

May 29th 2007

Division of Dockets Management (HFA- 305)
Food and Drug Administration
5630 Fishers Lane, room 1061
Rockville, MD 20852

Re: Comments on Draft Guidance for Industry and Review Staff –“Target Product Profile- A Strategic Development Process Tool”.
Docket No. 2007D-0089

Dear Sir/Madam:

The following comments on the draft guidance are submitted on behalf of Novartis pharmaceuticals corporation, an affiliate of Novartis AG (NYSE: NVS). Novartis Pharmaceuticals corporation researches, develops, manufacturers and markets leading innovative prescription drugs used to treat a number of diseases and conditions, including central nervous system disorders, organ transplantation, cardiovascular diseases, dermatological diseases, respiratory disorders, cancer and arthritis.

The publication “**Draft Guidance for Industry and Review Staff –Target Product Profile- A Strategic Development Process Tool**” provides information regarding target product profiles (TPPs). A TPP is described as “a format for a summary of a drug development program described in terms of labeling concepts”. The guidance document describes the purpose and potential usefulness of a TPP, provides a template and guidance on how to complete and use optimally, including case studies to demonstrate a TPP’s usefulness.

The TPP, which would be prepared and shared voluntarily, provides a tool to focus FDA- sponsor discussion of the development program and outcome of clinical studies in terms of desired labeling concepts from early on. The TPP, which is viewed as a complement to the briefing book, could be used during sponsor-FDA interactions throughout the drug development process to assist in constructive dialogue. The sponsor specifies the labeling concepts that are the goals of the development program (under “Target”), documents the specific studies intended to support the labeling concepts (under “Annotations”), and includes relevant additional information to aid the discussion and provide clarity (under “Comments”). The TPP is dynamic, evolving over time as knowledge of the drug increases. The TPP submitted at each FDA meeting can be limited to pertinent sections which the sponsor drafts or updates to reflect new information about the drug and changes in the development program, to be discussed with FDA review staff.

Novartis shares with the FDA a mutual interest in bringing safe and effective products to patients as efficiently as possible, and applauds FDA’s TPP initiative; we

agree that by framing discussions of the development program and study outcomes in terms of desired or potential labeling concepts, TPP- focused meetings will facilitate communication, aid in the mutual understanding between sponsor and FDA, and improve the efficiency of FDA-sponsor interactions.

The philosophy of beginning with the goal in mind and defining desired labeling goals aligns with Novartis' development philosophy: our development programs are planned/designed on the basis of a TPP and anticipated or desired claims. The ability to use the same approach with FDA will enhance our meetings. We therefore welcome /endorse the option of using a TPP to promote open dialogue and transparency between sponsor and Agency. Incorporating a TPP into the briefing materials when appropriate, will ensure that the Agency understands our label goals and gives input accordingly, and will increase our understanding of the Agency view and minimize misunderstanding.

We find the suggested **TPP template** to be easy to complete and to provide necessary flexibility to sponsors. The proposal to include three areas in each section—target, annotation and comments -- is a logical means to link drug development activities to specific concepts intended for inclusion in the label, in an easy to follow format. We find the “**Guidance for Industry and Review Staff –Target Product Profile- A Strategic Development Process Tool**” to be a well written and useful document, and have no major comments or suggestions for further revisions.

Nevertheless, we would like to take advantage of the opportunity that FDA has provided to offer some specific comments and suggestions on the draft guidance and TPP template. Please see the comments below for your consideration.

Specific Comments

1) To encourage uptake of the TPP and reduce any reluctance to its use, it may be helpful to state more clearly that the TPP is a *development tool* to guide FDA and sponsors during development, and is not be used during the review/registration period. Labeling concepts or directional label language and the adequacy of the planned clinical support should be the basis for "agreement in principle" for the potential label claim; however this would depend on the results of the clinical trials. Thus while “the TPP presented at a pre NDA meeting will be similar to the annotated draft labeling submitted with an NDA or BLA”, the TPP is a dynamic tool and not invariably a precursor to the final label: As knowledge of the drug increases and the development program evolves, the concepts and information in the TPP are expected to change. Irrespective of TPP concepts shared during the development phase, the final product label at the end of the review period should be based on results from the development program. Ensuring that this is made clear may facilitate acceptance, uptake, and willingness to use a TPP by both FDA and sponsors.

2) Label ‘concept’ vs. specific label ‘language’

The Guidance document describe the TPP as a “summary of the development program in terms of labeling **concepts**”, “linking development activities to specific **concepts** intended for inclusion in the drug labeling” (Introduction- line 23, Attributes- line 78). Thus the TPP is intended to specify the labeling **concepts** that are the goals of the development program. In contrast, Section IV.A.1.a-Target (line 204) directs the sponsor to “include labeling **language** sponsors hope to achieve”

Novartis strongly recommends consistent use of labeling ‘concept’ (rather than ‘language’) in the TPP guidance, when referring to the label goal. This will better capture the intent/spirit of the TPP, to guide the development program. The term “language” implies the need for sponsors to provide specific and precise words, which can logically only be determined after results are available, being data dependent. Notwithstanding, agreement between sponsor and FDA based on label concepts, about what supports claims will be helpful

3) Use of TPP for Proposed Promotional claims (line 234)

The guidance suggests **that the TPP can assist in constructive dialogue with FDA review staff regarding proposed promotional claims and/or presentations for use in product promotional materials, by linking drug development activities to specific concepts intended for proposed promotional claims** (line 236). It recommends that the target area should prominently state “Proposed promotional claims” and include these and/or the presentations for use

While it may occasionally be helpful to explore potential promotional claims prior to approval, to ascertain whether a particular study or data point could support specific promotional language, we suggest that (i) in most cases it is inappropriate/challenging for the sponsor to predict the specific promotional claim, and for FDA review staff to give guidance, until supporting data is available and has been fully assessed, and (ii) in cases where, based on precedent it is reasonable to discuss proposed promotional claims and the necessary data to support, in order to ensure consistency, it would be important to include reviewers from the appropriate oversight group e.g. the Division of Drug Marketing, Advertising and Communications (DDMAC), which reviews and regulates all promotional claims, or staff from the Study Endpoints and Labeling Group to such a discussion, in addition to review staff from the review division. We therefore recommend that the Agency provide clarification on the anticipated role of DDMAC vs. that of the review division and how they will interface, when the promotional claims option is used by sponsors

4) Statement of overall Intent

The guidance notes that “*Ideally, the TPP provides a statement of the overall intent of the drug development program, and gives information about the drug at a particular time in development*” (Attributes-Line 75). It is not clear where the ‘statement of overall intent’ would be provided on the template, nor whether it will be of value. As the TPP is a tool to discuss specifics of a development plan linked to proposed label concepts, we believe that inclusion of such a statement in the TPP is not necessary

and would rather be discussed in the accompanying briefing materials. If the agency believes that the statement should be provided in the TPP, further guidance should be provided on where in the template the *statement of the over all intent* should be captured. .

In summary, Novartis shares with the FDA a mutual interest in bringing safe and effective products to patients, and applauds FDA's TPP initiative. This development tool will facilitate communication and focus discussions in terms of potential labeling concepts to improve sponsor-FDA interactions. Novartis anticipates using the TPP as a useful accompaniment to the briefing book, and looks forward to its acceptance across the various divisions of FDA.

Novartis Pharmaceuticals is grateful for the opportunity to provide comments and offer suggestions and hope that the FDA will consider our minor suggestions when publishing the final guidance for the use of public in the near future.

On behalf of Drug Regulatory Affairs at Novartis

Yours faithfully,

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