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February 4, 2013

Dockets Management Branch
Food and Drug Administration
5630 Fishers Lane
Room 1061 HFA-305
Rockville, MD 20852

Re: Docket No. FDA-2012-P-1028;
Comment, Verification, and Request for Summary Denial of Petition
Submitted on behalf of Amneal Pharmaceuticals, LLC

Dear Sir or Madam:

Venable LLP submits this Comment and Request for Summary Denial of Petition on behalf of Amneal Pharmaceuticals, LLC (Amneal) in response to the citizen petition filed by Reckitt Benckiser Pharmaceuticals (RBP) dated September 25, 2012. The petition requests that FDA take the following actions:

1. Refrain from approving any buprenorphine NDA or ANDA for the treatment of opioid addiction that does not require a targeted pediatric exposure education program.
2. Refrain from approving an application for buprenorphine for opioid addiction that does not include a requirement for child-resistant unit-dose packaging.
3. Refrain from approving any buprenorphine/naloxone ANDA for addiction treatment until FDA determines whether the RLD for those drugs was discontinued for reasons of safety.

REQUEST FOR SUMMARY DENIAL OF PETITION

As set forth below, the petition must be summarily denied under section 505(q)(1)(E) of the Food, Drug, and Cosmetic Act (FDCA) with regard to pending ANDAs on the following grounds:

1. The petition is submitted to delay approvals of pending ANDAs.
2. The petition fails to demonstrate a safety issue regarding the buprenorphine products at issue.
3. FDA has no authority under the FDCA to grant the types of relief sought in the petition.

INTRODUCTION

On September 25, 2012, RBP filed its citizen petition requesting that FDA take measures designed to delay or prevent FDA approval of any ANDA or 505(b)(2) NDA that references Suboxone® (buprenorphine hydrochloride and naloxone) Tablets (Suboxone Tablets). Aware that Amneal and other companies hold pending ANDAs for Suboxone Tablets that are ready for approval upon FDA's acceptance of a proposed REMS, RBP asks FDA to go beyond the Suboxone REMS and require these applicants to implement RBP's unapproved and undefined "educational program" for Suboxone Tablets, and employ unit-dose packaging for their generic products, a requirement never before established by FDA for any prescription opioid, including Suboxone Tablets. RBP further seeks to prevent any possible generic competition for Suboxone Tablets by requesting that FDA deem RBP's voluntary withdrawal of Suboxone Tablets to have been done for reasons of safety.

RBP's arguments are without merit and are raised at this time solely to prevent or delay the final FDA approval of competing generic products. RBP's petition should thus be summarily denied pursuant to section 505(q)(1)(E).

BACKGROUND

RBP's petition is the latest chapter in a sophisticated, strategic campaign to preserve RBP's multi-billion dollar Suboxone monopoly by (1) preventing or delaying approval of generic versions of Suboxone Tablets, and (2) transitioning Suboxone patients to a patent-protected film dosage form.[1]

The story of Suboxone and RBP's anticompetitive campaign begins in 2002, with FDA's approval of Suboxone Tablets and Subutex® (buprenorphine hydrochloride) Tablets. The products became very successful, but had no patent protection and relied instead on orphan exclusivity that expired on October 8, 2009. With this limited exclusivity in mind, RBP began implementing a strategy of extending its Suboxone monopoly by commencing development of its patent protected Suboxone Film product. On October 20, 2008, RBP filed an NDA for Suboxone Film. RBP expected to receive approval for its film in October 2009; however, on August 21, 2009, RBP received a deficiency letter from FDA stating that RBP's application did not contain an adequate REMS to address the agency's concern regarding misuse and abuse. RBP filed a complete response letter on November 21, 2009, to address the REMS deficiency, and received final FDA approval of the Suboxone Film NDA in September 2010. RBP listed a patent in the Orange Book for Suboxone Film that will expire in September 2023. RBP also

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[1] RBP's 2011 Annual Report explains that:

> As a result of the loss of [Suboxone tablet] exclusivity in the US, up to 80% of the revenue and profit of the Suboxone tablet business in the US might be lost in the year following the launch of generic competitors, with the possibility of further erosion thereafter. However, in the event of generic competition to the Suboxone tablet, the Group expects that the Suboxone sublingual film will help to mitigate the impact.

2011 Annual Report at 11 (available at http://www.rb.com/Investors-media/Investor-information). *See also id.* ("The patent-protected Suboxone sublingual film continued to grow, and by the end of December had captured a 48% volume share of the total market and has further strengthened its position as market leader, ahead of tablets.").

received three-year exclusivity for the Suboxone Film dosage form. Based on publicly available information, it does not appear that an ANDA has been submitted to FDA seeking to market a generic Suboxone Film product prior to the expiration of the 2023 Orange Book patent. RBP has thus for the last two years focused significant efforts on transitioning patients from Suboxone Tablets to the patent- and exclusivity-protected Suboxone Film.

While seeking to extend its monopoly through Suboxone Film, RBP also undertook efforts to ward off the possibility of any generic versions of Suboxone Tablets or Subutex® (buprenorphine hydrochloride) Tablets (Subutex), prior to the expiration of orphan drug exclusivity for those products, by filing of two citizen petitions in 2009. On June 14, 2009, less than three months prior to the expiration of orphan drug exclusivity for both Suboxone and Subutex, RBP filed a petition proposing that FDA require ANDA applicants to conduct additional and extraordinary bioequivalence studies for individual strengths and over dosing ranges, and to make RBP's 2 mg tablet a distinct RLD *even though there was no approved 2 mg dosing for its products.* Docket No. FDA-2009-P-0325-0001. On August 21, 2009, barely six weeks before the potential ANDA approval date, RBP filed a supplemental petition in the same docket seeking to require ANDA applicants to comply with all impurity limits found in RBP's NDAs. Docket No. FDA-2009-P-0325-0004. On October 8, 2009, FDA denied these requested actions[2] and approved a generic version of Subutex Tablets.

FDA did not approve the Suboxone REMS until December 22, 2011. When it approved the REMS for Subutex, Suboxone Tablets and Suboxone Film, the agency had before it RBP's data on reported pediatric exposures associated with Suboxone Tablets and Subutex. *See* Summary Review for Regulatory Action, NDA No. 022410 (Aug. 30, 2010) (safety review of the application consisted of, *inter alia*, "[t]he Applicants evaluation of information about accidental pediatric exposure, which was submitted to substantiate the public health importance of the individually packaged strip product"). The agency addressed the pediatric exposure issue in the REMS, requiring that RBP address pediatric exposures associated with Suboxone Tablets through labeling, rather than through the educational program and packaging requirements RBP now seeks to impose on ANDA applicants.

On May 11, 2010, Amneal filed its ANDA for a generic version of Suboxone Tablets. On January 6, 2012, two weeks after its approval of the Suboxone REMS, FDA sent Amneal and all other sponsors of pending and approved ANDAs for oral transmucosal buprenorphine-containing products a REMS Notification Letter explaining that these drug products would be subject to a Single Shared REMS (SSRS) program. Exhibit 1. The Notification Letter advised Amneal to contact RBP to collaborate on the creation and implementation of an SSRS program. The Notification Letter also stated that pediatric exposure would be addressed in the REMS. FDA mandated a compliance date of May 6, 2012, for approved products, by which time it expected that the SSRS with RBP would be accomplished. FDA reasonably expected that the approved Suboxone REMS could be amended to add generic manufacturers in a relatively short time.

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[2] Letter to Ju Yang, RBP, from Janet Woodcock, FDA (Oct. 8, 2009). In denying these requests, FDA agreed to impose an impurity requirement for a specific genotoxic moiety agent that was imposed in RBP's NDAs. *Id.* at 8-9.

Because the SSRS was a precondition to the approval of Amneal's ANDA, Amneal promptly notified RBP of FDA's Notification Letter and requirement. RBP thereby became aware that Amneal and other companies had pending ANDAs. RBP took advantage of its access to this proprietary information by feigning cooperation in the SSRS development process and diligently working to delay the ANDA approvals.

During the next six months, Amneal and the other ANDA applicants for generic versions of Suboxone Tablets (along with ANDA holders for the single ingredient buprenorphine-containing products) sought to negotiate the SSRS with RBP in good faith and with due urgency to secure prompt approvals of their products. RBP, however, used every opportunity to delay the process, making unreasonable demands on the generic companies as a precondition to RBP's cooperation in the development of the SSRS.[3]

While ostensibly negotiating the SSRS, RBP at the same time retained the services of RADARS and the Venebio Group to prepare a study to explore the risk of pediatric exposure to Suboxone Tablets, a concern that RBP did not disclose at any time during the SSRS negotiations.

In May 2012, after months of futile discussions with RBP regarding a SSRS, during which period RBP refused to share any non-public information about its existing REMS program, Amneal and the other ANDA holders and ANDA applicants jointly requested a meeting with FDA to discuss the delays created by RBP. FDA scheduled the meeting for June 18, 2012, and invited RBP. After reviewing the written materials submitted by RBP and the BPMG, and hearing each party's oral presentations, FDA agreed at the meeting with Amneal and the generic sponsors that, as a result of RBP's refusal to cooperate and share information about

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[3] RBP initially informed the generic companies that it would wait until it received confirmation from FDA of the requirement for a SSRS before working on it. While waiting for a response from RBP, the ANDA sponsors joined together as a group in early February 2012 to form a Buprenorphine Products Manufacturers Group (BPMG), and submitted formal correspondence to RBP on February 8, 2012, regarding a request for collaboration on a SSRS. On February 14, 2012, RBP informed the BPMG that it had received the communication from FDA, but that, due to purported antitrust issues, its legal department would handle future communications regarding the SSRS. While waiting for a response from RBP's legal representative, the generic members of the BPMG initiated weekly meetings beginning on February 23, 2012. RBP turned down numerous invitations to participate in the meetings. On March 20, 2012, RBP's legal representative provided the BPMG with a list of legal and governance issues that it demanded be resolved before RBP would engage in any substantive discussions involving an SSRS. In particular, RBP's "gating issues" involved: (1) a mission statement describing the BMPG's commitment to patient safety; (2) an upfront agreement on cost-sharing for REMS implementation and activities; and (3) an upfront agreement that all manufacturers would share the costs of product liability for future potential lawsuits. These demands made clear that RBP was seeking to leverage access to its REMS program to its own commercial advantage. RBP finally agreed to meet with the BPMG in person on April 2, 2012. But at the meeting, RBP refused to engage in any substantive discussions about the REMS and would only provide legal staff to attend the meetings until the "gating issues" were resolved to RBP's satisfaction. Consistent with past experience and to expedite the process, the generic companies sought to develop the REMS in parallel with the discussions and negotiation of legal issues. RBP undermined the effort by refusing this approach while also refusing to share non-public information, documentation, or any description of its REMS program – despite having entered into a confidentiality agreement with the BPMG – until its gating issues were resolved. Although the gating issues had nothing to do with the content or administration of an SSRS, in a good faith effort at cooperation, the generic members of the BPMG worked on the issues for weeks with RBP. Ultimately, the BPMG members could not commit to a binding agreement on cost sharing until they reviewed the costs associated with RBP's program (which RBP refused to provide) and could not agree to RBP's unprecedented demand on product liability sharing as a required precursor to SSRS discussions.

its REMS and FDA's inability to compel RBP to share the information, the only viable alternative would be for the generic companies and RBP to develop a new SSRS based upon the requirements set forth in the REMS Notification Letter, without utilizing any of RBP's existing information (which RBP refused to provide claiming that it was proprietary and confidential). RBP advised FDA at the meeting that it would cooperate with the generic sponsors to develop this new SSRS, which RBP knew was necessary for generic sponsors to obtain approval of their respective ANDAs.[4] Through RBP's participation in that process, RBP obtained proprietary information regarding the filing status, timing, and content of the proposed new SSRS. Despite its commitment to cooperate, RBP's intransigence and delay tactics continued.[5]

In mid-August 2012, Amneal, together with other generic sponsors of buprenorphine-containing products (both pending and approved), filed the SSRS with the FDA as part of their respective applications. Despite its active involvement in the development of the SSRS, RBP refused to submit the new SSRS with its NDA filing.[6]

In mid-September 2012, FDA provided comments regarding the proposed new SSRS. Within two weeks, Amneal and the other generic sponsors jointly responded to the FDA comments. Despite RBP's refusal to file the SSRS as part of its NDA, RBP maintained that it desired to continue collaborating on the SSRS development. Such continued involvement allowed RBP to maintain its awareness of the status of the SSRS and to use such information to the detriment of the generic sponsors. On October 3, 2012, as a result of RBP's refusal to cooperate in good faith in the development of the SSRS, Amneal and the other generic companies elected to file a Waiver Request with the FDA, seeking the approval of a generics-only SSRS.

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[4] FDA told the parties that the structure of the SSRS, from a legal and operational perspective, should be consistent with other single shared programs approved by FDA. This guidance was critical to the development of the program since many generic members of the BPMG had been involved in the development of other shared SSRS programs. Further, FDA implored the parties to recognize that actions designed to "block or delay" approval of the BPMG member's ANDAs, or otherwise preventing the application of an SSRS to an ANDA drug, were prohibited by FDCA § 505-1(f)(8).

[5] For instance, RBP refused to sign a governing Memorandum of Understanding (MOU) for the group unless it was given veto authority or a super-majority vote for all issues relating to the administration of the SSRS. And it continued its demand that each BPMG member agree to share a pre-specified percentage of all product liability claims, regardless of fault, despite the fact that no other shared REMS program has adopted this approach. The FDA-negotiated Extended Release Long Acting Opioid SSRS does not have any provision dealing with the issue of sharing product liability claims, and other SSRS programs have standard cross-indemnification provisions for fault-based claims. Yet RBP insisted on unprecedented commercial obligations on the generic members of the BPMG for future product liability claims. Indeed, as certain generic members of the BPMG explained to RBP, the upfront agreement being sought by RBP would deprive these companies of coverage under their product liability insurance policies. Ultimately, the generic companies had no option but to file a Waiver Request seeking approval of a separate REMS program.

[6] Two days before the scheduled submission of the REMS documents to FDA in mid-August, RBP suddenly raised an issue regarding a prescriber outreach component of the SSRS involving the use of a field force, arguing that an important element of the REMS had been omitted. The ANDA sponsors were astonished that RBP raised this matter only a few hours before finalization of the REMS documents. The ANDA sponsors had no objection to exploring this option, but believed that it should be tabled until the group received comments from the FDA's review of the REMS documents about to be submitted.

Just prior to the submission of the REMS Waiver Request, on September 25, 2012, RBP revealed in the instant citizen petition the most current phase of its scheme to prevent generic versions of Suboxone Tablet from entering the market. RBP announced its intent to permanently withdraw Suboxone Tablets from the market for reasons of safety and filed the instant petition to block approval of all pending ANDAs on alleged safety grounds that RBP failed to disclose in the REMS negotiations. RBP's petition argues that, after 10 years on the market, RBP has suddenly discovered a safety issue so severe as to require the removal of Suboxone Tablets within the next six months, just as the REMS process comes to its expected close and the pending ANDAs are ripe for approval.

GROUNDS FOR SUMMARY DENIAL OF PETITION

I. Congress Has Directed that a Petition of This Nature Be Summarily Denied.

As described above, the instant petition is the most recent phase of RBP's well-orchestrated, but transparent, campaign to delay and/or prevent the approval of pending ANDAs that have for many months met the substantive requirements for approval. RBP's petition acknowledges that the petition is submitted under section 505(q) of the FDCA. Congress enacted section 505(q) to protect generic applicants and the American public from petitions such as RBP's, which are submitted late in the ANDA review process to forestall generic competition. Congress directed that such petitions not delay approval of a competitor's application in the absence of an extraordinary determination of public health necessity. FDCA § 505(q)(1)(A)(ii).[7] The statute further provides for summary dismissal of a petition "submitted with the primary purpose of delaying the approval of an application [that] does not on its face raise valid scientific or regulatory issues." FDCA § 505(q)(1)(E). As more specifically set forth herein, RBP's petition does not present a valid scientific or regulatory issue. In this instance, it is clear that the presence of the generic products on the market will have no negative effect on the public health. Indeed, RBP continues to market Suboxone Tablets as it has done over the last 10 years, and the generic products will be as safe as RBP's Suboxone Tablets, causing no greater pediatric exposures to buprenorphine. Hence, RBP's petition should be summarily denied.

II. RBP's Petition Is Submitted to Delay ANDA Approvals.

RBP has engaged in a textbook case of anti-competitive conduct designed to delay or inhibit generic entry into the market for Suboxone Tablets. From product-hopping (tablet to film), to its refusal to work in good faith to establish the SSRS, to its multiple citizen petitions, RBP has made every effort to prolong its multi-billion dollar Suboxone monopoly at the expense

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[7] In its guidance on petitions for delay, FDA sets forth the standard for determining public health necessity:

> If the application were approved before the Agency completed the substantive review of the issues in the petition and, after further review, the Agency concluded that the petitioner's arguments against approval were meritorious, could the presence on the market of drug products that did not meet the requirements for approval negatively affect the public health?

FDA, Guidance for Industry: Citizen Petitions and Petitions for Stay of Action Subject to Section 505(q) of the Federal Food, Drug, and Cosmetic Act ("FDA Citizen Petition Guidance"), at 8 (June 2011).

of generic competition and the public.[8] Analysts around the world have recognized and written about RBP's campaign.[9] As one author noted, "[t]o generic drug makers, some physicians and Wall Street analysts, the moves amount to a transparent one-two punch designed to delay lower cost generic tablets from reaching the market."[10] The author also noted increased pricing of tablets as part of RBP's transfer strategy: "Reckitt has gradually increased the price of Suboxone Tablets while keeping Suboxone Film prices steady in order to switch patients."[11] Others have noted the similarities between RBP's actions in connection with Suboxone and its anti-competitive conduct with respect to another of its products, Gaviscon®, for which RBP was investigated and fined in the U.K.[12]

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[8] *See, e.g., Abbott Laboratories v. Teva Pharmaceuticals USA, Inc.*, 432 F. Supp. 2d 408 (D. Del. 2006) (denying motion to dismiss antitrust claim arising from unlawful "product-hopping"); *In re Prograf Antitrust Litig.*, No. 1:11-md-2242, 2012 WL 293850, at *6 (D. Mass. Feb. 1, 2012) (denying motion to dismiss antitrust claim arising from unlawful abuse of the FDA citizen petition process).

[9] *See, e.g.*, Ed Silverman, *Reckitt's Suboxone Strategy Is Really About Patients or Profits?*, Forbes.com (Oct. 12, 2012, 5:13 PM), http://www.forbes.com/sites/edsilverman/2012/10/12/reckitts-suboxone-strategy-is-really-about-patients-or-profits/; SubOxDoc, *Dear CEO*, Suboxone Talk Zone, (Oct. 2, 2012), http://www.suboxonetalkzone.com/dear-ceo/; Simon Bowers, *Reckitt Benckiser's Expert Questions Moves to Withdraw Suboxone Tablets*, The Guardian (Oct. 1, 2012, 2:08 PM), http://www.guardian.co.uk/business/2012/oct/01/expert-questions-reckitt-benckiser-withdrawal-of-suboxone?newsfeed=true; Tracy Straton, *Reckitt Petitions FDA to Force 'Child Resistant' Packaging on Suboxone Rivals*, FiercePharma (Sept. 26, 2012), http://www.fiercepharma.com/story/reckitt-petitions-fda-force-child-resistant-packaging-suboxone-rivals/2012-09-26; Nick Fletcher, *Reckitt Benckiser to Stop Selling Tablet Form of Heroin Substitute Suboxone in the U.S.*, The Guardian (Sept. 25, 2012, 5:28 AM); Andrew Jack and Louise Lucas, *Reckitt Withdraws Suboxone® Over Abuse*, Financial Times (Sept. 25, 2012) (RBP was "citing a US Poison Control Center study that there was eight times a greater risk of accidental unsupervised exposure by young children to the tablets in a bottle than the tamper-proof film. However, a presentation it gave in July showed there were very few cases: six exposures to the under sixes per million units dispensed."), http://www.ft.com/intl/cms/s/0/fb04e75a-072d-11e2-b148-00144feabdc0.html#axzz27hNXkQqw; Jason Napodano, *Reckitt's Decision Opens The Door For Titan Pharma And BioDelivery Sciences*, Seeking Alpha (Sept. 26, 2012) ("[W]e see a clear ulterior motive to the decision. Suboxone® tablets lost patent protection in 2009. As of yet, generic competition from alternative buprenorphine and naloxone tablets is non-existent. However, Reckitt's goal is clearly to transition patients over to the still on-patent sublingual film. In fact, Reckitt has filed a Citizen's Petition asking the U.S. FDA to require all manufacturers of buprenorphine products implement public health safeguards around pediatric exposure through educational campaigns and child resistant packaging. Suboxone® tablets were previously sold in a bottle containing 30 pills. So while Reckitt may take a short-term hit to its top line by removing Suboxone® tablets from the market, in the long run the company benefits from seeing less generic competition and more (forced) migration over to its under-the-tongue film."), http://seekingalpha.com/article/889861-reckitt-s-decision-opens-the-door-for-titan-pharma-and-biodelivery-sciences.

[10] Silverman, *supra*.

[11] Silverman, *supra*.

[12] *See, e.g.*, Bowers, *supra*. According to an April 13, 2011 press release by the U.K. Office of Fair Trading (OFT), "[t]he OFT has today issued a decision that Reckitt Benckiser abused its dominant position by withdrawing NHS packs of its Gaviscon Original Liquid medicine, and has imposed a fine of £10.2m." *See* http://www.oft.gov.uk/news-and-updates/press/2011/53-11. According to the statement, "[t]he fine was the subject of an earlier agreement under which the company admitted its conduct infringed UK and European competition law and agreed to co-operate with the OFT." *Id.* The alleged conduct involved an OFT finding "that Reckitt Benckiser withdrew NHS packs of its profitable Gaviscon Original Liquid from the NHS prescription channel after the product's patent had expired but before the publication of the generic name for it, so that more prescriptions would be issued for its alternative product, Gaviscon Advance Liquid. Pharmacies that receive prescriptions for Gaviscon Advance Liquid must dispense it, as it is patent protected and there are no generic equivalent medicines." *Id.*

RBP's petition raising purported safety issues with Suboxone Tablets – which RBP has sold without competition for 10 years – is, as described above, just the latest maneuver in its effort to protect its Suboxone monopoly. RBP's stated concerns in the current petition over pediatric exposure and the need for unit-dose packaging are transparently disingenuous. Rather than work with generic companies on the SSRS to address pediatric exposures, RBP has sought to transform such exposures into a competitive advantage by (1) encouraging physicians to switch patients to the patent protected Suboxone Film, and (2) manipulating the ANDA approval process to forestall or prevent altogether the marketing of generic tablets.

If RBP were truly concerned over pediatric exposures, it could have addressed the issues raised in its petition years ago. RBP was aware of pediatric exposure concerns since 2004, yet never employed unit-dose packaging for Suboxone Tablets marketed in the U.S. even as it employed such packaging in Canada and the EU.[13] Moreover, RBP raised the issue of pediatric exposures associated with Suboxone Tablets in its NDA for Suboxone Film, and secured FDA approval of a Suboxone REMS that purports to address the risk of pediatric exposures (without the protections RBP now asserts). Only now, as generic approvals are imminent, does RBP suggest that additional protections must be imposed on Amneal and other ANDA applicants if buprenorphine tablets are allowed to remain on the market at all. To the extent that RBP's stated concerns are sincere, RBP elected to mute its concerns while transitioning patients to film and feigning engagement in the development of the SSRS, in an effort to further delay generic entry.

Whatever the case, as set forth below, the arguments and positions raised in RBP's petition are wholly without merit and serve to demonstrate the true intent of RBP's actions – to delay or inhibit generic competition. RBP has not offered data sufficient to establish any safety issue requiring FDA action, and FDA clearly does not have the authority to grant the type of relief RBP seeks.

This is evidenced at the outset by the fact that the petition fails to include the information upon which RBP claims a safety determination must be made. The data and analysis provided in summary form are clearly inadequate to substantiate RBP's claims or allow for substantive analysis by FDA or the ANDA applicants who are targeted by the petition. RBP's summaries cannot themselves form the basis for FDA safety standards and, as discussed more fully below, raise clear questions about RBP's data selections, methods of analysis, and motives.

RBP's delay tactics are also revealed by its petition proposal that generics should not be approved unless and until they incorporate RBP's undefined and unapproved "educational program" designed to reduce pediatric exposures. RBP attempts to categorize its educational program as "labeling" under the FDCA because the program is somehow tied to RBP's risk mitigation strategies. But RBP is well aware that the educational programs cannot be characterized as "labeling," and that RBP has actually addressed the pediatric exposure issue in labeling by including a pediatric warning in the product label as well as in its REMS supporting documents. Each such supporting document provided to patients, pharmacists, and prescribers

[13] Based on a comparison of the respective product's package inserts, it appears that RBP manufactures and packages Suboxone Tablets for the U.S. in the same manufacturing site in Hull, U.K., that is utilized for manufacture of the unit-dose packaged product sold by RBP in the U.K and other EU member countries.

cautions about keeping the product out of the reach of children. RBP's REMS program has been approved by FDA and is adequate to address the pediatric exposure issues. RBP's proposed educational program was not incorporated by RBP into its REMS program and has not been approved or otherwise required by FDA. While on the eve of filing of the new SSRS, RBP advised the ANDA sponsors that an "educational outreach program" should be incorporated, it never proposed that the SSRS address the pediatric exposure issue that RBP now claims must delay the generic approvals. Indeed, RBP never mentioned any concern over the pediatric exposure issue at any time during the REMS process.[14]

Similarly, RBP's request that FDA require unit-dose packaging to prevent pediatric exposures is clearly *ultra vires* and within the exclusive jurisdiction of CPSC rather than FDA. Again, RBP could have raised this issue years ago and could have addressed the issue directly with regard to Suboxone Tablets by providing the product in the same unit dose packaging that it has used for years in Canada and the E.U. Instead, it continued to sell billions of dollars worth of bulk containers of tablets in the U.S. without apparent concern, only to proffer an eleventh-hour demand that its competitors should be precluded from the market in the absence of such packaging.

It is thus abundantly clear that RBP's petition and, indeed its entire course of conduct related to its Suboxone product line, is not related to safety but is rather related to a sophisticated, multi-pronged effort to delay or inhibit ANDA approvals and maintain its multi-billion dollar Suboxone monopoly.

III. RBP Has Failed to Raise a Valid Scientific or Regulatory Issue.

RBP's petition is based on two contentions: (1) that RBP has discovered a new safety concern regarding Suboxone Tablets that warrants FDA action, and (2) that the FDCA mandates specific regulatory interventions, *i.e.*, imposition of approval standards for buprenorphine products that include an educational program and special child-resistant packaging, if ANDA approvals are to be allowed at all. It is clear from the face of RBP's petition, however, that the data and analyses included in RBP's petition do not demonstrate a safety concern warranting FDA action, and that the FDCA does not authorize the agency actions sought by the petition.

A. RBP Has Failed to Demonstrate a Safety Issue.

RBP argues in its petition that it has demonstrated a safety issue regarding Suboxone Tablets based on (1) various graphic presentations of data regarding pediatric exposures of products identified as buprenorphine, Suboxone Tablets, and Suboxone Film, and (2) an abstract of a study conducted by the Venebio Group (Venebio Study) (Petition, Ex. 1).

[14] RBP also failed to inform the ANDA sponsors that the proposed educational outreach program had not been approved by FDA.

1. RBP Fails to Include Its Data and Analyses.

RBP's petition is facially inadequate because it fails to include any of the data and analyses upon which it relies. For petitions submitted under section 505(q) that could delay approvals of pending applications, the petitioner is required to certify, *inter alia*, that the petition "includes all information and views upon which the petition relies." FDCA § 505(q)(1)(H). Although RBP provided this certification, Petition at 48, it failed to include any data, case notes, or actual analyses upon which it relies. RBP's failure to comply with section 505(q) and with its own certification denies the ANDA applicants who are targeted by the petition an opportunity to comment on the core data and analyses that RBP proposes should delay or preclude approval of their applications.[15] For this reason alone, FDA should deny RBP's petition. Nevertheless, even without the underlying data and analyses, it is clear from RBP's own summaries that RBP has failed to demonstrate a safety concern warranting the agency actions sought in the petition.

2. RBP's Data and Analyses Are Based on Spontaneous Reports, which Cannot Support the Safety Determination RBP Seeks.

RBP's data and analyses are based ultimately on spontaneous reports of pediatric exposures. As FDA has made clear, spontaneous reports can provide signals of potential safety issues but cannot, in and of themselves, demonstrate the nature, incidence, or cause of a reported event or the level of injury associated with the event, particularly for the types of reporting-rate comparisons in RBP's petition.[16] As explained in FDA guidance:

> FDA suggests that a comparison of two or more reporting rates be viewed with extreme caution and generally considered exploratory or hypothesis-generating. Reporting rates can by no means be considered incidence rates, for either absolute or comparative purposes.

FDA, Guidance for Industry: Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment ("FDA Pharmacovigilance Guidance"), at 11 (March 2005).

Moreover, if RBP believed at some point in time that reporting rate information represented a "signal of disproportionate reporting," the company should have acted to confirm the safety signal as it was emerging. *See* 21 C.F.R. § 314.80(b). Had RBP confirmed the signal to be an actual safety concern, one would have expected RBP to produce that data as evidence of a true risk of pediatric exposure.[17]

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[15] Should RBP seek to provide these or other data or analyses in the future, FDA should not permit the submissions to further delay approvals of pending ANDAs.

[16] For example, while RBP cites a study finding the buprenorphine side effects include CNS depression and death, that same study found buprenorphine overdoses to be "generally well-tolerated in children." *See* Petition at 10 n.22 (citing D.B. Hayes, *et al*., *Toxicity of Buprenorphine Overdoses in Children*, 121 Pediatrics 782 (2009)).

[17] FDA describes in the Guidance specific methods for investigating signals, including pharmacoepidemiologic studies (cohort, case-control), registries, and surveys. *See* FDA Pharmacovigilance Guidance at 12-17. No data are presented from any of these sources to confirm the safety signal for which the company alleges strict mitigation is warranted.

3. The Data and Analyses Reported in RBP's Petition Cannot Establish the Relative Safety of Suboxone Tablets.

RBP provides graphic representations of various types of information and comparisons related to different products and product classes, including Suboxone Tablets, Suboxone Film, and Subutex. These data sets do not substantiate RBP's claims and raise a number of questions regarding inferences related to risks associated with Suboxone Tablets, including the following:

- RBP's graph on trend in pediatric exposure (Fig. 1) is based on exposures to buprenorphine generally, as distinct from Suboxone Tablets. Petition at 20.
- RBP's graph on pediatric exposures to Subutex and Suboxone (Fig. 2) commingles data from Subutex (buprenorphine hydrochloride) tablets. *Id.* at 20. In addition, RBP uses doses distributed as the denominator. This number is used as a surrogate for sales, which is in turn used as a surrogate for exposure. This disproportionality necessarily requires signal clarification based on more rigorous data.
- RBP's graph on pediatric exposures "post education initiatives" (Fig. 3) is based on exposures to buprenorphine generally, as distinct from Suboxone Tablets. *Id.* at 21. In addition, the graph fails to include data from the entire period of RBP's "post education initiatives."
- RBP's trend line of exposures to Suboxone over time (Fig. 4) commingles data from Suboxone Tablets and Suboxone Film, and may also comingle data from Subutex. *Id.* at 23 ("By 2011, data from AAPCC had demonstrated a precipitous decline in the number of pediatric exposures to buprenorphine products . . . .").
- The Venebio Study uses unique recipients of a dispensed drug (URDD) as a denominator, *id.* at 25, while RBP uses doses as denominators in other comparisons.

RBP argues that its data presentations show that Suboxone Film is safer than Suboxone Tablets, relying primarily on the data reported Venebio Study regarding reported pediatric exposures from October 2009 through March 31, 2012. *Id.* It is clear, however, that these data cannot establish the relative safety of the two products. In addition to the fact that reported unintentional pediatric exposure data cannot establish actual exposure incidence or severity of related adverse events, the study compared reports from different time periods. While Suboxone Tablets were marketed during the entire 30-month time period of the study, Suboxone Film was not approved until August 30, 2010. Thus, data for Suboxone Tablets are present for the full time period and data for Suboxone Film were from a shorter, early market entry and are less stable and not directly comparable.

It is also important to note that, in its review of the Suboxone Film NDA, FDA refused to accept RBP's assertion that unit-dose packaging for the film product would ensure safer use. The Team Leader Review noted that, while such packaging would be "a helpful step," there would still be pediatric exposures and that such exposures would be more dangerous in the case of the film because of its greater bioavailability. Cross-Discipline Team Leader Review, NDA 22-410, at 4 (October 20, 2010). ("[T]he more rapid dissolution of this dosage form compared to the tablets, and the difficulty of spitting it out once it is placed in the mouth, could actually contribute to more severe outcomes when the product is accidentally taken by a small child."). RBP's

summaries of data and analyses do not address severity of injuries associated with reported pediatric exposures.

4. The Data and Analyses Do Not Establish the Risks Associated with RBP's Proposed Approval Requirements.

Even if RBP's data and analyses demonstrated a safety concern requiring mitigation, which is not the case, those data and analyses would not demonstrate the need for the safety standards proposed in the petition. In the only root-cause analysis identified in the petition, the Venebio Study reportedly examined a number of potential risk factors, including packaging and educational efforts. The report summary provided with the petition states clearly that the study failed to establish the risk associated with either packaging or educational efforts. Venebio Study at 4-5. The report summary notes that only 18% and 24% of cases had any information on dispensed drug packaging. *Id.* at 4. The report summary further notes that *none* of the Poison Center reports (representing more than 98% of the cases analyzed) included information on physician/patient education. *Id*. It is also important to consider that, although the report summary states that a number of risk factors were identified, it addresses only the two factors selected by RBP. There are clearly other potentially significant risk factors that might be relevant to differences in reporting rates, such as socioeconomic differences, and differences in presence and numbers of children.

IV. FDA Has No Authority to Grant the Types of Relief Sought in the Petition.

As noted above, RBP seeks three agency adjudications:

1. That all ANDAs and NDAs for buprenorphine products for opioid resistance implement RBP's non-REMS educational program;
2. That all ANDAs and NDAs for buprenorphine products for opioid resistance employ unit-dose packaging; and
3. That FDA determine whether RBP has withdrawn Suboxone Tablets from the market for safety reasons.

Even if RBP had demonstrated a safety issue regarding Suboxone Tablets, which is not the case, FDA could not grant the relief sought in the petition.

A. FDA Has No Authority to Mandate RBP's Education Program in ANDAs.

RBP argues that ANDA applicants must implement its educational program because drugs approved in ANDAs must have (1) the same labeling as the RLD under section 505(j)(4)(G), and (2) the same risk-benefit profile as the RLD. The FDCA imposes no such labeling or risk/benefit requirement on ANDAs.

RBP's proposed educational program cannot be imposed under the same labeling requirement because the program is not approved labeling. First, the consultative aspects of the outreach program are not labeling within the meaning of the FDCA. Rather, "labeling" is defined in section 201(m) of the FDCA as "labels and other written, printed, or graphic matter" on or accompanying the product. RBP's reference to Dr. Woodcock's statement regarding

ANDAs for generic versions of Accutane® is off-point. *See* Petition at 35. The statement cited in the petition referred specifically to FDA's requirement that the ANDA applicants have the same "educational materials" for Accutane®. *Id.* These "materials" were labeling within the meaning of FDCA.

Further, even if RBP's educational program were deemed labeling, which cannot be the case, it could not be required for ANDA applicants because its content was not reviewed and approved by the agency as part of the NDA. Section 505(j)(4)(G) requires that an ANDA contain information to "show that the labeling proposed for the drug is the same as the labeling *approved* for the listed drug . . . ." (Emphasis added.) RBP admits that FDA did *not* require and approve RBP's educational program as part of its REMS. Petition at 35 n.87.[18]

In addition, RBP's educational program cannot be imposed on an ANDA applicant based on a risk/benefit assessment. The standards for approval of an ANDA are set forth clearly and specifically in section 505(j)(4)(G). Those requirements do not include a determination of safety or effectiveness of the drug in the ANDA. ANDAs are rather approved based on bioequivalence and sameness criteria related to pharmaceutical equivalence and labeling. While ANDAs must meet REMS requirements, RBP's educational program has not been required in RBP's REMS, and FDA cannot impose requirements for ANDAs that are more demanding than those imposed on the RLD. *See Bracco Diagnostics, Inc. v. Shalala*, 963 F. Supp. 20, 27-28 (D.D.C. 1997) (similarly situated products cannot be subjected to differing regulatory requirements).[19]

B. FDA Has No Authority to Impose Unit Dose Packaging Requirements for Poison Prevention.

In 1970, Congress passed the Poison Prevention Packaging Act (PPP Act) to address potential unintended exposures to harmful products, including prescription drugs. 15 U.S.C. §§ 1471-1476. Although FDA was initially given authority to implement provisions of the PPP Act with regard to FDA-regulated products, FDA was divested of its authority in 1972, and the Consumer Products Safety Commission (CPSC) was given exclusivity jurisdiction over regulation of poison prevention packaging. *See* Consumer Product Safety Act, 15 U.S.C. § 2079(a); *see also Wahba v. H & N Prescription Ctr. Inc.*, 539 F. Supp. 352, 354 (E.D.N.Y. 1982). Although FDA in one instance attempted to assert authority over the PPP Act under the FDCA, as discussed below, the agency's effort was overturned in a dispositive ruling by the

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[18] RBP proposes that, should FDA not be able to impose RBP's educational program on ANDA applicants, the agency would have to consider imposing heightened labeling warnings for drugs approved in ANDAs. FDA can neither require nor permit labeling to highlight a difference between an ANDA drug and an RLD with regard to an educational program that falls outside the RLD approval. The exceptions to the same labeling requirement are "differences in expiration date, formulation, bioavailability, or pharmacokinetics, labeling revisions made to comply with current FDA labeling guidelines or other guidance, or omission of an indication or other aspect of labeling protected by patent or accorded exclusivity under section 505(j)(5)(F) of the act." 21 C.F.R. § 314.94(a)(8)(iv).

[19] It is also clear that FDA cannot impose RBP's outreach program on other NDAs because NDAs for drugs within the same drug class can differ in innumerable respects and require a risk/benefit assessment based on a constellation of factors. Even if RBP were to refine its proposal to address competitors' NDAs that are identical to the Suboxone NDA, its proposal would have to be rejected. FDA has not imposed RBP's outreach effort as a condition for the approval of Suboxone Tablets or any other buprenorphine product. Thus, the imposition of such a requirement on competitors would be impermissible. See *Bracco Diagnostics v. Shalala,* 963 F. Supp. at 27-28.

United States Court of Appeals for the Second Circuit, and the agency has otherwise refrained from attempting to impose PPP Act standards for prescription drugs and other FDA-regulated products.

1. Authority to Impose Poison Prevention Requirements Resides Exclusively with CPSC under the PPP Act.

In 1997, FDA reacted to a widespread problem of acute iron poisonings, including deaths from pediatric exposures, by promulgating standards for iron-containing dietary supplements. *See* 62 Fed. Reg. 2218, 2218 (Jan. 15, 1997) (final rule); 59 Fed. Reg. 51,030, 51,032-36 (Oct. 6, 1994) (proposed rule). The agency had found that, from 1986 through 1992, there were over 47,000 reports to poison control centers of adult product exposures to children under the age of six. 59 Fed. Reg. at 51,032.

The Nutritional Health Alliance challenged the FDA regulation, and on appeal, the Second Circuit ruled decisively that, regardless of safety standards under the FDCA, The PPP Act vests jurisdiction over PPP Act standards exclusively with CPSC. *Nutritional Health Alliance v. FDA*, 318 F.3d 92, 104 (2d Cir. 2003) (*NHA* case). The court specifically found that:

> (1) the PPP Act specifically and unambiguously targets the accidental poisoning problem and prescribes a specific regulatory approach to addressing the problem through packaging standards, (2) the CPS Act unambiguously transferred authority to administer and enforce the PPP Act from the FDA to the CPSC, and (3) the FDA's assertion of concurrent jurisdiction rings a discordant tone with the regulatory structure created by Congress.

Id.

In its opinion, the court provided a detailed analysis of the PPP Act and its relevance to poison prevention requirements for FDA-regulated products. *Id.* at 102-104. The court noted that the PPP Act was passed subsequent to the FDCA to address specifically concerns over pediatric poisonings from drugs and other products and that jurisdiction under the law was originally vested with FDA:

> Congress specifically targeted the problem of accidental poisoning of children caused by the ingestion of (or exposure to) a wide range of ordinary household products, *including drugs and medicines*, with a comprehensive yet circumscribed regulatory solution. Specifically, the PPP Act conferred to the FDA authority to establish and enforce regulatory standards for the "special packaging" of any "household substance" found to be a hazard to children (*i.e.*, poison prevention packaging).

Id. at 102-103 (emphasis added).

The court noted that the PPP Act set forth specific standards and procedures for addressing pediatric poisonings, stating: "It is particularly important that the PPP Act expressly set forth comprehensive 'instructions,' including specific regulatory constraints, as to how this

authority should be exercised." *Id.* at 103.[20] The court described Congress's intent to address the type issue that RBP raises here:

> In an opening statement before the Subcommittee for Consumers of the United States Senate Committee on Commerce for a hearing on S. 2162, the bill eventually enacted as the PPP Act, Senator Frank E. Moss, Chairman of the Subcommittee, described the problem as follows:
>
> > The problem is clear. At this very moment some small child is innocently exploring the limited environment of his home. In the process he is poking into the medicine cabinet, reaching into his mother's purse, crawling under the kitchen or bathroom sink, or rummaging in the garden shed and possibly swallowing a potential poison. Poisoning by household substances is the most common medical emergency facing young children. The loss that it imposes-in pain, suffering, and death-is incalculable.

Id. at 102 n.12 (quoting Hearings on S. 2162 Before the Consumer Subcomm. of the Senate Comm. on Commerce, 91st Cong. 1 (1969) (Statement of Senator Frank E. Moss)). The court found that FDA's unit-dose packaging requirement would constitute a "special packaging" standard under the PPP Act.[21] *Id.* at 103 n.13.

RBP attempts to distinguish the *NHA* case in a footnote and fails entirely. RBP points to the fact that that the case addressed standards for a dietary supplement rather than a drug. Petition at 41 n.99. The court's holding, however, was not addressed to a specific type of product. As described above, the court found that the PPP Act divested FDA entirely of authority to impose poison prevention requirements under the FDCA, including for "drugs and medicine." *See NHA*, 318 F.3d at 102-103. Rather, the pertinent question is whether the unit-dose packaging requirement sought in RBP's petition is a "special packaging standard" within the meaning of the PPP Act, which it clearly is. Indeed, the CPSC imposes special (child-resistant) packaging requirements on most prescription drugs, *see* 16 C.F.R. § 1700.14(a)(10),

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[20] The court elaborated as follows:

> First, special packaging standards can only be established where "packaging is required to protect children from serious personal injury or serious illness resulting from handling, using or ingesting [a] substance." 15 U.S.C. § 1472(a)(1). Second, special packaging must be "technically feasible, practicable, and appropriate." *Id.* § 1472(a)(2). Third, standards must be established pursuant to the following considerations listed in the PPP Act.

Id.

[21] The court explained:

> 'Special packaging' is defined as 'packaging that is designed or constructed to be significantly difficult for children under five years of age to open or obtain a toxic or harmful amount of the substance contained therein within a reasonable time and not difficult for normal adults to use properly, but does not mean packaging which all such children cannot open or obtain a toxic or harmful amount within a reasonable time.'

Id. at 103 n.13 (quoting 15 U.S.C. § 1471(4)).

just as it does the dietary supplements containing iron that were at issue in the *NHA* case, *see id.* § 1700.14(a)(12).

RBP further notes that the *NHA* case addressed a rulemaking rather than a petition. The court's holding, however, was not addressed to the process by which FDA sought to impose the PPP Act standards (*e.g.*, rulemaking vs. agency adjudication). The nature of the administrative action is not relevant to whether FDA has jurisdiction to impose PPP Act requirements. RBP's petition seeks to impose a special packaging standard, which must be done by CPSC under the PPP Act rather than by FDA under the FDCA.

RBP additionally argues that the court's decision was based on its interpretation of the FDCA safety standards under sections 402 and 351 of the FDCA, which are not at issue here. *Id.* The court held specifically, however, that regardless of the FDCA provision relied upon by the agency in its regulation, FDA was divested of *any* authority to require poison packaging prevention under the FDCA. While the court did address the scope of agency authority under the FDCA safety provisions at issue in the case, it was required to do so under Chevron step one. *Nutritional Health Alliance*, 318 F.3d at 99 (citing *Chevron U.S.A., Inc. v. Natural Resources Def. Council, Inc*., 467 U.S. 837, 842-43 (1984)). The court also conducted a full analysis under Chevron step two and most of the opinion was directed to its analysis of Congress's broad divestiture of FDA's jurisdiction over poison prevention packaging in the CPSA. *See id.* at 101-105.

2. Since the *NHA* Decision, FDA Has Refrained from Imposing Poison Prevention Packaging Standards for Drugs.

In its attempt to distinguish the *NHA* case, RBP points to FDA's approval of child-resistant packaging for Actiq®. This approval, however, occurred in 1998, predating the *NHA* decision. Since the *NHA* decision in 2003, there do not appear to be any examples of FDA imposing PPP Act standards through the drug approval process, and RBP cites to none. FDA's approach to pediatric poisonings associated with the fentanyl patch is particularly noteworthy. That product is a prescription drug, and most of the accidental exposures involving that product occurred in children under 2 years old, including 10 deaths and 12 cases requiring hospitalization. *See* FDA Consumer Health Information, "Fentanyl Patch Can Be Deadly to Children," http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm300803.htm (April 2012). There have been calls for child-resistant labeling for the product. *See* M. Grissinger, "Fentanyl Transdermal Patches: More Protection Needed for Patients and Their Families," 34 Medication Errors 390 (2009). FDA's response has not been to impose child-resistant packaging, but rather to address the issue in labeling and to issue public health advisories cautioning parents to exercise care in disposing used patches. *See* FDA Consumer Health Information, *supra*.

3. CPSC Is the Proper Venue for RBP's Unit-Dose Packaging Request.

CPSC is authorized to address RBP's proposed poison prevention packaging standards and is the appropriate venue for RBP's proposal. CPSC can more properly take into consideration the broader array of data and information related to drugs posing risks from pediatric poisonings. As noted above, CPSC addresses PPP Act standards for prescription drugs

and has amended its regulation on numerous occasions based on petitions to provide exceptions for specific prescription drugs. *See* 16 C.F.R. § 1700.14(a)(10)(i)-(xxiii). CPSC regulations, like FDA regulations, provide for petitions to amend regulatory requirements. *See* 16 C.F.R. § 1051. If RBP seeks to pursue this issue, it should thus petition CPSC, not FDA, which does not have authority to act on RBP's request.[22] In any event, RBP's request to FDA must be summarily denied for lack of jurisdiction.

D. FDA Has No Authority to Deny Approval to Buprenorphine ANDAs under Section 505(j)(4)(I).

RBP argues in its petition that FDA cannot approve ANDAs because RBP has voluntarily discontinued Suboxone Tablets for safety reasons, citing FDCA section 505(j)(4)(I). Petition at 43. But once again, RBP's conduct belies its claim. The cited provision applies only when a drug has been "withdrawn from sale." Here, despite RBP's purported safety concerns, RBP's Suboxone Tablets are currently on the market, and RBP has stated publicly that Suboxone Tablets will remain on the market for another six months. *See* RBP Press Release: "Reckitt Benckiser Pharmaceuticals Inc. Submits Citizen Petition to US FDA Requesting Action to Mitigate Risk of Pediatric Exposure with Opioid Dependence Treatment: Company Voluntarily Discontinues the Supply of Suboxone® Tablets (buprenorphine and naloxone sublingual tablets [CIII]) in the United States" (Sept. 25, 2012), http://www.prnewswire.com/news-releases/reckitt-benckiser-pharmaceuticals-inc-submits-citizen-petition-to-us-fda-requesting-action-to-mitigate-risk-of-pediatric-exposure-with-opioid-dependence-treatment-171174751.html. Indeed, after 10 years of a monopoly on the market, it is only now, on the cusp of generic approval for tablets, that RBP proposes to discontinue its product for alleged "safety reasons," a move designed to foreclose *any* generic competition for Suboxone.

Even if Suboxone Tablets were ultimately withdrawn from sale voluntarily by RBP, there would be no basis for an agency determination that the product was withdrawn for safety reasons. "Safety" in this context must reflect the safety standard for drug approvals. *See* FDCA §§ 505(c)(1), (d)(1)-(2); *see also Weinberger v. Hynson, Westcott, & Dunning, Inc.*, 412 U.S. 609, 631-32 (1973) (separate provisions of FDCA must be given "harmonious interpretation"). A determination by FDA that a product has been withdrawn for safety reasons is an integral component of a statutory mechanism for withdrawing ANDA approvals based on market withdrawals of the RLD by FDA. *See* 21 C.F.R. § 314.161(d). The statutory directive that ANDA approvals be withdrawn based on such RLD market withdrawals is to ensure that drugs not be marketed under ANDAs where the RLD has been determined not to meet the safety or efficacy standards of the FDCA. The question is thus whether the RLD was withdrawn from the

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[22] Certainly RBP – a household products company with an entire web page devoted to CPSC compliance, including a spreadsheet referencing PPP Act compliance for various products sold in the U.S. (http://www.rbnainfo.com/productpro/CPSIA.jsp) – must know that the CPSC is the proper agency to address this request. It is also inconceivable that RBP – with household "Powerbrands" such as Calgon, Air Wick, Clearasil, d-Con, Brasso, Mucinex, Lysol, RID-X, and Woolite – could not craft a childproof solution over the past 10 years if it truly believed that its packaging was insufficient. Indeed, as noted, it has for years sold unit-dose packaged Suboxone Tablets in Canada and the E.U.

market because it was unsafe within the meaning of section 505. Here, RBP has failed entirely to demonstrate a safety issue under the FDCA.

FDA made this approach clear in its determination that Xibrom® was not withdrawn for safety reasons. FDA addressed a petition that, like RBP's petition, was based on an alleged disproportionate number of adverse events associated with a single product and requested, *inter alia*, a specific container closure system based on potential impact on safety and efficacy. *See* Letter to Marvin Garrett, Ista Pharmaceuticals, from Janet Woodcock FDA, 7, 10 (May 11, 2011); Docket Nos. FDA-2008-P-0368 and FDA-2011-P-0128. In responding to the petition, FDA did not base its decision on the company's asserted motivation for market withdrawal, but rather assessed whether there was a safety issue under the standards for drug approval. *Id.* at 15-17.

In addition, and of particular significance in this case, FDA made clear in defending its Xibrom decision in court that the safety concern raised in Ista's petition could not support a determination of withdrawal based on safety under section 505(j)(4)(I) because the concern related to the packaging of the drug rather than to the drug itself. The agency stated in its brief as follows:

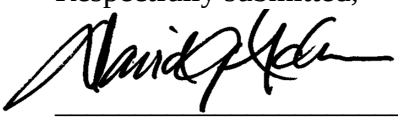
> Importantly, FDA is not aware of, nor has Ista raised, any safety concerns with the [BS] solution itself. FDA's concerns related only to bottle size and the risk of consumer usage leading to potential cross-contamination of post-operative eyes. For this reason, FDA properly concluded that Xibrom was not withdrawn from the market for reasons of safety or effectiveness.

Federal Defendants' Motion for Summary Judgment (Dkt. 40) at 27, *Ista Pharms, Inc. v. FDA*, No. 1:11-cv-0907, 2012 WL 2686106 (D.D.C. July 9, 2012). Thus, even if RBP demonstrated an issue that could be addressed by FDA under the FDCA, which it has not, its purported safety concern could not give rise to an FDA determination that Suboxone Tablets have been withdrawn from sale for safety reasons.

CONCLUSION

For all of the foregoing reasons RBP's Petition should be summarily denied. Amneal respectfully requests that the agency take immediate action on the petition to put an end to RBP's continued efforts to preserve its Suboxone monopoly by seeking to delay or prevent generic competition for Suboxone Tablets.

Respectfully submitted,



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VERIFICATION

I certify that, to my best knowledge and belief: (a) I have not intentionally delayed submission of this document or its contents; and (b) the information upon which I have based the action requested herein first became known to me on or about September 25, 2012. If I received or expect to receive payments, including cash and other forms of consideration, to file this information or its contents, I received or expect to receive those payments from the following persons or organizations: Amneal Pharmaceuticals, LLC. I verify under penalty of perjury that the foregoing is true and correct as of the date of the submission of this petition.

David G. Adams
Counsel to Amneal Pharmaceuticals, LLC