PPTA
Plasma Protein Therapeutics Association

August 23, 2004 **Via E-mail & USPS**
Reference No. **FDAA04018**

Dockets Management Branch, HFA-305
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

RE: Solicitation of Comments on Stimulating Innovation in Medical Technologies. Docket No. 2004S-0233.

Dear Sir or Madam:

The Plasma Protein Therapeutics Association (PPTA) is pleased to provide comments on the Department of Health and Human Services (HHS) Notice entitled, "Solicitation of Comments on Stimulating Innovation in Medical Technologies" [hereinafter "Proposal" or "Notice"]. We appreciate the opportunity to study and comment on this proposal, and believe that the HHS Proposal raises appropriate issues to address difficult areas of policymaking. In addressing the Proposal, PPTA also notes other areas that HHS and its agencies may pursue to aid innovation and cost-effective public-health measures.

PPTA is the international trade association and standards-setting organization for the world's major producers of plasma-derived and recombinant analog therapies. Our members provide 60 percent of the world's needs for Source Plasma and protein therapies. These include clotting therapies for individuals with bleeding disorders, immunoglobulins to treat a complex of diseases in persons with immune deficiencies, therapies for individuals who have alpha-1 anti-trypsin deficiency which typically manifests as adult onset emphysema and substantially limits life expectancy, and albumin which is used in emergency room settings to treat individuals with shock, trauma, burns, and other conditions. PPTA members are committed to assuring the safety and availability of these medically needed life-sustaining therapies.

*1) What strategies and approaches could HHS implement to accelerate the development and application of new medical technologies?*

The most basic strategies for accelerating development and application of new technologies consist of incentives and efficiencies. HHS should develop methods for incentivizing new and established sponsors to produce new products and new technologies; in the specific interest of the plasma industry, this should be done in the arena of rare diseases, perhaps through close study and review of the Orphan Drug Act. The second point, efficiency, stems from an acceptance of the new reality of a global marketplace which requires regulatory harmonization. The salient detail in any effort toward harmonization is that the regulatory effort must be science-based. Stringency for

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the sake of stringency contributes no safety but adds mammoth costs in terms of both time and resources; instead, regulations must be science- and risk-based. In addition, this requires the review and oftentimes removal of current requirements that are obsolete and do not add value. Similarly, it is not merely the Code of Federal Regulations that should be science-based and up to date, but other policy documents such as Guidance Documents, Inspection Guides, Policy Guides, Compliance Guides, and other communications.

*2) How can HHS helps its agencies (e.g., NIH (and its grantees), FDA, CDC, and CMS) to work together more effectively to eliminate obstacles to development of medical technologies? 3) How can the HHS scientific and regulatory agencies work more effectively with CMS to eliminate obstacles to development?*

Communications work as a foundation for any cooperative effort. While high-level meetings at the director level or higher are important and contribute to a clear and coherent policy view, it may also be that a finer level of granularity is required. To this end, a possible improvement could be to foster communications at a more technical, detailed level below that of the high-level policy questions. These communications should also include sponsor personnel or, if such a meeting is possible given any non-proprietary issues, other industry observers to ensure that any issues discussed are pertinent and relevant.

We understand that advisory committees serve a valuable role in lending expert scientific analysis to questions regarding safety and efficacy. We note that current advisory committee composition is diverse, and committees often include experts from sister agencies. We encourage such involvement as this is another area where specialized knowledge and technical expertise can improve, enrich, and focus discussion. Furthermore, in terms of focus, it is important that HHS agencies keep various advisory committees aligned with the mission contained in committees' respective charters. Scientific and technical advisory committees should be engaged in discussions congruent with the stated mission of the advisory committee, namely that the data presented by both the agency and the sponsor are meritorious and the analyses rigorous. We note that when overlap occurs between a policy-oriented advisory committee and a science-oriented advisory committee, confusion concerning proper meeting procedure and scope frequently arises. This can be avoided through proper advisory committee management and resource budgeting.

In conclusion for these questions, and as mentioned above, HHS sister agencies must have clear focus with regard to the real costs and meaning of regulation. Improving communications and having clear scientific bases for regulations are deep thematic elements for improving and fostering innovation.

*4) What forums should HHS use to survey constituents about obstacles to innovation (e.g., public meetings, contract research, focus groups)?*

PPTA and its member companies have long been supporters of open public dialogue and public process regarding non-proprietary industry issues and public health concerns. We think that public workshops and discussions would be the most effective avenue of survey at this stage of the initiative, as it will allow the broadest possible canvas for many interested stakeholders. While public process is highly important, the value of contract research in this same instance is highly questionable, as such research –whether sponsored by a governmental or nongovernmental entity—is, by definition, subject to contractual influence.

Focus groups will likely be useful in the context of narrow, technical issues. Such groups may also prove worthy when charting appropriate courses of action, though the composition of such a focus group would be of paramount importance and should include a broad spectrum of interested parties. Also, communications between initiative coordinators and focus group rapporteurs should be facilitated in such a way that interested agency officials receive pure focus group output.

Lastly, paper or electronic survey forms disseminated to stakeholders may present data that are quantifiable and amenable to statistical analysis. The greatest weakness in this approach, however, is in the survey or questionnaire design. As with any good data-gathering exercise, the survey questions should be appropriately neutral and in accordance with principles of cognitive science.

*5) How can the portability of information between HHS agencies be optimized?*

Information portability and exchange might be better facilitated by using agency personnel currently involved in projects as liaisons between sister agencies. Similar to the point above, which recommended that mid-level and technical committees meet to discuss specific issues, information liaisons may enhance communication between agencies.

In that same regard, drug development information is highly valuable. To maintain confidence in the regulatory review process, it is imperative that confidential and proprietary information remain safe and secure. Secure systems and methods of exchange for interagency communication are imperative; the corollary is that the secure systems and formats must be transferable from agency to agency. Secured, shared platforms and interagency liaisons could help accomplish these objectives.

Lastly, information portability is improved when sister agencies define meaningful terms in the same fashion. The current controversy regarding “generic biologics” is a case in point. Terms, such as “subsequent-entry,” “biosimilar,” “biogeneric,” “generic,” “follow-on,” and “second-generation” have all been used to greater or lesser extent by HHS sister agencies, and there does not appear to be any agreement on their use. A generic therapy for CMS may or may not be a generic therapy in the FDA Orange Book.

*6) Which HHS policies and programs effectively spur innovation? Which policies and programs at NIH (and its grantees), CMS, FDA, and CDC should be expanded to help spur innovation? Do any policies and programs pose obstacles to innovation?*

PPTA is encouraged by the dialogue created by FDA in initiating the Critical Path effort. While it is too early to measure any real progress by enacting this, we have observed that the risk-based regulatory approach announced by then-Commissioner McClellan has achieved measurable, positive results. The use of both the Critical Path initiative and risk- and science-based regulation should be expanded and refined to maximize safety and efficiency. PPTA is currently studying the NIH Roadmap Initiative and reserves its right to comment in the future.

The current FDA-CBER regulatory review system for plasma products should be studied and updated. As mentioned in PPTA comments to the FDA Critical Path initiative, some of our member companies have repeatedly experienced extensive redundant and unnecessary clinical testing requirements when simple changes are made to production processes. For example, companies that have been making an intravenous immunoglobulin product for more than a decade are frequently forced to "start at square one" in terms of licensure requirements for innocuous process changes that frequently result in safety and efficacy improvements.

*7) What role should be played by nongovernmental partners in assisting the Federal Government in this process?*

This query is an interesting one, but without appropriate parameters or definition of what a "nongovernmental partner" is, it is unanswerable. Corporations, civil society, nonprofit entities, international organizations, and contractors may all have valid roles, but what specific role played is highly dependent upon the HHS characterization in this context.

In conclusion, we believe that strong continued research and development will lead to improved lives for all of our patient population. HHS and its subsidiary agencies have extraordinarily important roles to play in this system, and PPTA is enthusiastic about the possibilities that exist in this Initiative. Our companies remain committed to providing safe, efficacious therapies. We look forward to further discussion of this important initiative.

Respectfully submitted,

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Plasma Protein Therapeutics Association