

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

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Guidance for Industry on Chemistry, Manufacturing, and Controls Information; Withdrawal and Revision of Seven Guidances

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice; withdrawal and revision.

SUMMARY: The Food and Drug Administration (FDA) is announcing the withdrawal of five and the revision of two guidances for industry, because some of the principles in these guidances are inconsistent with the agency’s initiative, Pharmaceutical Current Good Manufacturing Practices (CGMPs) for the 21st Century (CGMP Initiative). Several of the guidances listed in this notice are cross-Center guidances relating to products regulated by the Center for Drug Evaluation and Research (CDER), the Center for Biologics Evaluation and Research (CBER), and the Center for Veterinary Medicine (CVM).

FOR FURTHER INFORMATION CONTACT:

For products regulated by CDER: Jon Clark, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave.,

Bldg. 21, rm. 3550, Silver Spring, MD 20993–0002, 301–796–2020.

For products regulated by CBER: Christopher Joneckis, Center for Biologics Evaluation and Research (HFM–1), Food and Drug Administration 1401 Rockville Pike, suite 200N Rockville, MD 20852–1448, 301–435–5681.

For products regulated by CVM: Dennis Bensley, Center for Veterinary Medicine (HFV–140), Food and Drug Administration, 7500 Standish Pl., MPN II, Rockville, MD 20855, 301–827–6956.

SUPPLEMENTARY INFORMATION: FDA is announcing the withdrawal of five and the revision of two guidances for industry because of inconsistencies with the agency’s CGMP Initiative, announced by FDA on August 21, 2002. FDA introduced the Initiative for a number of reasons: (1) To enhance the CGMP, (2) to focus our resources and regulatory attention on those aspects of manufacturing that pose the greatest risk to the quality of the product, (3) to ensure that our work does not impede innovation in manufacturing, and (4) to promote consistency in our regulatory approach. A report on the outcome of the initiative and the recommended steps for implementing a pharmaceutical quality regulatory system for the future can be found on the FDA Web site at www.fda.gov/cder/gmp/gmp2004/GMP_finalreport2004.htm.

Many of FDA’s previously published guidances relating to chemistry, manufacturing, and controls information were drafted prior to the CGMP Initiative. FDA has begun a review of its guidances for their consistency with the CGMP Initiative and is withdrawing five guidances and revising two guidances as listed below. Several of the guidances are cross-Center guidances.

CDER—Only Guidance for Withdrawal

- *Format and Content of the Chemistry, Manufacturing, and Controls Section of an Application*, February 1987.

CDER/CBER Guidances for Withdrawal

- *Submitting Documentation for the Stability of Human Drugs and Biologics*, February 1987.
- *Stability Testing of Drug Substances and Drug Products (Draft)*, June 1998.
- *Drug Product: Chemistry, Manufacturing, and Controls Information (Draft)*, January 2003.
- *Submission of Chemistry, Manufacturing and Controls Information for Synthetic Peptides*, November 1994.

CDER/CBER Guidances for Withdrawal; CVM Guidances for Revision

CDER and CBER are withdrawing the following two guidances from their Web sites:

- *BACPAC I: Intermediates in Drug Substance Synthesis; Bulk Actives Postapproval Changes: Chemistry, Manufacturing, and Controls Documentation*, February 2001.
- *Drug Substance: Chemistry, Manufacturing, and Controls Information (draft)*, January 2004.

CVM made Level II revisions to the above two guidances to support their continued use in CVM for the approval of new animal drugs (e.g., removed references to human drug and biological products). The revised guidances are available on <http://www.fda.gov/cvm>. CVM is committed to and supports the CGMP Initiative and may draft additional guidance that supports the CGMP Initiative as it relates to new animal drugs.

We will continue to review our guidances for their consistency with the CGMP Initiative and may withdraw or revise other guidances if they do not reflect our current thinking or to align them with the concepts of the CGMP

Initiative, the Quality by Design Initiative, or Question-based Reviews. We also plan to develop new guidances to support these agency initiatives and to communicate guidance on submission of new drug applications and abbreviated new drug applications.

In the meantime, we recommend that the human drug pharmaceutical industry refer to the following International Conference on Harmonisation's (ICH) documents, which are available on FDA's Web sites, as alternate resources.

- *M4: Common Technical Document (CTD) for the Registration of Pharmaceuticals for Human Use (CTD)*, October 2001.
- *M4: The CTD—Quality*, August 2001.
- *Q1A(R2) Stability Testing of New Drug Substances and Products*, November 2003.
- *Q1B Photostability Testing of New Drug Substances and Products*, November 1996.
- *Q1C Stability Testing for New Dosage Forms*, May 1997.
- *Q1D Bracketing and Matrixing Designs for Stability Testing of New Drug Substances and Products*, January 2003.
- *Q1E Evaluation of Stability Data*, June 2004.
- *Q1F Stability Data Package for Registration Applications in Climatic Zones III and IV*, Revision 1, July 2004.
- *Q6A Specifications: Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances*, December 2000.
- *Q6B Specifications: Test Procedures and Acceptance Criteria for Biotechnological/Biological Products*, August 1999.

- *Q7A Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients*, August 2001.
- *Q8 Pharmaceutical Development* (Draft), February 2005.

The above list is not intended to be exhaustive. If questions arise that are not covered in the ICH guidances, we recommend that pharmaceutical manufacturers contact the appropriate review division.

Dated: May 18, 2006.

Jeffrey Shuren,

Assistant Commissioner for Policy.

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