meet the applicable regulatory requirements" and had reached the point where approval was "imminent." Amgen asserts that Roche is "systematically attempting" to meet the applicable FDA requirements to market CERA. But this proves nothing since any manufacturer seeking approval for a new or generic drug "systematically" attempts to meet the applicable regulations. If this were sufficient to constitute an unfair trade practice, then every applicant for FDA approval would be subject to a §337 action.

Amgen also ignores the fact that the defendant in Glaxo filed an Abbreviated New Drug Application ("ANDA"), not an NDA or its equivalent, a BLA. The difference is fundamental: ANDAs do not require safety and efficacy clinical trials and therefore do not involve the uncertainties associated with them. See Purepack Pharm. Co. v. TorPharm, Inc., 354 F.3d 877, 879 (D.C. Cir. 2004) ("Enacted to expedite the process by which companies gain approval to sell generic versions of already-approved brand-name drugs, the [Hatch-Waxman] amendments allow companies seeking such approval to submit . . . ANDAs, that 'piggyback' on the safety-and-effectiveness information that the brand-name manufacturers submitted in their NDAs."). Filing an ANDA, as opposed to an NDA or BLA, "substantially shorten[s] the time and effort needed to obtain marketing approval" which "enable[s] [generic] drugs to be marketed more cheaply and quickly," in particular by "avoid[ing] the costly and time-consuming studies required for a pioneer drug." Eli Lilly & Co. v. Medtronic, Inc., 496 U.S. 661, 676 (1990). In fact, the FDA is required to approve an ANDA immediately if there are no pending lawsuits after a 180 day waiting period. See 21 U.S.C. §355(c)(3)(C) ("[T]he approval shall be made effective immediately unless, before the expiration of 45 days . . ., an action is brought for infringement of the patent. . . .") (emphasis added).

Roche's importations of CERA are protected by 35 U.S.C. §271(e)(1). Accordingly, respondents respectfully request termination of the investigation with a determination of no violation.

Respectfully submitted,

Kent R. Stevens, Esq.
MORGAN & FINNEGAN, LLP
1775 Eye Street, N.W. Suite 400
Washington, D.C. 20006

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Of Counsel

George W. Johnston, Esq.
Patricia S. Rocha-Tramaloni, Esq.
HOFFMANN-LA ROCHE INC.
340 Kingsland Street
Nutley, NJ 07110-1199

Bartholomew Verdirame, Esq.
Michael P. Dougherty, Esq.
Tony V. Pezzano, Esq.
John C. Vassil, Esq.
MORGAN & FINNEGAN, LLP
3 World Financial Center
New York, NY 10281

Leora Ben-Ami
Patricia A. Carson
Thomas F. Fleming
Howard S. Suh
Peter Fratangelo
KAYE SCHOLER LLP
425 Park Avenue
New York, New York 10022
Telephone No.: (212) 836-8000

in October 1985. . . .") (emphasis added); In re Certain Minutiae-Based Automated Fingerprint Identification Systems, Inv. No. 337-TA-156, Order No. 10, 1983 ITC LEXIS 50 (Aug. 31, 1983) ("During the past year, the city of San Francisco and the State of Alaska have each contracted to purchase [an accused product] . . . from [respondent]") (emphasis added). Here there has been no sale for importation, much less a non-exempt one. Moreover, with respect to Amgen's request for a full blown investigation of whether there has been an offer for sale, the Commission has rejected this theory as a basis for a section 337 violation. See In re Certain Variable Speed Wind Turbines, Inv. No. 337-TA-376, 1996 ITC LEXIS 251, *11-*13 (Initial Determination, May 30, 1996) (sale requires at least a contract to provide the accused product), aff'd, Enercon GmbH v. U.S.I.T.C., 151 F.3d 1376 (Fed. Cir. 1998). In summary, Amgen's theories about proceeding on the basis of what it perceives may happen are not sustainable.

B. Amgen's Speculation About When Approval Might Be Granted Grossly Understates The Uncertainty Of The FDA Review Process

Amgen speculates that "Roche could have regulatory approval to market [CERA] . . . in the United States as early as the first quarter of 2007." Amended complaint ¶7.19. There are at least three problems with this allegation: (1) it is legally irrelevant because of the absence of any importation for sale of the accused product; (2) it is a question raised and rejected by the Commission as reflected by the Notice of Investigation; and (3) it is complete speculation. Amgen ignores the obvious facts that approval might not be granted within the time period that Amgen posits and that the FDA could require new clinical trials and significant changes to the product's label, safety statements, and manufacturing process, all of which could delay approval substantially. See Hoechst, 3 F. Supp. 2d at 112. 21 C.F.R. §314.125(b) provides no fewer than 18 grounds for rejecting an application, including:

> (1) The methods to be used in, and the facilities and controls used for, the manufacture, processing, packing, or holding of the drug substance or the drug product are inadequate to preserve its identity, strength, quality, purity, stability, and bioavailability.
>
> (2) The investigations required under section 505(b) of the act do not include adequate tests by all methods reasonably applicable to show whether or not the drug is safe for use under the conditions prescribed, recommended, or suggested in its proposed labeling.
>
> (3) The results of the tests show that the drug is unsafe for use under the conditions prescribed, recommended, or suggested in its proposed labeling or the results do not show that the drug product is safe or use under those conditions.
>
> (4) There is insufficient information about the drug to determine whether the product is safe for use under the conditions prescribed, recommended, or suggested in it proposed labeling.
>
> (5) There is a lack of substantial evidence consisting of adequate and well controlled investigations . . . that the drug product will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in its proposed labeling.
>
> * * * *
>
> (11) The drug will be manufactured or processed in whole or in part in an establishment that is not registered and not exempt from registration under section 510 of the act and part 207.

In papers supporting its declaratory judgment action in Massachusetts, Amgen has argued that by filing its BLA, "Roche is essentially representing to the FDA that it believes [CERA] is safe and efficacious to treat humans, and that its manufacturing process and product's characteristics are ready to be . . . finalized for marketing." But the same could be said of <u>any</u> applicant for approval of a new drug. Obviously, neither Roche nor any other rational company would go through the enormous expense of preparing and filing a new drug application or BLA without a reasonable belief that the application was approvable. This, however does not allow Roche to substitute its judgment for that of the FDA. As Amgen itself admitted in its March 30,

2006, press release announcing the filing of its BLA for the new drug pamitumumab: "Only the FDA can determine whether the product candidates are safe and effective for the use(s) being investigated." Wright Decl. Exh.2. See also Hoechst, 3 F. Supp. 2d at 112 ("Not only is FDA approval uncertain, but the process or product itself may be altered during the interval in ways that are material to an infringement analysis. Any declaration issued by this Court now may be rendered moot by such alterations.").

Moreover, contrary to Amgen's amended complaint, there is no assurance that the recently filed BLA for the use of CERA in the treatment of kidney disease will be approved in early 2007. In 2002-2004 the average approval time for a Standard[1] new chemical entity was about 22 months. Tufts Center for the Study of Drug Development, Impact Report Vol. 7, No. 6, Nov./Dec. 2005, Wright Decl. Ex. 3, at p. 4. See also FDA CDER[2] Approval Times for Priority and Standard NMEs and New BLAs Calendar Years 1993-2005, Wright Decl. Ex. 4 (median total approval time for 2004 was 24.7 months).[3] In addition, complications in certain patients taking Erythropoiesis Stimulating Agents ("ESAs") have required changes to product information of some currently marketed ESAs and a recommendation to discontinue use of ESAs in certain patients. Kingma-Johnson Decl. ¶10. These recent findings have caused increased scrutiny of ESAs. Id. This could lead to longer approval times for new ESAs such as CERA.

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[1] The FDA divides New Drug Applications into those that receive Priority and those that receive Standard review. See Tufts Center for the Study of Drug Development, Impact Report Vol. 7, No. 6, p. 4, November/December 2005, attached to the Wright Decl. as Ex. 3. CERA has been given Standard review status.

[2] Center for Drug Evaluation and Research. See also Wright Decl. Ex. 4 (therapeutic biologic products including Erythropoiesis Stimulating Agents such as CERA were transferred from CBER to CDER in October 2003).

[3] While the FDA Prescription Drug User Fee Act ("PDUFA") states that it is the agency's goal to complete review of 90% of new drug or biologic applications within 10 months, the actual number in recent years has been closer to 22-25 months as detailed above. See PDUFA Reauthorization Performance Goals and Procedures, Wright Decl. Ex. 5.

The uncertainty of the FDA approval process has only been exacerbated by recent high profile drug safety problems, such as those associated with Merck's Vioxx® product. As recently stated by the director of the Tufts Center for the Study of Drug Development, Kenneth Kaitin: "It's hard to imagine that the individual reviewers within the agency aren't more concerned about safety issues [than before] and as a result are being more cautious in their drug reviews, which is tending towards requesting more data and extension of the overall approval time." The Pink Sheet, Vol. 67, No. 45, Nov. 7, 2005, Wright Decl. Ex. 6, p. 17.

In papers supporting its declaratory judgment action in the Boston district court, Amgen has argued that the court should essentially ignore the above facts because Roche is a large, sophisticated company that is likely to complete the approval process quickly. The point about quick approval is pure speculation. Even if the approval process proceeds expeditiously, there can be no certainty as to when CERA will be approved. If it takes the average approval time in recent years, CERA will not gain approval for use in patients with kidney disease until 22-25 months from now. Roche's most recently approved BLA of its Pegasys® product took 29 months to approve. Wright Decl. Exh. 7 Aranesp® and Kineret® are among Amgen's two most recently approved biologics, and the review time for these were 21 and 23 months, respectively. Wright Decl. Exh. 8. The BLA for the use of CERA in cancer patients will not even be filed until 2009. Kingma-Johnson Decl. ¶11. This is hardly the type of imminent threat that would warrant proceeding with the investigation, and the Commission quite wisely chose not to do so.

Amgen's Boston papers also assert that approval of Roche's BLA is likely within 10 to 13 months, and that "Roche's data do not accurately reflect current approval rates" for BLAs. But it is Amgen's data that is not "current." Amgen cites a 2004 Performance Report to the President and the Congress for the Prescription Drug User Fee Act ("PDUFA"), which states

that the median approval time for original NDA and BLA standard applications was "12.8 months in FY 2002 and is estimated to be 13.8 months in FY 2003." According to the FDA, however, the actual median approval time for BLAs in 2003 was 30.0 months[4], and the approval time for BLAs and NDAs combined in 2004 was 24.7 months, and 23.0 months in 2005.[5] Further, the median approval time for BLAs alone in 2002 was much longer than the median approval time for BLAs and NDAs combined. According to the FDA, the median approval time for BLAs alone in 2002 was 19.9 months.[6] Thus, it is Amgen's statistics, not Roche's, that "do not accurately reflect current approval rates" for BLAs.

Amgen also argues that the FDA is meeting its performance goals, and is reviewing and acting on 90% of all standard new drug applications within 10 months. But the goal set forth in the PDUFA is only for the FDA to "act" on 90% of applications within 10 months, not to approve them. The FDA can act by issuing approvals, approvable letters, requests for additional clinical trials, or denials of the application. The 2004 Report to the President and Congress that Amgen relies on states, "[t]he percentage of first cycle approvals [within the initial 10 months] for standard applications was 36 percent in FY 2002 and 35 percent in FY 2003."[7] The approval rate was only about 20 percent in FY 2004. As Roche's BLA is a standard application, Amgen's own cited authority shows that, based on 2004 statistics, Roche has only

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[4] http://www.fda.gov/CBER/products/apprtime.htm

[5] http://www.fda.gov/cder/rdmt/NMEapps93-05.htm. Starting in 2004, certain groups of BLAs, recombinant proteins being one of them, were transferred to the Center for Drug Evaluation and Research ("CDER") from the Center of Biologics Evaluation and Research ("CBER"). That is why the number we use for 2004 is the combination of BLAs and NDAs from the CDER. The CBER median approval time for BLAs in 2004 was 19.77 months. See supra note 2.

[6] See supra note 2.

[7] Supra note 1 at pg. 4.

about a 20 percent chance of approval within the 10 month goal of the PDUFA (i.e., in the first review cycle).

Even without the ITC's requirement for a contract to sell the accused product as a threshold for cases in which there has been no infringing importation, the uncertainty of the approval process makes federal district courts reluctant to hear declaratory judgment cases under similar circumstances. In Hoescht, for example, even though the technical requirements for declaratory jurisdiction appeared to have been satisfied, the court declined to exercise that jurisdiction: "Not only is FDA approval uncertain, but the process or product itself may be altered during the interval in ways that are material to an infringement analysis. Any declaration issued by this Court now may be rendered moot by such alterations." 3 F. Supp. 2d at 112. See also Telectronics, 982 F.2d at 1526-27 (no declaratory judgment jurisdiction where defendant had not completed clinical trials and "[t]here was no certainty that the device when approved would be the same device that began clinical trials . . ."); Abbott Labs. v. Zenith Labs. Inc., 934 F. Supp. 925, 937-38 (N.D. Ill. 1995) (no declaratory judgment jurisdiction where defendant would not receive FDA approval until three months after complaint was filed).[8]

In support of its declaratory judgment action in Boston, Amgen relies heavily on Glaxo, Inc. v. Novopharm Ltd., 110 F.3d 1562, 1571 (Fed. Cir. 1997), where the court allowed a declaratory judgment action against an ANDA applicant who was "systematically attempting to

[8] Amgen has observed that its dispute with Roche over Amgen's EPO patents would be a "battle royal." Wright Decl. Exh. 9. Amgen would have the Administrative Law Judge launch this "battle royal" and proceed to trial without certainty regarding the chemical composition or processes that the FDA will be willing to approve. Further, given the ITC's fast schedule, the trial may be over before approval is granted. This general approach to litigating a case before a final product is certain was adopted by Judge Saxon in Certain Fluidized Bed Combustion Systems, Inv. No. 337-TA-213, 1985 ITC LEXIS 80 (Mar. 21, 1985), and, for good reason, has not been repeated. Further, the Fluidized Bed investigation did not involve a product that could not be finalized and sold due to the FDA prohibition of such acts.

complaint lacks merit, and Roche's motion to dismiss it for lack of a justiciable case or controversy was heard on May 10, 2006. The amended complaint here is equally meritless.

The Notice of Investigation here asks whether Roche has carried out any acts of importation, sales for importation, or sales within the United States after importation that are unfair because of alleged patent infringement, and directs any orders on summary determination of this issue to be forwarded to the Commission under the rules for final disposition of a case. Thus, Amgen's allegations concerning what Roche might do after the FDA approves CERA, if approval is ever granted, should not even be considered.

Even if the alleged future acts were within the scope of the Notice, Roche would still be entitled to summary determination. Few investigations have been allowed to proceed based on the "imminent" importation of an infringing product. The few "imminent" importation cases that have proceeded have involved respondents who have at least entered into a contract for commercial sale of the accused product to a customer in the United States, amounting to a "sale for importation" within the meaning of §337. See In re Certain Apparatus for the Continuous Production of Copper Rod, Inv. No. 337-TA-89, 214 USPQ 892 (1980) ("[Respondents] have entered into a contract for sale of a continuous copper rod system to be used [in the United States]. The proposed importation of the system is occurring, with a significant portion already imported.") (emphasis added); In re Certain Variable Speed Wind Turbines And Components Thereof, 337-TA-376, 1996 ITC LEXIS 251, *28 (May 30, 1996) ("Respondents . . . have entered into a contract for the sale and importation of accused devices. Therefore, there has been a "sale for importation" of accused devices as provided for in section 337.") (emphasis added); In re Certain Fluidized Bed Combustion Systems, Inv. No. 337-TA-213, 1985 ITC LEXIS 80, *15 ("the contract provides for delivery of the first piece of equipment