

May 29, 2007



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

**RE: Docket No. 2007D-0089 Draft Guidance for Industry and Review Staff on Target Product Profile – A Strategic Development Process Tool**

Merck & Co., Inc. is a leading worldwide human health products company. Through a combination of the best science and state-of-the-art medicine, Merck's Research and Development (R&D) pipeline has produced many important pharmaceutical and biological products available today. These products have saved the lives of or improved the quality of life for millions of people globally.

Merck Research Laboratories (MRL), Merck's research division, is one of the leading biomedical research organizations in the world. MRL tests many compounds as potential drug candidates through comprehensive, state-of-the-art R & D programs. Merck supports regulatory oversight of product development that is based on sound scientific principles and good medical judgment. In the course of bringing drug product candidates through developmental testing, clinical trials, and licensure, MRL encounters issues addressed by this draft guidance. We have extensive experience in the development and marketing of drug and biological products and we have utilized those experiences to author the comments below.

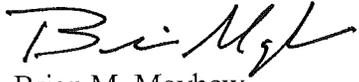
Merck commends the Food and Drug Administration (FDA or "the Agency") for its efforts to provide draft guidance regarding the Target Product Profile (TPP). We believe this is an important development tool for sponsors that may help facilitate discussions regarding product development programs. While we agree that the TPP can be a useful tool for sponsors, we believe that the information contained in a TPP should reflect the stage of development for the product program (e.g., based on available data). We note that the FDA uses the term "dynamic" in several instances throughout the draft guidance to imply that TPPs will change over time. However, we request that the Agency consider clarifying the term by stating explicitly that the FDA envisions TPPs will focus initially on broad concepts and over time contain more specific information with regard to program goals and achievements.

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In addition to the above, we have noted other areas of the draft guidance that we believe require clarification and have also provided recommendations for the FDA to consider as it finalizes the draft guideline (Table I).

Please contact me with questions or comments on this letter.

Sincerely,

A handwritten signature in black ink, appearing to read "Brian M. Mayhew". The signature is fluid and cursive, with the first name "Brian" being the most prominent part.

Brian M. Mayhew  
US Regulatory Policy

TABLE I.

Page, Section, paragraph, and Line number	Comments and Rationale	Recommendations, Clarifications, and Proposed Changes
<b>Line 75; Section III.B; Page 2</b>	The draft guidance states that TPPs provide a statement of the "overall intent of the drug development program." However, the draft guidance goes on to address how TPPs will be used to guide label information and resulting promotional claims. We believe that the FDA should be clear that TPPs apply only to labeling concepts and the intent of the FDA is not for the TPP to be used as the driver of the entire development program.	We recommend the following changes to the text of the final guidance: "the TPP provides a statement of the overall intent of the drug development program <u>in terms of labeling concepts</u> , and gives information about the drug at a particular time in development <u>based on the labeling goals of the program</u> ."
<b>Lines 78-80; Section III.B; Page 2</b>	The draft guidance states: "The sponsor can draft and update pertinent sections of the template that are intended to support the specific statements in labeling." We agree with the above statement, but would like to ensure that the TPP does not require sponsors to develop labeling targets for each section of the TPP template.	We request that the final guidance specifically state that, when sponsors decide to utilize a TPP, labeling targets will be determined based on the specific goals of the product program. Sponsors may not include labeling targets for each section of the TPP template. As such, inclusion of labeling targets for each section of the TPP template is optional.
<b>Line 82, 87-88; Section III.B; Pages 2-3; and Line 198; Section IV. A; Page 5</b>	We believe the text in these sections captures the idea that TPPs are flexible templates that will change over the course of the drug development process as more data is generated about specific drug products. Specifically, the draft guidance describes TPPs as "dynamic" and that early in development TPPs may capture only certain information "depending on the	In Line 82, the final guidance should read as follows: "The TPP is a <i>dynamic</i> summary that changes as knowledge of the drug increases. <u>Generally speaking, the FDA expects that TPPs will be broadly based on labeling concepts initially, but will progress to include more specific</u>

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	<p>drug, stage of development, and the questions and issues [sponsors] wish to discuss with the review staff."</p> <p>We agree with the Agency's approach that TPPs will change over time as more information is generated during the drug development process. However, we believe the FDA may want to consider stating this explicitly in the final guidance to ensure that the public understands the Agency's perspective.</p>	<p><u>information as the drug program matures over time."</u></p>
<p><b>Lines 207-211; Section IV.A.1.b; Page 5</b></p>	<p>Subparagraph (b) states "Sponsors should also include the protocol number, serial number, and submission date..." We believe that the inclusion of this type of information may be premature depending on the progress of a specific product program and may depend on when the submission of a TPP occurs.</p>	<p>We recommend that the text in this section be amended to indicate that specific study information (e.g., protocols, and study numbers) may be provided by sponsors when available. Therefore, the final guidance (Line 208) should read as follows: "<u>As studies are planned and implemented,</u> sponsors should also include the protocol number, serial number..."</p>
<p><b>Lines 236-237; Section IV.B; Page 6</b></p>	<p>We believe the process for the review of promotional claims and/or presentations requires further clarification. Specifically, it is unclear what type of information or materials the FDA would like sponsors to submit for review and whether CDER review divisions will involve staff from DDMAC to review this type of material and documentation.</p>	<p>We request clarification of the review process for promotional claims in the context of the TPP. Specifically, the final guidance should address the type of materials sponsors are expected to submit to review divisions in support of a TPP and whether other staff within CDER (e.g., DDMAC) will be involved in the review of such materials.</p>

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<p><b>Lines 511-512; Appendix C; Page 19</b></p>	<p>Under <i>12.1 Mechanism of Action</i> (MOA) the draft guidance states that sponsors should "...not include theorized mechanisms of action." However, we think it is important to note that, depending on the stage of the development program or the therapeutic area, many MOAs may be theoretical. As currently written, we believe the draft guidance may limit the discussion between sponsors and the Agency, precisely the opposite of what the TPP is designed to accomplish. Additionally, sponsors may benefit from discussion of theoretical MOAs by incorporating the Agency's feedback on theorized MOA's earlier in the development process.</p>	<p>We suggest that the FDA include the following edited language in the final guidance: "<u>Sponsors may include theorized mechanisms of action early in the development process and for therapeutic areas where MOA's may not always be completely known (e.g. Central Nervous System).</u>"</p>
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