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IPQ "In the News," February 10, 2011

FDA and EMA Will Launch Collaborative QbD Application Review Pilot

FDA and EMA will be conducting a pilot program for joint review of the quality-by-design component of new drug marketing applications – bringing the once-distant vision of a common review process a significant step closer to reality.

This pivotal step down the harmonization pathway was announced by FDA Office of New Drug Quality Assessment (ONDQA) Director Moheb Nasr and EMA Quality Working Party (QWP) Chair Jean-Louis Robert (Luxembourg Medicines Control Laboratory) at the conclusion of a February 7-9 CMC workshop in Washington, D.C. The workshop was sponsored by the Drug Information Association (DIA) and the American Association of Pharmaceutical Scientists (AAPS).

Nasr and Robert have both played key roles in helping define the new ICH Q8-10/QbD paradigm and serve together on the Q8-10 Implementation Working Group (IWG).

> **A formal release from FDA and EMA management providing further details on eligibility and participation in the pilot is expected imminently.**

Robert explained at the CMC workshop that the joint review will not "apply to the whole application file, but to the part relevant to quality by design – so mainly development, design space, real time release testing and so on."

He added that the pilot, as a first step, will include only chemical entities and not biologicals. It will encompass new drug applications and supplements/variations as well as scientific advice.

As in the FDA drug and biotech QbD pilots, participation will be voluntary, involving companies that are prepared to submit a filing at the same time in the US and Europe.

> **The pilot project was the fruit of several months of extended dialogue between Nasr, Robert and other key quality regulators at FDA and EMA on how to build on the increasingly solid foundation of harmonized guidelines, collaborative initiatives and information sharing efforts that has been laid across the CMC/review and GMP/inspection spectrum.** ***[Editor's Note: IPQ's May 2010 Special Report provides a comprehensive review of FDA and EMA progress in refining and implementing the ICH Q8-10 QbD paradigm.]***

Nasr highlighted the significance of having FDA and EMA "working collaboratively in assessing applications…. I think this is really a major step forward."

Regulators have been listening to industry on the challenges involved in having "different assessment expectations and requirements from different regulatory agencies," the ONDQA Director said. For the US

and Europe, he affirmed, the pilot represents "a sign that we are getting very close to complete alignment on regulatory expectations."

In approaching a joint CMC review effort, Nasr noted that the decision was made to "start with the most challenging one first, which is quality-by-design applications."

He emphasized that the pilot will involve collaboration between the FDA and EMA "before, during and after" the application review process, and will provide the opportunity for joint inspections that will include assessors/reviewers involved in QbD applications.

Joint Inspection Initiatives Help Lay the Groundwork

Some of the groundwork for the QbD review pilot has been laid by the two joint inspection initiatives in which the US and EU have been participating.

> **Of particular relevance is the FDA/EMA joint inspection pilot focused on preapproval inspections for finished product manufacturers. Under the pilot, companies that have submitted equivalent applications for the same product to both EMA and FDA have been eligible to request participation *(IPQ "In the News" August 12, 2010)*.**

In 2009 and 2010, a few joint inspections of manufacturing sites were carried out under the pilot, with enthusiastic reports back from the participating companies regarding the constructive interchange with the inspection teams involved.

Commenting on the "excellent alignment" he was hearing between the FDA and EU presenters at the DIA/AAPS CMC workshop, GlaxoSmithKline Product Development Manager Manish Gupta described GSK's participation in the joint inspection pilot as "first-hand experience" in that alignment. The "successful" combined week-long preapproval inspection included FDA and EU inspectors and reviewers and offered "a great exchange of information," the GSK official reported.

> **FDA and certain key agencies in Europe are also joining the European Directorate for the Quality of Medicines (EDQM) and Australia's Therapeutic Goods Administration (TGA) in conducting joint inspections of active pharmaceutical ingredient (API) manufacturers located globally.**

The API pilot, which began with a series of exploratory conference calls between the regulatory authorities in 2008, has enabled the rapid sharing of inspection reports for non-compliant sites, follow-up inspections at other facilities owned by the companies found to have non-compliant sites, and prompt notification of regulatory actions taken ***(IPQ "In the News" July 19, 2010)***

An "interim" progress report on the API pilot was issued in September, with a final report expected in the first quarter of 2011. The interim report indicated that seven joint inspections had been conducted to date in 2010 – each involving two of the participating agencies – and that numerous audit reports have been shared between the participating parties.

Jacques Morenas, Assistant Director of the French agency AFSSAPS, was on the podium with Robert and Nasr during their announcement of the QbD review pilot, and commented that the two joint inspection pilots represent important steps forward in decreasing the number of inspections and saving resources for "both competent authorities and industry."

Morenas has played a key role in helping set inspection policy in Europe and in its GMP/inspection harmonization and outreach efforts, such as the joint pilots, PIC/S, which he chaired from 2006 to 2009, and ICH. He now serves on the Q8-10 Implementation Working Group (IWG) with Nasr and Robert.

> **A confidentiality agreement signed in 2003 has provided the foundation for expanded quality regulatory information sharing between the FDA and EMA. The agreement provides for the exchange of information "during the review and evaluation of investigational and marketing applications and the post-marketing surveillance" of human and veterinary products.**

FDA and the EMA announced last September that they were extending the agreement "indefinitely without the need for further renewal" due to positive experiences by both agencies during the seven years the agreement has been in place ***(IPQ "In the News September 17, 2010)***.

[Editors note: On March 16, FDA issued a press release formally announcing the new pilot. In the release, CDER Director Janet Woodcock stressed the importance of the pilot in QbD information sharing and reducing redundancy (see box below)].

CDER's Woodcock on New FDA/EMA QbD Pilot

As the number of applications that follow the QbD approach steadily increases, collaborative assessments will enhance understanding of QbD concepts. The tools used by FDA and EU reviewers will increase information sharing and reduce redundancy. To fully implement QbD, we need to further harmonize the implementation of the guidelines, work collaboratively, and provide scientific, risk-based regulatory decisions in a timely manner.

LINKS:

FDA-EMA drug product joint inspection August 2010

API joint inspection interim report 2010

2003 FDA-EMEA confidentiality agreement

EMA 2010 statement of authority and confidentiality agreement with FDA

FDA 2010 statement of authority and confidentiality agreement with EMA

FDA Announcement of QbD Review Pilot

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