
Manual of Standard Operating Procedures and Policies

General Information

Tissue Reference Group

SOPP 8004

Version #2

June 7, 2002

1. Purpose

This guidance describes the process that the Tissue Reference Group (TRG) follows to schedule and document TRG meetings, prepare recommendations to the CBER and CDRH Center Directors based on discussions at these meetings, and maintain files to document responses and inquiries concerning human cells, tissue, and cellular and tissue-based products (HCT/Ps).

2. Background

The TRG was created as specified in the "Proposed Approach to the Regulation of Cellular and Tissue-based Products" published by FDA in February of 1997. The TRG is one component of the Tissue Action Plan (TAP), which was developed to implement the "Proposed Approach" on a timely basis, and reports regularly to the TAP Core Team. The TAP Core Team is composed of FDA staff, who oversee the progress on the commitments of the TAP. The TRG is composed of three representatives from the Center for Biologics Evaluation and Research (CBER) and three from the Center for Devices and Radiological Health (CDRH), including the product jurisdiction officer at each Center. An executive secretary carries out the functions described below. A liaison from the Ombudsman's Office and the Office of the Chief Counsel attends meetings. Other FDA staff are asked to attend meetings as needed, to discuss issues related to HCT/Ps in their area of expertise.

3. Policy

CBER and CDRH intend to provide a single reference point for product-specific questions received by the Centers or the Ombudsman's Office from manufacturers and sponsors or their designated representatives regarding existing or investigational products containing or consisting of HCT/Ps. The TRG considers these questions and prepares recommendations regarding jurisdiction, policy, and regulations related to novel HCT/Ps to promote consistency in the implementation of the Tissue Action Plan. Questions the TRG considers include whether HCT/Ps meet the criteria for regulation solely under section 361 of the PHS Act, are a device or biologic, or what the primary mode of action of a combination product is. The TRG does not publicly release correspondence received or TRG responses because of limits on disclosure of confidential information as contained in the Freedom of Information Act and the Privacy Act.

4. Responsibilities and Procedures

TRG meetings are routinely held on the first and third Monday of the month from 2:30pm to 4:00pm. A schedule of meetings for the year is generated at the beginning of the year and meetings will not be scheduled on Federal holidays.

Responding to Inquiries from Sponsors or Manufacturers to the TRG:

- The executive secretary of the TRG may be contacted directly by sponsors or manufacturers, concerning regulation of HCT/Ps. The name of the executive secretary and contact information are on the FDA TAP Website at www.fda.gov/cber/tissue/trgcont.htm. In addition, TRG members and other FDA staff forward all calls/inquiries from sponsors or manufacturers concerning regulation of novel HCT/Ps to the TRG executive secretary. The executive secretary, when appropriate, may inform the sponsor or manufacturer whether there is insufficient information to respond to the inquiry. The executive secretary may advise the sponsor or manufacturer what, if any, information would be helpful for the TRG to respond to the specific inquiry. Such information may relate to the factors specified in 21 CFR Part 1271.10 that determine whether an HCT/P will be regulated solely under section 361 of the Public Health Service (PHS) Act.
- Inquiries concerning regulation of products already designated as biologics or devices through regulation, policy statements, or other agency communications, are not within the scope of the TRG issues and will be directed to the appropriate reviewing Division with product responsibility. Inquiries that involve trade complaints will be forwarded to the respective CBER/CDRH Office of Compliance.
- Inquiries, with accompanying information about the product, are placed on the agenda for the next scheduled TRG meeting and should be reviewed in order of receipt. The executive secretary prepares the agenda, which is forwarded to TRG members by e-mail, in advance of the meeting, along with all background information received. The TRG attempts to respond within 60 calendar days of receiving an inquiry in writing. Sometimes, after reviewing the available information, the TRG may determine that there is insufficient information upon which to consider and respond to the inquiry. The executive secretary should communicate this information to the sponsor or manufacturer. The TRG should discuss any additional information provided to FDA at the next available meeting after receipt. A sponsor or manufacturer may request to meet with the TRG to present information. When the TRG reaches a recommendation, the TRG executive secretary prepares a draft response letter, which reflects the recommendation and the reasons supporting the recommendation. The draft response letter is circulated by e-mail for TRG review. Comments are due to the executive secretary within 7 working days after distribution. The letter is forwarded to CBER's Senior Policy Advisor and Counselor for Biologics, and to CBER and CDRH Center Directors for review and signature, and the signed letter is returned to the executive secretary for mailing.
- If the TRG cannot reach a recommendation in applying the factors in 21 CFR Part 1271.10, the matter is placed on the agenda of the TAP Core Team for discussion at its next scheduled meeting. If the TAP Core Team cannot reach a recommendation, the matter is referred to the Center Directors, with a summary of the TRG and TAP Core Team deliberations, for resolution.
- If the sponsor or manufacturer does not agree with the TRG or Center Directors recommendation, the sponsor or manufacturer may submit a Request for Designation (RFD) to the Ombudsman's Office, as provided under 21 CFR Part 3.
- If the TRG cannot reach a recommendation for regulation of a HCT/P identified, above, as not meeting the factors in 21 CFR Part 1271.10, the TRG executive secretary prepares a draft response letter (for review and sign off as above) recommending that the sponsor or manufacturer file a Request for Designation (RFD) with the FDA Ombudsman Office as described in 21 CFR Part 3.

Responding to a Request for Designation forwarded directly from the Ombudsman's Office

On issues of HCT/P jurisdiction, the manufacturers or sponsors may go directly to the FDA Ombudsman's Office by filing a RFD. RFDs involving HCT/Ps are sent to the Centers' product jurisdiction officers and to the TRG where appropriate. The TRG sends recommendations to the Centers' product jurisdiction officers, within 15 days, taking into consideration the time constraints of the Ombudsman's Office (60 calendar days from the time of receipt of the RFD). The Centers' product jurisdiction officers consider the TRG recommendations in drafting the Centers' recommendations (see SOPP 8003 Requests For Designation), as appropriate. The Centers' recommendations are forwarded to the Ombudsman's Office.

Responsibilities of the Executive Secretary:

- The executive secretary records meeting minutes. Minutes consist of a brief summary of the topics, with action items. Draft minutes are e-mailed to TRG members for review and comment. The executive

secretary finalizes the minutes, and provides copies to TRG members and liaisons. The meeting agenda and minutes are maintained and available for FDA personnel only on the TAP intranet site.

- The executive secretary distributes copies of letters (by e-mail or mail) signed by the Center Directors to TRG members, liaisons, and CBER- Office jurisdiction liaisons in product application Offices.
- The executive secretary maintains a file for each issue discussed by the TRG, as well as a file for agendas and minutes.
- The executive secretary maintains, updates and distributes a database of TRG recommendations to TRG and TAP Core Team members. The database is maintained on the TAP intranet site for FDA staff.
- Annually, the executive secretary prepares a list of TRG recommendation, redacted for confidential commercial information. The annual TRG report/update is maintained on the TAP Internet site at www.fda.gov/cber/tissue/tissue.htm.

5. Effective Date

June 7, 2002

6. History

Written/Revised	Approved	Approval Date	Version Number	Comment
Marty Wells, Sharon Riso, Diane Maloney, Jill Warner, Areta Kupchyk, Ruth Solomon, Marybeth Jacobs	Robert Yetter, Ph.D	June 7, 2002	2	This change incorporates language of the final rule (21CFR1271.10) published in January 2001, clarification of timeframes, staff responsibilities and formatting.
	Rebecca Devine, Ph.D	July 28, 1998	1	Original

Updated: June 11, 2002