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BY HAND DELIVERY

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

To Whom It May Concern:

Hyman, Phelps & McNamara, P.C. submits this petition pursuant to Section 505(q) of the Federal Food, Drug, and Cosmetic Act ("FDCA"), and in accordance with 21 C.F.R. §§ 10.20 and 10.30 to request that the Food and Drug Administration ("FDA") refuse to file any 505(b)(2) new drug application ("NDA") for a buprenorphine/naloxone drug product consisting of a polymer film for application to the oral mucosal membranes unless such NDA references the NDA for the SUBOXONE® sublingual film product, and to reaffirm that any such 505(b)(2) NDA will be subject to the impurity limits for naloxone established by FDA in response to a 2009 citizen petition (Docket No. FDA-2009-P-0325).[1]

A. Action Requested

The undersigned requests that FDA:

1. Refuse to file any 505(b)(2) NDA for a buprenorphine/naloxone drug product consisting of a polymer film for application to the oral mucosal membranes unless such 505(b)(2) NDA references NDA No. 22-410 (SUBOXONE®), which is the

[1] Reference is also made to Docket No. FDA-2011-P-0869, which contains a Citizen Petition dated Dec. 2, 2011, requesting the same actions cited herein, a comment dated May 3, 2012, filed by Foley and Lardner LLP, on behalf of their client, BioDelivery Sciences International, Inc. ("BDSI"), and our response to that comment dated June 13, 2013. Copies of these three submissions are included as Appendix 1 to this Citizen Petition.

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NDA for the sublingual film product, and makes the appropriate certifications with respect to all patents listed for NDA No. 22-410.

2. Refuse to approve any application for a buprenorphine/naloxone drug product unless the applicant can demonstrate that any genotoxic or potentially genotoxic impurities associated with naloxone are limited appropriately.

B. Statement of Grounds

Currently, oral buprenorphine/naloxone drug products are listed in FDA's "Approved Drug Products with Therapeutic Equivalence Evaluations" (commonly known as the "Orange Book"). The sublingual tablet product (now discontinued) was approved in NDA No. 20-733 for two strengths: EQ 8 mg base/2 mg base; and EQ 2 mg base/0.5 mg base. NDA No. 20-733 was approved on October 8, 2002. The sublingual film buprenorphine/naloxone product is approved in NDA No. 22-410. Four strengths of buprenorphine/naloxone sublingual film are approved: EQ 12 mg base/3 mg base; EQ 8 mg base/2 mg base; EQ 4 mg base/1 mg base; and EQ 2 mg base/0.5 mg base. NDA No. 22-410 was approved on August 30, 2010 for two strengths (EQ 8 mg base/2 mg base and EQ 2 mg base/0.5 mg base), and supplements to that NDA were approved on August 10, 2012 for two additional strengths (EQ 12 mg base/3 mg base; and EQ 4 mg base/1 mg base). Two patents are listed in the Orange Book for NDA # 22-140 (Patent No. 8,017,150 and Patent No. 8,475,832).

On August 1, 2013, BDSI announced that it had submitted an NDA to FDA for a "buccal film" buprenorphine/naloxone product for the maintenance treatment of opioid dependence.[2] According to information released by that company, the product "consists of a small, bioerodible polymer film" and the route of administration is "to the mucosal membranes (inner lining of cheek)."[3] As explained below, any 505(b)(2) NDA for such a product should be required to identify the sublingual film product approved in NDA No. 22-410 (SUBOXONE®) as the listed drug. In addition, the applicant must be able to demonstrate that any genotoxic or potentially genotoxic impurities associated with naloxone are limited appropriately.

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2 BDSI calls this product "BUNAVAIL." Press Release, BDSI, BioDelivery Sciences Announces Submission of NDA for BUNAVAIL (Aug. 1, 2013), *available at* http://bdsi.investorroom.com/2013-08-01-BioDelivery-Sciences-Announces-Submission-of-NDA-for-BUNAVAIL (Appendix 2).

3 *BEMA® Technology*, BDSI, http://www.bdsi.com/BEMA_Technology.aspx (last visited Aug. 1, 2013) (Appendix 3).

1. The 505(b)(2) NDA must reference NDA No. 22-410 (SUBOXONE®) and certify with respect to all patents listed for NDA No. 22-410

a. Statutory and Regulatory Background

FDCA § 505(b)(1) permits the submission of an NDA that contains full reports of investigations of safety and effectiveness (1) that are conducted by or for the applicant, and/or (2) for which the applicant has obtained a right of reference. FDCA § 505(b)(2) permits the submission of an NDA where at least some of the information required for approval comes from studies not conducted by or for the applicant, and for which the applicant has not obtained a right of reference. Section 505(b)(2) NDAs, therefore, enable the NDA applicant to rely, in part, on FDA's previous findings of safety and efficacy for an approved drug product (and/or published literature) in support of its application for the marketing of a new drug. If a 505(b)(2) applicant is relying on FDA's previous findings of safety and efficacy for an approved drug product, the applicant must identify the drug application forming the basis for FDA's conclusions.[4] The previously approved product is called the "listed drug" ("LD"). According to FDA regulations, a "listed drug" is:

> a new drug product that has an effective approval under section 505(c) of the act for safety and effectiveness or under section 505(j) of the act, which has not been withdrawn or suspended under section 505(e)(1) through (e)(5) or (j)(5) of the act, and which has not been withdrawn from sale for what FDA has determined are reasons of safety or effectiveness. Listed drug status is evidenced by the drug product's identification as a drug with an effective approval in the current edition of FDA's "Approved Drug Products with Therapeutic Equivalence Evaluations" (the list) or any current supplement thereto, as a drug with an effective approval. A drug product is deemed to be a listed drug on the date of effective approval of the application or abbreviated application for that drug product.[5]

Modifications to that LD, including a new route of administration or dosage form, can be approved in a 505(b)(2) application that need "contain only that information needed to support the modification(s) of the listed drug."[6] FDA may then approve the new product candidate for all or some of the label indications for which the LD has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

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4 21 C.F.R. § 314.54(a)(1)(iii).

5 Id. § 314.3(b).

6 Id. § 314.54(a).

Federal law provides for a period of three years of exclusivity following approval of a new drug that contains a previously approved active moiety, the approval of which was required to be supported by one or more clinical trials conducted by or for the applicant (e.g., a new dosage form, route of administration or combination, or for a new use), during which FDA cannot grant effective approval of an abbreviated new drug application (ANDA) or 505(b)(2) NDA for the LD's protected conditions of use.[7] To the extent that the 505(b)(2) NDA applicant is relying on FDA's previous findings for an already approved product, the applicant is required to certify to any patents listed for that LD in the Orange Book. Specifically, the applicant must certify that: (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or, (iv) the listed patent is invalid or will not be infringed by the new product.[8]

Once the 505(b)(2) applicant has identified the appropriate LD, the 505(b)(2) application must contain a "patent certification or statement required under section 505(b)(2) of the [FDCA] with respect to any relevant patents that claim the listed drug or that claim any other drugs on which the investigations relied on by the applicant for approval of the application were conducted, or that claim a use for the listed or other drug."[9] If there is a listed drug that is the pharmaceutical equivalent of the drug proposed in the 505(b)(2) application, the 505(b)(2) applicant should provide patent certifications for the patents listed for the pharmaceutically equivalent drug.[10] FDA has repeatedly refused to permit a 505(b)(2) applicant to "use the 505(b)(2) process to end-run patent protections that would have applied had an ANDA been permitted."[11] As FDA observed:

> [I]f a tablet and a capsule are approved for the same moiety with patents listed for the tablet and none listed for the capsule, an ANDA applicant seeking approval for a tablet should cite the approved tablet as the reference listed drug. It should not circumvent the patents on the tablet by citing the capsule as the reference listed drug and filing a suitability

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7 NDA No. 22-410 has been awarded three years of exclusivity through August 30, 2013 under this provision of law. The Orange Book indicates this exclusivity was awarded for the "new dosage form" (i.e., the film).

8 FDC Act § 505(b)(2)(A).

9 21 CFR § 314.54(a)(1)(vi).

10 FDA, Draft Guidance for Industry, Applications Covered by Section 505(b)(2), 8 (Oct. 1999).

11 FDA, Petition Response, Docket No. 2004P-0386, 9 (Nov. 30, 2004) (Appendix 4).

> petition under section 505(j)(2)(C) of the [FDCA] and 21 CFR 314.93 seeking to change to a tablet dosage form.[12]

Such an approach is a guiding principle in ensuring that the parallel structure and logic of the patent certification provisions in Sections 505(b)(2) and 505(j) in the Hatch-Waxman Amendments are interpreted faithfully.

b. The appropriate LD is "the most similar alternative"

As noted above, "[i]f there is a listed drug that is the pharmaceutical equivalent to the drug proposed in the 505(b)(2) application, that drug should be identified as the listed drug."[13] However, if there is no pharmaceutical equivalent, then FDA has stated that a 505(b)(2) NDA should reference the LD that is most similar to the drug for which approval is sought. As FDA explained:

> [I]f all the information relied on by FDA for approval (excluding information submitted in the 505(b)(2) application itself) is contained in a single previously approved application and that application is a pharmaceutical equivalent or the most similar alternative to the product for which approval is sought, the 505(b)(2) applicant should certify only to the patents for that application. This is the case even when another application also contains some or all of the same information. This approach ensures that patent certification obligations for 505(b)(2) applications and for ANDAs are parallel. Each application will certify only to patents listed for drugs on whose findings of safety and effectiveness FDA relies for approval (including patents for pharmaceutical equivalents or, if there is no pharmaceutical equivalent, for the most similar alternative), not to patents submitted for applications on which FDA could have relied but did not.[14]

In that case, FDA approved Abbott's NDA No. 19-304 for a 100 mg nonmicronized fenofibrate capsule on December 31, 1993 ("Abbott's first NDA"). On February 9, 1998, FDA approved a supplement to NDA No. 19-304 for 67 mg micronized fenofibrate capsules, and then later approved an additional supplement for 134 mg and 200 mg micronized capsules. "These two

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12 Id. at 9 n. 13.

13 FDA, Draft Guidance for Industry, Applications Covered by Section 505(b)(2), 8 (Oct. 1999).

14 FDA, Petition Response, Docket No. 2004P-0386, 10 (Nov. 30, 2004) (emphasis added).

supplements were approved based on studies in healthy volunteers that compared the bioavailability of the proposed drug products with that" of the 100 mg nonmicronized product and "did not include additional clinical or preclinical studies to establish safety or effectiveness."[15] On September 4, 2001, Abbott obtained approval for NDA No. 21-203 for 54mg and 160 mg fenofibrate tablets ("Abbott's second NDA"). "This NDA contained no new safety or effectiveness studies [and] was also supported by the clinical and preclinical studies previously submitted" in Abbott's first NDA "as well as by a newly conducted study in healthy volunteers comparing the bioavailability of the proposed Abbott tablets with that of the previously approved" product in Abbott's first NDA.[16] On February 18, 2004, Reliant submitted a 505(b)(2) NDA for micronized fenofibrate capsules (43 mg, 87 mg, and 137 mg strengths). Reliant's NDA identified as its LD Abbott's first NDA for fenofibrate capsules. Abbott filed a petition asking FDA to determine that Reliant was required to also identify Abbott's second NDA as its LD. FDA found that the 505(b)(2) applicant's choice of LD was appropriate since "[t]he fenofibrate capsules approved in [Abbott's] first NDA are the approved products that are most similar to the fenofibrate capsules described in Reliant's NDA."[17] FDA noted that Reliant's product and the product in Abbott's first NDA differed only in "strength," whereas the product in Abbott's second NDA differed in both "strength and dosage form."[18]

FDA also noted that Reliant used the product approved in Abbott's first NDA to conduct its bioavailability study, and was not required to reference other findings of safety and effectiveness to support its approval or product labeling.[19] Even if we assume these additional factors are relevant in the instant case, it does not obviate the need for the 505(b)(2) applicant to identify the LD that is "most similar" to the product in the 505(b)(2) when there is no pharmaceutical equivalent. As FDA observed, any other approach would circumvent appropriately listed patents and fail to "ensure[] that patent certification obligations for 505(b)(2) applications and for ANDAs are parallel."[20]

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15 Id. at 2.

16 Id.

17 Id. at 10 (emphasis added).

18 Id.

19 Id.

20 Id. The FDA response to a Citizen Petition filed by Osmotica (Docket No. FDA-2009-P-0356, Appendix 5), further explained the Agency's reasoning in the Abbott/Reliant decision, but did not expand on the general rule that the "most similar" NDA must be the LD. In that case, FDA addressed whether an ANDA must contain certifications with

c. The appropriate LD in this case is the sublingual film product

The 505(b)(2) applicant must identify as the listed drug "a pharmaceutical equivalent or the most similar alternative to the product for which approval is sought."[21] The Orange Book provides the definition of "pharmaceutical equivalent," and so the analysis must begin there.

> Pharmaceutical Equivalents. Drug products are considered pharmaceutical equivalents if they contain the same active ingredient(s), are of the same dosage form, route of administration and are identical in strength or concentration (e.g., chlordiazepoxide hydrochloride, 5mg capsules). Pharmaceutically equivalent drug products are formulated to contain the same amount of active ingredient in the same dosage form and to meet the same or compendial or other applicable standards (i.e., strength, quality, purity, and identity), but they may differ in characteristics such as shape, scoring configuration, release mechanisms, packaging, excipients (including colors, flavors, preservatives), expiration time, and, within certain limits, labeling.[22]

The first sentence of this definition identifies four key factors that must be compared in order to determine whether two drugs are pharmaceutical equivalents, or in this case, which LD is "most similar" to the product for which approval is sought. Examining each of those key factors in turn:

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respect to patents listed in the Orange Book for a drug relied on by a reference listed drug approved through a 505(b)(2) pathway. In contrast, the SUBOXONE NDAs were both 505(b)(1) NDAs. Morever, 505(b)(1) NDA applicants are encouraged not to resubmit information previously submitted to FDA, for example, information submitted in a previously approved NDA. "The applicant ordinarily is not required to resubmit information previously submitted, but may incorporate the information by reference." 21 C.F.R. §314.50(g)(1). Thus, FDA did not need to "rely" on its previous approval the SUBOXONE tablet NDA in order to approve the SUBOXONE film NDA since all of the data necessary for approval was in the SUBOXONE film NDA. BDSI simply chose to identify the inappropriate NDA as its LD in an effort to avoid the patents listed for the sublingual film product.

21 FDA, Petition Response, Docket No. 2004P-0386, 10 (Nov. 30, 2004).

22 See FDA, Approved Drug Products with Therapeutic Equivalence Evaluations, vi-vii (33rd ed. 2013); see also 21 C.F.R. § 320.1(c).

- **Active ingredient(s):** SUBOXONE film and tablets both contain identical active ingredients (buprenorphine hydrochloride and naloxone hydrochloride). The BDSI product apparently contains the bases of buprenorphine and naloxone, so on this factor, the LDs are equally similar. Therefore, this factor does not help determine which LD is most similar to BDSI's product.

- **Dosage form:** Appendix C to the Orange Book identifies certain uniform terms, including dosage forms. One of the dosage forms listed is "FILM."[23] The Orange Book does not define the term "film," but CDER's Data Standards Manual does define dosage forms, including "film," which is "[a] thin layer or coating."[24] A "tablet" is defined as "[a] solid dosage form containing medicinal substances with or without suitable diluents."[25] BDSI's product is undoubtedly a film, and therefore the "most similar" LD is the SUBOXONE film dosage form.

- **Route of administration:** The route of administration for both SUBOXONE products is sublingual. It is not yet clear how FDA will describe the route of administration of BDSI's product (e.g., "to the mucosal membranes (inner lining of cheek)," although Appendix C of the Orange Book suggests that one possibility may be "buccal"). In any case, the comparison of route of administration to the LDs will not help determine which LD is most similar to BDSI's product since both LDs are administered sublingually.

- **Strength or concentration:** Two strengths of the SUBOXONE tablet product were marketed: a 2 mg/0.5 mg tablet and an 8 mg/2 mg tablet (buprenorphine hydrochloride/ naloxone hydrochloride, content expressed in terms of free base). In contrast, four strengths of the film product are marketed: 2 mg/0.5 mg, 4 mg/1 mg, 8 mg/2 mg, and 12 mg/3 mg (buprenorphine hydrochloride/ naloxone hydrochloride, content expressed in terms of free base). BDSI has apparently not yet announced the strength of the buprenorphine/naloxone product for which it intends to seek approval. However, BDSI is currently enrolling patients into a clinical trial with the following strengths: 3.5/0.6 mg and 5.25/0.9 mg (buprenorphine/naloxone).[26] Thus, the strength of the BDSI product in the

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23 Id. at C-1.

24 FDA, CDER, Data Standards Manual (monographs), Monograph No. C-DRG-00201, *available at* http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/DataStandardsManualmonographs/ucm071666.htm.

25 Id.

26 BDSI, Clinical Trial, An Open Label Study to Assess the Safety and Tolerability of

NDA is likely "most similar" to the strength of a SUBOXONE film product (i.e., 4 mg/1 mg).

In sum, two of the four factors (active ingredients and route of administration) do not help determine which LD is most similar to BDSI's product. For one of the four factors (strength), it seems likely that the "most similar" LD will be the SUBOXONE film product. Finally, the dosage form factor clearly identifies the film product as the appropriate LD in this case.

To understand the fundamental similarities between SUBOXONE sublingual film and the BDSI BUNAVAIL film, and their fundamental differences from a tablet, it is important to compare the SUBOXONE sublingual products to BUNAVAIL from a pharmaceutics perspective. Table 1 lists several pharmaceutics characteristics that are relevant to the present case, and compares the anticipated BDSI product to the SUBOXONE film and tablet on each of those characteristics. The expected excipient profile for BUNAVAIL in Table 1 was taken from an example in "the USPTO granted US Patent No. 8,147,866 (issued from US Patent Application No. 13/184,306)," which, according to BDSI, "will extend the exclusivity of the BEMA® drug delivery technology for BEMA® Buprenorphine and BNX in the United States from 2020 to 2027."[27]

Table 1

	BUNAVAIL	**Suboxone Sublingual Film**	**Suboxone Sublingual Tablet**
Dosage Form	***Film***	***Film***	Tablet
Route of Administration	Buccal	***Sublingual***	***Sublingual***
Mucoadhesive	***Yes***	***Yes***	No
Erodible Polymeric Matrix	***Yes***	***Yes***	No
High Surface Area to Weight Ratio	***Yes***	***Yes***	No

BEMA® Buprenorphine NX In Opioid Dependent Subjects, *available at* http://clinicaltrials.gov/ct2/show/NCT01666119?term=BEMA&rank=1 (Appendix 6).

[27] BDSI, 2012 Annual Report to Stockholders, Form 10-K, 16, *available at* http://bdsi.investorroom.com/download/BDSI+2012+Annual+Report.pdf. We also note that if the actual excipient profile for BUNAVAIL in Table 1 differs to some extent from this expected profile based on the example in BDSI's '866 patent, it will not affect any of the points made in this submission. Copies of the pertinent pages of BDSI's 10-K are included as Appendix 7 to this Citizen Petition.

Polymeric Dosage Form	*Yes* ***Hydroxypropyl cellulose, hydroxyethyl cellulose, polycarbophil, carboxy methyl cellulose, buffer, sweetener, flavor, color and ink***[28]	*Yes* ***Polyethylene oxide, hydroxypropyl methylcellulose, sweetener, flavor, buffer, color and ink***	No Lactose, mannitol, cornstarch, povidone K30, buffer, color, magnesium stearate, sweetener and flavor
Buprenorphine/ Naloxone	***3.5/0.6 and 5.25/0.9 mg***[29]	12/3, 8/2, ***4/1*** and 2/0.5 mg	8/2 and 2/0.5 mg

Upon analysis of Table 1, it can be seen that the most similar dosage form to the BUNAVAIL film is definitively the SUBOXONE sublingual film product in NDA No. 22-410. To further explain, BDSI's BUNAVAIL buprenorphine/naloxone product is a mucoadhesive, high surface area to weight ratio polymeric dosage form that is orally delivered and applied to a mucosal surface (i.e., the inside of the cheek). Additionally, the excipient profile and associated functionality of the excipients are very different when compared to those of the SUBOXONE sublingual tablet, where traditional tableting excipients are used to create a non-polymeric, low surface area to weight ratio dosage form with no mucoadhesivity that disintegrates and dissolutes to deliver its drug payload.

Conversely, the BUNAVAIL buprenorphine/naloxone film and the SUBOXONE sublingual film both mirror the form and function that one would expect when comparing a film to a film rather than a film to a tablet. In fact, for film dosage forms, it is mandated that these polymeric excipients be used to obtain not only the desired physical manipulability, but also the overall functionality to enable proper dosing and pharmacokinetic performance.

In its 2012 annual report, BDSI stated: "In January 2013, the sublingual film formulation of Suboxone accounted for over 80% of volume sales, which helps to preserve the branded market for future buprenorphine/naloxone film products including [BUNAVAIL]."[30] The report also

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28 U.S. Patent No. 8,147,866, Example 3 (filed July 15, 2011) ("Preparation of Devices in Accordance with the Present Invention") (Appendix 8).

29 BDSI, Clinical Trial, An Open Label Study to Assess the Safety and Tolerability of BEMA® Buprenorphine NX In Opioid Dependent Subjects, *available at* http://clinicaltrials.gov/ct2/show/NCT01666119?term=BEMA&rank=1.

30 BDSI, 2012 Annual Report to Stockholders, Form 10-K, 15, *available at*

stated: "We believe [BUNAVAIL] has the potential to offer advantages over Suboxone® films and the more recently approved generic tablets."[31] Plainly, BDSI seeks to have it both ways: Marketing and characterizing its proposed film product to the investing public as poised to be the second film entrant in the market to compete against SUBOXONE film, while insupportably telling FDA that somehow its film is really more similar to the SUBOXONE tablet. Thus, as BDSI would have it, BUNAVAIL is most like SUBOXONE film when BDSI seeks to raise money and is most like SUBOXONE tablets when BDSI seeks to avoid the legal requirement of certifying against Orange Book-listed patents. FDA should not let would-be competitors to the SUBOXONE sublingual film product circumvent Orange Book patent protections by allowing the use of an inappropriate LD (i.e., SUBOXONE sublingual tablet) purely to circumvent patent certification and a potential patent infringement lawsuit. Such gamesmanship is not consistent with the 1984 Hatch-Waxman Amendments, and should not be countenanced by FDA.

d. FDA has the authority to refuse to file a 505(b)(2) NDA that does not identify the appropriate LD

As discussed above, the FDC Act requires a 505(b)(2) applicant to submit a certification for each patent for the LD. Likewise, FDA regulations also require the 505(b)(2) application to contain all appropriate patent certifications for the LD. In fact, FDA regulations explicitly state that, among other requirements, a 505(b)(2) application must contain

> any patent certification or statement required under section 505(b)(2) of the act with respect to any relevant patents that claim the listed drug or that claim any other drugs on which investigations relied on by the applicant for approval of the application were conducted, or that claim a use for the listed or other drug.[32]

Accordingly, a 505(b)(2) application that lacked an accurate patent certification would not "on its face" contain the information required under Section 505(b) of the FDC Act, or the information required under 21 C.F.R. § 314.50 and would thus satisfy the conditions for refusal to file under 21 C.F.R. § 314.101(d)(3). FDA has ample legal authority to refuse to file any 505(b)(2) NDA for a buprenorphine/naloxone drug product consisting of a polymer film for application to the

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http://bdsi.investorroom.com/download/BDSI+2012+Annual+Report.pdf. (emphasis added).

31 Id., Form 10-K, at 16 (emphasis added).

32 21 C.F.R. §314.54(a)(1)(vi).

oral mucosal membranes that does not reference the appropriate listed drug. As shown above, the appropriate LD in this case is NDA No. 22-410.

2. Impurities Associated with Naloxone Must be Limited

FDA has already stated that ANDA and 505(b)(2) applications containing naloxone are required to comply with a limit of 0.01% on 7,8-didehydronaloxone in naloxone.[33] Further, any naloxone impurity with the α,β-unsaturated ketone ("ABUK") moiety is subject to the same 0.01% limit, unless the applicant can demonstrate that the impurity is nongenotoxic.[34] Finally, the sum of ABUK impurities, including 7,8-didehydronaloxone, should not exceed 1.5 μg/day.[35] Accordingly, we ask FDA to re-affirm that any buprenorphine/naloxone product will be subject to these same requirements.

C. Environmental Impact

Petitioner claims a categorical exclusion under 21 C.F.R. § 25.31.

D. Economic Impact Statement

Petitioner will, upon request by the Commissioner, submit economic impact information, in accordance with 21 C.F.R. § 10.30(b).

E. Certification

I certify that, to my best knowledge and belief: (a) this petition includes all information and views upon which the petition relies; (b) this petition includes representative data and/or information known to the petitioner which are unfavorable to the petition; and (c) I have taken reasonable steps to ensure that any representative data and/or information which are unfavorable to the petition were disclosed to me. I further certify that the information upon which I have based the action requested herein first became known to the party on whose behalf this petition is submitted on or about the following date: October 10, 2009 (FDA response to Docket No. FDA-2009-P-0325); November 11, 2011 (BDSI press release announcing plans to develop a buprenorphine/naloxone product); August 1, 2013 (BDSI press release announcing the submission of an NDA). If I received or expect to receive payments, including cash and other forms of

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33 FDA, Petition Response, Docket No. FDA-2009-P-0325, 7 (Oct. 8, 2009). A copy of this response is included as Appendix 9 to this Citizen Petition.

34 Id. at 8-9.

35 Id. at 9.

consideration, to file this information or its contents, I received or expect to receive those payments from the following persons or organizations: Monosol Rx, Inc. I verify under penalty of perjury that the foregoing is true and correct as of the date of the submission of this petition.

Sincerely,

David B. Clissold

DBC/tee
Appendices