



United States  
General Accounting Office  
Washington, D.C. 20548

Health, Education, and  
Human Services Division

B-281553

February 26, 1999

The Honorable Thomas J. Bliley, Jr.  
Chairman  
The Honorable John D. Dingell  
Ranking Minority Member  
Committee on Commerce  
House of Representatives

The Honorable Fred Upton  
Chairman  
The Honorable Ron Klink  
Ranking Minority Member  
Subcommittee on Oversight and Investigations  
Committee on Commerce  
House of Representatives

Subject: Mutual Recognition Agreement: Food and Drug Administration's Progress in  
Assessing Equivalency of European Union Pharmaceutical Inspection Programs

On December 1, 1998, a mutual recognition agreement (MRA) between the United States and the European Union<sup>1</sup> became effective. The MRA affects billions of dollars in trade and includes six annexes covering telecommunications equipment, electromagnetic compatibility, electrical safety, recreational craft, medical devices, and good manufacturing practices (GMP) inspections of pharmaceutical facilities. The pharmaceutical GMP annex of the MRA provides that the United States will assess whether the pharmaceutical GMP inspection systems in the 15 European Union member states are equivalent to those in the United States during a 3-year transition period that began when the MRA became effective. The Food and Drug Administration (FDA)—which conducts GMP inspections in the United States and abroad to ensure the safety and quality of domestic and imported pharmaceutical products<sup>2</sup>—is responsible for making these assessments.

<sup>1</sup>The European Union, formerly referred to as the European Community, currently consists of 15 countries commonly referred to as member states. The 15 member states are Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, the Netherlands, Portugal, Spain, Sweden, and the United Kingdom.

<sup>2</sup>We use pharmaceutical products to refer to pharmaceuticals imported in finished dosage forms as well as bulk drug substances (for example, active pharmaceutical ingredients or bulk pharmaceutical chemicals).

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During the 3-year transition period, the United States and the member states of the European Union will jointly develop standard operating procedures for conducting inspections and a common inspection report format. They will also undertake equivalency assessments of the respective regulatory systems, which will include evaluations of laws, professional standards and conduct, administrative controls, inspection competence, and systems of enforcement and surveillance. The United States and the European Union will also establish an alert system for the exchange of information on the safety of drug products and conduct joint training sessions. For countries determined to have equivalent systems, the MRA provides for the exchange and endorsement of the U.S. and European Union pharmaceutical GMP inspection reports after the transition period. According to FDA, such an exchange will help it handle the growing demands to inspect foreign pharmaceutical facilities that manufacture drug products.

FDA has been involved in the negotiation of the MRA since 1994. In anticipation of the ratification of the MRA, FDA prepared in February 1998 a management plan that provided an organizational and procedural framework identifying the groups and functions needed for implementing the pharmaceutical GMP annex. In April 1998, FDA began drafting the regulation to implement the pharmaceutical section of the MRA. The final regulation was published on November 6, 1998, and became effective on December 7, 1998.

During a hearing on October 2, 1998, Subcommittee Members expressed concern about FDA's lack of progress in developing plans to implement the MRA. Specifically, the Members were concerned that FDA was not able to provide details on the tasks necessary to conduct FDA's equivalency determinations and the costs to complete this effort. Because of these concerns, you asked us to report on the status of FDA's efforts to implement the MRA.

In summary, we found that nearly 3 months into the transition period, FDA does not have a comprehensive plan that identifies the key tasks to complete an equivalency assessment of the European Union member states. In addition, FDA could not provide us an update of the estimated costs and resources that will be needed to implement the MRA.

More specifically, we found that FDA's current plan establishes an organizational framework, including a steering committee to oversee and coordinate MRA-related activities and a project management team to develop and execute a plan for the conduct of equivalency assessments. The plan also includes an implementation project time line, which provides a schedule of general activities and milestones that FDA anticipates completing during the transition period and through the operational period of the MRA.<sup>3</sup>

However, FDA has not yet identified in its plan the information needed to make equivalency determinations, even though the implementation project time line developed in February 1998 required that the plan be completed by about July 1998 to prepare the agency for the transition period. According to FDA officials, FDA did not begin to prepare the plan for making equivalency assessments until January 1999 because staff was involved in other

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<sup>3</sup>The operational period begins after the end of the transition period and continues for the life of the annex. Activities during the period include the sharing of alert information and establishment inspection reports among equivalent authorities, endorsement of establishment inspection reports among equivalent authorities, and monitoring equivalence among equivalent authorities.

related activities, such as developing regulations to implement the MRA. In commenting on a draft of this report, FDA officials said that another reason they waited until after the implementing regulations were in place to begin preparing the plan was to avoid the appearance of prejudging the outcome of the formal rulemaking process. This comment conflicts with FDA's February 1998 implementation project time line, which specifically states that the plan should have been completed by about July 1998—several months before FDA planned to have the final regulations in place. Moreover, FDA has not yet developed a strategic plan that describes the goals of the MRA and how FDA will measure its performance in achieving those goals. In our view, FDA could benefit by developing a strategic plan for implementing the MRA.

On February 2, 1999, FDA officials told us that an update of the plan for making equivalency determinations and cost estimates would not be available until March 1999 and the final plan would not be completed and shared with the European Union until about July 1999. However, this timetable appears to have changed. In their comments on this report, FDA said that a meeting is scheduled this spring with representatives of the European Union to discuss and exchange plans for conducting equivalence assessments. Once exchanged, the FDA officials said equivalency assessments would begin. It is not clear, however, whether the plan FDA now intends to share with the European Union this spring will be the final plan.

FDA officials acknowledged that there are several issues that will require the cooperation of the European Union to execute the MRA. These include issues such as developing a mutually agreed upon inspection report format as well as a joint alert system, joint inspection program, and joint training. FDA expects to address these issues either through informal discussions with the designated contact points in the European Union and its member states or through formal meetings of the committees established to oversee the implementation of the MRA.

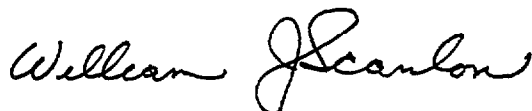
#### AGENCY COMMENTS

As indicated above, we obtained comments on a draft of this report from FDA and have included them where appropriate.

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We are sending copies of this report to the Secretary of Health and Human Services, the Commissioner of FDA and others who are interested. If you have any questions about this correspondence, please call me at (202) 512-7114 or John Hansen at (202) 512-7105. Other major contributors included Darryl Joyce and Claude Hayeck. A description of our methodology for conducting this study is enclosed.

Sincerely yours,



William J. Scanlon  
Director, Health Financing  
And Public Health Issues

Enclosure

ENCLOSURE

ENCLOSURE

METHODOLOGY

To examine FDA's implementation of the pharmaceutical GMP annex of the MRA, we reviewed the MRA to determine the requirements for the pharmaceutical GMP annex as well as materials gathered as a part of the Subcommittee's investigation on the negotiation and implementation of the MRA. To obtain information on FDA's plan for making equivalency determinations with European Union member states, estimates of costs for implementing the plan, and actions planned for addressing any unresolved matters, we met with FDA officials involved in implementing the pharmaceutical GMP annex. These included officials from the Center for Drug Evaluation and Research, the Center for Biologics Evaluation and Research, the Office of International Affairs, the Office of Regulatory Affairs, and the Office of Chief Counsel. We also reviewed correspondence dated November 6, 1998, and February 2, 1999, prepared by FDA in response to questions posed by the Subcommittee regarding FDA's progress in implementing the pharmaceutical GMP annex. We analyzed several implementation project time lines that were prepared by FDA between February 1998 and January 1999 to obtain an understanding of the planning process FDA will follow to implement the agreement.

We did our work between November 1998 and February 1999 in accordance with generally accepted government auditing standards.

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