



**Computer Systems Services
& Consulting, Inc.**

111 04 2004 11 24

Food and Drug Administration
Dockets Management Branch, HFA-305
5630 Fishers Lane, Room 1061
Rockville, MD 20852

November 24, 2004

Subject: Federal Register Docket 2004D-0443, *Guidance for Industry: Quality Systems Approach to Pharmaceutical Current Good Manufacturing Practice Regulations*

Summary

CSSC, Inc. feels that the expectations described in the draft Guidance for Industry mirror existing quality system requirements in 21 CFR 820, and we propose establishing clearer links between the existing regulation and the new Guidance. CSSC is concerned that a Quality System Guidance that is not linked to predicate regulations could potentially confuse firms attempting to comply with interdivisional expectations.

Introduction

In September 2004, FDA issued a draft guidance document whose stated purpose is to “help manufacturers that are implementing modern quality systems and risk management approaches to meet the requirements of the Agency’s current good manufacturing practices (CGMP) regulations,” specifically as described in 21 CFR Parts 210 and 211. This draft document solicits input from industry.

CSSC, Inc. is a worldwide regulatory and compliance consulting firm headquartered in Morristown, N.J. CSSC specializes in assisting pharmaceutical firms in meeting FDA compliance expectations, especially those involving Quality Systems and Good Manufacturing Practices. In response to an emphasis placed on Quality Systems inspections by FDA’s New Jersey District Office, CSSC has increased its expertise in this field by recruiting managers with strong backgrounds in Medical Devices Quality Systems—the ISO13485 standard and especially 21 CFR 820, the Quality System Regulation (QSR). CSSC therefore is providing comment on the draft Guidance as a representative consultant to the pharmaceutical industry.

2004D-0443

C4

The QSR and QSIT

The Quality System Inspection Technique, or *QSIT*, is an internal FDA document developed by the Center for Devices and Radiological Health (CDRH) to facilitate inspections of Medical Device firms. It directs Consumer Safety Officers and other Agency Inspectors to concentrate on a select sample of subsystems whose impact on product quality and regulatory compliance is well established. QSIT is not itself a law, regulation, or guidance; but it is predicated on quality concepts practiced throughout the industry and which are a subset of the expectations spelled out in CDRH’s *Medical Device Quality System Manual: A Small Entity Compliance Guide*.

As stated, QSIT (and the QSR it supports) applies only to the Medical Device industry. However, FDA has a long-standing policy of applying any division’s rules to wherever it may be pertinent to assuring the public health. For example, another CDRH document, *Guidance for Industry: General Principles of Software Validation* has found widespread application throughout the regulated Life Sciences industry. Furthermore, the Quality System Regulation contains an implicit statement that its scope far exceeds just Medical Devices: “The quality system regulation in this part supplements regulations in other parts of this chapter except where explicitly stated otherwise” (21 CFR 820.1(b)). It is therefore clear that drug firms are already subject to quality system requirements. While the draft guidance intimates this in Section I (“This guidance is not intended to place new expectations on manufacturers”), it never states clearly that firms have a pre-existing obligation to meet quality system expectations. A firm could therefore erroneously conclude that maintenance of a compliant quality system is entirely optional.

CSSC has performed an analysis of the individual quality elements contained in the draft guidance and compared them to 21 CFR 820. With the notable exception of Laboratory Controls—which do not have dedicated requirements in the current draft—every element maps directly to specific and *preexisting* expectations in the Quality System Regulation, as shown in the following table:

Draft Guidance Element	Corresponding QSR	Draft Guidance Element	Corresponding QSR
Quality by Design	820.20(d)	Outsourced Operations (purchasing)	820.50
Risk Analysis and Management	820.30(g)	Process Design	820.30(h), 820.70(a)
Resource Management	820.20(b)(2), 820.25(a)	Packaging and Labeling Control	820.40, 820.120, 820.130
Change Control	820.40, 820.70(b)	Input Requirements	820.30(c)
The Quality Unit (quality management)	820.20(a)	Output Verifications	820.30(d)
Defined Management Responsibilities	820.20(b)(1)	Process Monitoring (process control)	820.70(a)(2), 820.75(b)
Organizational Structure	820.20(b)	Nonconformity Processes	820.90
Quality Policies	820.20(a)	Continuous Improvement	820.5, 820.20(d), 820.100(a)
Quality System Review	820.20(c)	Internal Audits	820.22
CAPA	820.100	Trend Analysis	820.100(a)(1), 820.250(a)



Laboratory Controls are difficult to map into Part 820, which expects quality processes to be applied upon applicability and risk, rather than regulatory demarcations such as those found in 21 CFR 211.160 or Part 58. Nonetheless, the draft guidance does not appear to assign Laboratory Controls special status but instead reminds users that laboratories should be subject to the same quality expectations as other areas and functions.

In some cases, references have been made in this table to the Medical Device Design Control requirements. CSSC does not infer that drug manufacturers are, or should be, subject to 21 CFR 820.30; we recognize that the development of pharmaceuticals is substantially different than devices. However, it is axiomatic that the concepts behind design controls (as embodied by more general standards such as ISO9001) are vital to successful quality implementation. The concepts of documented design inputs, verified outputs, and management review and oversight have applicability across the entire quality system, and the draft guidance appears to embrace these widely accepted precepts.

Conclusion

Since it can be demonstrated that the elements of the proposed guidance map into Part 820—an existing regulation widely viewed as the premier quality standard in the Life Sciences—CSSC questions the approach taken in presenting essentially the same elements in a different format. We are concerned that this could result in confusion in the industry as to what standard to utilize, especially for firms engaged in production of Combination Devices.

CSSC therefore respectfully requests that the Agency modify the draft *Guidance for Industry: Quality Systems Approach to Pharmaceutical Current Good Manufacturing Practice Regulations* to explicitly cite 21 CFR Part 820 as an underlying structure and reorganize the elements to match those already found in *The Quality System Inspection Technique*, along with those additional Part 211-specific elements that are unique to drug and biologics manufacturers (for example, the explicit requirement for and duties of a dedicated Quality Control Unit under 21 CR 211.22). This way, firms will have a clear understanding of Agency expectations of their Quality System, regardless of whether they are audited by CDER, CDRH, or their local district office.

Should you should find that these comments were helpful, CSSC would welcome the opportunity to assist further. Thank you for your consideration.

Best Regards,



r. Jeff Boatman
Director of Quality, CSSC Inc.

