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

Re: **Docket No. 97N-484P,** Proposed Rule; Good Tissue Practice for Manufacturers of Human Cellular and Tissue-Based Products; Inspection and Enforcement; Federal Register January 8, 2001

PDA is pleased to provide these comments on the Proposed Rule for Good Tissue Practice for Manufacturers of Human Cellular and Tissue-Based Products; Inspection and Enforcement. PDA is an international professional association of more than 10,000 individual member scientists having an interest in the fields of pharmaceutical manufacturing and quality. Our comments were prepared by a group of international experts in this field.

We support the establishment of Current Good Tissue Practice (CGTP) regulations that would require cells and tissues to be handled according to procedures designed to prevent contamination and to preserve tissue function and integrity.

If you have any questions regarding our comments, or how we may assist with further development of the proposed rule, please contact me.

Sincerely,

Edmund M. Fry
President

Attachment: PDA comments on the Proposed Rule for Good Tissue Practice for Manufacturers of Human Cellular and Tissue-Based Products; Inspection and Enforcement.

97N-484P

C7

Major Comment

Orders of retention, recall, destruction, and cessation of manufacturing. 1271.440

- (a) This section provides FDA with the authority to take dramatic and far reaching enforcement actions for noncompliance with the CGTP regulations. Such noncompliance may range from deficiencies which allow product contamination to procedural or record keeping deficiencies which have no reasonable adverse impact on the quality of the product. As the stated impetus for proposing the regulations is to prevent cellular and tissue product contamination and to preserve product function and integrity, the standard for taking severe enforcement action (including the retention, recall and destruction of product and an order to cease manufacture) should be higher than mere CGTP deficiencies. The standard should include that the deficiencies reach the level of an imminent hazard to health, as defined in FDA regulation (21 CFR 2.5).

  Recommendation: Insert the phrase, "and constitutes an imminent hazard to public health" to subsection (a), second line, after the words, "...of the regulations in this part."

Other Comments

Definitions 1271.3

- (gg) The Adverse Reaction definition is unnecessarily broad in that it includes any "...reasonable possibility that the response may have been caused by the product." This broad interpretation of clinical responses may burden manufacturers and distributers in their review and evaluation of reports from clinicians, which have little probability of having significance to consumers. In contrast, current drug and biologic adverse reporting regulations narrow the scope of events to those with "reasonable probability" [21 CFR 201.57 (g)] or which are "associated with the use of the product" [21 CFR 600.80 (a)].

  Recommendation: Change the words "reasonable possibility" to "reasonable probability" in the definition.

- (nn) The Quality Audit definition indicates that an "...independent inspection...," take place, however, the term "independent" is not defined. Section 1271.160 (d) (2) provides a possible definition of the term "independent" but does not state that it is the agency's definition of the term.

  Recommendation: In order to clarify the regulatory expectation, define the term

"independent" through a reference to section 1271.160 (d) (2) or provide a separate definition in a footnote to 1271.3 (nn) in the definition section.

- (rr) Validation, the definition given here is not harmonized with the ICH definition as used in Q7A (GMPs for Active Pharmaceutical Ingredients).

  Recommendation: Change to read "A documented program that provides a high degree of assurance that a specific process, method, or system will consistently produce a result meeting predetermined acceptance criteria."

General 1271.50

- Compliance with parts 210, 211 and 820 of this chapter. This section states "...procedures...in this subpart...and the ...regulations in parts 210 and 211... and in part 820 of this chapter shall be considered to supplement, not supersede each other... In the event it is impossible to comply with all applicable regulations in these parts, the regulations specifically applicable to the biologic drug or device in question shall supersede any other requirements." As each of the subpart regulations cited (210, 211, 820) are general in nature, rather than specific, the last sentence of the section provides no useful guidance as to the appropriate standard to follow.

  Recommendation: Delete the last sentence of section 1271.50 (c).