

Statement



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**PhRMA Responses to
Agency Questions for:
CBER Stakeholder's Meeting**

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Good Morning,

I am Dr. Bert Spilker, Senior Vice President of the Pharmaceutical Research and Manufacturers of America. My comments this morning must of necessity be condensed in order to fit the allotted time. Further details and substantiation will be submitted to the Docket.

PhRMA appreciates the opportunity to provide input as FDA considers how best to achieve compliance with the Agency's various statutory obligations. It is important to underscore, however, that consultation with stakeholders like PhRMA does not relieve FDA from the ultimate responsibility to manage and, as necessary, re-allocate its resources to achieve the statutory timelines and other goals of the FD&C Act in a timely manner.

Question 1 on Agency Explanations

We wish to make three points:

1. It is important for FDA to make its procedures more transparent, particularly in terms of Good Review Practices - also known as GRPs.
2. Copies of GRPs and CBER and CDER reviewer handbooks plus MAPPS for NDA and IND Reviews should be provided to the industry, and other stakeholders -- even though these documents may still be in draft form. This step would provide industry with a better understanding of how these groups operate, and also enable industry to bring our procedures into conformity with FDA. This action is intended in the spirit of openness to foster improved collaboration. This action is also part of Section 119 of FDAMA.

98N-339B

Pharmaceutical Research and Manufacturers of America

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3. Allow more time for companies to respond to FDA proposed labeling changes near the end of the review period. At present, companies often have less than 24 hours to decide whether to accept FDA changes or get an approvable letter with FDA language that is not in the company's interest.

Question 2. Clarity of Information

We wish to make two points:

1. We appreciate that FDA is putting information about new drugs on the Internet. This is extremely positive. This practice should be followed for all products at the time of approval.
2. The FDA should allow companies and other groups to provide well documented information on marketed drugs using market forces.

Question 3

We wish to make five points:

1. There is nothing more important to the pharmaceutical industry than the safety of our products. Every day, worldwide, our companies are monitoring the safety of their products. We have extensive systems in place today to collect safety data and we report to the FDA all adverse reactions according to regulations.
2. The FDA should stress to Congress, the press and the public that the current safety standards for new drug approval are significantly higher than in the past. For example, in 1980 there were an average of 1500 patients studied in 34 clinical trials in the average NDA. These numbers have risen to over 4,000 patients in 68 clinical trials. The amount of safety data is related to the number of patients exposed to a new drug.
3. We support the views of 21 patient organizations, who wrote to USA Today last week to emphasize that
 - "the FDA has not comprised its world-class standards for the safety and effectiveness of new medicines" and

- They “fear that in overreaction to a small number of recent drug withdrawals, policy makers may decide to slow down the drug approval process. This would hurt public health and harm the patients we represent by denying them the new treatments and cures they are so anxious to receive.”
4. Both FDA and the pharmaceutical industry must educate Congress, the press and the public about the vast amount of safety activities already in place. Recent drug withdrawals demonstrate that the systems are basically working - not that they are broken.
 5. To the extent that the system for monitoring the safety of medicines after they are on the market can be improved, the pharmaceutical industry is eager to work with the FDA, patients, doctors, pharmacists, hospitals, Congress, and anyone else to achieve that goal.

Question 4. FDA Access to Scientific & Technical Expertise

We wish to make six points:

1. We support FDA conducting targeted research on regulatory policy, particularly if planned collaboratively with industry.
2. We support in-service training that supports the skills of staff who conduct reviews of marketing applications.
3. We support training of field staff, partly within pharmaceutical companies.
4. We support increased collaboration with other regulatory agencies world wide.
5. We support the establishment of periodic meetings for Division Directors in both CBER and CDER with no more than four industry representatives on a bimonthly or quarterly basis. The purpose of these meetings is to share scientific and technical information, management ideas, overall approaches, and creative thinking
6. We support increased efficiency in the use of current resources.

Question 5 on Review of Non-User Fee Products

1. The current level of full time support staff paid through user fees should not be diminished.

Question 6 on Ideas to Eliminate Backlogs

[Comments will be made to the Docket only.]

Question 7. Other Objectives Beyond the Six Questions

We wish to make three points:

1. It would be valuable for reviewers to have brief sabbaticals in the regulated industries. This will increase their knowledge of the industry, its procedures and its perspectives. Thus, they will better understand the industry they are regulating. It should be noted that CDER chemists currently have such sabbaticals.
2. The Agency should educate the public about benefit-to-risk ratios and the fact that medical interventions such as surgery, medicines, devices, and even diagnostics and food are not totally without risks.
3. There is a need for external advisory panels to advise FDA on efficient administrative policies and activities.

Improve the Review Process

In the last year the Center for Biologics Evaluation and Research (CBER) has made great strides toward improving the licensure process. The proposed rule to replace the Product License Application and Establishment License Application (PLA/ELA) has been published and the Biologics License Application (BLA) process shows great promise. The guidance document that implements the BLA, the so-called CMC Guidance, also was recently published. CFRR strongly encourages CBER to ensure that the paperwork reduction and regulatory efficiency goals of the BLA are maximized with its implementation.

In addition, FDA has a host of new tools for effecting modifications or changes to approved applications. These include the prior approval supplement (PAS), the Changes Being Effected (CBE30), and Annual Report (AR) submissions. These are important milestones; however, much work remains to be done in the area of biologics applications. FDA should utilize these tools to the greatest possible extent; the onerous PAS process should be used only for novel products or for a first-time request to license an establishment or product.

Areas where the agency has promised guidance and which industry desperately needs, include guidance specific to blood and plasma for CBE30 and, in particular, annual reports and comparability protocols. These are tools that may yield the greatest regulatory efficiencies but remain untapped. Many companies already have been required to submit annual reports without clear guidance on what the reports are supposed to contain or how the agency will use this information. Comparability protocols offer the promise of a standardized method for effecting certain application changes without the need for prior agency approval, but the scope of eligible changes and protocol contents remain undefined. These tools and others if used as intended, can relieve the agency's application review burdens for non-user fee industries.

Blood Action Plan

The Blood Action Plan holds promise for better communication of agency product quality expectations to industry. Based on FDA's public statements, the Blood Action Plan calls for a rewrite of the blood and plasma regulations. This includes formalizing requirements published through guidance and memoranda into regulations. CFRR applauds these efforts and hopes to work with the agency in achieving these goals.

It is important to note, however, that no publicly available documents currently exist to describe the Blood Action Plan, time frames for achieving the plan objectives have not been publicly announced and industry input has not been sought. One initiative of the plan is to develop a pilot program for approval of certain blood and plasma products through a monograph system. While this program holds promise for both FDA and industry in terms of the application process, without an industry-FDA dialogue this program may never get off the ground and an important opportunity may be lost.

Product Quality

Although GMPs are the cornerstone of quality products, the blood and plasma industries have lacked clear GMPs. Instead, the current GMPs contain many references to biologics that often do not directly bear on the blood and plasma industries. The current GMPs applicable to blood and plasma products span three sections of the Code of Federal Regulations – 21 C.F.R. §200, §600 and §800. A comprehensive rewrite of the GMPs is needed to incorporate these important requirements into one set of unified regulations for blood and plasma products.

Other regulatory requirements that bear on product quality include error and accident reporting, adverse event reporting, and product recalls and withdrawals. These tools are underutilized. Although industry expends vast resources submitting error and accident reports, FDA has failed to use this information as a quality assurance tool. Quarterly reports of errors and accidents are published but no meaningful analysis or trend reporting of submitted errors and accidents has ever been made publicly available. This is a missed opportunity. FDA can help industry better itself by making this kind of information available. Furthermore, error and accident reporting should not be extended to other industry segments without careful consideration.

Recalls and withdrawals are intended to help ensure that only quality products reach patients. However, the current recall regulations are not appropriate for blood and plasma products. Many if not most blood and plasma recalls involve only hypothetical risks, expired products or already transfused products. Other tools such as recipient notification may be more appropriate in such circumstances. A more rational recall and withdrawal policy would save agency resources and permit industry to concentrate its resources on delivering high quality products.

Closing

In closing, I would like to say that CFRR recognizes the magnitude of FDA's task – ensuring that only safe and effective products are made available to consumers. Without adequate funding CBER cannot carry out this mandate. Furthermore, this important mandate requires that the agency retain individuals with extensive skills and technical expertise. As such, CFRR fully supports CBER-based research needed to maintain an appropriate scientific infrastructure.

Thank you for the opportunity to comment. CFRR looks forward to working with the agency on current and future regulatory initiatives.