CONSUMER FEDERATION OF CALIFORNIA

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Response to Citizen Petition, FDA-2014-P-0594

EXPEDITED DECISION REQUESTED

The Consumer Federation of California ("CFC") respectfully submits this response ("Response") in support of the relief sought in the Citizen Petition submitted by Hyman, Phelps & McNamara, P.C. ("HPM Petition"), dated May 5, 2014. As the only persons advocating from the perspective of the interest of consumers (in particular, California consumers), we believe that it is long since time for the FDA to either approve Ranbaxy Laboratories Inc.'s ("Ranbaxy") generic version of delayed-release 40 mg Nexium (esomeprazole) capsules, or alternatively rule that Ranbaxy no longer holds the 180-day exclusivity for that product so that other generic makers may be approved and enter the market immediately. The FDA's delay has prolonged the already existing unlawful bottleneck preventing potential generic entrants from obtaining final approval of their ANDAs and beginning to sell generic esomeprazole. The resulting harm to consumers – no option to choose lower-priced versions of Nexium – flies in the face of the FDA's stated goals and regulations designed to promote timely access to less expensive generics.

We ask that, unless the FDA believes the Ranbaxy ANDA is ready for immediate approval in accordance with all applicable laws and regulations, (a) the FDA immediately determine that Ranbaxy has or must relinquish any 180-day exclusivity it may have for the marketing of generic esomeprazole and (b) undertake to review all other generic esomeprazole ANDAs for final approval and entry to market forthwith. The factual summary for this relief is straightforward.

First, the Ranbaxy esomeprazole ANDA was filed with the FDA in August of 2005 – *nine years ago*. As the apparent first-to-file, Ranbaxy has bottlenecked the ability of several other generic makers during all of this time.

Second, the FDA granted Ranbaxy preliminary approval for its esomeprazole ANDA in early 2008 – *six years ago*. The only impediment that should have been in the

way to FDA final approval at that time was pending patent litigation, issues that have long been resolved.

Third, in April of 2008, Ranbaxy resolved patent issues with AstraZeneca under terms in which Ranbaxy agreed to delay its efforts to gain market entry for its esomeparazole ANDA until no earlier than May 27, 2014 (adding essentially six years of delay for generic Nexium).

Fourth, in 2011 and despite Ranbaxy's ongoing issues with facilities in India, Ranbaxy worked with FDA to effectuate expedited approval for a site transfer to the U.S. and for final ANDA approval of a Ranbaxy atorvastatin in early 2012 (after an apparently extended period of negotiation). No explanation has been given as to why Ranbaxy has not done the same for generic Nexium.

Fifth, on January 25, 2012, the FDA entered into a consent decree with Ranbaxy that set a period of approximately one year to nearly three years – through September 30, 2014 – for first-filer Ranbaxy to remedy deficiencies and take other actions. The HPM Petition argues that the FDA's actions enabled and continue to enable Ranbaxy to delay its own generic entry and that of other generic companies.

Six, it appears that while Ranbaxy has not made efforts to gain prompt ANDA approval over the years for its generic product, Ranbaxy has received significant revenues from assisting the brand maker of Nexium, AstraZeneca, in the commercialization of branded Nexium in the U.S. (at high brand prices). Under Ranbaxy's 2008 pact with AstraZeneca, the two agreed to arrangements which (according to the few publicly revealed reports) indicate that Ranbaxy has supplied either or both of the active pharmaceutical ingredient or the Nexium finished product to AstraZeneca, receiving in return substantial money. Of course, FDA knows the details of these arrangements in so far as it needed to approve amendments or changes AstraZeneca's NDA for Ranbaxy to be able to provide these goods to AstraZeneca. So while all other generic makers remain barred from receiving final ANDA approval given the delayed approved of Ranbaxy's ANDA while it purports to hold its 180-day exclusivity, Ranbaxy has been able to receive substantial dollars from selling the reference listed product to AstraZeneca.

Seventh and finally, while Ranbaxy fulfilled its promise to AstraZeneca not to launch a generic Esomeprazole earlier than May 27, 2014, that date has come and gone. FDA has neither approved a Ranbaxy esomeprazole ANDA nor caused Ranbaxy's purported 180-day exclusivity to be relinquished, revoked, or lapsed.

The FDA's actions have enabled Ranbaxy to delay its marketing of a generic esomeprazole product for years, and certainly at least in the months since May 27, 2014 (the date upon which Ranbaxy agreed with AstraZeneca that Ranbaxy would not sell generic esomeprazole any earlier than). Not only did the FDA not grant final approval by this already delayed entry date of May 27, 2014, but it appears to have *extended* the date for Ranbaxy to remedy any deficiencies in connection with its generic esomeprazole ANDA further, through at least September 30, 2014.

At this time, there are no FDA-approved AB-rated generic alternatives to AstraZeneca's Nexium. California consumers (and, indeed, consumers across the United States) have no access to more affordable, lower priced generics. The manifest result of Ranbaxy's and the FDA's inaction is a dead stop bottleneck preventing more than a half-dozen generic manufacturers lined up behind Ranbaxy from entering the market. And there is no end of the delay in sight.

I. BACKGROUND OF THE CONSUMER FEDERATION OF CALIFORNIA AND INTEREST IN THE CITIZEN PETITION

The Consumer Federation of California is a non-profit education and advocacy organization established in 1960. CFC works to advance consumer protection laws and regulations, ensure their enforcement, and conducts education and research on consumer matters. CFC has authored, supported and testified on legislation affecting all California consumers, including laws protecting lower income Californians and consumers with limited English proficiency. Additionally, CFC has a lengthy record working on health care reform, quality and access, expansion of safety net programs, health insurance rate regulation, and regulation of the price and quality of prescription drugs. CFC has supported legislative and ballot measures for bulk purchasing and reimportation of prescription drugs, and sponsored a 2011 California law that prohibits retailers from selling expired over-the-counter medications.

In 2005, CFC supported Proposition 79 to establish a state prescription drug discount program for low- and moderate-income Californians, and opposed Proposition 78, which we believed was an illusory drug price discount measure funded by Pharma as a counter to Proposition 79.

CFC has also opposed and defeated measures that would have reduced state protection of the privacy of patient prescription records, including a special interest bill that would have empowered pharmaceutical companies to contract with intermediaries to deceptively market brand name drugs directly to patients who are prescribed generics. CFC opposed and defeated a proposal before the California Board of Pharmacy to reduce the professional educational and licensure standards for pharmacists, and supported legislation to make prescription drug labels easier to read for elderly and vision-impaired consumers. CFC also supported legislation to require physicians who dispense free prescription drug samples to supply the patient with the same disclosures that are required when sold through pharmacists, and to prohibit or require disclosure of benefits and emoluments that pharmaceutical companies provide to physicians and other prescribers of prescription drugs. CFC is currently supporting Proposition 46, a November 2014 ballot measure that would, among other things, require physicians to search a state-run prescription database for Schedule 2 and Schedule 3 controlled substances, as a method to reduce doctor shopping by drug abusers and drug dealers.

In these and other matters, CFC has demonstrated a lengthy track record of defending patients against unfair pharmaceutical industry practices, advocating for drug safety, and working for fairness in the pricing of prescription drugs.

California consumers have a major stake in Citizen Petition, FDA-2014-P-0594. Nexium is the nation's second top-selling drug, with over $6 billion in sales in 2013. Nearly one in eight Americans are California residents. If our state's share of the Nexium market reflects its share of the US population, annual Nexium sales in California are about $750 million.

It is difficult to project the cost savings to Californians should generic versions of Nexium reach the marketplace, but the annual savings to Californians would undoubtedly reach the hundreds of millions of dollars. A conservative estimate of a fifty percent price reduction would reduce the cost to Californians of this drug by $375 million a year. These savings include substantial savings, likely in the tens to hundreds of millions of dollars annually to the State of California, for prescriptions dispensed by state institutions including University of California's systems of hospitals, hospitals within state agencies such as the Department of Corrections and Rehabilitation, and through reduced costs of MediCAL and other state subsidized or funded health insurance programs. Additional substantial cost reductions, likely in the tens to hundreds of millions of dollars, would be enjoyed by health insurers and HMOs which, under the Affordable Care Act, may not exceed caps on their medical loss ratios, and would thereby be required to pass along their savings to individual and group health insurance subscribers, and to California Taft-Hartley Trust Funds which serve hundreds of thousands of California union-represented employees. Finally, uninsured and underinsured Californians would directly benefit by savings many millions of dollars a year as their costs for the purchase of generic Nexium would decrease substantially.

II. ACTION REQUESTED

We ask that, unless the FDA is prepared to conclude that Ranbaxy's ANDA is in a position for immediate final approval, the FDA enforce its existing regulations and policies take the following actions:

1. Determine that Ranbaxy has either forfeited or must relinquish any 180-day exclusivity it may have had for the manufacture, formulation, and supply of generic delayed-release 40 mg Nexium capsules; and

2. Grant final approval to all other pending esomeprazole ANDAs that are otherwise ready for such final approval.

We join in HPM's request that FDA act quickly to ensure that a generic esomeprazole product or products will enter the market soon, and hopefully well before the outside date of September 30, 2014.[1]

Any further delay by Ranbaxy, or inaction by the FDA, would unnecessarily delay consumers' access to generic esomeprazole products and undermine the purpose of the 180-day exclusivity period provisions. FDA is authorized by the provisions of its January 25, 2012 consent decree entered into with Ranbaxy, current law, FDA

[1] *See* Consent Decree, *United States of America v. Ranbaxy, Inc., et al*., D. Md., 12-cv-0250, D.E. no. 5.

regulations, and FDA policy, to take the requested actions. A quick response to our requests will ensure that consumers have access to lower priced esomeprazole as soon as possible.[2]

III. STATEMENT OF GROUNDS

A. Regulatory Background

We refer to the discussion set forth in the HPM Petition regarding the competitive effects of AB-rated generic competition, the value of exclusivity to a first generic filer, and the further drop in prices to consumers when multiple generics enter the market.

It is important to repeat, here, however, that typically, generics are at least 25% less expensive than their brand equivalents when there is only one generic available, and this discount typically increases to 50% to 80% (or more) when there are multiple generics on the market for a given brand. Consequently, the launch of a generic drug usually results in significant cost savings for consumers. And any actions that prevent generic competition directly cause prices to remain artificially high and injures consumers.

B. Factual Background

On February 20, 2001, AstraZeneca received approval from the FDA to market Nexium. The active ingredient in Nexium is esomeprazole magnesium ("esomeprazole"). AstraZeneca listed fourteen patents in the FDA Orange Book as covering Nexium or a method of using Nexium.[3] These patents expire between April 20, 2007 and November 3, 2019.

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[2] An additional reason for the FDA to render the requested relief immediately is to avoid further conflict between the results sought the HPM Petition, Ranbaxy's dilatory actions and in meeting all of its consent decree milestones and the FDA's role in this matter. The FDA recently acknowledged the significance of the HPM Petition in a public statement regarding its approval for the marketing of generic valsartan:

"The Agency notes the submission of a citizen petition dated May 5, 2014, by attorneys representing a generic manufacturer with an unidentified tentatively approved ANDA. Docket No. FDA-2014-P-0594. This petition requests that FDA determine that Ranbaxy has forfeited or is not eligible for first-to-file status for valsartan, among other drugs, and that FDA must immediately approve all tentatively approved ANDAs for which final approval is blocked by Ranbaxy's alleged eligibility for 180-day exclusivity. The agency has not made a decision with respect to this petition, and any such decision, when made, will be announced in the petition docket . . . . Because ANDA 077492 is eligible for final approval today regardless of the ultimate decision on the issues raised in the petition, today's action with respect to ANDA 077492 is taken in order not to further delay the availability of generic valsartan while the issues raised in the petition are under consideration."

See FDA Approval Letter from Kathleen Uhl, M.D. to Ohm Laboratories Inc. regarding ANDA 077492 for the commercial marketing of generic valsartan, dated June 26, 2014, n.3.

[3] *See AstraZeneca AB v. Ranbaxy Pharms. Inc.*, Civ. Action No. 3:05-cv-05553-JAP-TJB (D.N.J. Nov. 21, 2005), Dkt. 1 (AstraZeneca AB's Complaint against Ranbaxy Pharmaceuticals Inc.).

1. Ranbaxy's status as first-filer of generic esomeprazole ANDA.

Ranbaxy announced that it was the first to file an ANDA seeking to market generic esomeprazole, on August 5, 2005.[4]

On November 21, 2005, AstraZeneca sued Ranbaxy for patent infringement in federal district court for the District of New Jersey on ten of the fourteen patents AstraZeneca listed in the Orange Book as covering Nexium.[5]

2. FDA tentatively approves Ranbaxy's ANDA.

While that litigation was ongoing, on February 5, 2008, Ranbaxy received tentative approval of its ANDA.[6] Due to the Hatch-Waxman statutory 30-month stay of final FDA approval (which went into effect when AstraZeneca filed suit against Ranbaxy for patent infringement) Ranbaxy could not enter the market with generic Nexium until April 14, 2008.[7]

3. The 30-month stay expires and Ranbaxy and AstraZeneca agree that Ranbaxy will not sell generic Nexium before May 27, 2014.

On April 14, 2008, the day on which the statutory 30-month stay against Ranbaxy expired, Ranbaxy and AstraZeneca signed numerous agreements, including an agreement settling their Nexium patent litigation.[8] Ranbaxy reported that the settlement terms

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[4] Ranbaxy website, *Ranbaxy Receives Tentative Approval To Manufacture And Market Esomeprazole Magnesium DR Capsules in USA*, dated February 7, 2008, ("Ranbaxy believes that it has a FTF (First to File) status on the drug [generic Nexium], providing it with a potential 180 days marketing exclusivity, thereby offering a significant opportunity in the future.") *available at:*

http://www.ranbaxy.com/ranbaxy-receives-tentative-approval-to-manufacture-and-market-esomeprazole-magnesium-dr-capsules-in-usa/. *See also* the FDA's list of drug products for which ANDAs have been received by the Office of Generic Drugs (OGD) containing a "Paragraph IV" patent certification *available at:* http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/ucm047676.htm (listing August 5, 2005 as the date on which the first substantially complete generic drug application for esomeprazole magnesium was submitted to the FDA).

[5] *Id.*

[6] *See Ranbaxy website, Ranbaxy Receives Tentative Approval To Manufacture And Market Esomeprazole Magnesium DR Capsules in USA*, dated February 7, 2008, *available at:*

http://www.ranbaxy.com/ranbaxy-receives-tentative-approval-to-manufacture-and-market-esomeprazole-magnesium-dr-capsules-in-usa/. *See also* FDA webpage for ANDA 07-7830, Approval History, *available at*: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.DrugDetails; No. 12-md-2409-WGY (D. Mass.), Dkt. 228 (Answer of AstraZeneca to Direct Purchasers' Consolidated Amended Complaint, dated May 17, 2013) at ¶ 10 ("AstraZeneca admits the FDA granted tentative approval to Ranbaxy's generic Nexium products on February 5, 2008"); No. 12-md-2409-WGY (D. Mass.), Dkt. 234 (Ranbaxy's Answer to Direct Purchasers' Consolidated Amended Complaint, dated May 17, 2013) at ¶ 10 ("Ranbaxy admits that, on or about February 5, 2008, the FDA granted tentative approval to Ranbaxy for ANDA No. 77-830").

[7] § 505(c)(3)(C)(i).

[8] Ranbaxy press release, *Ranbaxy and AstraZeneca reach agreement in esomeprazole litigation*, dated April 15, 2008, *available at* http://www.ranbaxy.com/us/ranbaxy-and-astrazeneca-reach-agreement-in-esomeprazole-patent-litigation/.

permit it to "launch the generic version of Nexium under a license from AstraZeneca, on May 27, 2014. Ranbaxy announced that it would be the only company to market this product *with a 180 days exclusivity*, in the US market."[9] (Emphasis added.)

May 27, 2014 has come and gone. Ranbaxy has not received final approval of its ANDA for generic esomeprazole. No generic esomeprazole product has entered the market. Consumers remain bereft of the benefit of cost-saving generic drugs until full generic entry in this market.

4. Ranbaxy effectuated expedited approval for a site transfer and final approval of Ranbaxy's atorvastatin (Lipitor) ANDA in early 2012.

Following the AstraZeneca-Ranbaxy settlement, on February 25, 2009, the FDA invoked its Applications Integrity Policy against Ranbaxy. Among other things, the FDA announced that it would not review ANDAs containing data generated from Ranbaxy's Paonta Sahib and Dewas (India) facilities until the FDA was satisfied certain conditions regarding the reliability of that data were met. Upon publicly available information and belief, Ranbaxy's 2005 generic esomeprazole ANDA contained data generated from Ranbaxy's Paonta Sahib facility.[10]

5. Under a consent decree with the FDA, Ranbaxy, cannot manufacture or sell its generic esomeprazole until it meets all FDA milestones, and Ranbaxy has not done so.

In order to avoid repetition, we hereby incorporate by reference the facts set forth in the HPM Petition setting forth particulars of a consent decree between the FDA and Ranbaxy and dated January 25, 2012.[11]

It is important to note for purposes of our Response, however, that: (1) the consent decree, among other things, set milestones for Ranbaxy to bring certain generic products to market, including Ranbaxy's generic Nexium product;[12] and (2) Ranbaxy agreed to relinquish any 180-day marketing exclusivity that it might have for several generic drug applications – which, upon publicly available information and belief, include its generic esomeprazole ANDA – if it fails to meet certain decree requirements by specified dates and to do so no later than September 30, 2014.[13]

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[9] Ranbaxy Laboratories Limited (RLL) Board of Directors Meeting Report, Q1 Jan.-Feb. 2008, April 22, 2008, *available at*: http://www.ranbaxy.com/global-sales-at-usd-409-mn-rs-16231-mn-15/.

[10] *See* http://www.fda.gov/newsevents/newsroom/pressannouncements/ucm382736.htm.

[11] While the consent decree addressed issues at Ranbaxy's Pahib and Dewas facilities, in September 2013, the FDA added Ranbaxy's Mohali facility to the CGMP provisions of the decree. In January 2014, the FDA added Ranbaxy's Toansa facility to the provisions of the consent decree. *See* http://www.fda.gov/newsevents/newsroom/pressannouncements/ucm382736.htm.

[12] *See* Ranbaxy Quarterly Call Transcript, February 5, 2014, Q4, FY2014, *available at*: http://www.ranbaxy.com/investor-relations/financial-information/quarterly-results-2/.

[13] *Id*. *See United States of America v. Ranbaxy, Inc., et al.,* D. Md., 12-cv-0250, D.E. no. 5, p. 14, ¶ XIII. *See also* http://www.fda.gov/newsevents/newsroom/pressannouncements/ucm289224.htm.

6. Ranbaxy has received significant revenues from helping AstraZeneca commercialize *branded* Nexium.

The caustic rub of there being no generic Nexium available to consumers is particularly egregious because, in the wake of its delay and FDA scrutiny, Ranbaxy has turned its first-to-file status into substantial profits by helping AstraZeneca manufacture branded Nexium.

On the same day that AstraZeneca and Ranbaxy settled their litigation, April 14, 2008, Ranbaxy and AstraZeneca also entered into other agreements, including an agreement by which "*Ranbaxy will formulate a significant portion of AstraZeneca's U.S. supply of Nexium from May 2010*, including provisions for the manufacture of [e]someprazole magnesium [API] from May 2009."[14] (Emphasis added.)

In September 2010, upon publicly available information and belief, Ranbaxy began to ship Nexium API to AstraZeneca.[15] By the first quarter of 2012, Ranbaxy was selling finished Nexium capsules to AstraZeneca and earning substantial revenue.[16]

In September 2010, upon publicly available information and belief, Ranbaxy began to manufacture and sell Nexium API to AstraZeneca.[17]

By the first quarter of 2012, Ranbaxy was formulating finished Nexium capsules for purchase by AstraZeneca and booking substantial sales revenues. In a May 9, 2012 conference call addressing first quarter 2012 results, Managing Director of Ranbaxy Laboratories Limited, Arun Sawhney, stated: "we have started the formulation supplies . . . per the plan." Mr. Sawhney also confirmed that Ranbaxy booked the revenue from the sales of Nexium capsules under "US businesses."[18] Updated AstraZeneca labeling

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[14] *See id. See also* Ranbaxy Laboratories Limited (RLL) Board of Directors Meeting Report, Q1 Jan.-Feb. 2008, April 22, 2008, *available at*: http://www.ranbaxy.com/global-sales-at-usd-409-mn-rs-16231-mn-15/.

[15] Ranbaxy Annual Report, 2010, p. 21, *available at:* www.moneycontrol.com/bse_annualreports/5003591210.pdf ("The company's Toansa site started supplying Esomeprazole to AstraZeneca from September 2010."); Ranbaxy Annual Report, 2011, p. 33, *available at*: http://www.ranbaxy.com/investor-relations/financial-information/annual-report/ ("As per our agreement, we also supplied API for Esomeprazole, another big global molecule to AstraZeneca for the US market. Although we started initial supplies in September 2010, the majority of demand was met in 2011. Ranbaxy is catering to a substantial part of the API demand for Esomeprazole in the US.").

[16] *See* Ranbaxy Laboratories Limited, Post Results Conference Call for Quarter 1 2012, Transcript, pp. 20, 23, *available at:* http://www.ranbaxy.com/investor-relations/financial-information/quarterly-results-2/ ("[Ranbaxy has] started the formulation supplies.").

[17] Ranbaxy Annual Report, 2010, p. 21, *available at*: www.moneycontrol.com/bse_annualreports/5003591210.pdf ("The company's Toansa site started supplying Esomeprazole to AstraZeneca from September 2010."); Ranbaxy Annual Report, 2011, p. 33, at: http://www.ranbaxy.com/investor-relations/financial-information/annual-report/ ("As per our agreement, we also supplied API for Esomeprazole, another big global molecule to AstraZeneca for the US market. Although we started initial supplies in September 2010, the majority of demand was met in 2011. Ranbaxy is catering to a substantial part of the API demand for Esomeprazole in the US.").

[18] Ranbaxy Laboratories Limited, Post Results Conference Call for Quarter 1 2012, Transcript, pp. 20, 23,

available at: http://www.ranbaxy.com/investor-relations/financial-information/quarterly-results-2/, stating:

information for its Nexium NDA shows that by January 2012, AstraZeneca had listed OHM Laboratories Inc., Ranbaxy's wholly owned subsidiary, as a manufacturer of AstraZeneca's Nexium capsules and Ranbaxy Laboratories Ltd. as the manufacturer of Nexium API for AstraZeneca.[19]

In 2013, Ranbaxy continued to sell and receive substantial revenue from its Nexium API and finished capsule sales to AstraZeneca.[20]

In early 2014, Ranbaxy sold Nexium API and finished capsules to AstraZeneca, manufacture at its Ohm facility in New Brunswick, New Jersey.[21]

Ranbaxy's end-run to participate in the marketing of Nexium and sharing in the proceeds from Nexium sales, free of any generic competition is further (and compelling grounds) to end the delay and open the market to other waiting generic drug companies. It is the very type of manipulation that the FDA has repeatedly stated it will not tolerate in favor of a first to file generic applicant.

7. Recent events underscore Ranbaxy's continued delay and bottlenecking of the marketing of generic esomeprazole.

More than two-and-a-half years have passed and, it appears, that Ranbaxy has not sufficiently remedied its deficiencies to obtain FDA final approval for its generic Nexium

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Rahul Sharma: Sir, just wanted to know the Nexium supplies. Have you started formulation supplies as your API number is basically moving down from this quarter onwards?

Arun Sawhney: Yes, we have started the formulation supplies.

[19] *See* http://www.accessdata.fda.gov/spl/data/cb9f9b6c-2fdb-4d80-4c8b-5ae5c6b132bc/cb9f9b6c-2fdb-4d80-4c8b-5ae5c6b132bc.xml. *See also* http://www.iodine.com/label/Nexium, (citing http://lables.fda.gov) and showing a revised listing as of November 2012 listing the product codes for the finished capsules manufactured by

[20] Ranbaxy Laboratories Limited Q1CY13 Results Conference Call, May 8, 2013, Q1 2013, Transcript, pp. 10, 12, *available at*: http://www.ranbaxy.com/global-sales-at-usd-409-mn-rs-16231-mn-15/, stating:

Kartik Mehta: So is it fair to assume the sales of API that we have now would that include any [Nexium] API sales that we do to the Innovator under our settlement in the past or is it actually recorded under some other ad?

Arun Sawhney: It is a total universe of API sales that we make.

Kartik Mehta: So which includes Nexium also, right?

Arun Sawhney: Yeah.

[21] *See* Nexium label stating: "Mfd. for: AstraZeneca LP . . . By: Ohm Laboratories Inc., 14 Terminal Road, New Brunswick, NJ 08901 Product of India," attached hereto as Exhibit A. *See also* Ranbaxy Laboratories Limited Q4 FY14 Earnings Conference Call, February 5, 2014, Transcript, p. 13, *available at*:

http://www.ranbaxy.com/global-sales-at-usd-409-mn-rs-16231-mn-15/.

product. Recent events underscore the apparent lack of progress. In January 2014, FDA added Ranbaxy's facility at Toansa, India, to the consent decree's coverage.[22] It has been widely reported that Ranbaxy planned to manufacture its generic esomeprazole capsules using API from Toansa.[23]

Currently, as of June 2014, Ranbaxy has not launched a generic product, although it claims it has met all of the milestones set forth in the consent decree.[24]

8. At least nine other drug companies have filed ANDAs for generic esomeprazole.

It is publicly known that at least nine other drug companies have also filed ANDAs seeking to market generic esomeprazole.[25] AstraZeneca sued each one of the nine companies for patent infringement in federal district court.[26]

Upon publicly available information and belief, these generic drug companies would market their generic esomeprazole products upon final approval of the FDA. The generic drug companies cannot receive final FDA approval, however, until any 180-day exclusivity which Ranbaxy may have had has either elapsed or (as requested here) been determined by the FDA to have been either forfeited or relinquished.

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[22] *See* http://www.fda.gov/newsevents/newsroom/pressannouncements/ucm382736.htm.

[23] *See e.g.*, CNBC, JM Financial, Anmol Ganjoo, *Ban may hit Ranbaxy's new product launches*, January 24, 2014, *available at*: http://www.moneycontrol.com/news/market-outlook/ban-may-hit-ranbaxys-new-product-launches-jm-fin_1030820.html (". . . [The] Nexium generic launch may get delayed because of the ban on the Toansa plant. Had this ban not come through, the company would have launched the two products from the Toansa facility - that is procured API from the Toansa facility and formulated in Ohm Laboratories in the US."); FiercePharma, *Ranbaxy asks the FDA to let it make generic Diovan in U.S.*, January 16, 2014, at: http://www.fiercepharmamanufacturing.com/story/sources-ranbaxy-asks-fda-let-it-make-generic-diovan-us/2014-01-16#ixzz2vWPWwsqv ("Ranbaxy this week announced the FDA has issued a Form 483 for its active pharmaceutical plant (API) in Toansa, a facility that supplies about 70% of the raw ingredients for U.S. production.").

[24] *See* Ranbaxy Quarterly Call Transcript, February 5, 2014, Q4, FY2014, *available at*: http://www.ranbaxy.com/investor-relations/financial-information/quarterly-results-2/.

[25] Other drug companies that subsequently filed ANDAs under section 505(j) also seeking to market generic esomeprazole include: Ivax Corp., Dr. Reddy's Laboratories Ltd., Sandoz, Inc., Lupin Ltd., Hetero Drugs, Ltd., Torrent Pharmaceuticals Limited, Watson Laboratories, Inc., Wockhardt Limited, and Mylan.

[26] *See AstraZeneca AB v. Ivax Corp., Teva Pharmaceutical Industries, Ltd., Teva Pharmaceuticals USA, et al.,* Civ. Action No. 06-cv-01057-JAP-TJB (D.N.J. Mar. 8, 2006), Dkt. # 1; *AstraZeneca AB v. Dr. Reddy's Labs., Ltd.*, Civ. Action No. 08-cv-00328-JAP-TJB (D.N.J. Jan. 17, 2008), Dkt. # 1; *AstraZeneca AB v. Sandoz, Inc*., No. 09-cv-00199-JAP-TJB, (D.N.J. Jan. 14, 2009), Dkt. # 1; *AstraZeneca AB v. Lupin Ltd.*, No. 09-cv-05404-JAP-TJB (D.N.J. Oct. 21, 2009) , Dkt. # 1; *AstraZeneca AB v. Hetero Drugs, Ltd.*, No. 11-cv-04468-JAP-TJB (D.N.J. Aug. 2, 2011) , Dkt. # 1; *AstraZeneca AB v. Torrent Pharmaceuticals Limited*, No. 12-cv-00506-JAP-TJB (D.N.J. Jan. 26, 2012), Dkt. # 1; *AstraZeneca AB v. Watson Laboratories, Inc. – Florida*, No. 13-cv-01669, (D.N.J. Mar. 19, 2013), Dkt. # 1; *AstraZeneca AB v. Wockhardt Limited*, No. 13-cv-04854 (D.N.J. Aug. 12, 2013), Dkt. # 1, and *AstraZeneca AB, et al. v. Mylan Laboratories Limited, et al.*, Civil Action No. 12-cv-01378 (D.N.J. Oct. 9, 2013), Dkt. # 1.

C. Legal Authority.

1. Regulatory and legal authority, as well as FDA policy, support the requested relief.

In the Drug Price Competition and Patent Term Restoration Act of 1984 ("Hatch-Waxman"),[27] Congress sought to "make available more low cost generic drugs."[28] Hatch-Waxman creates an incentive for generic drug companies to challenge brand name drug patents by, among other things, permitting a company wishing to manufacture and market a generic version of a previously approved drug to file an "Abbreviated New Drug Application" or "ANDA."[29] The fundamental purpose of the generic drug approval provisions of Hatch-Waxman is to expedite and maximize the introduction of cost-saving generic drugs, while providing drug product innovators with research incentives, but – as the FDA has noted – without providing unintended "market 'windfall[s]' for crafty, albeit industrious, market players.'"[30] The main purpose of the Hatch–Waxman Amendments which is to "bring generic drugs onto the market as rapidly as possible."[31]

On December 8, 2003, Congress enacted the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 ("MMA"), amending Hatch Waxman.[32] Under 21 C.F.R. § 314.1 07(c)(3), "if FDA concludes that the applicant submitting the first application is not actively pursuing approval of its abbreviated application, FDA will make the approval of subsequent [ANDAs] immediately effective if they are otherwise eligible for an immediately effective approval." As set forth in the HP Petitions, in promulgating this rule, FDA stated that:

> For purposes of this rule, the phrase 'actively pursuing approval' is intended to encompass a drug sponsor's good faith effort to pursue marketing approval in a timely manner. In determining whether a sponsor is actively' pursuing marketing approval, FDA will consider all relevant factors, such as the sponsor's compliance with regulations and the timeliness of its responses to FDA's questions or application deficiencies during the review period.

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[27] Drug Price Competition and Patent Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (1984), 21 U.S.C. §355(j) ("Hatch-Waxman" or the "Act").

[28] H.R. Rep. No. 98-857, pt. 1, at 14 (1984).

[29] Drug Price Competition and Patent Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585, 21 U.S.C. §355(j) ("Hatch-Waxman" or the "Act"). An ANDA must show that the generic drug contains the same active ingredient(s), dosage form, route of administration, and strength as the brand name drug, and is absorbed at the same rate and to the same extent as the brand drug—that is, that the generic drug is pharmaceutically equivalent and bioequivalent (together, "therapeutically equivalent") to the brand named drug. 21 U.S.C. § 355(j)(2)(A)(iv).

[30] *See* Docket No. 00P-1446KPl, Letter from Janet Woodcock, Director, Center for Drug Evaluation and Research, to Deborah Jaskot, Senior Director, Regulatory Affairs, Teva Pharmaceuticals USA, Inc., dated February 6, 2001, p. 5 (citing *Teva Pharmaceuticals v. FDA*, 182 F.3d 1003, 1009 (D.C. Cir. 1999) (quoting *Mylan Pharmaceuticals Inc. v. Henney*, 94 F. Supp.2d 36, 54 (D.D.C. 2000))).

[31] *Mova Pharmaceutical Corp. v. Shalala*, 140 F.3d 1060 at 1068 (D.C.Cir.1998).

[32] Pub. L. No. 108-173, 117 Stat. 2066 (2003).

59 Fed. Reg. 50,338, 50,354 (Oct. 3, 1994) (emphasis added).

At issue here is Ranbaxy's delay of more than two years in obtaining final approval of its generic esomeprazole ANDA – delay that reached past even its own agreed entry date with AstraZeneca. The FDA clearly recognized the issue of potentially inappropriate delay in putting an outside date of September 30, 2014 on four of the ANDAs that were subject to the consent decree, including Ranbaxy's generic esomeprazole ANDA.[33]

This delay should end now. Unless the FDA believes that Ranbaxy's esomeprazole ANDA is ready for immediate approval in accordance with all applicable laws and regulations, the FDA should immediately consider whether Ranbaxy has forfeited or waived any 180 day exclusivity it may otherwise have been entitled to. We suggest that the record supports the conclusion that waiver or forfeiture have already occurred.

2. The FDA should determine that Ranbaxy has either forfeited or must relinquish any 180-day exclusivity it may otherwise have been entitled to and immediately approve the otherwise approvable ANDAs.

The FDA has observed that an objective of the 180-day exclusivity provision is to enhance market competition.[34] The FDA has also expressed concern that the 180-day exclusivity provision not be used in a manner which enables "market access for subsequent ANDA holders [to be] substantially delayed, potentially for years [such that] marketplace competition could be anticipated to develop more slowly, a result that would be inconsistent with this legislative objective."[35] The FDA has further acknowledged that interpretation of governing exclusivity regulations "prevent[s] one company from "manipulat[ing] the system in order to block or delay generic competition."[36]

Specifically, the FDA has applied the following "principles" in addressing issues of 180-day exclusivity. "First, the statute is to be interpreted in a manner consistent with 'the statute's interest in affording market access and incentives for both generic and non-, generic makers,' and to maintain 'an incentive for the parties to follow the purposes of Hatch-Waxman.' Second, FDA should avoid an interpretation that excessively favors the first generic and the innovator parties' 'anticompetitive hold' over the drug. . . . Finally

[33] Ranbaxy has publicly addressed the consent decree in the context of meeting milestones for marketing its products, including Nexium. *See* footnote <>, *supra*.

[34] *See e.g.*, Letter from William K. Hubbard, Associate Commissions for Policy and Planning, FDA, to Bert W. Rein and William A. McGrath, dated July 2, 2004, at 12 (". . . the Hatch-Waxman amendments reflect two fundamental legislative goals: continued pharmaceutical innovation and enhanced competition in the pharmaceutical marketplace. In granting l80-day exclusivity, Congress intended to reward patent challenges based on non-infringement or invalidity to promote the latter of these basic legislative objectives-- enhanced marketplace competition." (Citations omitted.)).

[35] Letter from William K. Hubbard, Associate Commissions for Policy and Planning, FDA, to Bert W. Rein and William A. McGrath, dated July 2, 2004, at 12.

[36] *Teva Pharmaceuticals v. FDA*, 182 F.3d 1003, 1009 (D.C. Cir. 1999) (citation omitted).

FDA should avoid interpreting Hatch-Waxman so the decision on whether a generic applicant is entitled to exclusivity rests entirely in the patent holder's hands.'"[37]

Those principles counsel in favor of determining that (1) Ranbaxy has either forfeited or must relinquish any statutory exclusivity it may have for generic esomeprazole, and (2) grant final approval to the generic drug companies who stand next in line that are otherwise ready for such final approval.

To determine otherwise would lead to the practical effect (and the absurd result) that generic products which would come to market except for Ranbaxy's claimed 180-day exclusivity are further delayed, Ranbaxy enjoys the benefit of having sold AstraZeneca's Nexium product while looking forward to exclusive profits when it obtains final approval of its generic esomeprazole product at some indefinite time, and consumers are penalized with no recourse to less expensive products. Ranbaxy would enjoy an unprecedented windfall – based upon an inexcusable delay of the very generic competition that Hatch-Waxman intended should *not* result from the application of the exclusivity provisions – at the expense of consumers.

For these reasons, given the consent decree, the legislative intent behind 180-day exclusivity, and the FDA's goals and stated position, we ask that – unless the FDA is prepared to conclude that Ranbaxy's esomeprazole ANDA is eligible for final approval – the FDA (a) determine that Ranbaxy has forfeited or must relinquish any 180-day exclusivity it may have had with respect to esomeprazole and (b) grant final approval to all other pending esomeprazole ANDAs that are otherwise approvable.

IV. REQUEST FOR EXPEDITIOUS RULING

The FDA is still withholding final approval of Ranbaxy's ANDA for a generic esomeprazole product. With a mere 90 days before the outside date on which FDA and Ranbaxy agreed that Ranbaxy must relinquish its claims to exclusivity for certain ANDAs – which, upon publicly available information and belief, includes Ranbaxy's generic esomeprazole ANDA – Ranbaxy has not obtained FDA approval nor met all of its milestones for doing so.

We respectfully request that the Commissioner adjudicate this petition in an expeditious fashion. Consumers have a strong interest in having this matter resolved promptly so that consumers may benefit from the advent of competition in the generic esomeprazole drug market as soon as possible.

We agree with the HPM Petition and Teva Response[38] that FDA must decide *now*. Consumers have paid too much for esomeprazole for far too long. The action we believe is needed is an immediate decision whether there is any reason justifying the current bottleneck.

[37] Docket No. 00P-1446KPl, Letter from Janet Woodcock, Director, Center for Drug Evaluation and Research, to Deborah Jaskot, Senior Director, Regulatory Affairs, Teva Pharmaceuticals USA, Inc., dated February 6, 2001, p.5 (citing *Teva Pharmaceuticals v. FDA*, 182 F.3d 1003, 1009 (D.C. Cir. 1999) (quoting *Mylan Pharmaceuticals Inc. v. Henney*, 94 F. Supp.2d at 54 (D.D.C. 2000))).

[38] May 14, 2014 Response of Teva Pharmaceuticals Response to Citizens Petition, FDA-2014-P-0594.

V. ENVIRONMENTAL IMPACT

The subject matter of this petition is not within any of the categories of action for which an environmental assessment is required. We claim a categorical exclusion under 21 C.F.R. §§ 25.30 and 25.31.

VI. ECONOMIC IMPACT

We are not providing economic information because no economic information has been requested by the Commissioner.

VII. CERTIFICATION

The undersigned certify, that, to the best of their knowledge and belief, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to us that are unfavorable to the petition.

Respectfully submitted,

Richard Holober
Executive Director