

December 16, 2010

Margaret A. Hamburg
Commissioner of Food and Drugs
Food and Drug Administration
10903 New Hampshire Ave.
Silver Spring, MD 20993-0002

Donald M. Berwick
Administrator
Centers for Medicare & Medicaid Services
200 Independence Avenue S.W.
Washington, D.C. 20201

By Electronic Delivery

RE: Parallel Review of Medical Products (Docket No. FDA-2010-N-0308)

Dear Commissioner Hamburg and Administrator Berwick:

The Plasma Protein Therapeutics Association (PPTA) appreciates this opportunity to comment on the Notice published by the Food and Drug Administration (FDA) and Centers for Medicare and Medicaid Services (CMS) regarding the parallel review of medical products.¹ As an association deeply committed to the health and safety of the patients it serves, these comments on the proposed parallel review process are intended to ensure that the process the agencies develop is one that will promote, and not impede, access to innovative medical technologies.

PPTA is the association that represents the manufacturers of plasma protein therapies. These therapies are produced from donations of human blood plasma and, in the case of blood clotting factors, also through biotechnology. Therapies produced from plasma and by the use of recombinant technology are collectively referred to as plasma protein therapies. Most importantly, plasma protein therapies treat serious medical conditions for a very small, fragile patient population in the United States. PPTA members produce more than 80 percent of the plasma protein therapies for the U.S. market and more than 60 percent of such therapies for global consumption. From this perspective, PPTA offers some general comments on the proposed parallel review process and then addresses some of the specific questions listed in the Notice.

¹ Parallel Review of Medical Products, 75 Fed. Reg. 57045 (Sept. 17, 2010) (the Notice).

Comments on Proposed Parallel Review

As FDA and CMS acknowledge in the Notice, despite advances in scientific discoveries, there are barriers to bringing innovative medical products to market. In particular, FDA and CMS note that the number of drug and biological applications is decreasing for reasons that are unclear. PPTA believes that the decline is attributable in part to the fact that there is increasing uncertainty with regard to coverage, causing hesitancy on the part of manufacturers to move forward in developing drugs and biologicals. The cost of clinical trials is also increasing rapidly, making it harder to afford the cost of developing new drugs and biologicals. PPTA supports the agencies' efforts to ensure timely patient access to medically appropriate care and foster medical innovation by addressing these barriers through a parallel review process. Because the proposal to pursue this goal through a parallel review process raises several issues and potential concerns, our comments are intended to help the agencies develop a parallel review process that, if adopted, will in fact ease the barriers to the timely access to innovative medical technologies and avoid injecting additional uncertainty or cost into the approval and review processes.

1. Should anyone other than the product sponsor be able to initiate a request for parallel review (for example, the FDA, CMS, or an interested third party)?

Participation in the parallel review process should be voluntary. In order to ensure that it is, FDA and CMS should initiate the process only at the request of the product sponsor. A competitor or other interested party should not be able to initiate a request for parallel review to avoid a product sponsor's feeling compelled to participate even though they do not believe it is in their best interests to do so. For the same reason, FDA and CMS must ensure that a decision not to request parallel review or not to participate in parallel review initiated by the agencies will not result in any negative inference or consequences for the product sponsor in terms of FDA approval or CMS coverage.

2. For which classes of products would consumers, payers, or sponsors benefit most from parallel review? Why?

With regard to drugs and biologicals, parallel review may be most useful where there is an existing non-coverage decision or where coverage is very restricted because those are the cases in which the national coverage determination (NCD) process is most likely to be initiated. The majority of coverage determinations currently are made by local contractors, either by processing a claim or by issuing a local coverage determination (LCD). As a general matter, the Medicare contractors make these coverage determinations in a timely and efficient manner and moving more review to the national level could unnecessarily tax CMS resources and delay resolutions via the parallel review process. The guidance FDA and CMS issue should make clear that the parallel review process is not intended to supplant the existing local coverage process, but simply provide another option for addressing coverage of new products in a more expedited fashion.

3. FDA and CMS may propose to limit the number of products concurrently under parallel review. How should limits be placed on the number and/or type of products concurrently under parallel review? Should CMS be permitted to review indications for which the sponsor is not seeking FDA clearance or approval under parallel review?

CMS should not be permitted to review indications for which the sponsor is not seeking FDA approval. Such review would not be “parallel” insofar as FDA clearance or approval is not being sought for the indication. It would also be unfair to sponsors who have prepared their clinical literature and other documentation for the review of the particular indication they are seeking to have approved or cleared by the FDA.

4. Are there disadvantages to parallel review?

There would be a distinct disadvantage to parallel review if Medicare contractors were to make negative coverage inferences about the products undergoing parallel review (e.g., no coverage until parallel review is complete) or the decision not to participate in parallel review.

The greater danger, however, is not that there will be disadvantages to parallel review, but that there will be no incentive to participate in the first place. As noted above, the number of drug and biological applications is decreasing partly due to the uncertainty and cost involved with the current system. To the extent that the parallel review process exacerbates these problems, it may in fact inhibit the marketing of innovative medical technologies, and not be a viable option for product sponsors. Similarly, any benefits to be gained by the parallel review process would be lost to the extent that CMS and FDA are unable to coordinate with regard to the information that they are seeking and streamline the process to avoid unnecessary duplication.

6. Should a voluntary process be put in place to encourage the conduct of clinical trials that are appropriately designed to support both FDA approval/clearance and CMS national coverage decisions? If so, what process should be established?

In principle, a voluntary process to encourage the conduct of clinical trials appropriately designed to support both FDA and CMS could offer certain benefits for the agencies and sponsors. However, the idea also poses significant risk that such coordination would actually increase the cost and complexity of clinical trials by resulting in *additional* requirements or considerations that lead to greater cost and delay. There is also a risk that collaboration of this kind could inappropriately conflate the separate missions of FDA and CMS. As the Notice recognizes, FDA is a science-based agency that makes determinations regarding a product’s safety and effectiveness, whereas CMS’ role is to determine whether coverage of products is reasonable and necessary for beneficiaries of government health care program. Any process should be developed with these considerations in mind.

8. At what point during FDA premarket review for prescription drugs, biologics, and medical devices, should parallel review begin in order to reduce the time between FDA

marketing approval or clearance decisions and CMS national coverage decisions while avoiding the risk that CMS would initiate an NCD for a product whose premarket application the FDA subsequently does not approve or clear?

If a parallel review process is adopted, the CMS component of the review should begin as soon as practical to avoid unnecessary duplication. The Notice makes reference to the need to ensure that parallel review is “carefully staged” because of the statutory deadlines for CMS’s coverage review. The statutory deadlines, however, are not relevant until CMS formally opens a national coverage analysis (NCA). Much of CMS’s review can occur before the NCA is opened, and this would be consistent with CMS’s current practice of informally meeting with manufacturers and becoming familiar with a new product before a request for an NCD is made or an NCA is opened. In addition, although CMS is required to issue the proposed NCD within 60 or 90 days of opening an NCA, nothing prevents it from doing so sooner. Proceeding in this manner (i.e., informally considering a product before formally opening an NCA) may actually allow CMS to expedite the issuance of a proposed coverage decision after the NCA is opened (and thereby reduce the time between FDA marketing approval or clearance and the CMS national coverage decision). Thus, we are not convinced the timeframes in the statute for national coverage determinations pose the practical hurdle suggested by the Notice, so long as CMS does not formally open the NCA until an appropriate time.

9. How should parallel review be implemented? Should the agencies use means in addition to a guidance document, such as designating agency liaisons, to educate sponsors about parallel review?

The parallel review process should be set forth in guidance documents issued by FDA and CMS and not in regulations; this will give the agencies more flexibility to tailor the process as it gains experience. At the same time, for the initial guidance for the parallel review process, PPTA urges the agencies to do as suggested by the Notice – issue draft guidance, accept comments, and then issue final guidance.

It is critical that any guidance that is issued provide sufficient clarity on the parallel review process. Greater clarity can reduce the type of uncertainty that can inhibit the use of the parallel review process for new drugs and biologicals. Finally, in developing guidance, FDA and CMS should be sure that implementation does not create additional hurdles to review (e.g., extra meetings, additional applications, etc.), as this will eliminate any of the benefits that might be gained by providing for a parallel review process in the first place.

10. When, if at all, should the agencies offer joint meetings to interested sponsors during parallel review? Before parallel review begins? Before a premarket application is submitted to the FDA?

Any meeting with a product sponsor should be offered as early as possible once the sponsor has volunteered for parallel review and the agencies have selected the

sponsor's product for the process. This initial meeting should be designed to ensure that the product sponsor has a good understanding of how the parallel review will proceed with regard to its particular product and can make any adjustments that are necessary to realize the benefits of such a review.

11. Should the FDA and CMS have access to the same data and information about the product during parallel review? (Note: Both agencies will protect the confidentiality of proprietary information used in the parallel review process, as they currently do under their respective approval/clearance and coverage processes.)

If a parallel review process is adopted and includes any level of data sharing between FDA and CMS, the agencies must develop protocols for information sharing to ensure that the confidentiality of proprietary information/trade secrets will be protected. Any such information sharing should not occur without prior notice to and consent of the sponsor.

12. It is CMS' policy to inform the public when it begins an NCD process for a particular product. However, under applicable statutes and FDA's regulations, the existence of a premarket application is considered confidential commercial information prior to approval or clearance unless the sponsor has publicly acknowledged the application. With the consent of the sponsor, should CMS make public that it has begun the NCD process, as part of parallel review, for a product still undergoing FDA premarket review? As a condition of the agencies' agreement to initiate parallel review, should a sponsor have to inform the public, or consent to the agencies informing the public, that the product will be evaluated under parallel review? If the sponsor declines to consent to disclosure, should it be permitted to request parallel review anyway, which would prevent CMS from disclosing the NCD process until after the product is approved by the FDA? How can the transparency of CMS' NCD process be reconciled with the need to retain confidentiality of certain commercial information?

Participation in the parallel review process should remain confidential until FDA approves the product or CMS officially opens an NCA, unless the product sponsor publicizes its participation in the process at an earlier point. The time between FDA approval and the opening of an NCA need not be great if CMS is willing to consider coverage for the product informally before opening the NCA, as discussed above.

13. At present, sponsors whose medical products will undergo both FDA premarket review and CMS national coverage review submit separate application packages to FDA and CMS that, in part, contain the same data, and, in part, contain different data. Keeping in mind the limited resources available to the agencies, what steps can the agencies take to minimize duplication of data submissions? Would the use of electronic submissions reduce submission burdens and facilitate data transfers? Are there other steps the agencies can take to streamline a parallel review process without modifying the regulatory standards and evidentiary requirements of both agencies? Would the transparency of CMS' NCD process subject the FDA to additional public pressure regarding marketing authorization?

As discussed above, the benefits to be gained by the parallel review process may be realized only to the extent that CMS and FDA are able to coordinate with each other and with the sponsor with regard to the information that they are seeking and streamline the process to avoid unnecessary duplication. CMS and FDA would need to work together and with product sponsors that volunteer for parallel review to identify areas where their requests for information are duplicative or where they may be able to rely on the same information to address their unique review standards.

15. What other concerns or considerations should the agencies take into account when developing a process for parallel review?

The parallel review process proposed by FDA and CMS addresses FDA approval or clearance and CMS coverage. Once a drug or biological product has received both approval or clearance and coverage through the parallel review process, CMS should expedite the coding and payment decisions for the product. Specifically, simultaneous with approval and a positive coverage determination for a drug or biological, CMS should provide a temporary code (e.g., a Q code) for the product to ensure that there is no unnecessary delay in claims processing for the covered drug or biological. CMS also should use the parallel review process to expedite drug and biological pass-through applications as much of the information used to make a coverage determination also is relied on in the pass-through application. Finally, CMS should expedite inclusion of drugs and biologicals in the average sales price (ASP) payment files as part of the parallel review process. Sometimes, it takes a few quarters for CMS to include new drugs in CMS's ASP payment files. Expediting such inclusion would provide manufacturers with added incentive to utilize the parallel review process. These steps will further expedite the marketing of innovative drug and biological products, helping further the purpose of the parallel review process.

16. Once FDA and CMS have opened a parallel review should a sponsor be able to terminate or withdraw the request for parallel review? If this happens, should that information be made public?

Product sponsors should be able to withdraw from parallel review at any point. The fact that the sponsor had been engaged in parallel review and the fact that the sponsor decided to withdraw should be kept confidential. In addition, there should be no negative consequences associated with a product sponsor's decision to withdraw from parallel review with regard to FDA approval or clearance or CMS coverage.

Conclusion

PPTA appreciates the opportunity to comment on the proposed parallel review process. We appreciate FDA and CMS's efforts to reduce the barriers to the marketing of innovative medical technologies. We hope that our comments will help the agencies develop a process that does in fact limit the uncertainty and cost involved in bringing new products to market. Please contact either Jon McKnight or Jay Greissing at (202)

789-3100 if you have any questions regarding our comments. Thank you for your attention to this very important matter.

Respectfully submitted,

A handwritten signature in black ink that reads "Julie Birkofer". The signature is written in a cursive, flowing style.

Julie Birkofer
Senior Vice President
PPTA North America