of 2009 ("BPCIA").[2] The BPCIA's transition provisions are applicable to biological products that, for historical reasons, are subject to approval under section 505 of the Federal Food, Drug, and Cosmetic Act ("FD&C Act") rather than section 351 of the Public Health Service Act ("PHS Act") (hereinafter referred to as "transitional biologics").

Mylan is the world's third largest generic and specialty pharmaceutical company and the largest global generics company headquartered in the United States. Today, one out of every 11 prescriptions dispensed in the United States, brand or generic, is a Mylan product. Over the course of its 50-year history, Mylan has demonstrated an unwavering commitment to enhancing patient access to high-quality, affordable generics, which are equally as safe and efficacious as their brand counterparts. As part of that commitment, Mylan is taking a leading role in the development of biosimilars and interchangeable biologics for the U.S. marketplace and currently has fifteen products in various stages of development, including transitional biological products. Mylan thus has a strong interest in ensuring that any scientific or regulatory policies regarding transitional biological products are consistent with the intent and purpose of the BPCIA.

For the reasons discussed below, Mylan strongly opposes FDA's plan to withhold approval of transitional biological products that have not yet been approved by March 23, 2020, the statutory

[1] *See Draft Guidance for Industry on Implementation of the "Deemed to be a License" Provision of the Biologics Price Competition and Innovation Act of 2009* (March 2016) ("Draft Guidance"); 81 Fed. Reg. 13373 (March 14, 2016) (Docket No. FDA-2015-D-4750).
[2] BPCIA, Pub. L. No. 111-148, § 7002(e) (2010).

transition date, and require withdrawal and a different, new submission under the PHS Act. This proposal, if implemented, will have a devastating effect on current development programs for many important protein products, including insulin, thereby impairing competition from lower-cost biological medicines, increasing healthcare costs in the United States, and, most importantly, limiting patient access to affordable biological products. Mylan believes these results are antithetical to the overriding goals of the BPCIA, which were to *increase* competition and access and *lower* healthcare costs in the United States. Moreover, FDA's proposed actions are arbitrary, capricious, contrary to the clear language of both the BPCIA and the FD&C Act, and beyond the scope of FDA's authority.[3]

For all of these reasons, Mylan respectfully requests that FDA modify its proposed policy regarding pending applications prior to finalizing the Draft Guidance. In particular, FDA should adopt a new interpretation that (a) is consistent with the statutory language and underlying goals of the BPCIA, and (b) minimizes disruptions to the development, review and approval of, and patient access to, affordable transitional biological products. Mylan believes there are several available options that meet these criteria, which are discussed in more detail in section III below. Moreover, because FDA's current interpretation creates a regulatory "dead zone" that could already be disrupting development programs for transitional biologic products (as described in section I below), FDA should take immediate steps to mitigate this effect. In particular, FDA should announce that it is immediately withdrawing the proposed interpretation described in the Draft Guidance while it considers which of the permissible options to adopt in a final guidance document. The grounds for Mylan's requests are set forth below.[4]

I. FDA's Proposed Policy Will Have a Devastating Impact on Ongoing Development Programs That Will Unnecessarily Reduce Competition, Increase Healthcare Costs and Limit Patient Access to Affordable Biological Products

According to the BPCIA's transition provisions, an approved application under section 505 of the FD&C Act for a biological product – which includes full New Drug Applications ("NDA"), 505(b)(2) applications, and Abbreviated New Drug Applications ("ANDA") – "shall be deemed" to be an approved Biologics License Application ("BLA") on March 23, 2020.[5] The transition provision also explicitly permits a sponsor to submit a section 505 application for certain transitional biological products up until the transition date.[6] The BPCIA, however, does not

[3] 5 U.S.C. § 706.

[4] Although Mylan's comments focus on its opposition to FDA's proposed policy regarding pending applications, Mylan wishes to emphasize that it supports many other aspects of the Draft Guidance. In particular, Mylan agrees with FDA's position that section 505 applications "deemed" to be Biologics License Applications on March 23, 2020, are not entitled to the 4- or 12-year exclusivity periods described in the BPCIA. Draft Guidance at 7. Those exclusivity periods are available only to biological products that are "first licensed" under the PHS Act, and the "deeming" procedure under section 7002(e)(4) of the BPCIA does not qualify as a first licensure. Moreover, granting such exclusivity to biological products that have been marketed for years (or even decades – Lantus® was first approved in 2000) would bestow a massive and entirely undeserved economic windfall on brand name manufacturers in a manner that is inconsistent with the goal of the BPCIA to facilitate patient access to affordable alternatives to existing biological products.

[5] BPCIA, § 7002(e)(4).

[6] BPCIA, § 7002(e)(2).

explain how FDA should treat section 505 applications submitted before March 23, 2020 (as permitted) that are unapproved or otherwise pending on March 23, 2020.

In its Draft Guidance, FDA proposes to address this statutory gap in a manner that the Agency concedes could have a "significant impact" on development programs for transitional biological products. In particular, FDA states that it "will not approve any application under section 505 of the FD&C Act for a biological product subject to the transition provisions that is pending or tentatively approved 'on' March 23, 2020."[7] Instead, FDA advises that such applications should be withdrawn and a new submission made under section 351(a) or 351(k) of the PHS Act, as appropriate, presumably triggering new user fees and review timeframes.[8] In other words, although Congress explicitly permitted sponsors to submit section 505 applications up until March 23, 2020, FDA has decided it will not review or approve them after that date.

FDA's proposed policy not only conflicts with the BPCIA and FD&C Act (as discussed more fully in section II below) but, more importantly, will have a disastrous effect on ongoing development programs for transitional biologics. This, in turn, will reduce competition, increase healthcare costs, and impair patient access to affordable alternatives to transitioned brand name biologics. FDA's proposal thus will benefit sponsors of brand name transitional biologics, who will remain free from meaningful competition during the delays caused by FDA's policy, but it will do little to advance the underlying goals of the BPCIA. FDA's proposed policy, in fact, will seriously undermine these important BPCIA goals.

The Agency itself concedes that its proposed interpretation of the BPCIA "could have a significant impact on development programs for any proposed protein products intended for submission under section 505 of the FD&C Act that are not able to receive final approval by March 23, 2020."[9] Mylan believes the effects of FDA's proposal on current development programs will be highly disruptive, delaying the development and approval of competing transitional biological products for several years in at least two ways.

First, and most importantly, FDA's proposal will create what the Generic Pharmaceutical Association ("GPhA") aptly describes in its comments as a regulatory "dead zone."[10] This is the period of time during which prospective sponsors cannot submit ***any*** abbreviated applications for approval of follow-on versions of transitional biological products under either the FD&C Act or the PHS Act and thus during which development, review and approval activities will come to a standstill. This period will vary from drug to drug based upon the expected delays inherent in the review process and the blocking effect of Hatch-Waxman patent and exclusivity protections but, as discussed further below, it likely will extend at least several years prior to March 23, 2020.

On the front end, reasonable sponsors will refrain from submitting 505(b)(2) applications or ANDAs at some point well before March 23, 2020 because of the meaningful risk that such

[7] Draft Guidance, at 5.
[8] FDA does not provide any guidance regarding user fees or review goals in the Draft Guidance but instead promises to do so in a subsequent guidance document. Draft Guidance, at 5 n. 7.
[9] Draft Guidance, at 6.
[10] Comments of GPhA, Docket No. FDA-2015-D-4750, at 4 (May 13, 2016).

applications will not be approved prior to that date and thus will need to be withdrawn and a new submission made under section 351(a) or 351(k) of the PHS Act. On the back end, FDA's policy will block sponsors from submitting 351(k) applications for biosimilar or interchangeable biological products until after March 23, 2020 because of the absence of any "reference product" prior to that date.[11] FDA's proposed policy, therefore, will create strong disincentives for sponsors to submit section 505 applications for transitional biologics prior to March 23, 2020 while simultaneously blocking submission of 351(k) applications until after that date, thereby creating a period of several years during which no applications are feasible under either approval pathway.

The scope of this regulatory dead zone may vary but is likely to be lengthy. At a minimum, it will extend at least a year, *i.e.*, from March 2019 to March 2020, because of FDA's 10-month user fee goal for reviewing 505(b)(2) applications and ANDAs.[12] Reasonable sponsors are unlikely to submit applications within, or even close to, this 10-month review period because of the unlikelihood, and in some cases impossibility, of receiving FDA approval by March 23, 2020. This one-year period, however, is only a minimum: FDA's review times for complex products historically have extended well beyond a year. For example, the review times for Basaglar® (insulin glargine injection), Omnitrope® (somatropin [rDNA origin] for injection), and enoxaparin were 2 years, 4½ years and 5 years, respectively.[13] Reasonable sponsors will factor these historical review times into their planning and make submission decisions accordingly. They also will consider Hatch-Waxman patent and exclusivity protections, which could block approvals for 30 months or more if innovator products are protected by patents or non-patent exclusivity.[14] Consequently, for many transitional biological products, a more realistic estimate is that *the regulatory dead zone will last anywhere from two to four years*.[15]

Second, for applications that are submitted but not approved prior to March 23, 2020, FDA's proposed policy will cause unnecessary disruptions to the review process that will further delay approval of competing transitional biological products. According to FDA, pending 505(b)(2) applications and ANDAs that have not been approved by March 23, 2020, will need to be "withdrawn and resubmitted under section 351(a) or 351(k) of the PHS Act, as appropriate."[16]

---

[11] In its Draft Guidance, FDA admits that a sponsor could not submit a biosimilar application until "such time as there is a biological product licensed under section 351(a) of the PHS Act that could be a reference product." Draft Guidance, at 8. For most transitional biological products, this will not occur until March 23, 2020.

[12] *PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2013 Through 2017*, p. 4 ("PDUFA Goals Letter") (review performance goal for standard, non-NME original NDAs is 10 months from receipt), *available at* http://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM270412.pdf; *Generic Drug User Fee Act Program Performance Goals and Procedures*, p. 9 ("GDUFA Commitment Letter") (review performance goals for ANDAs in the Year 5 cohort is 10 months from the date of submission), *available at* http://www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/UCM282505.pdf.

[13] *See* Basaglar Approval Letter (Dec. 16, 2015), *available at* http://www.accessdata.fda.gov/drugsatfda_docs/appletter/2015/205692Orig1s000ltr.pdf; Omnitrope Approval Letter (May 30, 2006), *available at* http://www.accessdata.fda.gov/drugsatfda_docs/appletter/2006/021426s000LTR.pdf; Enoxaparin ANDA Approval Letter (July 23, 2010), *available at* http://www.accessdata.fda.gov/drugsatfda_docs/appletter/2010/077857s000ltr.pdf.

[14] *See* 21 U.S.C. § 355(c)(3)(C) (establishing 30-month stay period for 505(b)(2) applications).

[15] If the regulatory dead zone extends 4 years prior to March 23, 2020, it would have started on March 23, 2016, approximately a week after FDA issued the Draft Guidance.

[16] Draft Guidance, at 6.

This will require sponsors to prepare entirely new applications rather than amend or update existing applications, a process that could be especially time-consuming if FDA requires new data or new analyses of existing data. More significantly, FDA's proposal will require the Agency to initiate a new review of the "resubmitted" 351(a) or 351(k) applications that likely will be subject to new user fee goal dates. This, of course, could extend the review timeline by an additional 10 months or more (and require payment of a new user fee).[17] Mylan believes that restarting review processes in this manner is wasteful and unnecessary for all transitioned applications, but it is particularly unjustified for pending applications that are tentatively approved prior to March 23, 2020.

For the foregoing reasons, FDA's proposed policy will cause major disruptions to the development and review of transitional biological products and result in significant delays in the approval of lower-cost, competing products. By impairing competition, FDA's proposal will in turn have a significant impact on healthcare costs and patient access to affordable biological products. The Federal Trade Commission ("FTC") has recognized that "[b]iosimilar competition is important because biologics are among the most promising medicines for the treatment of a variety of medical conditions for which patients have no other alternative."[18] Transitional biologics, which include insulin, human growth hormone, and pancrelipase, are no different and offer important treatment options to millions of patients suffering from potentially debilitating diseases. For example, the Centers for Disease Control estimates that diabetes affects 29.1 million people in the United States, and the total costs (direct and indirect) associated with the disease are approximately $245 billion.[19] Insulin and insulin analogues, which are regarded as transitional biologics, thus are important treatment options for millions of patients suffering from diabetes.

Competition is particularly important for biologics because of their relatively high cost. According to the FTC, biologics are 22 times more expensive, on average, than traditional medications.[20] Moreover, biologic prices are increasing rapidly, with price increases of "about 10 to 15 percent each year, with the average price of biologics doubling from 2006 to 2012."[21] For example, the price of Lantus, a brand name insulin glargine product that is also a transitional biologic, has skyrocketed in recent years. According to a recent analysis of drug prices by Reuters, the list price of Lantus Solostar has increased by 94% since December 31, 2010, nearly doubling in the span of approximately five years.[22] Sanofi, the sponsor of Lantus, realized almost $9 billion in sales in the fiscal year ending in October 2015.

---

[17] PDUFA Goals Letter, p. 4; *Biosimilar Biological Product Authorization Performance Goals and Procedures Fiscal Years 2013 Through 2017*, p. 3 (review performance goals for original biosimilar applications is within 10 months of receipt), *available at* http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/UCM281991.pdf.

[18] FTC Comments to INN Proposal, Docket No. FDA-2013-D-1543, pp. 2-3 (Oct. 27, 2015) ("FTC Comments").

[19] National Diabetes Statistics Report, 2014, http://www.cdc.gov/diabetes/pubs/statsreport14/national-diabetes-report-web.pdf.

[20] FTC Comments, pp. 2-3.

[21] FTC Comments, p.3.

[22] Caroline Humer, *Factbox: Price hikes shore up revenue for top-selling U.S. drugs*, Reuters (April 4, 2016), *available at* http://www.reuters.com/article/us-usa-healthcare-drugpricing-factbox-idUSKCN0X10U9?mod=related&channelName=healthNews.

These high and continuously increasing prices result in rising healthcare costs for everybody, not just those using biologics.[23] Competition from lower-priced biosimilars, however, can stem this tide by garnering potential price reductions of 10% to 30%.[24] Competition from interchangeable biologics could be even more effective at reining in prices: Mylan estimates that a therapeutically equivalent version of Lantus could result in approximately $6.65 billion per year in savings to the U.S. healthcare system and benefit millions of patients suffering from diabetes.[25]

Competition not only reduces healthcare costs; it also increases patient access to needed medications. The FTC has recognized this link between competition, price reductions, and patient access in recent comments to the FDA on its biosimilar naming proposal. According to the FTC, "the relatively high prices of biologics, combined with patient cost-sharing requirements, can limit patient access to biologics."[26] The remedy for this is increased competition, which leads to "reduced prices for, and thus greater patient access to, biologics and biosimilars."[27] Consequently, by impairing competition from lower-cost, follow-on and generic transitional biological products, FDA's proposed policy not only impacts sponsors seeking to develop such products but, more importantly, adversely affects millions of patients by limiting their access to affordable biological medications.

In sum, Mylan respectfully requests that FDA modify its proposed policy regarding pending applications because of the significant negative effects it will have on competition, healthcare costs, and patient access to affordable biological products. As discussed in Section III below, there are several alternative policies that could be adopted by the Agency that not only comply with the BPCIA transition provisions but also minimize disruptions and delays to the development, submission, review and approval of lower-cost, competing transitional biological products like insulin. FDA should adopt one of these alternatives when it finalizes the Draft Guidance.

II. FDA's Proposed Refusal to Approve Pending Applications for Transitional Biological Products After March 23, 2020, Is Arbitrary, Capricious, Contrary to Law, and Beyond FDA's Authority

In the Draft Guidance, FDA proposes to interpret section 7002(e)(4) of the BPCIA "to mean that the Agency will not approve any application under section 505 of the FD&C Act for a biological product subject to the transition provisions that is pending or tentatively approved 'on' March 23, 2020."[28] Although FDA acknowledges that another section of the BPCIA's transition provisions "expressly permits" submission of an application under section 505 for a transitional biological product up until March 23, 2020, FDA nevertheless concludes that "an application for

[23] FTC Comments, at 3.
[24] *Emerging Health Care Issues: Follow-on Biologic Drug Competition*, Federal Trade Commission Report, p. v (June 2009).
[25] Data on file (based upon IMS data for the 12-month period ending October 2015).
[26] FTC Comments, p. 3.
[27] FTC Comments, p. 3.
[28] Draft Guidance, p. 5.

a protein product that has been submitted under section 505 of the FD&C Act and is pending on March 23, 2020, will not be able to be approved."[29] FDA thus recommends that sponsors withdraw such applications and make new submissions under section 351(a) or 351(k) of the PHS Act, as appropriate. For the reasons discussed below, FDA's proposed interpretation is arbitrary, capricious, contrary to law, and beyond FDA's statutory authority. As such, it must be modified or, if challenged, it will be set aside by the federal courts.

A. FDA's Interpretation Is Contrary to the Clear Language of the BPCIA and the FD&C Act and Beyond the Scope of FDA's Authority

The Agency's interpretation of the BPCIA transition provisions is impermissible because it conflicts with the clear statutory language of both the BPCIA and the FD&C Act and is beyond the scope of FDA's authority. First, FDA's interpretation ignores and makes inoperative the BPCIA transition provision that expressly permits sponsors to submit applications under section 505 up until March 23, 2020. It also leads to an absurd result, *i.e.,* the submission of section 505 applications that are inherently futile because they can never be approved. Second, FDA's interpretation conflicts with the express provisions of the FD&C Act and its implementing regulations that define the specific grounds upon which FDA can refuse to approve a 505(b)(2) application or ANDA, none of which are implicated by the "deeming" process. As such, FDA's proposed policy to refuse to approve any pending section 505 application after March 23, 2020 is "contrary to law" and "in excess of statutory jurisdiction, authority, or limitations."[30]

FDA's interpretation of the BPCIA transition provisions must be analyzed under the well-known, two-step *Chevron* test established by the United States Supreme Court in 1984.[31] Under the first step of the *Chevron* test, a reviewing court must determine "whether Congress has directly spoken to the precise question at issue."[32] If the court determines that "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."[33]

Courts use traditional tools of statutory construction to determine Congressional intent, including an examination of the statute's text, structure, purpose, and legislative history, as well as established canons of statutory construction.[34] Typically, the statutory language itself and the structure and purpose of the statute as a whole are the most powerful indicators of Congressional intent.[35] In addition, courts are careful not to interpret a statutory provision in isolation but instead

---

[29] Draft Guidance, p. 5.

[30] Pursuant to the Administrative Procedure Act ("APA"), a reviewing court must "hold unlawful and set aside agency action" that is "in excess of statutory jurisdiction, authority, or limitations" or "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2)(A), (2)(C).

[31] *Chevron U.S.A. Inc. v. Natural Res. Def. Council, Inc.*, 467 U.S. 837 (1984).

[32] *Mova Pharmaceutical Corp. v. Shalala*, 140 F.3d 1060, 1067 (D.C. Cir. 1998) (quoting *Chevron*, 467 U.S. at 842).

[33] *Chevron* at 842-843; *see also Carcieri v. Salazar*, 555 U.S. 379, 387 (2009).

[34] *Serono Labs., Inc. v. Shalala*, 158 F.3d 1313, 1319 (D.C. Cir. 1998); *Bell Atl. Tel. Co. v. FCC*, 131 F.3d 1044, 1047 (D.C. Cir. 1997); *Stat-Trade Inc. v. FDA*, 869 F. Supp. 2d 95, 102 (D.D.C. 2012).

[35] *See Amalgamated Transit Union v. Skinner*, 894 F.2d 1362, 1368 (D.C. Cir. 1990) (quoting *K Mart Corp. v. Cartier, Inc.*, 486 U.S. 281, 291 (1988)); *Watson Labs, Inc. v. Sebelius*, 2012 WL 6968224, at *9 (D.D.C. Oct. 22, 2012), (internal citation and quotation omitted).

strive to consider the context in which it is used, taking into account the entire statutory scheme and the overriding goals of the legislation.[36] If the court concludes that the statute is either silent or ambiguous, the second step of the court's review process under the *Chevron* test is to determine whether the interpretation proffered by the agency is "based on a permissible construction of the statute."[37]

1. FDA's Proposed Interpretation Conflicts With the BPCIA

In this case, FDA's interpretation conflicts with the clear language of the BPCIA. Section 7002(e)(2) of the BPCIA explicitly allows a sponsor to submit an application for a transitional biological product under section 505 of the FD&C Act "not later than" March 23, 2020. FDA's blanket policy not to approve such applications after that date, however, voids this provision by effectively prohibiting sponsors from submitting section 505 applications months or years prior to March 23, 2020.

An application submitted close to the transition date could not, as a practical matter, be approved by FDA prior to March 23, 2020, and, under FDA's policy, would never be approved thereafter. Because the typical review timeline for applications submitted under section 505 of the FD&C Act is ten months, FDA's proposed policy essentially bans the submission of such applications for a minimum of ten months prior to March 23, 2020. For products blocked by patents or exclusivity, this ban could extend much longer.[38] FDA's interpretation thus makes the March 23, 2020, date established by Congress inoperative and replaces it with a date that is a least ten months earlier, i.e., May 23, 2019, and in many cases, may be much earlier than that. It is well-established, however, that an interpretation of a statute that renders any provision inoperative must be rejected.[39]

FDA's interpretation also must be rejected because it would lead to absurd results. As the Supreme Court has instructed, even a "literal application of a statute which would lead to absurd consequences is to be avoided whenever a reasonable application can be given which is consistent with the legislative purpose."[40] In this case, Congress was certainly aware that the usual review

---

[36] *Robinson v. Shell Oil Co.*, 519 US 337 (1997); *Stat-Trade Inc. v. FDA*, 869 F. Supp. 2d 95, 102 (D.D.C. 2012); *Serono Labs.*, 158 F.3d at 1319.

[37] *Chevron*, 467 U.S. at 843.

[38] For example, the ban could extend to 30-months prior to March 23, 2020 for 505(b)(2) applications and ANDAs that make a Paragraph IV certification to a listed patent and are sued by the innovator, since FDA approval typically would be blocked by a 30-month stay. 21 U.S.C. §§ 355(c)(3)(C), 355(j)(5)(B)(iii).

[39] *See Milner v. Dept. of Navy*, 131 S. Ct. 1259, 1268 (2011); *TRW Inc. v. Andrews*, 534 U.S. 19, 31 (2001) (noting canon of statutory interpretation that statutes should be read to avoid making any provision "superfluous, void, or insignificant" (internal quotation marks omitted)); *Edison Elec. Inst. v. EPA*, 996 F.2d 326, 335 (D.C. Cir. 1993) (applying "the elementary canon of construction that a statute should be interpreted so as not to render one part inoperative") (citation omitted); *FTC v. Manager, Retail Credit Co.*, 515 F.2d 988, 994 (D.C. Cir. 1975) ("The presumption against interpreting a statute in a way which renders it ineffective is hornbook law.").

[40] *United States v. Ryan*, 284 U.S. 167, 175 (1931); *see also Haggar Co. v. Helvering*, 308 U.S. 389, 394 (1940) ("All statutes must be construed in the light of their purpose. A literal reading of them which would lead to absurd results is to be avoided when they can be given a reasonable application consistent with their words and with the legislative purpose.").

timeline for a 505(b)(2) application or ANDA is ten months and thus that it would be impossible from a regulatory viewpoint for an application submitted a day or two before March 23, 2020 – or even a month or two – to be reviewed and approved by FDA prior to that date. Yet under FDA's interpretation, Congress specifically authorized the submission of applications like this that it knew could never be approved and, in fact, would need to be withdrawn and re-submitted shortly after initial submission. In other words, Congress specifically authorized the submission of applications that are inherently futile. This, of course, is absurd. Congress authorized the submission of section 505 applications until March 23, 2020, because it expected FDA to review and approve those applications without interruption after March 23, 2020. Because "courts will not construe a statute in a manner that leads to absurd or futile results[,]"[41] FDA's interpretation is impermissible.

In a footnote, FDA suggests that its decision to ignore Section 7002(e)(2) of the BPCIA is justified because that provision is an example of "inartful drafting."[42] But this explanation is too facile. Federal agencies are required to interpret statutes in a manner that makes all parts operative and, short of impossibility, cannot ignore entire statutory provisions by pleading "inartful drafting."[43] In this case, even if the BPCIA transition provisions are inartfully drafted, there are several reasonable ways for FDA to interpret them that make all parts effective and that avoid the disruptions, delays, regulatory dead zones, and absurdity inherent in FDA's proposed interpretation (see section III below). Mylan thus respectfully requests that FDA adopt one of these alternatives when it finalizes the Draft Guidance.

2. FDA's Proposed Interpretation Conflicts With the FD&C Act and Its Implementing Regulations

FDA's proposed interpretation not only conflicts with the clear language of the BPCIA but also with the unambiguous provisions of the FD&C Act and FDA's regulations governing approval decisions. In the Draft Guidance, FDA announces a blanket policy that "[a]fter March 23, 2020, FDA will not approve any pending or tentatively approved 505(b)(2) application (or ANDA) for a biological product that relied on an approved NDA that was deemed to be a BLA on March 23, 2020."[44] FDA's purported basis for this position is that such NDAs will be removed from the Orange Book after March 23, 2020, and thus no longer will be considered "listed drugs" that can be relied upon by a 505(b)(2) application or ANDA.[45] But neither the FD&C Act nor FDA's regulations grant FDA authority to deny approval of a pending 505(b)(2) application or ANDA under these circumstances.

---

[41] *Nixon v. Missouri Municipal League*, 541 U.S. 124, 138 (2004) (citing *United States v. American Trucking Assns., Inc.*, 310 U.S. 534, 543 (1940); *SEC v. DiBella*, 587 F.3d 553, 572 (2d Cir. 2009) ("Where an examination of the statute as a whole demonstrates that a party's interpretation would lead to absurd or futile results plainly at variance with the policy of the legislation as a whole, that interpretation should be rejected.") (quoting *Yerdon v. Henry*, 91 F.3d 370, 376 (2d Cir. 1996)); *Clinton v. City of New York*, 524 U.S. 417, 429 (1998) (rejecting a government interpretation of a statute that "'would produce an absurd and unjust result which Congress could not have intended.'") (quoting *Griffin v. Oceanic Contractors, Inc.*, 458 U.S. 564, 574 (1982)).

[42] Draft Guidance, p. 5 n. 10 (citing *King v. Burwell*, 135 S.Ct. 2480, 2492 (2015)).

[43] *Edison Elec.*, 996 F.2d at 335; *FTC v. Manager, Retail Credit Co.*, 515 F.2d at 994.

[44] Draft Guidance, p. 6.

[45] Draft Guidance, p. 6.

With respect to 505(b)(2) applications, the FD&C Act and FDA's regulations specify the grounds upon which FDA can refuse to approve an application.[46] For instance, FDA can refuse to approve a 505(b)(2) application if there is a lack of substantial evidence of effectiveness or the drug is unsafe.[47] Significantly, however, the status of the NDA for the listed drug is not identified in either the statute or FDA regulations as a basis to deny approval of a 505(b)(2) application. This makes sense because, in approving a 505(b)(2) application, FDA is not relying upon the NDA for the listed drug itself, or even any of the specific studies contained in that NDA, but rather on the Agency's own prior findings of safety and effectiveness.[48] These prior findings, once made, reside with the Agency separate and apart from the specific NDA upon which they are based and thus can be relied upon by a 505(b)(2) applicant regardless of the status of the NDA. Indeed, they can be relied upon by a 505(b)(2) applicant even if the NDA is withdrawn in its entirety (as would be the case here).

The withdrawal of the NDAs for transitional biologic products identified as "listed drugs," therefore, provides no basis for FDA to deny approval of pending or tentatively approved 505(b)(2) applications after March 23, 2020. FDA itself has recognized that once a 505(b)(2) application "has been appropriately submitted and is under review, FDA may refuse to approve the application only if one or more specific conditions warranting refusal apply."[49] In this case, because none of those "specific conditions" apply to the "deeming" process, FDA lacks authority to adopt a blanket policy refusing to approve pending section 505 applications for transitional biological products after March 23, 2020.

The FD&C Act and FDA's regulations also specify the grounds for refusing to approve an ANDA and illustrate the problems with FDA's interpretation with even greater clarity than the 505(b)(2) provisions.[50] The ANDA provisions, unlike the provisions applicable to 505(b)(2) applications, specifically address situations where the approval status of the listed drug changes. In particular, under both the statute and FDA's regulations, the Agency may deny approval of an ANDA if the NDA for the listed drug is suspended or withdrawn, *but only if the suspension or withdrawal is based on safety or effectiveness reasons*.[51] In other words, an ANDA cannot be refused approval if the NDA for the listed drug is suspended, withdrawn and/or no longer in effect for reasons other than safety or effectiveness.

In this case, of course, there are no safety or effectiveness reasons for the withdrawal of the NDAs for transitional biological products on March 23, 2020; on the contrary, those products will continue to be commercially marketed under approved BLAs after March 23, 2020 and will continue to be regarded as safe and effective. Accordingly, there is no basis under the FD&C Act

[46] 21 U.S.C. § 355(d); 21 C.F.R. § 314.125.
[47] 21 U.S.C. § 355(d)(1), (2).
[48] *Guidance for Industry: Applications Covered By Section 505(b)(2)*, p. 2 (Oct. 1999) (Draft); FDA 505(b)(2) Petition Response, Docket Nos. 2001P-0323, 2002P-0447, 2003P-0408, p. 14 (Oct. 14, 2003).
[49] FDA Response to GenPharm Petition, Docket No. FDA-2003-P-0338, p. 4 (June 24, 2004).
[50] 21 U.S.C. § 355(j)(4); 21 C.F.R. § 314.127.
[51] 21 U.S.C. § 355(j)(4)(I); 21 C.F.R. § 314.127(a)(9), (10), (11). It is also possible for FDA to deny approval if the NDA is withdrawn or suspended because the labeling is false or misleading or required patent information was not submitted with the NDA, but Mylan is not aware of any instances where these latter two reasons were implicated.

or FDA's regulations for FDA to deny approval of pending or tentatively approved ANDAs after March 23, 2020, simply because the NDAs for the listed drugs are withdrawn and "deemed" to be BLAs by operation of the BPCIA.

Finally, Mylan believes that FDA lacks authority to remove NDAs for transitional biological products from the Orange Book after March 23, 2020. The contents of the Orange Book are specified in the FD&C Act and must include any drug that has been approved by FDA via an NDA.[52] This category, of course, includes transitional biological products, all of which were initially approved via NDAs.[53] Moreover, the sole basis provided in the FD&C Act for removing a drug from the Orange Book list, once included, is if the NDA (or ANDA) is withdrawn or suspended, or the drug is voluntarily withdrawn from sale, for safety or effectiveness reasons.[54] As noted above, this provision does not apply to transitional biological products, which continue to be considered safe and effective after March 23, 2020.

FDA nevertheless contends that its actions are justified because "the BPCIA does not explicitly provide a basis for the Agency to treat approved NDAs or ANDAs for biological products as both NDAs and BLAs after such applications are deemed to be BLAs on March 23, 2020."[55] But FDA unquestionably could treat the NDAs as "withdrawn" as a result of the "deeming" process. Moreover, because the withdrawal of such applications would be for reasons other than safety or effectiveness, FDA could keep them listed in the Discontinued section of the Orange Book where they could continue to be relied upon as listed drugs by pending 505(b)(2) applications and ANDAs.[56] Accordingly, there is no statutory or regulatory basis for FDA to remove NDAs for transitional biological products from the Orange Book after March 23, 2020, and any effort to do so would conflict with the clear language of the FD&C Act.[57]

[52] 21 U.S.C. § 355(j)(7)(B).
[53] BPCIA, § 7002(e) (applicable to "products previously approved under section 505")
[54] 21 U.S.C. § 355(j)(7)(C).
[55] Draft Guidance, p. 6.
[56] Moreover, there is no risk that the continued listing of these NDAs in the Discontinued section of the Orange Book would permit the submission of 505(b)(2) applications or ANDAs after March 23, 2020, since the BPCIA explicitly prohibits this. BPCIA, §§ 7002(e)(1), (2). Rather, the benefit of these continued listings would inure exclusively to pending applications submitted prior to March 23, 2020, as explicitly permitted by the BPCIA.
[57] The above analyses demonstrate that FDA's interpretation is impermissible under step one of the *Chevron* test. Even under step two, however, the Agency's interpretation is unreasonable and must be rejected. As noted above, it leads to absurd results which, by definition, are unreasonable. Moreover, because the Agency has a potential pecuniary interest in advancing this particular interpretation of the BPCIA transition provisions – which could lead to additional user fees for FDA – the Agency's position would not be entitled to the usual *Chevron* deference. *Amalgamated Sugar Co. LLC v. Vilsack*, 563 F.3d 822, 834 (9th Cir. 2009), *cert. denied*, 130 S. Ct. 280 (2009); *see also Transohio Sav. Bank v. Director, OTS*, 967 F.2d 598, 614 (D.C. Cir. 1992) (voicing concern about deferring to the statutory interpretation of an agency with a financial interest in the interpretation).

B. FDA's Interpretation Is Arbitrary and Capricious

FDA's interpretation of the BPCIA transition provisions also is impermissible because it is arbitrary and capricious. Under the Administrative Procedures Act ("APA"), a reviewing court must set aside agency action that is "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law."[58] In this case, FDA's proposed interpretation is arbitrary and capricious within the meaning of the APA because it: (a) fails to treat similarly situated products in a similar manner, (b) and departs from established Agency precedent without adequate justification.

First, FDA's proposed "non-approval" policy treats full NDAs for transitional biological products differently than 505(b)(2) applications and ANDAs. The Draft Guidance explains that the Agency will not approve 505(b)(2) applications or ANDAs after March 23, 2020 because of the removal of relevant listed drugs after that date. This explanation, however, does not apply to full NDAs, which do not rely upon listed drugs for approval, and the Draft Guidance does not provide any other grounds that could justify refusing to approve a pending, full NDA for a transitional biological product after March 23, 2020. Accordingly, FDA's proposed policy, of necessity, would block approval of 505(b)(2) applications and ANDAs after March 23, 2020 but not full NDAs, which do not rely upon a listed drug.

This disparate treatment, however, is unwarranted. The BPCIA transition provisions make no distinctions whatsoever between full NDAs, 505(b)(2) applications and ANDAs, referring to them collectively as applications submitted under section 505 of the FD&C Act.[59] For purposes of the BPCIA transition provisions, therefore, these different application types are similarly situated and must be treated in a consistent manner. It is well-established that "[i]f an agency treats similarly situated parties differently, its action is arbitrary and capricious in violation of the APA."[60] Because FDA's proposed policy would permit full NDAs to be approved after March 23, 2020, but not similarly situated 505(b)(2) applications and ANDAs, it is arbitrary and capricious and must be modified.

Second, FDA's proposed policy deviates from established precedent without adequate justification or explanation. On numerous occasions in the past, the Agency has moved products from one regulatory category to another, both on its own initiative and, like here, in accordance with statutory transition provisions.[61] In each case, the Agency has adopted a policy of "ensur[ing] that the transition from one jurisdictional category to another would take place with minimal disruption to the marketplace and minimal prejudice to the firms subject to the move."[62]

---

[58] 5 U.S.C. § 706(2)(A).
[59] BPCIA, § 7002(e).
[60] *Bracco Diagnostics, Inc. v. Shalala*, 963 F. Supp. 20, 27-28 (D.D.C. 1997) (quoting *Allergan. Inc. v. Shalala*, 6 Food and Drug Rep. 389, 391, No. 94-1223 (D.D.C. Nov. 10, 1994) (Greene, J.)).
[61] *See, e.g.*, FDA Guidance, *Repeal of Section 507 of the Federal Food, Drug, and Cosmetic Act*, (explaining how FDA will move approved and pending antibiotic applications to approved and pending drug applications); 47 Fed. Reg. 46139 (Oct. 15, 1982) (redesignation of liquid tear ophthalmic product from device to drug); 40 Fed. Reg. 31311 (July 25, 1975) (reassignment of radioactive biological products from biologic to drug).
[62] FDA Consolidated Response to Pending Citizen Petitions on the Regulation of Ultrasound Contrast Agents, Docket No. 96P-0511, p. 59 (July 25, 1997) ("Consolidated Response").

In this case, by contrast, FDA proposes to adopt a policy that it acknowledges will have a "significant impact on development programs" for transitional biological products. Indeed, given the sizeable regulatory "dead zones" likely to arise for key biological products (as discussed in section I above), it is difficult to imagine an interpretation of the BPCIA transition provisions that would be *more disruptive* to the marketplace or *more prejudicial* to sponsors subject to the transition. Moreover, this is not a situation where FDA's actions are constrained by the statutory language; FDA's proposed policy, in fact, conflicts with the statutory language.

It is a basic principle of administrative law that "an agency must provide a reasoned explanation for any failure to adhere to its own precedents."[63] "[A]gency action cannot stand when it is 'so inconsistent with its precedents as to constitute arbitrary treatment amounting to an abuse of discretion."[64] Consequently, FDA's failure to follow past precedent by ensuring that the BPCIA transition takes place with "minimal disruption" to the marketplace and "minimal prejudice" to affected sponsors is arbitrary and capricious in violation of the APA. As such, it must be modified.

C. FDA's Interpretation Is Inconsistent With the Purpose of the BPCIA

Finally, Mylan respectfully requests that FDA modify its proposed policy because it is inconsistent with the overriding goals of the BPCIA. The Supreme Court has cautioned that "[w]e cannot interpret federal statutes to negate their own stated purposes."[65] In *King v. Burwell*, which addressed a different provision of the same legislation in which the BPCIA is contained, the Supreme Court rejected an interpretation that would have undermined the statutory scheme as a whole and "likely create the very 'death spirals' that Congress designed the Act to avoid."[66] The Court reasoned that it was "implausible that Congress meant the Act to operate in [a] manner" antithetical to its underlying goals.[67]

In this case, FDA's proposed interpretation is antithetical to the purpose and goals of the BPCIA in at least two ways. First, one of the primary goals of the BPCIA is to spur competition among biological products and thereby increase access to affordable biological products by patients in the United States. As described in more detail above, however, FDA proposed policy will hamper competition and impair access by creating regulatory "dead zones" and other hurdles that disrupt and delay the development, submission, review and approval of lower-cost transitional biological products. FDA itself acknowledges that its proposed policy "could have a significant impact on development programs" for competitive products.[68]

---

[63] *Hatch v. FERC*, 654 F.2d 825, 834 (D.C. Cir. 1981).
[64] *Garrett v. FCC*, 513 F.2d 1056, 1060 (D.C. Cir. 1975) (quoting *Herbert Harvey Inc. v. NLRB*, 424 F.2d 770, 780 (D.C. Cir. 1969)); *Greater Boston Television Corp. v. FCC*, 444 F.2d 841, 852 (D.C. Cir. 1970) (citations omitted), *cert. denied*, 403 U.S. 923 (1971) ("an agency changing its course must supply a reasoned analysis indicating that prior policies and standards are being deliberately changed, not casually ignored, and if an agency glosses over or swerves from prior precedents without discussion it may cross the line from tolerably terse to the intolerably mute.").
[65] *King v. Burwell*, 135 S.Ct. 2480, 2493 (2015) (quoting *New York State Dept. of Social Servs. v. Dublino*, 413 U.S. 405, 419-20 (1973).
[66] *Id.*
[67] *Id.* at 2494.
[68] Draft Guidance, p. 6.

Second, FDA's proposed interpretation undermines the specific purpose of the transition provision itself. Although the legislative history is scant, the purpose of the transition provision is not difficult to discern: it is intended to reduce uncertainty, ensure continuity, and minimize disruptions to the approval process of transitional biological products. The Draft Guidance, however, undermines all of these goals. Sponsors now face increased uncertainty regarding the appropriate approval pathway for transitional biological products and the allowable timing of such applications. Although Congress promised that sponsors could submit section 505 applications at any time up until March 23, 2020, FDA's proposed policy revokes that promise and forces applicants to guess when it would be feasible to submit a section 505 application based upon estimated review times and existing patent and exclusivity protections. Likewise, FDA's proposed policy causes major disruptions to the review and approval process by requiring withdrawal and re-submission of applications that are not approved by March 23, 2020.

FDA's proposed policy thus creates the very consequences that Congress sought to avoid by enacting the BPCIA and its transition provisions. Because it is "implausible that Congress meant the Act to operate in [a] manner" antithetical to its underlying goals,[69] FDA's proposed interpretation is not permissible.

III. Alternate Interpretations Are Available That Not Only Conform to the Statutory Language But Also Minimize Disruptions to the Development and Approval of Affordable Transitional Biological Products

Although the proposed policy set forth the Draft Guidance is impermissible, Mylan believes there are several available alternatives that are consistent with the BPCIA and FD&C Act and that would minimize delays and disruptions to the approval process. Because these alternatives better comport with the overriding goals of the BPCIA to facilitate competition and thereby increase patient access to affordable biological products, Mylan respectfully requests that FDA revise the Draft Guidance to adopt one of the alternatives described below.

First, Mylan believes that FDA could interpret the BPCIA transition provision to allow pending 505(b)(2) applications and ANDAs to continue to be reviewed and approved under section 505 of the FD&C Act after March 23, 2020. As discussed above, FDA could treat the "deeming" process for the listed drug to involve the *de facto* withdrawal of the NDA upon its transition to a BLA. Because such withdrawals would not be the result of safety or effectiveness concerns (but rather would flow from operation of the BPCIA itself), 505(b)(2) applications and ANDAs could continue to rely upon withdrawn NDAs, and FDA could continue to review and approve such applications, after March 23, 2020.[70] This not only would make section 7002(e)(2) of the BPCIA effective, but also would allow such applications to be reviewed and approved by FDA under section 505 of the FD&C Act without any disruptions or unnecessary delays.

[69] *Id*. at 2494.
[70] *See* 21 C.F.R. §§ 314.127(a)(9), (10), (11).

Moreover, FDA could take administrative action to ensure regulatory uniformity after such applications are approved under section 505. Although FDA appears to be concerned that the BPCIA does not provide a mechanism to transition an approved 505(b)(2) application or ANDA to an approved BLA after March 23, 2020,[71] Mylan believes this concern is unfounded. The Agency has inherent administrative authority to move products from one regulatory category to another to, among other things, "bring regulatory uniformity to a class of products."[72] Moreover, the Agency has exercised this authority numerous times in the past.[73] The BPCIA transition provisions do not in any way prohibit FDA from exercising this inherent authority. Consequently, if FDA is concerned about maintaining uniformity among transitional biological products after March 23, 2020, it could simply use its inherent authority to transition 505(b)(2) applications and ANDAs approved after that date to approved BLAs.

Second, FDA could simply "deem" all *pending* applications submitted under section 505 of the FD&C Act to be pending BLAs on March 23, 2020, and continue to review them without interruption and in accordance with the same user fee review goals. Because applicants would not need to withdraw and re-submit such applications, this alternative would minimize disruptions and delays in the review process, ensure continuity, and expedite the approval of affordable transitional biological products.

FDA has adopted this approach in numerous similar situations in the past. For example, before 1976, FDA regulated several medical devices as drugs under the FD&C Act, requiring them to have NDA approval prior to commercial marketing. After enactment of the Medical Device Amendments of 1976,[74] the regulatory status of these "transitional devices" was switched from "drug" to "device." For transitional devices with pending NDAs, Congress directed FDA to consider those applications to be pending Premarket Approval applications ("PMAs") and to calculate the 180-day review timeline as if it had started on submission of the original NDA (rather than re-starting it on the transfer date).[75] Neither the statute nor FDA required the withdrawal of pending NDAs or the submission of new PMAs.

Likewise, when section 507 of the FD&C Act was repealed in 1997, FDA deemed pending antibiotic applications submitted under that section to be pending drug applications under section 505 of the FD&C Act. Significantly, FDA took this action on its own initiative without specific authorization from Congress. In that case, like here, the statutory transition provision addressed only "approved" applications, not pending applications.[76] This Congressional silence regarding pending applications, however, did not prevent FDA from administratively transferring pending

[71] Draft Guidance, p. 5.
[72] Consolidated Response, p. 58.
[73] *See, e.g.*, 40 Fed. Reg. 31311 (July 25, 1975) (moving radioactive products from biologics to drugs); 47 Fed. Reg. 46139 (Oct. 15, 1982) (moving liquid tear ophthalmic products from devices to drugs); 51 Fed. Reg. 37976 (Oct. 27, 1986) (moving human thrombin products from devices to biologics); 55 Fed. Reg. 5892 (Feb. 20, 1990) (moving certain diagnostic test kits from devices to biologics); Consolidated Response, p. 59 (moving ultrasound contrast agents from devices to drugs).
[74] Medical Device Amendments of 1976, Pub. L. No. 94-295 (1976).
[75] 21 U.S.C. § 360j(l)(3)(B).
[76] Food and Drug Administration Modernization Act of 1997, Pub. L. No. 105-115, § 125(d) (1997).

section 507 applications to pending section 505 applications. Following the precedent established for transitional devices, FDA did not require pending antibiotic applications to be withdrawn and resubmitted under section 505, thereby minimizing disruptions and delays in the review process.[77] Instead, the Agency continued to review such applications without interruption.[78] The Agency even revised its final regulations governing patent term extensions to ensure that affected applicants were not prejudiced by the administrative transfer of their applications from section 507 to section 505.[79]

Finally, in 1997, FDA took action *without any statutory directive whatsoever* to transfer a pending PMA for an ultrasound contrast agent to a pending NDA.[80] Like the precedent discussed above, FDA did not require the applicant to withdraw its PMA and submit a new NDA. Moreover, the Agency did not re-start the review process or "repeat the review of those portions of the PMA on which [FDA] officials have already completed substantial work."[81] Instead, FDA assigned the application a new NDA number and transferred the review from the device center to the drug center, explaining that the NDA reviewers would "rely, as appropriate, on the extensive analyses already done by [the PMA reviewers], the comments and recommendations of the February 24, 1997, advisory panel, and any conclusions already reached by CDRH officials regarding the data and information in the PMA."[82] Although there are some differences in the requirements between an NDA and a PMA, FDA concluded that these could be handled through submission of an amendment to the pending NDA following the re-designation.[83] In addition, FDA calculated the PDUFA "goal date" based upon the date the application was initially filed as a PMA, not the date it was "deemed" to be an NDA.[84] In this way, FDA accomplished the re-designation of the PMA as an NDA "without a significant interruption in the pre-market review process."[85]

Mylan believes FDA could follow this precedent with respect to pending applications for transitional biological products submitted under section 505 of the FD&C Act. FDA adopted this approach in the above cases, in part, because the review standards under the old and new jurisdictional categories were similar and the new reviewers had familiarity with the pending applications.[86] In this case, the same factors are present. First, FDA's requirements for full NDAs and full BLAs have been harmonized for years,[87] and the standards for approving a 505(b)(2)

---

[77] FDA Guidance, *Repeal of Section 507 of the Federal Food, Drug, and Cosmetic Act*, p. 5 ("All action letters must use the 505(b) or 505(j) templates, even for drugs that originally were submitted under section 507, but are the subject of Agency action on or after November 21, 1997.").

[78] *See, e.g.*, FDA Review Package for Periostat (doxycycline hyclate) Capsules, *available at* http://www.accessdata.fda.gov/drugsatfda_docs/nda/98/50744.cfm.

[79] 64 Fed. Reg. 396, 400 (Jan. 5, 1999) (amending 21 C.F.R. § 60.22(a) to clarify that the approval phase begins on the date an application under section 507 was initially submitted, not the date the application was "deemed" to be a section 505 application).

[80] FDA Consolidated, p. 59.

[81] Consolidated Response, pp. 59-60.

[82] Consolidated Response, p. 60.

[83] Consolidated Response, p. 60.

[84] Consolidated Response, p. 59.

[85] Consolidated Response, p. 60.

[86] Consolidated Response, p. 60.

[87] Food and Drug Administration Modernization Act of 1997, Pub. L. No. 105-115, § 123(f) (directing FDA to "take measures to minimize differences in the review and approval" of NDAs and BLAs).

application for a protein product are highly similar to the requirements for approving a 351(k) application.[88] To the extent there are differences in the approval requirements, FDA could permit sponsors to make post-transfer amendments to add new or missing information, as the Agency did in the similar situations discussed above. Second, the transfer of pending NDAs to pending BLAs is unlikely to cause significant disruptions within the Agency, since the same reviewers and review divisions will be involved in the review of both application types. Under the BPCIA, biosimilar applications must be reviewed by the same review division responsible for the reference product.[89]

Accordingly, although there is no explicit provision in the BPCIA authorizing FDA to treat one type of pending application as a different type of pending application, as discussed above, FDA has ample authority to do so. Moreover, exercising that authority not only would allow FDA to adopt an interpretation of the BPCIA transition provisions that is consistent with the statutory language but also would "ensure that the transition from one jurisdictional category to another would take place with minimal disruption to the marketplace and minimal prejudice to the firms subject to the move."[90]

IV. Conclusion

In conclusion, Mylan respectfully requests that FDA modify its proposed policy regarding pending applications prior to finalizing the Draft Guidance. The proposed policy, if implemented, will have a devastating effect on development programs for many important protein products, including insulin, thereby impairing competition from lower-cost biological medicines, increasing healthcare costs in the United States, and, most importantly, limiting patient access to affordable biological products. Mylan believes these results are antithetical to the overriding goals of the BPCIA to *increase* competition and access and *lower* healthcare costs in the United States. For the reasons discussed above, Mylan also believes FDA's proposed actions are arbitrary, capricious and contrary to the clear language of both the BPCIA and the FD&C Act and beyond the scope of FDA's authority.

To remedy this situation, FDA should adopt a new interpretation that (a) is consistent with the statutory language and underlying goals of the BPCIA, and (b) minimizes disruptions to the development, review and approval of, and patient access to, affordable transitional biological products. Mylan has identified two options that meet these criteria (see section III above), and there may be additional ones as well. Moreover, because FDA's current interpretation creates a regulatory "dead zone" that could already be disrupting development programs for transitional

[88] For example, a 505(b)(2) application, like a biosimilar application, is compared to a reference product and may be supported by one or more clinical studies establishing safety, effectiveness and/or comparable immunogenicity. In addition, protein products have been approved under section 505(b)(2) based upon the same "highly similar" standard used for biosimilar applications. *See* 42 U.S.C. § 262(i)(2). For example, Omnitrope® (somatropin [rDNA orgin] for injection) was approved based upon a showing that its active ingredient is "highly similar" to the somatropin in the reference product. FDA Response to Omnitrope Petition, Docket No. FDA-2004-P-0339, at 14 (May 30, 2006).

[89] 42 U.S.C. § 262(k)(5)(B). For ultrasound contrast agents, for example, FDA explained that its transition plan was permissible because, among other things, the review standards for drugs and devices are similar and CDER review staff already had familiarity with the pending application. Consolidated Response, at 61.

[90] Consolidated Response, at 59.

biologic products (as described in section I above), FDA should announce that it is immediately withdrawing the proposed interpretation described in the Draft Guidance while it considers which of the permissible options to adopt in a final guidance document. FDA should publish this announcement in the Federal Register immediately.

Mylan appreciates your consideration of these comments. Please do not hesitate to contact the undersigned if you have any questions.

Sincerely,

Carmen M. Shepard
Global Head of Policy, Regulatory Counsel,
and Operations Auditing