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Office of The Attorney General
State of Connecticut

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Division of Dockets Management
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Docket N. FDA-2014-P-0594

COMMENTS OF THE OFFICE OF THE CONNECTICUT ATTORNEY GENERAL TO THE HYMAN, PHELPS & McNAMARA, P.C. PETITION AND RANBAXY, INC.'S COMMENTS IN OPPOSITION

EXPEDITED DECISION REQUESTED

The Attorney General for the State of Connecticut ("Connecticut Attorney General") offers these comments ("Comment") in response to the above-referenced Citizen Petition submitted by Hyman, Phelps & McNamara, P.C. ("HPM Petition"), dated May 5, 2014, and the Comments in Opposition to the HPM Petition submitted by Ranbaxy Inc. dated July 10, 2014, specifically with regard to the generic drug esomeprazole magnesium ("esomeprazole"), currently only marketed under the brand name Nexium®.

One of the overriding public policy goals of the Hatch Waxman Amendments to the Drug Price Competition and Patent Term Restoration Act of 1984 (the "Hatch-Waxman Act") was that all consumers would benefit from the rapid availability of lower-priced generic versions of innovator drugs.[1] With regard to a generic form of Nexium (esomeprazole), however, this has not happened.

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[1] *See, e.g.*, H.R. Rep. No. 98-857, 98th Cong., 2d Sess. at 14-15 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2647-48 (The Hatch-Waxman Amendments were intended to balance innovation in the development of new drugs with accelerating the availability to consumers of lower cost alternatives to innovator drugs); *Federal Trade Comm'n v. Actavis, Inc.*, 570 U.S. ___, 133 S.Ct. 2223, 2228, 186 L.Ed.2d. 343 (2013) ("The Hatch-Waxman process . . . 'speed[s] the introduction of low-cost generic drugs to market,' thereby furthering drug competition") (citation omitted).

While the above-referenced docket involves only a discrete dispute between drug manufacturers concerning the development of one generic drug, it represents only the tip of the iceberg of a much larger and more important national health policy issue: access to affordable generic drugs. More precisely, a systemic problem has developed in the pharmaceutical industry whereby some branded and generic drug manufacturers have rigged the system by settling patent infringement lawsuits with the intent and effect of delaying entry of generic drugs for as long as they possibly can. Although their methods and forms of settlement have been evolving in an attempt to avoid government enforcement or regulation, the results have been the same: consumers pay significantly more for branded drugs while lower-cost generic alternatives are kept out of the market.

Here, the manufacturer for the branded drug Nexium®, AstraZeneca Pharmaceuticals LP ("AstraZeneca"), agreed to pay the first-to-file generic manufacturer, Ranbaxy Inc. ("Ranbaxy") to significantly delay entry of the first generic Nexium® drug into the market by approximately six years. During that six-year delay period, they split AstraZeneca's monopoly profits for the brand drug. The two companies agreed that Ranbaxy would delay marketing a generic version of Nexium until May 2014, however Ranbaxy has still yet to enter the market – allegedly due to manufacturing problems that the FDA correctly addressed in a previous action against Ranbaxy, but which Ranbaxy has not yet corrected. While still profiting from sales of the brand drug, Ranbaxy's delay in marketing its generic version of Nexium is blocking the efforts of many other generic manufacturers to come to market and lower costs for consumers. Ranbaxy or AstraZeneca should bear the consequences of their failure to address those manufacturing problems, not consumers.

AstraZeneca and Ranbaxy are the only winners here, reaping monopoly profits for the branded drug Nexium®. Consumers and payers are the clear losers. Only the FDA can put an end to this injustice through swift action.

As the only person advocating for the interest of consumers in this forum, and as the Connecticut official charged with protecting the Connecticut citizens from anticompetitive behavior and securing a competitive marketplace,[2] the Connecticut Attorney General believes that the Food and Drug Administration ("FDA") should either approve promptly Ranbaxy Laboratories Inc.'s ("Ranbaxy") generic version of delayed-release 40 mg Nexium (esomeprazole) capsules if it is ready for immediate approval,[3] or alternatively rule that Ranbaxy no longer holds the 180-day exclusivity for that product so that other generic drug makers may be approved and enter the market immediately. The delay in Ranbaxy approval to market esomeprazole has created a bottleneck preventing other potential generic drug entrants from obtaining final approval of their Abbreviated New Drug Applications ("ANDAs") and beginning to sell lower cost generic esomeprazole. The resulting harm to *all* consumers – including federal and state government, municipal and employee health plans and the uninsured – leaves these

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[2] The Connecticut Attorney General is also the Co-Chair of the Antitrust Task Force of the National Association of Attorneys General.

[3] The Connecticut Attorney General urges the FDA to grant immediate approval *only* if the FDA has fully resolved, to its satisfaction, that Ranbaxy has corrected any manufacturing or potential safety problems associated with the production of generic esomeprazole. If it has not, the Connecticut Attorney General would alternatively urge the FDA to find that Ranbaxy has forfeited its 180-day exclusivity for marketing that drug.

payers no option to choose lower-priced versions of Nexium and flies in the face of the FDA's stated goals and regulations designed to promote timely access to less expensive generics.

To put this issue in context, Nexium® is among the drugs with the highest utilization in the state. Since January 1, 2012, the State of Connecticut has spent nearly $75 million on Nexium® through its Medicaid program and various other state employee/retiree health plans. That is an average outlay of approximately $2.3 million per month in Connecticut taxpayer funds. Moreover, there is no reason to assume that Connecticut is unique in the amount its health care programs spend on Nexium®. In fact, AstraZeneca's nationwide sales of Nexium® – *the second highest selling pharmaceutical drug in the United States* – were approximately $5.99 billion in 2013.[4] That means that consumers across the United States are spending, on average, $16.4 million *per day* on Nexium®. Obviously, these costs will be greatly reduced through the introduction of generic competition in this market.

The Connecticut Attorney General requests that, unless the FDA believes the Ranbaxy ANDA is ready for immediate approval and commercialization in accordance with all applicable laws and regulations, the FDA should (a) immediately determine that Ranbaxy 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 and compelling:

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 effectively blocked the ability of several other generic makers to come to market since that time.

Second, the FDA granted Ranbaxy preliminary approval for its esomeprazole ANDA in early 2008 – *six years ago*. The only impediment to FDA final approval at that time was pending patent litigation.

Third, in April of 2008, Ranbaxy resolved the pending patent litigation with Nexium® brand manufacturer AstraZeneca under terms in which Ranbaxy agreed to delay its efforts to gain market entry for its esomeparazole ANDA until May 27, 2014 at the earliest (adding an additional six years of delay for generic Nexium).

Fourth, on January 25, 2012, the FDA entered into a consent decree with Ranbaxy that set a period of approximately one year to three years – through September 30, 2014 – for first-filer Ranbaxy to remedy deficiencies[5] and take other actions. The HPM Petition argues that the

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[4] *See* http://www.drugs.com/stats/nexium.

[5] *See* HPM Petition at pp. 3-13. The HPM Petition provides great detail regarding the deficiencies identified by the FDA with regard to Ranbaxy drug products, including violations of Current Good Manufacturing Practices ("cGMPs") concerning the company's analytical raw data, undocumented stability sample test intervals, inadequate staffing and resources in the stability laboratory, lack of information in batch records, incomplete failure investigations, failures related to the Quality Control Unit and procedures related to aseptic operations, among others. The HPM Petition also describes two instances where Ranbaxy's atorvastatin drug was recalled

consent decree enables and continues to enable Ranbaxy to delay the commercialization of generic Nexium and thwart the entry of other generic drug companies.

Fifth, it appears that while Ranbaxy has been dilatory in its efforts to gain prompt ANDA approval over the years for its generic product, it has received significant revenues by assisting the brand maker of Nexium, AstraZeneca, in the commercialization of branded Nexium® in the U.S. (at much higher brand prices). Under Ranbaxy's 2008 pact with AstraZeneca, the two companies agreed to a financial arrangement that (according to the few publicly revealed reports) indicates that Ranbaxy has supplied either or both of the active pharmaceutical ingredient ("API") or the actual Nexium finished product to AstraZeneca, receiving in return substantial payments. Of course, the FDA knows the details of these arrangements insofar as it needed to approve amendments or changes to AstraZeneca's New Drug Application ("NDA") for Ranbaxy to be able to provide the product to AstraZeneca. So, while all other generic drug manufacturers remain barred from receiving final ANDA approval given Ranbaxy's status as the first ANDA filer, in actuality Ranbaxy has very little incentive to gain prompt ANDA approval because it has been able to (and presumably will continue to) reap substantial compensation from selling the reference listed product to AstraZeneca.

Finally, while Ranbaxy fulfilled its promise to AstraZeneca to delay launching generic esomeprazole before May 27, 2014, that date has come and gone. Ranbaxy has not commercialized generic esomeprazole in the time period since May 27th, causing public and private payers to pay what are, in effect, artificially inflated prices for Nexium®. Meanwhile, the FDA has perpetuated this situation by failing to either approve a Ranbaxy esomeprazole ANDA or require Ranbaxy's purported 180-day exclusivity to be relinquished, revoked, or lapsed.

These circumstances have enabled Ranbaxy to delay its marketing of a generic esomeprazole product for many years, and certainly at least in the months since May 27, 2014 (the date upon which Ranbaxy agreed with AstraZeneca that Ranbaxy could begin selling generic esomeprazole). Not only was final approval not granted by this already delayed entry date of May 27, 2014, but the problem has been compounded by Ranbaxy's failure to remedy any deficiencies in connection with its commercialization of generic esomeprazole by September 30, 2014, the date on which the FDA has mandated it do so[6]

At this time, there are no FDA-approved AB-rated generic drug alternatives to AstraZeneca's Nexium®. Consumers, including the State of Connecticut's health programs, municipal and private payers and individual consumers, have *no* access to more affordable, lower-priced generic Nexium. The manifest result of this inaction is higher prices and a dead-stop bottleneck preventing more than a half-dozen generic drug manufacturers lined up behind Ranbaxy from entering the market. And there is no end to the delay in sight.

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after (1) finding glass particles in batches of the drug and (2) finding a 20 mg tablet of the drug inside a sealed bottle of atorvastatin 10 mg. *Id.* at 12.

[6] *See* Consent Decree, *United States of America v. Ranbaxy, Inc., et al.*, D. Md., 12-cv-0250, Doc. 2, § XIII at pp 13-14 (January 25, 2012).

I. ACTION REQUESTED

The Connecticut Attorney General requests that, unless the FDA is prepared to immediately approve Ranbaxy's ANDA, the FDA take the following actions as soon as possible:

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

2. Immediately grant final approval to all other pending esomeprazole ANDAs that are otherwise eligible for such final approval.

The Connecticut Attorney General joins in HPM's request that FDA act quickly to ensure that a generic esomeprazole product or products will enter the market as soon as possible.[7]

Any further delay would unnecessarily prolong consumers' access to generic esomeprazole products and undermine the intended purpose of the 180-day exclusivity period provisions as well as the underlying policies of the Hatch-Waxman Act. The FDA is authorized by the provisions of its January 25, 2012 consent decree entered into with Ranbaxy, current law, FDA regulations, and FDA policy, to take the requested actions. A quick response to this request will ensure that consumers have access to lower priced esomeprazole as soon as possible.[8]

II. STATEMENT OF GROUNDS

A. Regulatory Background

The Connecticut Attorney General refers to the discussion set forth in the HPM Petition regarding the competitive effects of AB-rated generic competition, the economic value of

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[7] *See* Consent Decree, *United States of America v. Ranbaxy, Inc., et al.*, D. Md., 12-cv-0250, Doc. 2, § XIII at pp. 13-14 (January 25, 2012).

[8] An additional reason for the FDA to render the requested relief immediately is to avoid further conflict between the results sought in 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.

exclusivity to a first generic filer, and the further drop in prices to consumers when multiple competing generic drugs enter the market.

It is important to repeat, here, however, that typically, generic drugs 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.[9] Consequently, the launch of a generic drug usually results in significant cost savings for consumers. Conduct that prevents generic competition directly will invariably cause prices to remain artificially high and injure consumers.[10]

B. Factual Background

On February 20, 2001, AstraZeneca received approval from the FDA to market Nexium. The active ingredient in Nexium is esomeprazole. AstraZeneca listed fourteen patents in the FDA Orange Book as covering Nexium or a method of using Nexium.[11] These patents expire between April 20, 2007 and November 3, 2019.

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

Ranbaxy announced that it was the first to file an ANDA seeking to market generic esomeprazole on August 5, 2005.[12]

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.[13]

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[9] *See, e.g.,* GAO, Drug Pricing: Research on Savings from Generic Drug Use (Jan. 31, 2012), *available at* http://www.gao.gov/assets/590/588064.pdf; *see also* Fed. Trade Comm'n Staff Study, Pay-for-Delay: How Drug Company Pay-Offs Cost Consumers Billions (Jan. 2010), *available at* http://www.ftc.gov/os/2010/01/100112payfordelayrpt.pdf.

[10] Analysts have already observed such injury to consumers in the context of Nexium. *See e.g.,* Wall Street Journal, Hester Plumridge, Sean McLain, Ed Silverman, June 17, 2014, Drug Delays Cost U.S. Health-Care Payers Millions of Dollars ("Delays to an Indian company's generic versions of three blockbuster drugs annually cost U.S. health-care payers millions of dollars—and preserve millions of dollars in revenue for the makers of the brand-name versions. . . provided no generic version is available, the big drug companies can continue cashing in."), *available at*: http://online.wsj.com/articles/drug-delays-cost-u-s-health-care-payers-millions-of-dollars-1403020482.

[11] *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.).

[12] 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).

2. FDA tentatively approves Ranbaxy's ANDA.

While that litigation was ongoing, on February 5, 2008, Ranbaxy received tentative approval of its ANDA.[14] Due to the Hatch-Waxman Act's 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.[15]

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.[16] Ranbaxy reported that the settlement terms 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."[17] (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 deprived of the benefit of cost-saving generic drugs until full generic entry in this market.

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[13] *See* footnote 5, *supra.*

[14] *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").

[15] 21 U.S.C. § 355(j)(5)(B)(iii).

[16] 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/.

[17] 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/.

4. 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, the Connecticut Attorney General hereby incorporates 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.[18]

It is important to note for purposes of this Comment, however, that: (a) the consent decree, among other things, set milestones for Ranbaxy to bring certain generic products to market, including Ranbaxy's generic Nexium product;[19] and (b) 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.[20] Ranbaxy does not dispute any of these contentions in its July 10, 2014 Comments in Opposition to the HPM Petition.

5. Ranbaxy has received significant revenues from assisting AstraZeneca to manufacture *branded* Nexium®.

The unfairness to consumers of the fact that there is no generic Nexium available is further compounded because, in the wake of its delay and FDA scrutiny, Ranbaxy has turned its first-to-file status (and failure to enter the market for generic esomeprazole) into substantial profits by helping AstraZeneca manufacture and sell branded Nexium®.[21]

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."[22] (Emphasis added.)

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[18] While the consent decree addressed issues at Ranbaxy's Pahib and Dewas facilities in India, 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.

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

[20] *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.

[21] Rather than falling, prices for Nexium® have actually increased. Therefore, if Ranbaxy's agreement with AstraZeneca includes compensation based on a percentage of Nexium® revenues, a fact unknown to this office, Ranbaxy further profits at the expense of consumers.

[22] *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/.

In September 2010, upon publicly available information and belief, Ranbaxy began to manufacture and sell Nexium API to AstraZeneca.[23]

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."[24] Updated AstraZeneca labeling 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.[25]

In 2013, Ranbaxy continued to sell and receive substantial revenue from its Nexium API and finished capsule sales to AstraZeneca.[26]

In early 2014, Ranbaxy sold Nexium API and finished capsules to AstraZeneca, which were manufactured at its Ohm facility in New Brunswick, New Jersey.[27]

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[23] 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.").

[24] 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:

> **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.

[25] *See* http://www.accessdata.fda.gov/spl/data/cb9f9b6c-2fdb-4d80-4c8b-5ae5c6b132bc/cb9f9b6c-2fdb-4d80-4c8b-5ae5c6b132bc.xml.

[26] 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 [sic] 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.

[27] *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/.

Ranbaxy's end-run to participate in the manufacture and marketing of Nexium® and sharing in the proceeds from Nexium® sales, free from any generic competition, is further (and compelling) grounds to end the delay and open the market to other generic drug companies that have filed ANDAs for esomeprazole. It is the very type of market manipulation that the FDA has repeatedly stated it will not tolerate in favor of a first-to-file generic applicant.[28]

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

More than two-and-a-half years have passed and it appears that Ranbaxy has not sufficiently remedied the deficiencies identified by the FDA as necessary to obtain final approval for its generic Nexium product. Recent events further illustrate the apparent lack of progress. In January 2014, FDA added Ranbaxy's facility at Toansa, India, to the consent decree's coverage.[29] It has been widely reported that Ranbaxy planned to manufacture its generic esomeprazole capsules using API from Toansa.[30]

Currently, as of August 2014, Ranbaxy has not launched a generic product, although it claims it has met all of the milestones set forth in the consent decree.[31]

7. 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.[32] AstraZeneca sued each one of the nine companies for patent infringement in federal district court.[33]

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[28] *See* footnote 33, *infra*.

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

[30] *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.").

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

[32] Other drug companies that subsequently filed ANDAs under section 21 U.S.C. § 355(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.

[33] *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. #

Upon publicly available information and belief, these generic drug companies are prepared to market their generic esomeprazole products pending final approval of their ANDAs by 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 due to Ranbaxy's failure to commercialize its esomeprazole by September 30, 2014. Thus, if Ranbaxy loses its ANDA, it is possible, if not likely, that a number of generic drug manufacturers will be able to enter the market with their generic esomeprazole and, through the benefit of competition, significantly lower the price of the drug.

C. Legal Authority

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

In the Hatch-Waxman Act,[34] Congress sought to "make available more low cost generic drugs."[35] The Hatch-Waxman Act 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 ANDA.[36] The fundamental purpose of the generic drug approval provisions of the Hatch-Waxman Act is to expedite and maximize the introduction of cost-saving generic drugs, while providing the branded pharmaceutical manufacturers with economic incentives to develop new drugs, but – as the FDA has noted – without providing unintended "market 'windfall[s]' for crafty, albeit industrious, market players.'"[37] The main purpose of the Hatch–Waxman Act is to "bring generic drugs onto the market as rapidly as possible."[38]

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.

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

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

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

[37] *See* Docket No. 00P-1446KPI, 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))).

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

On December 8, 2003, Congress enacted the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 ("MMA"), amending the Hatch Waxman Act.[39] 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 HPM Petition, 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.

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 extends well beyond even its own agreed market entry date with AstraZeneca. The FDA clearly recognized the issue of potentially inappropriate delay in putting a deadline of September 30, 2014 on four of the Ranbaxy ANDAs that were subject to the consent decree, including Ranbaxy's generic esomeprazole ANDA.[40]

The FDA should put an end to this delay, now. Unless the FDA finds 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. The Connecticut Attorney General urges the FDA to find that the record supports the conclusion that waiver or forfeiture have already occurred.

2. The FDA should immediately approve the otherwise approvable ANDAs.

The FDA has observed that the purpose of the 180-day exclusivity provision is to incentivize generic drug manufacturers to bring a generic equivalent product into the system and hence, enhance market competition.[41] The FDA has also expressed concern that the 180-day exclusivity provision not be used in a manner that enables "market access for subsequent ANDA holders [to be] substantially delayed, potentially for years [such that] marketplace competition

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

[40] Ranbaxy has publicly addressed the consent decree in the context of meeting milestones for marketing its products, including Nexium. *See* footnote 17, *supra*.

[41] *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.)).

could be anticipated to develop more slowly, a result that would be inconsistent with this legislative objective."[42] The FDA has further acknowledged that its interpretation of governing exclusivity regulations "prevent[s] one company from "manipulat[ing] the system in order to block or delay generic competition."[43]

The FDA has applied the following "principles" in addressing issues of 180-day exclusivity.

> First, the [Hatch-Waxman Act] 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 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.'[44]

Those principles counsel in favor of determining that (a) Ranbaxy has either forfeited or must relinquish any statutory exclusivity it may have for generic esomeprazole, and (b) final approval should be considered and granted 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 (a) generic drug products which would otherwise come to market except for Ranbaxy's claimed 180-day exclusivity are further delayed, (b) Ranbaxy enjoys the economic benefit of already having sold AstraZeneca's Nexium product while also reaping additional and exclusive profits when it obtains final approval of its generic esomeprazole product at some indefinite time, and (c) consumers pay monopoly rents – artificially higher prices – because they are prevented from access to less expensive esomeprazole. Ranbaxy would unfairly enjoy an unprecedented windfall – based upon an inexcusable delay of the very generic competition that the Hatch-Waxman Act intended– at the expense of taxpayers and consumers.

For these reasons, given the consent decree, the legislative intent behind 180-day exclusivity, and the FDA's goals and stated position, the Connecticut Attorney General requests that – unless the FDA is prepared to immediately approve Ranbaxy's esomeprazole ANDA – the FDA should (a) determine that Ranbaxy must forfeited or relinquish any 180-day exclusivity

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[42] 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.

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

[44] Docket No. 00P-1446KPI, 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))).

it may have had with respect to esomeprazole and (b) immediately grant final approval to all other pending esomeprazole ANDAs that are otherwise approvable.

III. REQUEST FOR EXPEDITIOUS RULING

The FDA is still withholding final approval of Ranbaxy's ANDA for a generic esomeprazole product. With less than 30 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.

The Connecticut Attorney General respectfully requests 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.

The Connecticut Attorney General agrees with the HPM Petition and Teva Response[45] that FDA must decide *now*. United States taxpayers and consumers have paid too much for esomeprazole – for far too long. An immediate decision is needed on whether there is any reason justifying the current bottleneck.

Very truly yours,

George Jepsen
Attorney General of the State of Connecticut

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