

Guidance for Industry Quality Systems Approach to Pharmaceutical ~~Current Good~~ ~~Manufacturing Practice Regulations~~

~~DRAFT GUIDANCE~~

~~This draft guidance document is being distributed for comment purposes only.~~

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~~For questions regarding this draft document contact (CDER) Monica Caphart, 301-827-9047, (CBER) Robert Sausville, 301-827-6201, (CVM) June Liang, 301-827-8789, and (ORA) Patricia Maroney-Benassi, 240-632-6819.~~

**U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
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Office of Regulatory Affairs (ORA)**

**September ~~2004~~
~~Pharmaceutical CGMPs~~**

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Center for Drug Evaluation and Research
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Manufacturers Assistance, HFM-40
Center for Biologics Evaluation and Research
Food and Drug Administration
1401 Rockville Pike, Rockville, MD 20852-1448
<http://www.fda.gov/cber/guidelines.htm>.
(Tel) 800-835-4709 or 301-827-1800*

or

*Communications Staff, HFV-12
Center for Veterinary Medicine
Food and Drug Administration
7519 Standish Place, Rockville, MD 20855
(Tel) 301-827-3800
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Guidance for Industry¹

Quality Systems Approach to Pharmaceutical Current Good Manufacturing Practice Regulations

This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

~~I. INTRODUCTION~~

This draft guidance is intended to help manufacturers that are implementing modern quality systems and risk management approaches to meet the requirements of the Agency's current good manufacturing practice (CGMP) regulations (21 CFR parts 210 and 211). The guidance describes a *comprehensive quality systems (QS) model*, highlighting the model's consistency with the CGMP regulatory requirements for manufacturing human and veterinary drugs, including biological drug products. The guidance also explains how manufacturers implementing such quality systems can be in full compliance with parts 210 and 211. This guidance is not intended to place new expectations on ~~manufacturers~~ nor to replace the CGMP requirements. Readers are advised to always refer to parts 210 and 211 to ensure full compliance with the regulations.

FDA's guidance documents, including this ~~draft~~ guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the ~~agency's~~ current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in ~~agency~~ guidances means that something is suggested or recommended, but not required.

II. BACKGROUND AND PURPOSE

A. Background

In August 2002, the FDA announced the Pharmaceutical CGMPs for the 21st Century Initiative. In that announcement, the FDA explained the Agency's intent to integrate *quality systems* and *risk management* approaches into ~~existing programs with the goal of encouraging the adoption of~~ modern and innovative manufacturing technologies. The CGMP initiative was spurred by ~~the~~

¹ ~~This draft~~ guidance was developed by the Office of Compliance in the Center for Drug Evaluation and Research (CDER) in cooperation with the Center for Biologics Evaluation and Research (CBER), the Center for Veterinary Medicine (~~CVM~~) and the Office of Regulatory Affairs (ORA).

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II. BACKGROUND AND PURPOSE

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43 fact that since 1978, when the last major revision of the CGMP regulations was published, there
44 have been many advances in manufacturing technologies and in our understanding of quality
45 systems. Many pharmaceutical manufacturers are implementing comprehensive, modern quality
46 systems and risk management approaches. The Agency also saw a need to address the
47 harmonization of the CGMPs and other non-U.S. pharmaceutical regulatory systems as well as
48 FDA's own medical device quality systems regulations.

49
50 The CGMP initiative steering committee created a Quality System Guidance Development
51 working group (QS working group) to compare the current CGMP regulations, which call for
52 specific quality management elements, to other existing quality management systems. The QS
53 working group mapped the relationship between CGMP regulations (parts 210 and 211 and the
54 1978 Preamble to the CGMP regulations²) and various quality system models, such as the Drug
55 Manufacturing Inspections Program (i.e., systems-based inspectional program),³ the
56 Environmental Protection Agency's Guidance for Developing Quality Systems for
57 Environmental Programs, ISO Quality Standards, other quality publications, and experience
58 from regulatory cases. The QS working group determined that, although the regulations do
59 provide great flexibility, the CGMP regulations do not consider all of the elements that today
60 constitute most quality management systems. The CGMP regulations and other systems differ
61 somewhat in organization and in certain constituent elements; however, they are very similar and
62 share underlying principles. For example, the CGMP regulations stress quality control. More
63 recently developed quality systems stress quality management, quality assurance, and the use of
64 risk management tools, in addition to quality control. The QS working group decided that it
65 would be very useful to examine exactly how the CGMP regulations and the elements of a
66 modern, comprehensive quality system fit together in today's manufacturing world. This
67 guidance is the result of that examination.

68 69 **B. Goal of the Guidance**

70
71 This guidance describes a comprehensive quality systems model, which, if implemented, will
72 allow manufacturers to operate robust, modern quality systems that are fully compliant with
73 CGMP regulations. The guidance demonstrates how and where the requirements of the CGMP
74 regulations fit within this comprehensive model. The inherent flexibility of the CGMP
75 regulations should enable manufacturers to implement a quality system in a form that is
76 appropriate for their specific operations.

77
78 The overarching philosophy articulated in both the CGMP regulations *and* in robust modern
79 quality systems is:

80
81 ***Quality should be built into the product, and***
82 ***testing alone cannot be relied on to ensure product quality.***
83

¹ See Reference #1.

² See Reference #2.

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there have been many advances in manufacturing science and in our understanding of quality systems. In addition, many pharmaceutical manufacturers are already implementing comprehensive, modern quality systems and risk management approaches. This guidance is intended to help manufacturers implementing modern quality systems and risk management approaches to meet the requirements of the Agency's CGMP regulations. The Agency also saw a need to harmonize the CGMPs with other non-ILS pharmaceutical regulatory systems and with FDA's own medical device quality systems regulations. This guidance supports these goals. It also supports the objectives of the Critical Path Initiative, which intends to make the development of innovative medical products more efficient so that safe and effective therapies can reach patients sooner.

The CGMPs for the 21st Century Initiative steering committee created a Quality System Guidance Development working group (QS working group) to compare the current CGMP regulations, which call for some specific quality management elements, to other existing quality management systems. The QS working group mapped the relationship between CGMP regulations (parts 210 and 211 and the 1978 Preamble to the CGMP regulations²) and various quality system models, such as the Drug Manufacturing Inspections Program (i.e., systems-based inspectional program),³ the Environmental Protection Agency's Guidance for Developing Quality Systems for Environmental Programs, ISO Quality Standards, other quality publications, and experience from regulatory cases. The QS working group determined that, although the CGMP regulations do provide great flexibility, they do not incorporate explicitly all of the elements that today constitute most quality management systems.

The CGMP regulations and other quality management systems differ somewhat in organization and in certain constituent elements; however, they are very similar and share underlying principles. For example, the CGMP regulations stress quality control. More recently developed quality systems stress quality management, quality assurance, and the use of risk management tools, in addition to quality control. The QS working group decided that it would be very useful to examine exactly how the CGMP regulations and the elements of a modern, comprehensive quality system fit together in today's manufacturing world. This guidance is the result of that examination.

B. Goal of the Guidance

This guidance describes a comprehensive quality systems model, which, if implemented, will allow manufacturers to support and sustain robust, modern quality systems that are consistent with CGMP regulations. The guidance demonstrates how and where the elements of this comprehensive model can fit within the requirements of the CGMP regulations. The inherent flexibility of the CGMP regulations should enable manufacturers to implement a quality system in a form that is appropriate for their specific operations.

The overarching philosophy articulated in both the CGMP regulations *and* in robust modern quality systems is:

¹ See Reference #1.

² See Reference #2.