



Joint Council  
of Allergy,  
Asthma and  
Immunology

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Docket No. 98N-0339

September 18, 1998

Docket Management Branch  
HFA-305  
Food and Drug Administration  
5630 Fishers Lane, Rm. 1061  
Rockville, MD 20852

Dear Sir/Madam:

The Joint Council of Allergy, Asthma and Immunology (JCAAI) is pleased to submit public comments to the Food and Drug Administration's solicitation for comments in accordance with the Food and Drug Administration Modernization Act of 1997 406(b). The JCAAI has valued our working relationship with the Food and Drug Administration (FDA). We commend the agency for seeking input from its stakeholders.

The JCAAI is a professional, nonprofit organization comprised of the American Academy of Allergy, Asthma and Immunology (AAAAI) and the American College of Allergy, Asthma and Immunology (ACAAI), and it consists of more than 4,000 researchers and clinicians who are dedicated to providing care for the 50 million Americans who suffer from allergic or immune disorders.

We have considered the questions outlined in the *Federal Register* notice and offer the following recommendations.

What can FDA do to improve its explanation of the agency's submission review processes and make explanations more available to product sponsors and other interested parties?

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JCAAI encourages the agency to take steps to make information about the FDA's application and review processes more available to product sponsors and others. More guidance and education about the review process would facilitate communication between FDA and product sponsors before the process is initiated.

Specifically, FDA might consider hosting an open-house with a "walk-through" workshop explaining the submission and review process. These types of opportunities could further serve as an opportunity for industry scientists, academics and relevant associations to meet FDA personnel. Such workshops would be particularly helpful for individuals involved in clinical drug development when the agency makes changes in regulations.

In addition, we recommend that the FDA consider placing a succinct document explaining the steps involved in the application and review processes on the Internet as well as broadly disseminating them to industry and academia.

**How can the agency maximize the availability and clarity of information concerning new products?**

The product package insert is a major source of information for patients as well as physicians. It is our experience that the package inserts help patients feel secure about their medical care and treatment and as physicians we value the role that these documents play in care delivery.

In that context, the JCAAI recommends that the FDA might strengthen this important patient teaching tool and facilitate improved therapeutic compliance by considering a few changes to the current package insert. We urge the agency to maximize the availability and clarity of information concerning new products through package inserts by considering the following:

- 1). phrase information about the product in a more sympathetic and comprehensible manner. The technical language utilized in the insert may be confusing for average consumers.
- 2). weight adverse side effects according to their severity. Some side effects are of more consequence than others and should be presented accordingly. The inclusion of minor side effects may be confusing to the reader and could be unnecessary. Due to the breadth of information presented in the current document, there is the potential to detrimentally impact compliance with treatment regimes among patients who become more concerned about potential side effects from the treatment rather than the symptoms caused by the underlying disease.

From a practical perspective, the FDA could encourage new pharmaceutical companies to make information available to physicians. The FDA might want to consider publishing "approvable" information or findings and recommendations of advisory panels in

therapeutic journals, providing more information than is currently available through the *Pink Sheet* and industry publications. In addition, this would provide the FDA with a direct conduit to physicians about approvable products. FDA could further facilitate publication of product information in the lay press.

Another concern of allergy and immunology specialists with the function of the CBER and CDER at FDA relates to biopharmaceutical products. As an example, CBER has a long history of carrying out research designed to improve the labeling and standardization of the extracts of biopharmaceuticals employed. While progress has been slow, there has been steady improvement. Advances in immunology and protein chemistry are emerging that should speed progress toward the goal of rational labeling. There is concern, however, that the progress will become slower because of FDA policies that limit the number of people and resources necessary to in-house research on biopharmaceuticals.

JCAAI recommends that the FDA add to its investigational capabilities rather than subtract from them. The Committee on Standardization of Allergens of the AAAAI has developed detailed recommendations for action on standardization. We urge FDA to consider using these recommendations in executing its responsibilities in this area. There are other biopharmaceuticals under development and a well established, clearly defined approach dealing with these products will be necessary.

**How can FDA work with its partners to ensure that products-both domestic and foreign-produced and marketed by the regulated industry are of high quality and provide necessary consumer protection, and how can FDA best establish and sustain an effective, timely, and science-based postmarketing surveillance system for reporting, monitoring, evaluating, and correcting problems associated with use-consumption of FDA-regulated products?**

We have a few recommendations for FDA to review regarding improvement of the agency's capacity. We urge FDA to consider a simplified reporting system. The collaboration between industry and FDA is vital to reducing drug development, and we urge the agency to continue its efforts in this regard.

The postmarketing surveillance system could be improved to increase its effectiveness and timeliness. The process for reporting adverse reaction information to FDA is cumbersome for physicians and others. Establishing a simplified reporting system would improve the postmarketing surveillance system.

A more efficient system would likely increase the numbers of adverse reaction reports, thereby improving the scientific basis for the data. JCAAI recommends that the FDA consider adopting an email and/or fax system to simplify and streamline the reporting process.

We believe that the present review process is too private and that privacy may not be in the best interest of industry, patients, researchers and physicians. We recognize that there is an important proprietary aspect to industry and FDA activities with regard to the review of products; however, aside from the proprietary aspects which would not be appropriate to open up to greater scrutiny, JCAAI would like to see aspects of this process be more open.

Collaboration in the development process between industry and FDA is vitally important at the beginning of the process. FDA might consider an advisory panel approach during the development where peers review data, instead of at the end of the clinical program. We further recommend that the FDA consider mandating and standardizing the conduct of Phase IV programs.

The FDA may also consider providing for a central method of notifying IRBs. The current process, in which dozens of IRBs operate independently, may increase the difficulty of reporting.

**What approach should FDA use to assure an appropriate scientific infrastructure, with continued access to the scientific and technical expertise needed to meet its statutory obligations and strengthen its science-based decision making process?**

One of the key issues in this regard is resources. FDA needs to provide pay that is competitive to the private sector in order to attract and retain high quality scientists. In addition, JCAAI believes that FDA scientists could be provided more interaction with the private sector--industry and academia--to expose the FDA scientists to the development process by the private sector. It is important that FDA scientists have a keen understanding of the intricacies of this process.

JCAAI would like to see increased utilization of outside expertise in the review process. The cost of products are ultimately effected by the expediency of the FDA review process. FDA must be diligent in executing its responsibilities in a timely fashion, and it is important that the FDA have the staff or the wherewithal to bring on board the appropriate experts to carry out a review in a timely fashion that will provide the maximum benefit to patients waiting for innovative products. Currently, review panels frequently lack experts in the specific area of review. JCAAI recommends that the agency consider opening review panels to outside experts that have appropriate information not available on the panel on a product-by-product basis. The agency might supplement review panels with experts from the appropriate discipline relating to the specific area of review. Further, we recommend that these experts should include practitioners and not be limited to "bench" immunologists.

Further, FDA might consider expanding the role of expert panels beyond the review process. For instance, FDA could consider

having a minimum of two or more meetings of their expert panels, or advisors, to discuss ongoing issues related to the responsibilities of CDER or CBER. The panel could be charged with the responsibility of advising the agency about decisions of CDER or CBER regarding important policy and scientific issues. Current policy is adversely affecting the antigen manufacturing industry, reducing the availability of antigens to patients. The FDA needs to activate the expert panels it already has. The constitution of these panels could be formulated in conjunction with the professional societies; each panel member could serve for three years on a sequential rotation to ensure continuity of the membership of the panel.

In addition, FDA might want to consider holding open forums, at least annually, where outside agencies with whom the Centers interact by regulation have the opportunity to provide input to the individual Center regarding regulation. For instance, we would appreciate the opportunity to participate in a public dialogue with the agency and other stakeholders on the regulation of allergy and immunology products and have those discussions made available publicly.

**What do you believe FDA should do to adequately meet the demands that are beginning to burden the application review process, especially for non-user fee products, so that it can meet its statutory obligations to achieve timely product reviews?**

The review process for drugs has improved in its timeliness and efficiency, but further progress is possible to benefit consumers.

JCAAI suggests that the FDA consider ways to facilitate the review of applications. For example, within a month or two of the submission of an application, the agency should know what additional information is necessary, and what will be the duration of application process. Appropriate parties could be notified so that all the necessary resources could be directed toward meeting that target.

We also believe that too many studies may be required as a part of a New Drug Application (NDA) due to fear of the FDA requesting more data, rather than for reasons of good science. One solution to this problem is that FDA establish a policy of developing its suggestions made during minutes of meetings with FDA and sponsors and providing them to all parties to ensure that documentation of the agreements exist. When FDA reviewers change during a project, FDA may consider requiring the new reviewer to accept the recommendations of the previous FDA agreements unless issues of safety exist.

JCAAI also suggests that the agency streamline the review process. Currently, the agency generally requires two clinical trials followed by submission of safety data. Perhaps the agency

could greatly increase the speed of the review process by starting the review process based upon clinical efficacy trials. Final approval would, of course, be contingent on the submission of product safety data.

**What suggestions do you have for the agency to eliminate backlogs in the review process?**

Per our earlier suggestion we believe that the review process could be expedited if the FDA increased its utilization of outside experts or vendors. Specifically, independent CROs could review statistics sections, repeat tests and undertake other initiatives integral to the review process. In addition, improved planning up front with product sponsors (collaboration), should decrease timelines and backlog.

**What other objectives related to the agency's statutory obligations or public expectations-beyond the six objectives-should be included in FDA's plan?**

The JCAAI recommends that the FDA become more aggressive in putting forth its resource requirements to the Congress, and the Administration. Over the past 10-15 years, the FDA has not aggressively addressed the issue of additional responsibilities mandated by Congress and the Administration without the necessary resources to carry out those mandates. The agency may want to consider a change in posture. There has been a significant erosion of core FDA responsibilities in order to meet "emerging" responsibilities. JCAAI suggests that FDA officials consider ways that the agency could become a better advocate for itself. Furthermore, the agency could provide the critical insight for its stakeholders -- academia, clinicians, patients, industry -- in this regard in order to facilitate broad public support for FDA's resource needs.

JCAAI appreciates the opportunity to submit comments in the process of the FDA Modernization Act of 1997 406 (b). We thank the agency for soliciting comments and commend the FDA for reaching out to its stakeholders.

Sincerely,



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