

November 5, 2001

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

Re: Current Good Tissue Practice for Manufacturers of Human Cellular and Tissue-Based Products; Inspection and Enforcement

To Whom It May Concern:

The Food and Drug Administration (FDA) issued a proposed rulemaking seeking comments on its plan to develop and institute current good tissue practice (CGTP) for manufacturers of human cellular and tissue-based products, hereinafter referred to as the CGTP rule.¹ The regulation would seek to assure that manufacturers follow CGTP, which includes methods used in, and the facilities and controls used for, the manufacture of human cellular and tissue-based products; recordkeeping; and the establishment of a quality program. The rulemaking identifies the extensive nature of the industries that will be affected by the CGTP rule, including eye banks, conventional tissue banks, hematopoietic stem cell facilities and reproductive tissue facilities.

The Office of the Chief Counsel for Advocacy of the United States Small Business Administration was created in 1976 to represent the views and interests of small business in Federal policy making activities. The Chief Counsel participates in rulemakings when he/she deems it necessary to ensure proper representation of small business interests. In addition to these responsibilities, the Chief Counsel monitors compliance with the RFA, and works with Federal agencies to ensure that their rulemakings demonstrate an analysis of the impact that their decisions will have on small businesses.

The Office of Advocacy appreciates and commends the FDA on the public policy objectives behind the CGTP rule. Advocacy agrees that there is a public benefit derived from protecting patient safety in the manufacture of human cellular and tissue-based products. However, Advocacy is concerned that the rule will be particularly onerous on small businesses. Further, Advocacy wants to insure that the FDA is not creating artificial market barriers to small business by implementing the rule. Based on the rule's provisions and the findings contained in the FDA's analysis of impacts, Advocacy is of

¹ 66 Fed. Reg. 1508 (January 8, 2001).

the opinion that the FDA should make every attempt to assure that small businesses are given the opportunity to compete in the human cellular and tissue-based marketplace. This request is not meant to provide special competitive advantages for affected small businesses, rather it is meant to lessen the rule's economic burden that falls primarily on the shoulders of small businesses. This has heightened importance in light of evidence that suggests that small businesses are vital to the development and success of new and emerging technologies, especially in areas such as those covered by this rule.

The FDA analyzed the CGTP rule under the Regulatory Flexibility Act (hereinafter RFA). The FDA chose not to certify that the rule would not have a significant impact on a substantial number of small entities. Because it was unable to certify no impact, the FDA appropriately performed an analysis of the rule's cost impacts. The FDA admitted that many of the establishments within the tissue industry would be classified as small businesses, and a number of those entities will incur new costs. The FDA characterized the costs on such entities as uncertain. The FDA could not fully assess small business impacts because it was unable to determine accurately current practices and compliance with industry standards at the facilities covered by the rule, and because the agency lacked data on business revenues. Therefore, the FDA asked industry to comment on: the number of facilities involved in the manufacture of cellular and tissue products; the net change in quality assurance efforts needed for those facilities to comply with the proposed rule; the percentage of firms that qualify as small businesses; and industry revenues. Advocacy believes that the FDA should increase its outreach to small entities in an effort to obtain the information necessary to fully assess the rule's impacts before finalization.

Pursuant to Section 604 of the RFA, Advocacy asserts that upon publication of the final rule, the FDA should address comments received regarding small business impacts and provide an assessment of small business revenues that are likely to be affected by the rule's implementation. A determination of facility revenue is vitally important as the FDA measures the impact of CGTP by calculating the ratio of industry compliance costs to industry revenues. Despite a dearth of information on these issues, the rule's assessment of small business impacts estimates that compliance costs for the affected firms will be small when based on the annual revenue per firm. The FDA should make every effort to confirm whether this conclusion is in fact the case. It is obvious that if the FDA significantly underestimated firm revenues the rule's resultant costs to the firms could be far greater than those estimated.

Section 1271.155 of the rule seems to allow all businesses affected by the regulation to seek an exemption or alternative from the requirements of the rule. For the purposes of this letter Advocacy will assume that section 1271.155 of the rule is FDA's attempt to comply with Section 603(c) of the RFA, which requires agencies to identify any significant alternatives available to small entities in their initial regulatory flexibility analysis. While Advocacy applauds the FDA for providing businesses with exemptions/alternatives to the rule, the end result is that section 1271.155 lacks teeth. In fact, the FDA concludes, "that there is currently no basis for predicting industry requests for exemptions or alternatives." In fact, the FDA concludes, "that there is currently no basis for predicting industry requests for exemptions or alternatives." Further, "FDA anticipates that very few facilities will consider it appropriate to be exempted from the quality standards specified in the proposed rule." If the FDA is inclined to allow for exemptions and alternatives to the rule then the FDA should evaluate reasonable exemptions and alternatives, especially as to how small entities may qualify for such treatment.

Despite the lack of information on the firms expected to be affected by the rule, the FDA hypothesizes that many of the affected industries already have operations in place that meet or exceed the specifications required by the CGTP rule. FDA estimates that the affected industries are already between 75-100% compliant. If the above is true, then Advocacy questions whether the rule will result in creating another layer of unnecessary recordkeeping and training requirements for the affected firms. Any additional financial burden placed on small entities at this time could make a difference in the survival of the businesses and ultimately could hinder innovation in these important scientific areas.

Lastly, Advocacy is concerned that the FDA places the ultimate responsibility for the product in the hands of the firm distributing the product, while other companies will undoubtedly participate in the manufacturing process. Pursuant to Section 1271.150(b)(2) of the rule the distributor of the product will be responsible for maintaining documents from all other companies involved in the manufacturing process. Advocacy is concerned that this methodology will place an unacceptable burden on the administrative costs to small entities. Advocacy suggests that the FDA adopt the alternative discussed in the proposed rule that allows for a cascading set of responsibilities. This will give each company involved in the process a stake in assuring that the product is manufactured in compliance with the rule thereby reducing disease and minimizing the administrative costs to all companies. The alternative should include a uniform method for tracking the product. This will also serve to establish chain-of-custody in the event that a product is found to be deficient.

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Thank you for your attention to the above matters. If you have any questions concerning the contents of this letter or Advocacy's position on this matter in general, please do not hesitate to contact Linwood Rayford at (202) 401-6880.

Sincerely yours,

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