DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

February 27, 2004

Kenneth C. Cancellara, Q.C.
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Re: Docket Nos. 99P-2778/CP1 and 00P-1556/CP1

Dear Mr. Cancellara and Mr. Dormer:

This letter responds to the citizen petition dated July 27, 1999, submitted on behalf of Biovail Corporation International (Biovail), and the citizen petition dated October 4, 2000, submitted by Robert Dormer, Esq., of Hyman, Phelps & McNamara, P.C. (HP&M). Both petitions request that the Food and Drug Administration (FDA) make available to the public through its Web site certain information relating to first-filers of abbreviated new drug applications (ANDAs) with Paragraph IV certifications. For the reasons explained below, the Biovail petition is granted and the HP&M petition is granted in part and denied in part.

Biovail requests that FDA disclose to the public through its Web site (1) the name of the innovator drug and approved dosage strengths, (2) the date the first Paragraph IV-containing ANDA is submitted, and (3) the dosage strengths included in that ANDA.

HP&M requests that FDA disclose to the public through its Web site (1) the date on which the first Paragraph IV-containing ANDA was received by FDA, and (2) the patents to which ANDA applicants have made Paragraph IV certifications and the date of the first such certification for each patent. HP&M also requests that FDA adopt new policies whereby (1) if an ANDA holder inquires whether it holds the first-filed ANDA with a Paragraph IV certification on a drug product, the Agency will answer in the affirmative or in the negative without divulging the name of other applicants or other confidential information, and (2) if an ANDA holder inquires whether it has filed the first Paragraph IV certification for a specific patent, the Agency will answer in the affirmative or negative.

I. DISCUSSION

Under sections 505(b)(1) and (c)(2) of the Act, an innovator drug applicant must include information in its NDA about patents that claim the drug or the method of using the drug that is

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the subject of the NDA. When an NDA is approved, the name of the drug product (referred to as the listed drug) and the related patent information are published in FDA's *Approved Drug Products With Therapeutic Equivalence Evaluations* (the Orange Book).

Under section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), FDA may approve an ANDA that duplicates a listed drug (a previously approved innovator drug) without submission of all the information contained in a new drug application (NDA). When seeking approval of an ANDA referencing a particular listed drug, a generic drug applicant must include in its ANDA a patent certification for each patent for the listed drug that is listed in the Orange Book.[1] Under section 505(j)(2)(A)(vii)(IV) of the Act, one possible certification, a Paragraph IV certification, claims that the patent is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the drug product for which the ANDA is submitted.[2]

A. List the Name and Approved Strength of the Innovator.

In response to Biovail's petition, FDA has established a pilot program to list Paragraph IV certifications on the Internet at http://www.fda.gov/cder/ogd/ppiv.htm. The pilot program list includes:

- the generic name of the drug
- the dosage form of the reference listed drug (RLD)
- the dosage strengths of the RLD, and
- the trade name of the RLD

The pilot program list is updated monthly. FDA regards the institution of this pilot program as granting Biovail's first request that the FDA Web site list the name and approved dosage strengths of the innovator drug if an ANDA is submitted that contains a Paragraph IV certification.

B. List the Date of Submission of the first Paragraph IV-containing ANDA.

Biovail also requests that FDA list the date that the first Paragraph IV-containing ANDA is submitted. The Agency grants Biovail's request to disclose this date for the following reasons.[3]

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[1] See Section 505(j)(2)(A)(vii) of the Act.

[2] Under section 505(j)(5)(B)(iv) of the Act, the first ANDA applicant with a Paragraph IV certification may be eligible for 180 days of market exclusivity (180-day exclusivity). This is the only means by which exclusivity for a generic drug may be obtained under the Act. Therefore, there is often significant competition to be the first ANDA applicant with a Paragraph IV certification.

[3] HP&M requests that FDA disclose on its Web site the date on which the first Paragraph IV-containing ANDA was received by the Agency. This request is similar to the second request made by Biovail, except that it turns on the date that the Agency received the first Paragraph IV-containing ANDA, rather than the date that such ANDA was submitted. As outlined in the text, the difference between the date that a Paragraph IV certification is submitted and the date that it is received is not one of semantics. The date of submission of such a certification in a subsequently received ANDA is normally the relevant date for exclusivity purposes. As modified to reflect the request made by Biovail, HP&M's request is granted for the reasons stated above.

Our regulations are very specific regarding the disclosure of information from unapproved NDAs and ANDAs. We will not disclose the existence of an application or abbreviated application before an approvable letter is sent unless the existence of that application is publicly known. Regardless of whether the existence of an application or abbreviated application is known, no data or information in that unapproved application or abbreviated application are publicly available before the Agency sends the applicant an approval letter. See 21 CFR § 314.430. On the date that a Paragraph IV certification is first made in an ANDA with respect to a particular drug, that ANDA is always unapproved.

However, it is possible that certain information regarding unapproved applications can be made publicly available without revealing specific information regarding a specific application. In accordance with this principle, when the Agency receives an ANDA with a Paragraph IV certification, we currently post on our Web site the generic name of the drug for which an ANDA has been submitted, the dosage form of the reference listed drug, the dosage strengths of the RLD, and the trade name of the RLD. Although this information is contained in ANDAs, none of this information identifies the applicant or potentially discloses information that could identify that applicant. Similarly, we have also responded to individual inquiries concerning the existence of an ANDA for a particular drug with a Paragraph IV certification. Although we have not identified which ANDA contains the certification, since 1994, we have stated whether we have received an application containing such a certification. See 59 Fed. Reg. 50334, 50354 (October 3, 1994).

The Agency's policies regarding the release of general information regarding pending ANDAs containing Paragraph IV certifications have been in place for some time. Given the current state of technology, we now believe that our practice should be updated. In 1994, the Internet was not widely used. Responding to individual telephone requests for non-application specific information was an appropriate means of disseminating that information. Today, however, we believe that this practice is inadequate for a number of reasons. First, the Agency's resources are unduly burdened by repetitive telephonic inquiries from multiple applicants and potential applicants who call the Agency on a daily basis to ask whether a particular drug has become the subject of an ANDA containing a Paragraph IV certification. Second, the process of responding to individualized requests made to the Agency without making affirmative disclosures to the public as a whole effectively rewards more sophisticated entities who are able to learn whether such an ANDA has been submitted at the expense of less sophisticated entities who may not be aware that this information can be obtained through this informal process. Posting this information on the Internet gives all interested parties access to the information at the same time, thereby reducing the Agency's resource burden and equalizing access to information by all requesters through affirmative transparency.

The HP&M petition asks that we disclose the date that a Paragraph IV certification for a drug is first received, whereas the Biovail petition asks that we post the date that such a certification is first submitted. We had previously stated that we would not disclose the specific date that the

first Paragraph IV certification was received, or the applicant's identity.[4] This practice was adopted "to preserve the confidentiality of the applicant." Id. However, disclosing the date of submission of the first Paragraph IV certification (which may not be the same as the date that the application containing this certification was received), does not disclose the identity of the applicant.[5] Our practice has been to encourage individual potential applicants who wished to inquire whether an ANDA had been received for a particular drug to contact the Agency, id.; the Agency would then answer their question in either the affirmative or the negative.

The date an ANDA is submitted is crucial to determining whether an ANDA is eligible for 180-day exclusivity under section 505(j)(5)(B)(iv)(II)(bb) of the Act. First applicant status turns on the date that an applicant first "submits [for approval] a substantially complete application that contains and lawfully maintains a [Paragraph IV] certification. . . ." The date of submission is the date that an ANDA with a Paragraph IV certification is stamped by the appropriate FDA mail room. The ANDA is not received at that time, however. The determination on whether the application is substantially complete, and thus may be received, is made within 60 days after the date of submission. If the application is determined to be substantially complete, the Agency will receive the application for review. See 21 CFR 314.101(b)(1). In that circumstance, the date of the Paragraph IV certification contained in the ANDA will be the date that the application was submitted, not the date that it was received, in accordance with the statutory provision. If, however, a Paragraph IV certification is submitted in an ANDA that is not substantially complete, the ANDA will be refused to be received. In that circumstance, the applicant will have the opportunity to file an amendment to the ANDA to make it substantially complete. If such an amendment is received, the date that the substantially complete application containing a Paragraph IV certification was submitted is the date that the amendment is submitted.

The date that the first Paragraph IV certification is submitted cannot be determined until the application is received for review. Thus, there will of necessity be a delay between the time that the first Paragraph IV certification in a substantially complete application is submitted and the time that information appears on the Web site. As described above, the Agency currently discloses non-specific ANDA-related information on its Web site on a monthly basis. To enhance the usefulness of the disclosure of the submission date of the first Paragraph IV certification, the Agency will update its Web site disclosures of this information at least bi-

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[4] As we wrote in 1994, "The agency, therefore, will disclose whether an ANDA has been received for a particular drug, but, in order to preserve the confidentiality of the applicant, will not disclose when the application had been received or the applicant's identity." 59 Fed. Reg. 50334, 50354 (October 3, 1994).

[5] We do not believe that we are required to go through notice and comment rulemaking to implement a change in our disclosure of the date of submission. Cf. Parlayzed Veterans of America v. D.C. Arena, 117 F.3.d 579, 586 (D.C. Cir. 1997); Alaska Professional Hunters Ass'n v. FAA, 177 F.3d 1030 (D.C. Cir. 1999). FDA's statement in 1994 appeared to implicitly address disclosure of the date of an ANDA's submission along with the identity of the applicant, rather than disclosure of the date of submission alone, because disclosure of the submission date alone does not raise confidentiality concerns. Moreover, individuals who inquire on a daily basis could effectively estimate the date that an ANDA containing a paragraph IV certification was received by noting when the Agency changed its answer from the negative to the affirmative in responding to individual inquiries. Although the date the ANDA is received is not the same as the date the ANDA is submitted, the 60-day time frame for decisions on receiving ANDAs can permit an outside party to effectively estimate when the ANDA was submitted.

monthly. To reduce the burden on Agency resources, the disclosure of the first dates of submission of substantially complete, Paragraph IV-containing ANDAs will be made only on a prospective basis.

Determining whether a particular ANDA applicant is eligible for 180-day exclusivity, whether multiple ANDA applicants might be eligible, and whether forfeiture provisions have removed the eligibility of particular applicants are complicated statutory and factual inquiries. The determination regarding which applicant(s) is or are "first" is not made until one or more ANDAs are ready for approval. The determination turns on a multitude of contingencies that can arise after the date that a substantially complete ANDA with a Paragraph IV certification is first submitted for a particular drug. Knowledge of the date that an ANDA applicant first submitted a Paragraph IV certification alone will not enable anyone to conclude definitively that 180-day exclusivity will be awarded to an applicant that submitted a Paragraph IV certification on that date, or even whether that applicant will be among any applicants ultimately awarded exclusivity. The Agency therefore will post disclaimers on the Web site that will help ensure that the information disclosed is understood in context and will caution persons reading it not to use the information posted to draw final conclusions on an award of 180-day exclusivity.

C. List the Dosage Strengths included in the ANDA.

Biovail also asks that the Agency disclose the dosage strength as to which the first ANDA that contains a Paragraph IV certification seeks approval. The Agency will do so. As noted above, FDA currently discloses the dosage strength of the RLD. When the RLD is available in only one dosage strength, the dosage strength of the ANDA product and the RLD will generally be the same unless FDA has approved an ANDA suitability petition under 21 CFR 314.93, requesting a change in dosage strength from that of the RLD. When there is more than one dosage strength for an RLD, an ANDA applicant is usually not required to seek approval for all dosage strengths. Nonetheless, an ANDA applicant that submits a Paragraph IV certification on the first day such certifications are submitted for a particular drug might seek approval for more than one dosage strength. As is the case with disclosure of the date of first Paragraph IV certifications, disclosure of the dosage strengths in ANDAs with such certifications is consistent with our practice of providing non-identifying information that will assist in considerations of eligibility for 180-day exclusivity periods.

D. List the Patents to which an ANDA Applicant has made a Paragraph IV Certification.

HP&M requests that the Agency disclose the patents to which ANDA applicants have made Paragraph IV certifications and the date of the first certification for each patent. The Agency declines to do so. The request was based on the former wording of the Act, which provided that eligibility for exclusivity was to be determined on a patent-by-patent basis. The date that a Paragraph IV certification was first submitted for a particular patent was highly relevant under the former statutory language. An ANDA applicant that was first to submit a Paragraph IV certification to any patent submitted for the listed drug might obtain 180-day exclusivity. However, since HP&M filed its citizen petition, the statutory language has changed. Eligibility

for 180-day exclusivity for applications governed by the amended statute no longer turns on individual patents, but is product-based. Under section 505(j)(5)(B)(iv) of the Act as amended, 180-day exclusivity eligibility is determined by the date that an ANDA containing one or more Paragraph IV certifications is submitted for a particular drug. Once a substantially complete ANDA that is subject to the amended statutory provisions has been submitted with a Paragraph IV certification for any patent for the listed drug, the date of such a certification closes the eligibility for such exclusivity. Disclosing the specific patents for which Paragraph IV certifications have been made and the date of the first such certification for each patent might create confusion and thus would serve no public purpose. The request is therefore denied.

E. Answer Questions Regarding First Applicant Status.

HP&M requests that FDA adopt new policies whereby (1) if an ANDA holder inquires whether it holds the first-filed ANDA with a Paragraph IV certification on a drug product, the Agency will answer in the affirmative or in the negative without divulging the name of other applicants or other commercial information, and (2) if an ANDA holder inquires whether it holds the first-filed position on a Paragraph IV certification for a specific patent, the Agency will answer in the affirmative or negative. For the reasons that follow, these requests are denied.

The Agency is adopting through this response the practice of displaying on its Web site the dates that a Paragraph IV certification is first made for a drug. As stated above, the reasons for this decision are conservation of resources and transparency. Responding to individual requests regarding first applicant status would harm these goals. Moreover, because the requests seek "yes" or "no" answers to the question of whether an applicant is the first to file, such a practice would be inherently misleading. There will often be multiple first Paragraph IV certifications for a particular drug. An applicant that is told that it is "the first" will not receive comprehensive information concerning its eligibility for 180-day exclusivity, or what such eligibility may mean. Similarly, an applicant that was told that it was not "the first" would not know whether it was one of multiple "first" applicants or not a "first" applicant at all. Moreover, information concerning whether an applicant is the "first" to file with respect to any particular patent is of no public value for applications affected by intervening statutory changes. These requests are therefore denied.

II. CONCLUSION

The Agency believes the pilot program has successfully provided to industry and the public current, non-confidential information regarding ANDAs with Paragraph IV certifications. Therefore, the Agency will continue listing on its Web site the same information provided during the pilot program, and will update this list more frequently than the current monthly basis. In addition, the Agency will include prospectively on that Web site the date that a drug first becomes the subject of a Paragraph IV certification and the dosage strengths that are the subject of the certification. However, the Agency will not reveal to the public or to the individual applicant whether a particular ANDA applicant with a Paragraph IV certification holds first applicant status for a drug product or a patent listed for a drug product; nor will it disclose on its

Web site the date that a Paragraph IV certification was submitted for any particular patent. Accordingly, Biovail's petition is granted, and HP&M's petition is granted in part and denied in part.

Sincerely yours,

William K. Hubbard
Associate Commissioner for
Policy and Planning