US Food and Drug Administration – European Medicines Agency
Good Clinical Practice Initiative
Frequently Asked Questions and Answers

I. Overview of the Program

Q1. Why did the Food and Drug Administration (FDA) and the European Medicines Agency engage in this bilateral initiative on good clinical practice (GCP)?

There are several factors that prompted this initiative:

a. *Globalization of clinical trials*
The development of new medicines has become a global enterprise, with clinical trials increasingly being conducted by clinical investigators who are scattered throughout the world. Both the Food and Drug Administration (FDA) and the European Medicines Agency conduct inspections of clinical trials in order to validate data in US new drug applications/European centralised marketing authorisation applications. Each regulatory authority has finite inspectional resources so it makes sense to join forces in sharing information about inspections and in conducting inspections in order to use resources more efficiently.

b. *The success of recent collaborative efforts*
There are several initiatives between the FDA, the European Medicines Agency and other regulatory authorities underway, including information sharing and inspection collaboration on manufacturing sites producing active pharmaceutical ingredient outside the territories of the involved regulatory authorities. The success of the 2008 FDA-European Medicines Agency Good Manufacturing Practices (GMP) inspection pilot led the two agencies to consider extending the effort to good clinical practice in clinical trials.

To read more about the FDA-European Medicines Agency Good Manufacturing Practices (GMP) inspection pilot, please go to: http://www.fda.gov/InternationalPrograms/FDABeyondOurBordersForeignOffices/EuropeanUnion/EuropeanUnion/EuropeanCommission/ucm114333.htm or to http://www.emea.europa.eu/Inspections/docs/43043807en.pdf

c. *Barriers to product development and duplication of inspections*
Sponsors of new drug applications (NDAs) and marketing authorisation applications (MAAs) have complained to the FDA and the European Medicines Agency of the burden they face in hosting inspections conducted by each regulatory authority in succession, often at the same sites. Since both authorities validate the same information, sponsors have suggested combining the inspections. By minimizing duplicative inspections and harmonizing regulatory approaches to good clinical practice, sponsors' resources may be focused on greater innovation leading to improved access to promising new medicines.

Q2. Have the FDA and European Medicines Agency previously shared information? If so, how would that change under the initiative?

This initiative builds on the general framework of the FDA–European Commission/European Medicines Agency 2003 Confidentiality Arrangement. In the past, the FDA and the European Medicines Agency have shared information on inspections but the effort was limited and not as effective as it might have been. Under the current initiative more efficient ways are being developed to share information and regular forums are being developed in which the exchange will take place. This includes standardizing the data and format of inspection information to be shared and instituting regular telephone conferences.

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Q3. What will the initiative entail?

There are three main components to the initial 18- month pilot part of the initiative:

a. Enhancement of information sharing on inspections conducted separately by each regulatory authority
b. Collaborative GCP inspections to evaluate and enhance mutual understanding and confidence in each agency's inspectional process and inspectional findings
c. Information sharing on good clinical practice (GCP), and keeping each other informed of new or developing GCP-related legislation and guidance.

II. Scope of Program

Q4. What subset of regulated products will be addressed in this pilot?

The pilot will address those products submitted as new drug applications (NDAs) and biologics license applications (BLAs) regulated by the Center for Drug Evaluation and Research (CDER) in the US FDA and the same products submitted as marketing authorisation applications to the European Medicines Agency.

Q5. Will medical devices be covered?

No, medical devices will not be covered.

Q6. What type of sites will be inspected?

Clinical investigator and sponsor/CRO sites located in the European Union (EU) and the United States (US) will be involved in this pilot GCP initiative.

Q7. As part of the GCP initiative, are the FDA and European Medicines Agency working to harmonize risk based approaches to inspections?

At the present time, risk based approaches to inspections are not included as a formal part of this initiative, but to the extent that selecting sites for inspection contributes to each regulatory agency's risk management, it is hoped that the initiative will lead to more consistent approaches in the agencies' risk-based site selection.

III. Potential Benefits

Q8. What benefits might develop out of this initiative?

Potential benefits of this collaboration include sharing of best practices, leveraging of finite inspectional resources, enhanced knowledge of evolving policies and guidance, and collaborating on interpretation of good clinical practice.

The pilot will evaluate processes of information exchange, share inspection planning and enhance mutual understanding and confidence in each other agency's processes. This will allow duplicative inspections to be avoided thus improving the range of sites being inspected with the available resources.

For companies that are developing new medicines, it is hoped that the effort will decrease the regulatory burden by minimizing duplicative inspections and by improving harmonization in how the FDA and the European Medicines Agency approach good clinical practice in the conduct of clinical trials.

For clinical investigators and others involved in planning and conducting clinical trials, it is hoped that the initiative will make it easier to conduct high quality research by improving understanding of what the FDA and the European Medicines Agency expect in the clinical trials and by minimizing differences in the interpretation of good clinical practice.

For consumers, it is hoped that it will help to improve access to promising new therapies on both sides of the Atlantic.

Overall goals include enhancing human subject protections internationally and ensuring that the highest quality data are used for regulatory decision making.

Q9. What does the FDA/European Medicines Agency expect the effect of the collaboration to be, in terms of how many more sites, or what larger proportion of sites, can be monitored?

The FDA/European Medicines Agency hope to be able to expand the coverage of inspections by avoiding duplication and using resources to widen inspection coverage to additional sites/countries but the agencies have not determined at this time how many more sites or what proportion that will be. More will be known when the results of the 18-month pilot are analyzed. In the analysis, the extent to which each agency can utilize information on the other's inspections in regulatory decision making will be considered.

IV. Sponsor/Applicant Information

Q10. Can sponsors/applicants volunteer to participate in this initiative?

Yes, any sponsor/applicant who intends to market the same medicinal product (e.g., same indications for use; same chemical entity/dosage form) in both the US and the EU, through MAA via the centralised procedure, can volunteer. The FDA and the European Medicines Agency may, in any case, select applications for inspections.

Q11. How many applications could the collaboration handle? Why would companies be interested in participating?

There is no set limit on the number of applications that will be handled during the pilot phase. It is anticipated that information sharing on inspections will occur on most, if not all, NDAs/BLAs and MAAs submitted to CDER and the European Medicines Agency, respectively, during the time frame covered by the pilot phase. As far as joint inspections to be conducted during the pilot phase, it is anticipated that between 4 and 6 applications will be handled. Prior to launching this initiative, sponsors have noted that both agencies often conducted duplicative inspections when the same medicinal product was submitted separately in marketing application to both regulatory authorities. These sponsors have expressed the wish that regulatory authorities minimize duplicative inspections.

Q12. How many sponsors/applicants does FDA/European Medicine Agency want to work with?

Although there is no set limit on the number of sponsors/applicants to be engaged with the pilot or the number of applications that will be handled during the pilot phase, it is anticipated between 4 and 6 applications will be involved with joint inspections.

Q13. Is it necessary that market applications be submitted to the FDA and the European Medicines Agency at the same time?

It is not necessary for the market applications to be submitted to both agencies at the same time. However, for FDA and the European Medicines Agency to take full advantage of this pilot, it will be important for applications to be submitted in parallel in order to conduct joint inspections.

Q14. Is there specific information that might be helpful to submit in the market applications to FDA and the European Medicines Agency?

Yes. It would be very helpful for sponsors/applicants to include inspectional information in the market application. If not already included in the submission, any of the following information may be included in the cover letter:

a. Any information about any inspections conducted by foreign regulatory authorities of sites from which clinical data will be used to support approval of the NDA/BLA/MAA. It would be most helpful to include in a table in the application the following information: 1) site inspected (name and address); 2) type of site (sponsor, CRO, investigator etc.); 3) dates of inspection; 4) identification of the inspecting regulatory authority; 3) summary of inspectional findings; and 4) inspectional outcome (if known).

b. Information about the market application submitted to the other regulatory agency. It would be most helpful to include the following information in the application: 1) the name of the medicinal product that is intended to be marketed in the other region; 2) the date the market application was submitted to the other agency; 3) other significant information such as any delay in the review/approval process.