MDMA MEDICAL DEVICE MANUFACTURERS ASSOCIATION

Serving the Innovator and Entrepreneur in the Medical Device Industry

May 11, 2001 4164 '01 MAY 14 A9:53

Stephen J. Northrup
202-496-7150
snorthrup@medicaldevices.org

VIA FEDERAL EXPRESS

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

Re: Comments to Docket No. 97N-484P
Proposed Rule: Current Good Tissue Practice for Manufacturers of Human Cellular and Tissue-Based Products; Inspection and Enforcement

Dear Sir or Madam:

On January 8, 2001, the Food and Drug Administration ("FDA") published in the *Federal Register* a proposed rule entitled, "Good Tissue Practice for Manufacturers of Human Cellular and Tissue-Based Products." These comments are submitted by the Medical Device Manufacturers Association ("MDMA") on behalf of its members and address the content of the preamble as well as the proposed rule itself.

The proposed rule appears to mirror current Good Manufacturing Practices ("cGMPs")/Quality System ("QS") Regulations for *in vitro* diagnostics and current blood borne pathogen guidelines, and to that extent appears reasonable. However, MDMA maintains that many provisions of the proposed rule are duplicative of the regulations and guidelines already in place and only create another layer of unnecessary record keeping for its members.

Furthermore, MDMA believes that several provisions of the proposed rule extend beyond its original intent – to minimize the actual risk of disease transmission during the manufacturing process of human cellular and tissue-based products – and therefore place an undue regulatory burden on the limited resources of its members. If enacted, the proposed rule would bring to a halt the innovative activities of companies which manufacture human cellular and tissue-based products. A discussion of these provisions follows.

97N-484P C39

Proposed 21 C.F.R. § 1271.150(b)(2)

FDA has tentatively concluded that the best approach is to assign ultimate responsibility for the product to the company that is responsible for making the product available for distribution. Under this provision, FDA would require every company to collect and store documents from all other companies participating in the manufacturing process. However, this provision would place an excessive administrative burden on its members, especially smaller companies with limited resources. Alternatively, FDA discussed adopting the "cascading" set of responsibilities, in which each company (1) would be responsible for ensuring that its own operations comply with applicable requirements, and (2) would bear the burden of proof that operations performed by other companies prior to its receipt of cells or tissues were performed in compliance with applicable requirements. Assigning the responsibility for the product to all companies participating in the manufacturing process would not only help minimize the risk of disease transmission but also reduce the administrative burden on all companies.

Recommendation: FDA should reconsider its tentative conclusion and adopt the "cascading" set of responsibilities.

Proposed 21 C.F.R. § 1271.160(b)(2)

Under this provision, FDA would require every company to establish procedures for sharing and receiving information that could affect the integrity and function of a human cellular or tissue-based product, the possible contamination of the product, or the potential transmission of communicable disease by the product. However, this provision would be impractical if all companies were required to share and receive information, because a particular company may have to disclose proprietary information (e.g., customer lists and manufacturing processes) to competitors. Alternatively, FDA should assign the responsibility for sharing and receiving information to the vendor, who is in the best position to contact all its customers in the event of an emergency. This arrangement is common in industry practice.

Recommendation: FDA should narrow the scope of this provision to require only the vendor to share and receive information among its customers.

Proposed 21 C.F.R. § 1271.160(b)(7)

Under this provision, FDA would require every company to investigate and document all product deviations in manufacturing. However, the definition of

product deviation under proposed 21 C.F.R. § 1271.3(kk) is sufficiently broad to include even minor events. As a result, an FDA inspector, who would have the authority to determine what constitutes a *product deviation* during a site inspection, could cite a company for alleged violations that do not increase the risk of disease transmission.

Recommendation: FDA should narrow this provision to include only product deviations in manufacturing that would increase the risk of disease transmission.

Proposed 21 C.F.R. § 1271.220(c)

Under this provision, FDA would prohibit the pooling of human cells or tissues from two or more donors during manufacturing. In the preamble, FDA states this provision is consistent with recommendations made by the Transmissible Spongiform Encephalopathy ("TSE") Advisory Committee with respect to the pooling of dura mater. However, this provision contradicts many years of established industry practice with regard to other human cells and tissue. Since all human source material is already tested on an individual donor basis by validated methods, subsequent commingling of human cells or tissues would not increase the risk to recipients of exposure to infectious agents.

This provision appears to be an overreaction to the current fears regarding TSEs. Since the recommendation of the TSE Advisory Committee was limited to the pooling of dura mater, expanding this recommendation to include all human cells and tissues is premature because not all human cells and tissues have been shown to transmit TSEs. The current regulation (21 C.F.R. Part 1270) appears to respond to concerns about the known transmission risks of HIV and hepatitis, while the proposed rule appears to respond to concerns about the hypothetical transmission risks of infectious disease. Furthermore, the current regulations allow for the pooling of human blood, even though the overall risk of disease transmission is greater in human blood than it is in other human cells and tissues.

Recommendation: FDA should consider revising this provision to reflect the known risks of disease transmission by various human tissue types.

Proposed 21 C.F.R. § 1271.290

FDA would require every company to track human cellular or tissue-based products. However, unless all companies adopt a uniform method of tracking, it would be impossible to establish a *chain-of-custody* from donor to recipient. Furthermore, this provision would limit the number of vendors available to

customers because vendors may elect not to participate in tracking due to potential disclosure of proprietary information.

Recommendation: FDA should clarify this provision to require every company to maintain the necessary records in order for FDA to preserve a *chain-of-custody* from donor to recipient.

Respectfully Submitted,

Stephen J. Northrup SK

Stephen J. Northrup

SJP/sk

FedEx. USA Airbill

FedEx Tracking Number: 8131 2415 5104

Form I.D. No. 0215

Recipient's Copy

SP1122

RECIPIENT: PEEL HERE

1 From This portion can be removed for Recipient's records.

Date 7/12/04

FedEx Tracking Number 813124155104

Sender's Name Stu Kim

Phone 202 496-7500

Company MCKENNA & CUNEO LLP

Address 1900 K ST NW STE 100

Dept./Floor/Suite/Room

City WASHINGTON State DC ZIP 20006

2 Your Internal Billing Reference 16523-0001

3 To

Recipient's Name Document Management Branch

Phone

Company HFA-305 FDA

Address 5630 Fishers Lane, Room 1061

We cannot deliver to P.O. boxes or P.O. ZIP codes.

Dept./Floor/Suite/Room

To "HOLD" at FedEx location, print FedEx address here.

City Rockville State MD ZIP 20852

8131 2415 5104

0097663638

4a Express Package Service — *Packages up to 150 lbs.* Delivery commitment may be later in some areas.

- [x] FedEx Priority Overnight — Next business morning
- [ ] FedEx Standard Overnight — Next business afternoon
- [ ] FedEx First Overnight — Earliest next business morning delivery to select locations
- [ ] FedEx 2Day* — Second business day
- [ ] FedEx Express Saver* — Third business day

* FedEx Letter Rate not available. Minimum charge: One-pound rate

4b Express Freight Service — *Packages over 150 lbs.* Delivery commitment may be later in some areas.

- [ ] FedEx 1Day Freight* — Next business day
- [ ] FedEx 2Day Freight — Second business day
- [ ] FedEx 3Day Freight — Third business day

* Call for Confirmation:

5 Packaging * Declared value limit $500

- [x] FedEx Letter*
- [ ] FedEx Pak*
- [ ] Other Pkg. — Includes FedEx Box, FedEx Tube, and customer pkg.

6 Special Handling

- [ ] **Saturday Delivery** — Available for FedEx Priority Overnight and FedEx 2Day to select ZIP codes
- [ ] **Sunday Delivery** — Available for FedEx Priority Overnight to select ZIP codes
- [ ] **HOLD Weekday at FedEx Location** — Not available with FedEx First Overnight
- [ ] **HOLD Saturday at FedEx Location** — Available for FedEx Priority Overnight and FedEx 2Day to select locations

Does this shipment contain dangerous goods? One box must be checked.

- [x] No
- [ ] Yes — As per attached Shipper's Declaration
- [ ] Yes — Shipper's Declaration not required
- [ ] Dry Ice — Dry Ice, 9, UN 1845 ____ x ____ kg
- [ ] Cargo Aircraft Only

Dangerous Goods cannot be shipped in FedEx packaging.

7 Payment *Bill to:* Enter FedEx Acct. No. or Credit Card No. below.

- [ ] Obtain Recip. Acct. No.
- [x] Sender — Acct. No. in Section 1 will be billed.
- [ ] Recipient
- [ ] Third Party
- [ ] Credit Card
- [ ] Cash/Check

Total Packages	Total Weight	Total Charges
1		Credit Card Auth.

†Our liability is limited to $100 unless you declare a higher value. See the *FedEx Service Guide* for details.

8 Release Signature *Sign to authorize delivery without obtaining signature.*

By signing you authorize us to deliver this shipment without obtaining a signature and agree to indemnify and hold us harmless from any resulting claims.

Questions? Call 1·800·Go·FedEx® (800-463-3339)

Visit our Web site at www.fedex.com

359