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Re: Reply to the FTC's Response to Citizen Petition by
IVAX Pharmaceuticals, Inc.
Docket No. 2005P-0008/CP-1

Ranbaxy Laboratories, Inc. ("Ranbaxy"), through its undersigned counsel, submits this reply to the response by the Federal Trade Commission ("FTC"), dated April 5, 2005, to the Citizen Petition filed by IVAX Pharmaceuticals, Inc. ("IVAX") (hereafter the "FTC Response" or "FTC's Response"). In its petition, IVAX argued that FDA should not remove from the Orange Book two patents, U.S. Patent No. RE 36,481 (the "'481 patent") and U.S. Patent No. RE 36,520 (the "'520 patent"), listed by Merck & Co. ("Merck") as claiming Zocor®. IVAX argues it is entitled to 180-day exclusivity as to these patents, because it was the first to file an Abbreviated New Drug Application ("ANDA") containing a paragraph IV certification,[1] and removing these patents from the Orange Book without expressly reserving IVAX's 180-day exclusivity would prevent IVAX from receiving 180-day exclusivity.[2] IVAX notes that FDA's regulation, 21 C.F.R. § 314.94(a)(12)(viii)(3), delays delisting to protect exclusivity where the first applicant has been sued for infringement. IVAX's position is that its right to 180-day

1. IVAX asserts in its petition that it believes that it was the first to file an ANDA for simvastatin tablets 5 mg, 10 mg, 20 mg, and 40 mg, which contains a paragraph IV certification as to the '481 and '520 patents.

2. Ranbaxy believes that it was the first to file an ANDA for simvastatin tablets, 80 mg, with a paragraph IV certification as to the '481 and '520 patents. Ranbaxy has also filed a Citizen Petition, requesting that FDA refrain from the approval of any ANDA for simvastatin 80 mg tablets until Ranbaxy's 180-day exclusivity has expired and confirm that Ranbaxy's rights to 180-day exclusivity with regard to ANDA No. 76-285 for simvastatin 80 mg have not been affected by FDA's delisting of the '481 patent and the '520 patent. Citizen Petition filed on behalf of Ranbaxy Laboratories Limited (February 1, 2005) ("Ranbaxy Citizen Petition") available at http://www.fda.gov/ohrms/dockets/dockets/05p0046/05p0046.htm (last visited May 12, 2005).

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exclusivity must be preserved by delaying the delisting of the patents without regard to whether the first applicant is sued for infringement.[3]

The FTC's Response

The FTC opposes IVAX's petition, arguing that, were FDA to adopt IVAX's interpretation of the pertinent regulations, a New Drug Application ("NDA") sponsor could no longer correct an improper Orange Book patent listing following the submission of an ANDA with a paragraph IV certification. Making the assumption that the patents at issue here were listed improperly, FTC urges FDA to reject IVAX's request because perpetuating improper listings "would have significant negative, implications for competition in the pharmaceutical industry, to the detriment of consumers."[4] The FTC discusses four kinds of potential harm that might flow from perpetuating improper listings. First, it notes that improper listings may lead to unwarranted 30-month stays, which inappropriately delay generic competition.[5] Second, it argues that improper listings may lead to abuses of 180-day exclusivity, which may also delay generic entry.[6] Third, it argues that 180-day exclusivity resulting from an improper listing harms consumers by temporarily preventing access to lower-cost generic versions of the drug.[7] Finally, it argues that FDA should avoid an interpretation that would prevent the FTC or a court from requiring the delisting of an improperly listed patent.[8] In addition to arguing competitive harm, FTC argues that IVAX is wrong in characterizing the 180-day exclusivity to which it is entitled as a right,[9] and that the FDA's regulation distinguishing between delisting when litigation is underway and delisting when no litigation has been instituted is appropriate.[10]

Ranbaxy's Reply

The FTC's comments rest on two erroneous assumptions: that IVAX seeks to prevent patent delistings and that the purpose of delisting will be to correct improper listings. In fact, IVAX and Ranbaxy seek to preserve 180-day exclusivity. That can be accomplished while still allowing NDA sponsors to remove patents from the list. Further, not all delistings will correct improper listings. Where delisting is undertaken for some other purpose, the policy concerns are different than those discussed by the FTC. In adopting a delisting policy, FDA must consider both proper and improper delistings.

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3. Citizen Petition filed by IVAX Pharmaceutical re: 180-Day Exclusivity and ANDA 76-052 (January 5, 2005) at 21-22.

4. FTC Response at 6.

5. Id.

6. Id.

7. Id. at 6-7.

8. Id. at 7-8.

9. Id. at 9-11.

10. Id. at 10.

Even if the FTC's assumptions were correct, Ranbaxy does not believe that FTC's predictions of anticompetitive consequences from failing to delist immediately are well-founded. Delayed delisting will not lead to abusive 30-month stays or "parking" 180-day exclusivity, and it will not disadvantage consumers. Nor will recognizing 180-day exclusivity impede the FTC's or a court's ability to rectify abusive practices.

Ranbaxy believes that the FTC's concerns can be addressed while still granting the relief sought by IVAX, and that doing so will promote, not discourage, competition. FDA has already recognized that it can and should defer delisting where litigation has been initiated. There is no principled reason to take a different position simply because litigation has not begun.

In addition, the FTC argues that 180-day exclusivity is an incentive rather than a right. However characterized, FDA must recognize that 180-day exclusivity is statutorily conferred, as demonstrated by IVAX and Ranbaxy in their respective Citizen Petitions. FTC has not addressed these legal arguments.

I. Recognizing 180-Day Exclusivity Does Not Necessarily Prevent Delisting.

The FTC response assumes that adopting IVAX's position would prevent the correction of improper listings. Neither IVAX nor Ranbaxy, however, has urged FDA to interpret its regulations in any way that would prevent the correction of improperly listed patents. Rather, IVAX and Ranbaxy seek to have FDA recognize the 180-day exclusivity to which they are entitled under the statute and regulations because each was the first to file an ANDA with a paragraph IV certification to a listed patent.[11] FDA could accomplish this objective in several ways. For example, FDA could delist the patent but continue to recognize the 180-day exclusivity and so inform subsequent ANDA applicants, either by letter or by entry of a notation in the Orange Book. Alternatively, FDA could accept the NDA holder's statement that the patent was submitted for listing in error, but maintain the Orange Book listing until the 180-day exclusivity expired.

In an analogous situation, FDA has elected to recognize a generic applicant's exclusivity by continuing the listing of even an acknowledged invalid patent in the Orange Book until the 180-day exclusivity expired.[12] Once this purpose is achieved and the exclusivity expired, FDA updates the Orange Book entry to reflect a patent's status. Preserving the 180-day exclusivity affects only the timing of the correction. Were FDA to apply the same approach when a patent is delisted following a paragraph IV certification, there would be no greater inaccuracy in Orange Book listings nor any additional disincentive to entry than exists under FDA's current approach.

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11. See e.g., Ranbaxy Citizen Petition at 1-2; Supplement to Citizen Petition filed by IVAX Pharmaceutical re: 180-Day Exclusivity for ANDA 76-052 (April 11, 2005) at 2.

12. See 21 C.F.R. § 314.94(a)(12)(viii)(B) (maintaining patent listing to preserve exclusivity even though patent declared invalid by a court after litigation).

II. The FTC Erroneously Assumes That Delisting Will Correct An Improper Listing.

The FTC's response assumes that patents will be delisted to correct listing errors, but fails to address the situation in which the delisting is in error. In this case, for example, it is the delisting that was in error. FTC summarily asserts that the simvastatin patents that Merck is attempting to delist do not claim the drug and implies that Merck seeks to delist the patents in response to FDA's 2003 regulation clarifying certain patents that may not be listed.[13] The FTC's assertion that the patents at issue here should not be listed is unwarranted, and its implication concerning Merck's motivation for delisting is based on speculation.

The two patents at issue claim a number of compounds per se, and in pharmaceutical compositions, related to simvastatin that are created when Zocor is manufactured. Ranbaxy has tested Zocor tablets for the presence of the compounds in the '481 patent and the '520 patent, and has found that several of these claimed compounds are present in Zocor.[14] The '481 and the '520 patents cover not only ingredients present in Zocor, but also the formulation, and composition, of Zocor.[15] For example, claim 24 of the '481 patent claims a pharmaceutical composition that include a pharmaceutically acceptable carrier and an effective amount of the compound of claim 1.[16] Several compounds claimed by claim 1 of the '481 patent are found in Zocor tablets and the tablets include a pharmaceutically acceptable carrier.[17] Under FDA's regulation, therefore, the '481 and the '520 patent claims the approved drug product, Zocor[18], and Merck properly listed the patent as claiming Zocor.[19]

Further, there is no reason to suppose that Merck delisted these patents in response to FDA's 2003 rule. In 2003 FDA amended 21 C.F.R. § 314.53(b) to clarify that patents that claimed packages, intermediates and metabolites are not properly listable patents because they are not present in the finished drug product.[20] Neither the '481 nor the '520 patent is a patent that

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13. FTC Response at 4.

14. Declaration of William D. Hare ("Hare Declaration") ¶ 20.

15. Hare Declaration ¶¶ 26,31.

16. Hare Declaration ¶¶ 26-28.

17. Hare Declaration ¶¶ 25-26.

18. 21 C.F.R. § 314.53(b)(1) provides that NDA sponsors must submit patent information for drug substance patents and for drug product (formulation and composition) patents. A drug product is defined as a finished dosage form that contains a drug substance generally in association with one or more other ingredients. 21 C.F.R. e.g., § 314.3. Both the '481 and the '520 patents cover ingredients combined with a drug substance (e.g., simvastatin) present in the finished dosage form approved by FDA. See also Applications for FDA Approval to Market a New Drug, 68 Fed. Reg. 36,676, 36,679 (June 18, 2003) (explaining that FDA's regulation will not allow the submission of "any patents claiming formulations or inactive ingredients not contained in the drug product described in the NDA") (emphasis added).

19. Hare Declaration ¶¶ 20-33.

20. Applications for FDA Approval to Market a New Drug, 68 Fed. Reg. at 36,680.

claims a package, intermediate or metabolite.[21] Merck's attempt to delist therefore seems unlikely to have been related to this rule.

The consequences of delisting an appropriately listed patent, and thereby extinguishing 180-day exclusivity, are even less acceptable than delisting an incorrectly listed patent. In such situations, a generic company is harmed by an action that is not in compliance with the Food, Drug, and Cosmetic Act.[22] Permitting NDA sponsors to delist, regardless of the obligations created by the FDCA, would significantly undercut the system's effectiveness. The FTC's response sidesteps any comment on these consequences, avoiding the issue by confining its remarks to the correction of improper listings. Once all the consequences are weighed, the balance falls decisively towards preserving 180-day exclusivity.

III. The Balance of Costs and Benefits Favors Recognition of 180-Day Exclusivity.

When an innovator seeks to delist a patent, it need not declare the reason for its action, and FDA will not know whether the delisting is appropriate or not. In an ideal world, when an NDA sponsor requested delisting, FDA would make a judgment about whether a patent should or should not be delisted. FDA, however, has decided not to make these judgments, a decision that Ranbaxy does not contest as part of this proceeding.[23] Given that FDA will not make case-by-case decisions, it must choose a policy that takes into account that any given delisting may be correct or incorrect. Leaving aside the requirements of law, which are addressed in IVAX's and Ranbaxy's Petitions, the appropriate policy inquiry should turn on which approach achieves the most equitable result and does the least harm to generic applicants, to innovators, and to the public. On balance, the harm associated with robbing an ANDA applicant of legitimate, and legitimately earned, 180-day exclusivity seems far greater than the harm, if there is any, associated with delaying the delisting of an incorrect listing.

A. Generic Applicants will be Harmed if NDA Sponsors can Negate 180-day Exclusivity.

The FTC's comments fail to recognize the harm to generic applicants caused by a withdrawal of the right to 180-day exclusivity. The ANDA applicant will lose a benefit on which it has relied in making business decisions, which it earned at substantial cost, and which

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21. Hare Declaration, Attachment B. Indeed, it appears Merck did not seek to delist either patent in 2003 when FDA promulgated its final rule amending 21 C.F.R. § 314.53(b). The delisting of the '481 and '520 patents occurred in mid-2004, well after the amendment of the regulation.

22. The FDCA requires that all patents that claim the drug and on which an infringement action could be based must be listed. Federal Food, Drug and Cosmetic Act § 355(b)(1).

23. Ranbaxy believes that FDA has an obligation to exercise some diligence in this respect. To reduce the possibilities of mistakes in listing, FDA has at least designed forms calculated to reduce the probability that a patent will be erroneously listed by an NDA sponsor. Applications for FDA Approval to Market a New Drug, 68 Fed. Reg. 36,676, 36,686-87 (June 18, 2003). FDA has done nothing at all to avoid delisting mistakes; allowing a patent holder to delist for any reason whatsoever. Yet the adverse consequences to third parties of incorrect delisting are markedly greater.

has affected the design of its product. This is a real, immediate harm to which the ANDA applicant has in no way contributed.

Equally important, generic applicants are likely to be harmed by allowing the NDA sponsor to decide whether the generic applicant will or will not receive 180-day exclusivity. The FTC's proposal to allow NDA holders to delist their patents after an ANDA applicant has qualified for 180-day exclusivity would empower NDA sponsors to nullify the exclusivity accorded to a first ANDA applicant at no cost to the innovator, merely by submitting a patent withdrawal notice. It is difficult to predict how that power might be used, but it is not difficult to think of hypotheticals. For example, an NDA sponsor might enter into an agreement with a subsequent ANDA applicant to remove the exclusivity awarded to the first applicant.

One can even imagine NDA sponsors listing and delisting for the purpose of undermining the incentives to file paragraph IV certifications. NDA sponsors intent on deterring ANDA applicants could react by withdrawing listed patents after the ANDA applicant has successfully invested time and resources designing around the patents and filed an application with a paragraph IV certification. Over time such conduct will act as a deterrent to ANDA applicants challenging patents. The result will be delayed generic entry, to the detriment of generic manufacturers and consumers alike.

Further, making 180-day exclusivity contingent on litigation may force ANDA applicants to provoke litigation in order to safeguard their 180-day exclusivity. Thus, for example, an ANDA applicant might decide to provide the minimum required information to the NDA sponsor in notifying the sponsor of a paragraph IV certification, rather than, as is often the practice now, providing more than is necessary so that the NDA sponsor will not have to file suit to make a fully informed judgment about the factual situation. Creating incentives for more patent lawsuits helps no one, not the NDA sponsor or generic applicant, which must finance the lawsuit, and not the public, which will suffer the delay in generic approval while the litigation proceeds.[24]

B. NDA Sponsors Should have No Interest In Whether Patents Are Removed From The Orange Book.

An NDA sponsor suffers no harm from a delay in delisting. The only consequence of delisting is to extinguish 180-day exclusivity; thus, once an NDA sponsor has notified FDA of its view that a product should be delisted, the NDA sponsor should have no reason to care whether FDA actually removes the patent from the Orange Book.

24. Patent lawsuits trigger 30 month stays, which clearly delay competition for longer than 180-days.

C. Delayed Delisting Will Not Harm Consumers.

The FTC's comment assumes that 180-day exclusivity may unduly delay generic entry and therefore prevent access to lower-cost generic drugs.[25] This is an argument against 180-day exclusivity in general, not one that is specific to delisting. It is surprising that the FTC should make it, inasmuch as the FTC has supported 180-day exclusivity in the past. As the FTC has recognized, the existing Hatch Waxman regulatory framework with its incentives for market entry by generic drug manufacturers has yielded a "remarkable record of success."[26] There is no reason to change the incentives for entry by generics.

It is not correct to assert, as FTC does, that 180-day exclusivity will always be detrimental to consumers. The extent to which consumers benefit from generic entry is a function both of when generics enter the market for any given drug , as well as how many ultimately enter the market. The earlier a generic enters, the greater the benefit to consumers. A generic company's decision to challenge patents and attempt to enter early to compete with the NDA sponsor depends on the expected return anticipated by the generic manufacturer.[27] Because the return expected with the 180-day exclusivity is so much higher than the return otherwise would be, the prospect of 180-day exclusivity may actually result in earlier entry than would occur if the patent had not been listed in the Orange Book. Consumers may receive a greater benefit from earlier entry by one or more generics that receives 180-day exclusivity, followed by the entry of additional generics, rather than a later entry by many, regardless of whether the patent was appropriately listed.

At worst, delaying delisting of an inaccurately listed patent has, if one accepts the FTC's logic, the consequence that, for 180-days, prices for the drug at issue may not fall as far as they otherwise would have. Prices will, of course, still fall, and fall dramatically. Much of the consumer benefit is captured when the first generic enters, and the remainder follows quickly.[28] When the exclusivity leads to entry occurring earlier than it would if no exclusivity were available, this can represent a net gain to consumers. If delisting at the whim of the NDA sponsor were to have a chilling effect on the submission of paragraph IV certifications, however, as Ranbaxy believes it would, any price reduction would come much later.

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25. FTC Response at 6.

26. FTC Statement at 1.

27. See David Reiffen & Michael R. Ward, Generic Drug Industry Dynamics, 3 (Feb. 2002) available at http://www.ftc.gov/be/workpapers/industrydynamicsreiffenwp.pdf (last visited May 12, 2005).

28. FTC itself has concluded that the 180-day exclusivity provision generally has not created a bottleneck to prevent FDA approval of subsequent eligible generic applicants. FTC, Generic Drug Entry Prior to Patent Expiration: An FTC Study, viii (July 2002) ("FTC Study") available at http://www.ftc.gov/os/2002/07/genericdrugstudy.pdf (last visited May 12, 2005). FTC's data indicates that "when not sued, first generic applicants, upon receiving FDA approval, begin commercial marketing in a timely manner that triggers the running of the 180 days and allows FDA approval of any subsequent eligible generic applicant once the 180 days has run." FTC Study at viii, 58.

In addition, allowing an NDA sponsor to decide, via listing or delisting, whether the first generic filer will get 180-day exclusivity will impart a random, unpredictable quality to 180-day exclusivity. Adding a variable which makes it uncertain whether a generic first applicant will in fact receive 180-day exclusivity, can only diminish, not increase, competition. To be successful, proactive strategies for early entry require significant resources in intellectual property capability and design expertise. A generic company that anticipates a substantial expected return for 180 days will have a greater incentive to develop the capacity to challenge innovator patents and enter the market than one that expects a lower return. The greater the uncertainty associated with obtaining 180-day exclusivity, however, the lower the expected return and the less likely a generic firm will be to challenge listed patents. If generics do not challenge patents, consumers will pay the higher prices associated with the NDA holder's monopoly for a longer period of time. There is therefore every reason for FDA to make 180-day exclusivity awards as certain as possible.

Allowing an innovator to defeat an ANDA applicant's 180-day exclusivity would result in: (1) direct and immediate harm to the ANDA applicant; (2) according NDA sponsors leverage over a first generic applicant; and (3) harm to consumers from any delay in entry by any generic applicant due to the expectation of lower return for the first-filer. Preserving 180-day exclusivity, on the other hand, results in: (1) preserving the incentives to competition by generics; (2) depriving the innovators of unfair leverage over generic competitors; and (3) fair treatment of the first generic applicant.

D. The FTC and FDA Have Already Recognized That Undermining Incentives To Challenge Patents Is Not In The Public Interest.

In 1994, FDA had to balance exactly the same costs and benefits in deciding whether it would delist if the first generic applicant with a paragraph IV certification had been sued. There, FDA observed that "[T]he agency agrees that the protection offered by 180-day exclusivity should not be undermined by changes from paragraph IV certification or by filing of original certifications other than paragraph IV certifications,"[29] and concluded that it should leave the delisted patents in the Orange Book. The result should be no different here.

The FTC supports FDA's regulation, 21 C.F.R. § 314.94(a)(12)(viii)(B), which delays delisting to protect exclusivity where the first applicant has been sued for infringement. In voicing support for this regulation, the FTC acknowledges that a delay in delisting is appropriate in order to protect the "incentive to challenge weak patent claims provided by the 180-day exclusivity."[30] The FTC fails to acknowledge, however, that the "incentive to challenge weak patent claims" provided by the statute is, in fact, the incentive to file a paragraph IV certification. If consumers benefit by challenges to weak patents, as FTC concedes they do, they do so regardless of whether patent litigation is filed or not.

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29. Abbreviated New Drug Application Regulations; Patent and Exclusivity Provisions, 59 Fed. Reg. 50,338, 50,348 (Oct. 3, 1994).

30. FTC Response at 10.

The FTC further states that, without the delay in delisting afforded by the regulation, "the delisting would provoke a perverse result by extinguishing the first ANDA filer's 180-day exclusivity based on its bringing a successful patent challenge."[31] Again, the FTC's argument rests on an erroneous assumption – in this case, the assumption that a successful patent challenge occurs only through litigation. In fact, the most successful patent challenge occurs when the NDA sponsor is convinced by the ANDA applicant's notification of filing of its paragraph IV certification, and chooses not to sue, allowing the generic competition without the costs and years of delay associated with litigation. Thus, the "perverse result" the FTC seeks to avoid is actually fostered by its proposal.[32]

The FTC's comments fail to acknowledge that the statute conditions the award of 180-day exclusivity based on the first applicant's notifying the NDA holder of its paragraph IV certification, not on the first applicant's actually defending an infringement suit. This issue was laid to rest in several court decisions.[33] The FTC ignores these decisions and proposes that FDA resurrect the "litigation" requirement as a basis for protection of a first applicant's entitlement to 180-day exclusivity. But, the FTC proposal would, in fact, undermine the incentive to challenge patents by submitting paragraph IV certifications.

IV. There Is No Principled Reason To Protect Exclusivity After Litigation Has Begun, But Not Before.

The FTC encourages FDA to continue to award 180-day exclusivity by deferring delisting during litigation,[34] but not before litigation. This distinction first arose when FDA determined that 180-day exclusivity would be triggered only by a successful defense by an ANDA applicant of a patent infringement suit brought by the NDA holder.[35] Since then, the courts have held that the statute does not permit FDA to condition the award of exclusivity on the successful defense of patent litigation.[36] Thus, there is no basis in the Hatch-Waxman scheme for such a distinction.

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31. Id.

32. In fact, Ranbaxy believes that this scenario may have occurred when Ranbaxy was the first applicant to submit an ANDA with a paragraph IV certification for tolterodine. There, the NDA sponsor delisted the relevant patent on receiving the notification from Ranbaxy that it had filed a paragraph IV certification and explaining why the listed patent was not infringed.

33. See Purepac Pharm. Co. v. Friedman, 162 F.3d 1201, 1203-05 (D.C. 1998); Granutec, Inc. v. Shalala, No. 97-1873 and No. 97-1874, 1998 U.S. App. LEXIS 6685, at *17-22 (4th Cir. Apr. 3, 1998); Mova Pharm. Corp. v. Shalala, 955 F. Supp. 128 (D.D.C. 1997) aff'd, 140 F.3d 1060 (D.C. Cir. 1998).

34. See FTC Response at 10-11.

35. Abbreviated New Drug Applications; Patent and Exclusivity Provisions, 59 Fed. Reg. 50,338, 50,367 (Oct. 3, 1994).

36. Mova Pharm. Corp. v. Shalala, 140 F.3d 1060 (D.C. Cir. 1998); FDA, Guidance for Industry: 180-Day Generic Drug Exclusivity Under the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act, 4 (June 1998).

There is no reason to think that an ANDA applicant that is sued will have incurred greater total expense than one that is not sued, or that consumers will benefit more from a generic that was the subject of litigation. There simply is no material distinction between the expenditures required to defend a lawsuit and those required to design around a patent. From the perspective of an ANDA applicant, the costs of defending a suit can range from the insignificant into the millions, but so too can the cost of designing around an infringing patent. Thus, the investment required to earn exclusivity is not dependent on whether an ANDA applicant was sued or not; in either case, the actual expenditures can be of similar magnitude.[37] Nor is the nature of the benefit reaped by consumers dependent on whether opening a market to generics is due to litigation or to successful patent design. Thus, no meaningful distinction can be drawn between the two situations. It is manifestly unfair, and legally unsound, to treat similarly situated ANDA applicants differently.[38]

V. Neither FTC's Nor A Court's Ability to Rectify Abusive Patent Listings Would Be Affected By Granting IVAX's Petition.

FDA's resolution of the delisting issue should not affect the FTC's or a court's ability to restrain anticompetitive behavior. The reason for the FTC or a court to order delisting is not because the listing alone causes an anticompetitive result; the problem to be remedied is the 30-month stay that can, in some circumstances, flow from the listing, or, potentially, abuse of 180-day exclusivity. It is not necessary for a patent to be delisted to prevent abuse of the 30-month stay provisions. A court or the FTC can order that a lawsuit not be brought within 45 days; or order that the NDA sponsor do nothing to initiate a 30-month stay. A company seeking to avoid enforcement action can assure the government that it will not institute a lawsuit within 45 days or take action that would result in a 30-month stay. The FTC's Consent Order with Bristol-Myers Squibb Company ("BMS"), which FTC references in its response, illustrates the point. There, BMS agreed not to make patent infringement claims with respect to particular patents and to do nothing that would trigger a 30-month stay for certain drugs.[39]

Similarly, it is not necessary to require delisting to police misuse of 180-day exclusivity. As FTC explains in its response, the principal abuse of 180-day exclusivity has involved

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37. Any assumption that litigation expenses necessarily exceed design expenses is unwarranted. Indeed, exclusivity can be triggered by a court decision in litigation involving other parties. FDA, Guidance for Industry: Court Decisions, ANDA Approvals, and 180-Day Exclusivity Under the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act, 4 (Mar. 2000). Or litigation can be swiftly concluded by a concession that a patent is not enforceable. Teva Pharm., USA, Inc. v. FDA, 182 F.3d 1003 (D.C. Cir. 1999).

38. See, e.g., El Rio Santa Cruz Neighborhood Health Center v. HHS, 300 F. Supp. 2d 32, 42-43 (D.D.C. 2004), aff'd, 396 F.3d 1265 (D.C. Cir. 2005); Bracco Diagnostics v. Shalala, 963 F. Supp. 20, 27-28 (D.D.C. 1997).

39. In the Matter of Bristol-Myers Squibb Co., Docket No. C-4076 (Decision and Order), at ¶¶ IV-VII (Apr. 14, 2003), available at http://www.ftc.gov/os/2003/04/bristolmyersquibbdo.pdf (last visited May 20, 2005).

"parking." FTC and the courts have direct remedies to sanction "parking," such as ordering the termination of the agreement. Thus, preventing delisting in circumstances in which a paragraph IV ANDA has been submitted will not interfere with antitrust remedies.[40]

VI. The FTC Need Not Be Concerned That Failures To Delist Immediately Will Lead To Abuse.

A. Unwarranted 30-Month Stays.

Ranbaxy shares the FTC's concern that ANDA approvals not be delayed based on 30-month stays resulting from erroneously listed patents. That concern is irrelevant here, however, because the delay in delisting a patent to preserve 180-day exclusivity would not result in additional delays in ANDA approval based on 30-month stays.

First, as a practical matter, an NDA sponsor that plans to try to enforce its patents by suing a generic applicant and thereby obtaining a 30-month stay is not going to try to delist the patent. Because 30-month stays are dependent on listing, only an NDA sponsor that did not intend to obtain a 30-month stay would seek to delist.

Second, even if an NDA sponsor's delisting was delayed during the 180-day exclusivity, and it did choose to sue an ANDA applicant and obtain a 30-month stay during that time, once the 180-day exclusivity delay came to an end, the patent would be delisted. In those circumstances, the ANDA subject to the 30-month stay would not have been delayed because it was already subject to the first ANDA filer's exclusivity and could not have been approved in any event.[41]

It is also important to note in this context that the FTC supports FDA's regulation under which patents proposed for delisting remain listed until exhaustion of exclusivity if the first applicant has been sued for infringement. The rules regarding 30-month stays are the same whether litigation ensues or not. Thus, it is inconsistent to approve of them in one scenario and not the other.

B. Exclusivity "Parking"

Ranbaxy also agrees with the FTC that it is important to prevent abuse of 180-day exclusivity through "parking" arrangements under which first applicants delay generic competition by delaying the triggering of exclusivity. This potential abuse, however, is not relevant to the question of whether 180-day exclusivity should be preserved in the case of an NDA sponsor's attempt to delist a patent. Again, as a practical matter, an NDA sponsor that has

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40. Moreover, following the amendments to the exclusivity provisions enacted in the Medicaid Prescription Drug Improvement and Modernization Act ("MMA") of 2003, ANDA applicants will not be able to enter into "parking agreements" without forfeiting their exclusivity. Federal Food, Drug, and Cosmetic Act § 505(j)(5)(D).

41. If the patent was improperly listed and does not claim the drug, it is likely that the NDA holder will not sue, and, even if it does, that litigation could be concluded relatively quickly.

a "parking" agreement with the first ANDA paragraph IV filer will not attempt to delist the patent because doing so would eliminate the 180-day exclusivity that keeps later ANDA applicants off the market. To the contrary, in those circumstances, the NDA sponsor will do everything it can to maintain the listing.

Second, even if delisting delays did increase the potential for "parking," the appropriate remedy is to take enforcement action against the "parking," not to penalize ANDA applicants who are not engaged in abusive behavior. The *potential* for abuse of a statutory right should not be a basis for denying the right.

Third, as is the case with the 30-month stay, FTC supports FDA's regulation, 21 C.F.R. § 314.94(a)(12)(viii)(B), which also delays patent delisting to protect exclusivity where the first applicant has been sued for infringement. Again, the FTC does not object to the rule when litigation is present though it raises exactly the same potential for "parking."

VII. The FTC Is Mistaken In Its Analysis Of The Food, Drug, And Cosmetic Act (FDCA) And Its Implementing Regulations.

In its response, the FTC quarrels with IVAX's characterization of 180-day exclusivity as a "right" rather than an "incentive." How to characterize 180-day exclusivity need not be resolved as part of this petition.[42] Whether a right, an incentive, or both, FDA must recognize that 180-day exclusivity is mandated by statute, and delisting in circumstances that would interfere with the statutory mandate is contrary to the FDCA.

Conclusion

The FTC response is based on an assumption that all attempted delistings will be to correct an improper Orange Book listing. In fact, there is no reason to think that delisting will necessarily be undertaken to correct improper listings. There are many reasons why a company might seek to delist, some of which could have serious anticompetitive consequences.

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42. FTC's comments do not address the case law that governs the assessment of whether a right is constitutionally protected. This case law supports IVAX's conclusion that 180-day exclusivity is a protected right. A statute can create a constitutionally protected interest when it places substantive limitations on official discretion. See, e.g., Olim v. Wakinekona, 461 U.S. 238, 249 (1983); see also Board of Regents v. Roth, 408 U.S. 564, 577 (1972). Hatch-Waxman, together with the MMA amendments and FDA's regulations, specifically identify the substantive factors that give rise to 180-day exclusivity, and limits FDA's ability to award or deny 180-day exclusivity. The statute, for example, provides how exclusivity is to be awarded depending on a number of specific factors, such as the certifications contained in other ANDAs or the result of court decisions and how the right is forfeited. Under these statutory provisions an applicant that complies with the existing substantive provisions has a legitimate vested right to 180-day exclusivity.

Even if the FTC's assumptions were correct, the competitive harm that the FTC foresees is not realistic. IVAX's proposal will not delay generic approvals based on unwarranted 30-month stays or "parking" arrangements. The short-term delay in competition that may result from 180-day exclusivity is less harmful to consumers than the disincentive to challenge patents that would be created by immediate delisting and loss of 180-day exclusivity. Further, it is simply unfair to an ANDA applicant that has spend millions of dollars developing a non-infringing product and exposed itself to patent litigation in reasonable reliance on the patent listing to allow the NDA sponsor to rob the applicant of exclusivity. FDA recognized all of these principles in 1994 when it declined to allow NDA sponsors to extinguish 180-day exclusivity in the context of litigation. There is no reason to distinguish between situations in which litigation has begun and those in which it has not, and the policy goals that impelled FDA to refuse to delist where litigation has begun should apply to the simvastatin patents as well.

Respectfully submitted,

Kate C. Beardsley

Carmen M. Shepard

DECLARATION OF WILLIAM D. HARE

I, William D. Hare, do hereby declare as follows:

1. I hold the position of Senior Counsel – Global Intellectual Property for Ranbaxy Inc. I submit this Declaration in support of the position of Ranbaxy Pharmaceuticals Inc., Ranbaxy Inc., and Ranbaxy Laboratories Limited (together, "Ranbaxy").

2. I obtained a B.S. in Chemical Engineering in 1985 from Clemson University in Clemson, SC; an M.S. in Bioengineering in 1988 from Clemson University; and a J.D./MBA in 1995 from the University of Houston in Houston, TX.

3. I was an attorney at Hogan & Hartson from 1995-1997 and Fish & Richardson from 1997-2002. I have practiced patent law since 1997.

4. I am a member of the bars of Oregon, Washington, D.C., and the United States Patent and Trademark Office.

5. In my position as Senior Counsel – Global Intellectual Property for Ranbaxy Inc., I share responsibility for all intellectual property and regulatory legal aspects of Ranbaxy's pharmaceutical business in the United States and in the rest of the world.

6. Ranbaxy Pharmaceuticals Inc., is a wholly owned subsidiary of Ranbaxy Inc., which is ultimately a wholly owned subsidiary of Ranbaxy Laboratories Limited, a publicly traded company. Ranbaxy Inc. is the agent of Ranbaxy Laboratories Limited in the United States. Ranbaxy Laboratories Limited has dealt and continues to deal with the United States Food and Drug Administration ("FDA") through Ranbaxy Inc. and Ranbaxy Pharmaceuticals Inc.

7. Ranbaxy manufactures and markets generic and branded generic pharmaceuticals, as well as active pharmaceutical ingredients. Ranbaxy Laboratories Limited also is engaged in the research and development of novel drugs.

8. Zocor®, manufactured by Merck & Co. ("Merck"), was approved by FDA on December 23, 1991 for the 5 mg, 10 mg, 20 mg, and 40 mg strengths, and on July 10, 1998 for the 80 mg strength.

9. Zocor® is one of the most widely prescribed drugs in the United States and had sales of approximately $4.5 billion in 2004.

10. In 1998, Ranbaxy began to explore the possibility of developing a generic version of Zocor® 80 mg strength, as well as other strengths.

11. Since its approval, Merck had listed a number of patents as claiming Zocor®. Among these are U.S. Patent Nos. RE 36,520 ("the '520 patent") and RE 36,481 ("the '481 patent"), and U.S. Patent No. 4,444,784 ("the '784 patent"). The '784 patent expires December 23, 2005, but has a pediatric exclusivity for an additional six months beyond the patent expiry.

12. In order to obtain approval of its generic version as quickly as possible, Ranbaxy determined that it must develop a generic drug product that did not infringe the listed patents.

13. Ranbaxy spent several million dollars developing its generic simvastatin products. In November 2001, Ranbaxy submitted to FDA, pursuant to 21 U.S.C. § 355(j), an abbreviated new drug application ("ANDA") for an 80 mg generic version of simvastatin (trade name Zocor®) tablets (ANDA No. 76-285). In accordance with 21 U.S.C. § 355(j)(2)(A)(vii)(IV), Ranbaxy included a statement in its ANDA

certification that U.S. Patent Nos. RE36,520 ("the '520 patent") and RE36,481 ("the '481 patent") were not infringed (a "paragraph IV certification").

14. Ranbaxy had reason to believe it would be the first to file a paragraph IV certification as to one or more of the Zocor® patents and therefore would qualify for 180-day exclusivity for the 80 mg tablet which would enable it to recoup its investment.

15. Ranbaxy included a paragraph III certification with respect to the '784 patent in its ANDA certification in accordance with 21 U.S.C. § 355(j)(2)(A)(vii)(III). Ranbaxy's paragraph III certification states the date of expiry of the '784 patent and requests approval of ANDA No. 76-285 upon expiry of the patent. The FDA will approve the ANDA upon that expiry date (as extended by pediatric exclusivity).

16. Ranbaxy was not sued by Merck for filing ANDA No. 76-285 with a paragraph IV certification within the 45 days specified at 21 U.S.C. § 355(j), or at any time since.

17. On September 26, 2003, FDA, by letter, granted "tentative approval" to Ranbaxy's ANDA No. 76-285. The tentative approval of Ranbaxy's ANDA signified that the ANDA has satisfied all requirements for approval, but that the effective date of the approval was deferred due to the paragraph III certification against the '784 patent.

18. Ranbaxy believes that it is the first ANDA applicant to submit a substantially complete ANDA containing a paragraph IV certification for simvastatin tablets (80 mg) with regard to the '481 and '520 patents.

19. On September 27, 2004, Ranbaxy discovered a statement on the FDA website for the "Electronic Orange Book" that FDA had "delisted" the '481 and '520 patents. This "delisting" came as a surprise to Ranbaxy. These patents claim compounds related to simvastatin that are synthesized during Merck's manufacture of Zocor® and that are present in Zocor®. A patent issued by the U.S. Patent and Trademark Office is presumed to be valid, Ranbaxy has no knowledge to cause a belief that these patents are not valid, and therefore does not believe that these patents were erroneously listed in the Orange Book.

The Patents Claim the Approved Drug - Zocor.

20. Ranbaxy has conducted Liquid Chromatography – Mass Spectrometry/Mass Spectrometry (LC-MS/MS) testing of Merck's Zocor® tablets which is described in detail in the declaration of Dr. T.G. Chandrashekhar, provided in **Attachment A**. That LC-MS/MS testing demonstrates that at least eight compounds claimed in the '481 patent and at least one compound claimed in the '520 patent are present in Merck's Zocor®. The '481 and '520 patents are provided as **Attachment B**.

21. The appendix to this declaration relates the compounds found in Merck's Zocor® to the claims in the '481 and '520 patents. This relationship was determined by generating structures for the compounds claimed by name in the '481 and '520 patents, calculating molecular weights for the compounds, and using that information to interpret the results provided by LC-MS/MS testing. The results include retention times, molecular weights, and fragmentation patterns. This testing is described in the declaration of Dr. T.G. Chandrashekhar (**Attachment A**).

The '481 Patent

22. Claim 1 provides a skeleton structure of the claimed molecule in which two side groups (R and R^1) are specified such that they can be substituted according to a listing in the claim of substitutable groups. Some of the substitutable groups are further substitutable with other groups. I estimate that the number of compounds potentially claimed in claim 1 is in the thousands, if not the tens of thousands.

23. The '481 Patent has a total of 29 claims. Claims 2-23 and 26-29 are dependent claims that claim a compound according to the compound of claim 1 or an intervening claim. Claims that depend from a prior claim incorporate all of the limitations of the claim from which it depends. As such, any limitations on claim 1 would also be limitations on all of the dependent claims. Claims 24 and 25 are independent claims that are directed to a pharmaceutical composition and a method of inhibiting cholesterol biosynthesis, respectively, using the compound of claim 1. Accordingly, even though claims 24 and 25 are independent claims, they include the compound claimed in claim 1.

24. Claims 10, 12, 13, 20, 23, 26, and 28 are dependent claims that ultimately depend from claim 1. These dependent claims describe and claim specific subsets from the large set of compounds claimed in claim 1.

25. Based on my experience as a patent attorney, claims 1, 10, 12, 13, 20, 23, 26, and 28 of the '481 patent cover compounds that Ranbaxy has determined by LC-MS/MS testing to be present in Merck's Zocor® tablets. See Appendix (describes information on claims 1, 10, 12, 13, 20, 23, 26, and 28 of the '481 patent). The '481

patent, therefore, claims Zocor®. These claims of the '481 patent do not claim a package, intermediate or metabolite.

26. In addition, claim 24 is a formulation and composition patent claim that claims Zocor®.

Claim 24 of the '481 patent reads as follows:

> 24. A hypocholesterolemic, hypolipidemic pharmaceutical composition comprising a pharmaceutically acceptable carrier and a nontoxic effective amount of a compound as defined in claim 1.

Zocor® is a pharmaceutical composition that is indicated for treatment of hypercholesterolemia and hyperlipidemia. As evident from the labeling, Zocor® contains pharmaceutically acceptable carriers (including cellulose, hydroxypropyl cellulose, and hydroxypropyl methylcellulose). Zocor® also contains nontoxic effective amounts of the compounds recited in claims 1, 10, 12, 13, 20, 23, 26, and 28. As detailed below, this claim covers the commercially available Zocor®.

27. The term "effective" as used in claim 24 means that there must be enough compound in the composition to cause HMG-CoA reductase inhibitory activity, but not necessarily enough to cause a therapeutic effect. See col. 26, lines 16-28. Compare, claim 25 (describing a method of inhibiting cholesterol biosynthesis by administering a therapeutically effective level of the compounds of claim 1). I reach this meaning of "effective" based on applying well-accepted law of claim construction to claim 24 and, in particular, to the difference in usage of "effective" in the phrases "non toxic effective amount" of claim 24 and "nontoxic therapeutically effective amount" of claim 25. In general, there is presumed to be a difference in meaning and scope when different words or phrases are used in separate claims. Because there is a difference in

the words and phrase used in claims 24 and 25, claim 24 cannot be interpreted to mean a therapeutically effective amount of the compound of claim 1.

28. The presence in Merck's Zocor® of the compounds described above is sufficient to meet the requirement of claim 24. Further, as described above, Merck's Zocor® includes a pharmaceutically acceptable carrier. As such, Merck's Zocor® falls within the scope of claim 24 of the '481 patent.

The '520 Patent

29. The '520 patent claims also cover both ingredients in Zocor® tablets as well as formulations and compositions of Zocor® tablets.

30. Based on my experience as a patent attorney, claims 1 and 18 of the '520 patent cover a compound that Ranbaxy has determined by LC-MS/MS testing to be present in Merck's Zocor® tablets. See Appendix (describes information on claims 1 and 18 of the '520 patent). These claims of the '520 patent do not claim a package, intermediate or metabolite.

31. Claim 24 of the '520 patent makes a formulation and compositional patent claim over Zocor® tablets. This claim reads as follows:

> 24. A hypocholesterolemic, hypolipidemic pharmaceutical composition comprising a pharmaceutically acceptable carrier and a nontoxic effective amount of a compound as defined in claim 1.

This claim covers the commercially available Zocor®. As described above, Zocor® is a pharmaceutical composition that is indicated for treatment of hypercholesterolemia and hyperlipidemia. As evident from the labeling, Zocor® contains pharmaceutically acceptable carriers including cellulose, hydroxypropyl cellulose, and hydroxypropyl

methylcellulose. Zocor® also contains nontoxic effective amounts of the compound recited in claims 1 and 18.

32. For the same reasons described above with respect to the '481 patent, the term "effective amount" in claim 24 of the '520 patent should be interpreted to mean enough compound in the composition to cause HMG-CoA reductase inhibitory activity, but not necessarily enough to cause a therapeutic effect. Notably, as in claim 25 of the '481 patent, claim 25 of the '520 patent claims a method of inhibiting cholesterol biosynthesis by administering a nontoxic therapeutically effective amount of the compound of claim 1. Because of this difference in usage of the words and phrases "nontoxic effective amount" in claim 24 and "nontoxic therapeutically effective amount" in claim 25, claim 24 cannot be interpreted to mean a therapeutically effect amount.

33. The presence in Merck's Zocor® of the compounds described above is sufficient to meet the requirement of claim 24. Further, as described above, Merck's Zocor® includes a pharmaceutically acceptable carrier. As such, I conclude that Merck's Zocor® falls within the scope of claim 24 of the '520 patent.

* * * * *

I declare under penalty of perjury that the foregoing is true and correct. Executed this 19th day of May, 2005 in Princeton, NJ.

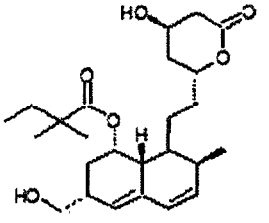
William D. Hare

William D. Hare

APPENDIX

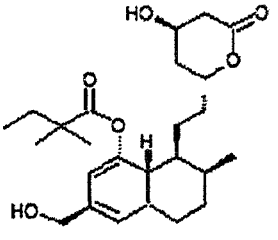
Information on the '481 Patent

1. Two compounds detected in Zocor® tablets have a molecular weight of 434 and may be one of the following structures recited in claim 1 of the '481 patent:



Molecular Formula = $C_{25}H_{38}O_6$
Formula Weight = 434.5656
Monoisotopic Mass = 434.26684 Da

(a)



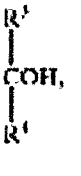
Molecular Formula = $C_{25}H_{38}O_6$
Formula Weight = 434.5656
Monoisotopic Mass = 434.26684 Da

(b)

These compounds result by making the following substitutions in claim 1:

R^1 is a C_{1-10} alkyl (see col. 54, line 26);

R is the following structure found at col. 54, line 20:



;

R^3 and R^4 are hydrogen, as specified in claim 1 at col. 55, lines 36-37; and

In compound (a), a is a double bond, b is a single bond, and c is a double bond, as specified in claim 1 at col. 57, lines 49-51.

In compound (b), a is a single bond, b is a single bond, and c is a single bond, as specified in claim 1 at col. 57, lines 49-51.

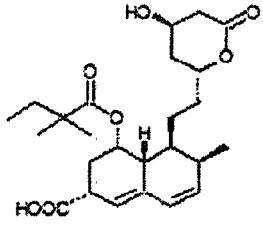
2. The compound (a) above is the first named compound of claim 10 of the '481 patent. The relevant portion of claim 10 reads as follows:

> 10. A compound of claim 9 selected from the group consisting of:
>
> (1) 6(R)-[2-[8(S)-(2,2-dimethylbutyryloxy)-2(S)-methyl-6(R)-hydroxymethyl-1,2,6,7,8,8a-(R)-hexahydronaphthyl-1(S)]ethyl]-4(R)-hydoxy-3,4,5,6-tetrahydro-2H-pyran-2-one;

3. The compound (b) above is the named compound of claim 26 of the '481 patent. Claim 26 reads as follows:

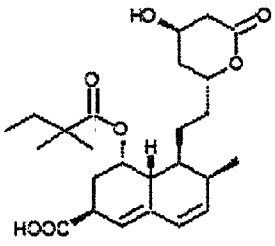
> 26. The compound of claim 9 which is 6(R)-[2-[8(S)-(2,2-dimethylbutyryloxy)-2(S)-methyl-6(S)-hydroxymethyl-1,2,3,4,4a(R)-hexahydronaphthyl-1(S)ethyl]-4(R)-hydoxy-3,4,5,6-tetrahydro-2H-pyran-2-one.

4. Four compounds detected in Zocor® tablets have a molecular weight of 448 and may be one or more of the following structures recited in claim 1 of the '481 patent.



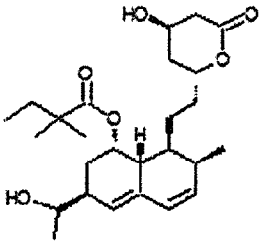
Molecular Formula = $C_{25}H_{36}O_7$
Formula Weight = 448.5491
Monoisotopic Mass = 448.246105 Da

(a)

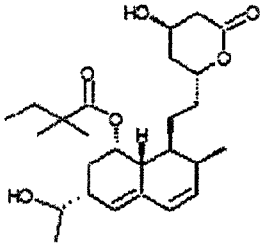


Molecular Formula = $C_{25}H_{36}O_7$
Formula Weight = 448.5491
Monoisotopic Mass = 448.246105 Da

(b)



Molecular Formula = $C_{26}H_{40}O_6$
Formula Weight = 448.5922
Monoisotopic Mass = 448.28249 Da



(c) (d)

These compounds result by making the following substitutions in claim 1 of the '481 patent:

R^1 is a C_{1-10} alkyl (see col. 54, line 26)

For compounds (a) and (b) above, R is the following structure found at col. 54, line 20:

CO_2R^6;

with R^6 being hydrogen, as specified in claim 1 at col. 55, lines 27-28.

For compounds (c) and (d) above, R is

;

with R^3 being hydrogen and R^4 being a C_{1-5} alkyl, as specified in claim 1 at col. 55, lines 36-38.

Each of a and b represents a double bond and c represents a single bond, as specified in claim 1 at col. 57, lines 49-51.

5. The compound (a) above is the first compound named in claim 12 of the '481 patent. The relevant portion of claim 12 reads as follows:

> 12. A compound of claim 11 selected from the group consisting of:
>
> (1) 6(R)-[2-[8(S)-(2,2-dimethylbutyryloxy)-2(S)-methyl-6(R)-carboxy-1,2,6,7,8,8a(R)-hexahydro-naphthyl-1(S)]ethyl]-4(R)-hydroxy-3,4,5,6-tetrahydro-2H-pyran-2-one;

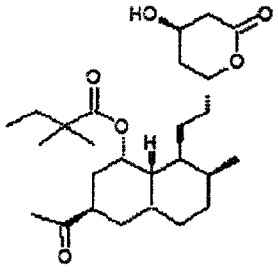
6. The compound (b) above is the compound named in claim 28 of the '481 patent. Claim 28 reads as follows:

> 28. The compound of claim11 which is 6(R)-[2-[8(S)-(2,2-dimethylbutyryloxy)-2(S)-methyl-6(S)-carboxy-1,2,6,7,8,8a(R)-hexahydronaphthyl-1(S)]ethyl]-4(R)-hydroxy-3,4,5,6-tetrahydro-2H-pyran-2-one.

7. The compounds (c) and (d) above are the first and second named compounds, respectively, of claim 13 of the '481 patent. The relevant portions of claim 13 read as follows:

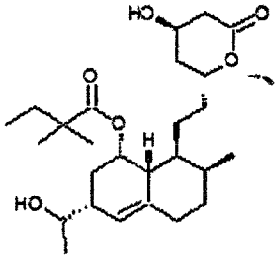
> 13. A compound of claim 9 selected from the group consisting of:
>
> (1) 6(R)-[2-[8(S)-(2,2-dimethylbutyryloxy)-2(S)-methyl-6(S)-(1-hydroxyethyl) 1,2,6,7,8,8a-(R)-hexahydronaphthyl-1(S)]ethyl]-4(R)-hydroxy-3,4,5,6-tetrahydro-2H-pyran-2-one;
> (2) 6(R)-[2-[8(S)-(2,2-dimethylbutyryloxy)-2(S)-methyl-6(R)-(1-hydroxyethyl) 1,2,6,7,8,8a (R)-hexahydronaphthyl-1(S)]ethyl]-4(R)-hydroxy-3,4,5,6-tetrahydro-2H-pyran-2-one;

8. Three compounds detected in Zocor® tablets have a molecular weight of 450 and may be one or more of the following structures recited in claim 1 of the '481 patent:



Molecular Formula = $C_{26}H_{42}O_6$
Formula Weight = 450.6081
Monoisotopic Mass = 450.29814 Da

(a)



Molecular Formula = $C_{26}H_{42}O_6$
Formula Weight = 450.6081
Monoisotopic Mass = 450.29814 Da

(b)

These compounds results by making the following substitutions in claim 1 of the '481 patent:

R^1 is a C_{1-10} alkyl (see col. 54, line 26);

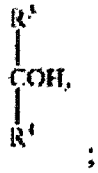
For compound (a), R has the following structure at col. 54, line 20:

;

R^3 is a C_{1-10} alkyl, as specified in claim 1 at col. 55, lines 36-37, and

each of a, b and c are single bonds, as specified in claim 1 at col. 57.

For compound (b), R has the following structure found at col. 54, line 20:



;

R^3 is a hydrogen and R^4 is a C_{1-10} alkyl, as specified in claim 1 at col. 55, lines 36-37; and a is a double bond and b and c each are single bonds, as specified in claim 1 at col. 57, lines 49-51.

9. The compound (a) is named in claim 20 of the '481 patent. Claim 20 reads as follows:

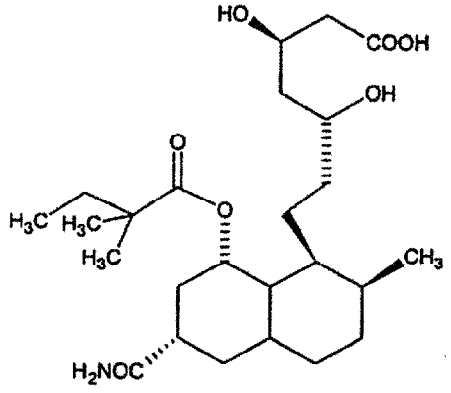
> 20. A compound of claim 19 which is:
> 6(R)-[2-[8(S)-(2,2-dimethylbutyryloxy)-2(S)-methyl-6(S)-(1-oxoethyl)-1,2,3,4,4a(S),5,6,7,8,8a(S)-decahydro-naphthyl-1(S)]ethyl]-4(R)-hydroxy-3,4,5,6-tetrahydro-2H-pyran-2-one.

10. The compound (b) is named as the third compound in claim 23 of the '481 patent. The relevant portion of claim 23 reads as follows:

> 23. A compound of claim 22 selected from the group consisting of:
> [. . . .]
> (3) 6(R)-[2-[8(S)-(2,2-dimethylbutyryloxy)-2(S)-methyl-6(R)-(1 hydroxyethyl) 1,2,3,4,6,7,8,8a(R)-octahydronaphthyl-1(S)]ethyl]-4(R)-hydroxy3,4,5,6-tetrahydro-2H-pyran-2-one.

Information on the '520 Patent

11. One compound detected in Zocor® tablets has a molecular weight of 469 and the following structure, as claimed in claim 1 of the '520 patent:



with the following substitutions in the compound formula II of claim 1:

R = H_2NCO- (aminocarbonyl) (see claim 17 and claim 5)

R_1 = 1,1-dimethylpropyl (see claim 6)

R_2 = hydrogen (see claim 1, column 56, line 35)

a, b, and c are all single bonds (see claim 14)

12. This compound is the third named compound of claim 18 of the '520 patent. The relevant portion of claim 18 reads as follows:

> 18. The compound of claim 17 selected from the group consisting of:
>
> [. . . .]
>
> (3) 7-[1,2,3,4,4a(S),5,6,7,8,8a(R)-decahydro-2(S)-methyl-6(S)-aminocarbonyl)-8(S)-(2,2-dimethylbutyryloxy)-1(S)-naphthyl]-3(R),5(R)-dihydroxyheptanoic acid;