FDA Takes First Step in Recognizing the Role of Emerging Technologies in the Area of Process Validation

Effective March 12, 2004, FDA revised a long-standing policy document regarding the validation of pharmaceutical manufacturing processes for drugs that are subject to pre-market approval requirements. This policy guide is now titled *Process Validation Requirements for Drug Products and Active Pharmaceutical Ingredients Subject to Pre-Market Approval* (formerly titled *Process Validation Requirements for Drug Products Subject to Pre-Market Approval*). Compliance Policy Guides (CPG) are intended for agency staff and are for the purpose of consolidating agency compliance policy decisions.

As with the previous version of this policy guide, the new version reaffirms that agency drug product pre-market review units may approve applications for marketing before a firm has manufactured one or more conformance batches at commercial scale (also sometimes referred to as "validation" batches). The revised CPG again recognizes certain conditions under which a firm may market batches of drugs while gathering data to confirm the validity of the manufacturing process.

New to this version is the recognition of the role of emerging advanced engineering principles and control technologies in ensuring batch quality. For drugs produced using these new principles and technologies, this CPG provides for possible exceptions to the need for manufacturing multiple conformance batches prior to initial marketing. This version also deletes the previous reference to "three" validation (or conformance) batches at commercial scale as adequate minimum proof of process validity — a number is no longer suggested. Also, this version further clarifies the importance of post-market information gathering especially for those batches released to market concurrent with the manufacture of the initial conformance batches. And, finally, this version adds a reference to the currently recognized standard for CGMPs in the manufacture of active pharmaceutical ingredients: Guidance for Industry, Q7A, GMP Guidance for Active Pharmaceutical Ingredients, issued August 2001.

This is an important first step in the Agency's plan to address the area of process validation. The next step will be to update the *Guideline of General Principles of Process Validation* (May 1987), to reflect modern manufacturing principles, technology, and science. This update will be revised in accordance with the agency's Good Guidance Practice procedures and include public notice and comment before being finalized. The final step of this process will be addressing the proposed revisions of the CGMPs, the *Federal Register* dated May 3,1996, *Current Good Manufacturing Practice; Proposed Amendment of Certain*

requirements for Finished Pharmaceuticals. This effort is being taken in concert with FDA's initiative on the regulation of pharmaceutical quality known as "Pharmaceutical cGMPs for the 21st Century: A Risk-Based Approach." Progress on these issues will be included in future announcements on the initiative.

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