

## COMMENT TO DOCKET 2005D-0286

I am deeply disturbed by the draft guidance, **Approaches to Complying with CGMP During Phase I**. This response to the docket provides some specific reasons for my concern that this draft guidance is deeply flawed.

1. **Emphasis on “quality control (QC) principles” and not on quality systems.** Throughout the draft guidance there is mention of “QC principles”; I could not even find the term “quality system” in the draft guidance. The term, “Quality control principles” is not defined, however “quality control”, as it is currently used in the pharma industry, is generally limited to analytical testing and release. What happened to the “quality systems” thinking that CDER, et al have been emphasizing? Why are quality systems apparently not applicable to a lab that makes a product for Phase I? If quality systems are not applicable, how can FDA make a case for them in large-scale manufacturing? Why should Phase I facilities be exempt from the “many advances in manufacturing technologies and in our understanding of quality systems” that was mentioned in FDA’s Draft Guidance on Quality System Approaches?

2. **Inconsistency with other regulatory authorities.** It is ironic that while FDA is working with ICH, PIC/S, and other agencies/groups as they together try to globally harmonize GMP, this draft document seems to stray far from the path taken by EU in its Annex 13.

3. **Recommendation “that QC responsibilities be performed independently from production responsibilities”.** This statement is troublesome as it violates one of the key concepts of GMP: there must be checks and balances. In GMP, one person does not verify his or her own work. This principle does not require a large staff or infrastructure: It simply says that someone else must be convinced that the product was made properly and according to GMP before it can be released.

4. **Forgetting that small manufacturing operations can adversely affect public health.** One of the closest comparators to facilities making Phase I clinical trial materials are pharmacies that do compounding – a segment of the pharmaceutical industry that has contributed to numerous problems. FDA Warning Letters over the past five years show this.

5. **Attempting to achieve short-term benefits in a way that could have a dramatic negative long-term impact.** FDA is right in looking at ways to improve the “critical path” to encourage innovation. However, if Phase I materials are found to cause or contribute to injury or deaths of study subjects, consider how this might cause profound, long-term effects on clinical studies. Would study subjects be more or less likely to be part of these important research efforts?

I urge FDA to reconsider this draft guidance. Yes, guidance is needed, particularly for the number of new laboratories that are being created in hospitals, medical centers, and non-traditional research facilities to produce Phase I materials. The guidance needs to be quality system focused and have integrity with GMP concepts and practices that have been evolving since the 1960s.

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