Biological Product Deviation Reporting

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Introduction

cGTP Final Rule in effect as of May 25, 2005

Two parts:
- Biological Deviation Reports
- Adverse Event Reporting

Applies to non-reproductive Human Tissues and Cellular and Tissue-Based Products (HCT/Ps) regulated under section 361 of the PHS
FDA guidelines

Biological Deviation Reporting Guidelines

- http://www.fda.gov/cber/biodev/biodev.htm
- The important thing to remember is that it doesn’t refer to every deviation that occurs in your lab, only the ones that are related to transmission of communicable disease.
Definition of a Deviation

The term “HCT/P deviation” is defined in 21 CFR 1271.3(dd) as an event:

1. that represents a deviation from applicable regulations or from applicable standards or established specifications that relate to the prevention of communicable disease transmission or HCT/P contamination; or

2. that is an unexpected or unforeseeable event that may relate to the transmission or potential transmission of a communicable disease or may lead to HCT/P contamination
FDA Codes

Importance of familiarizing yourself with the codes

Deviation Codes
- http://www.fda.gov/cber/biodev/devcode.htm
- Three types
  - Blood BPD codes
  - Non-Blood BPD codes
  - HCT/P BPD codes

Product Codes
- http://www.fda.gov/cber/biodev/nbldcode.htm
“…(A)n event is only required to be reported [see 1271.350(b)(2)] if it relates to “core Current Good Tissue Practices” [see 1271.150(b)], involves a distributed HCT/P, and occurs in your facility or a facility that performs a manufacturing step for you under contract, agreement, or other arrangement.”

DE - Donor Eligibility
DS - Donor Screening
DT - Donor Testing
EC - Environmental Control and Monitoring
SR - Supplies and Reagents
RE - Recovery
PC - Processing and Processing Controls
LC - Labeling Controls
ST - Storage
SD - Receipt, Pre-Distribution, Shipment, and Distribution
Deviation Codes

Examples

- **DT-**-**-** DONOR TESTING
  - **DT-03-** Unacceptable specimen tested
    - **DT-03-01** - Specimen collected more than 7 days before or after recovery
    - **DT-03-02** - Specimen collected from donor 1 month of age or younger, instead of from birth mother
    - **DT-03-03** - Specimen collected from a peripheral blood stem cell donor more than 30 days before recovery
Deviation Codes

Examples

- **RE -**-** RECOVERY**
  - **RE-01-** Manner of recovery
    - **RE-01-01** - HCT/P contaminated, potentially contaminated, or cross-contaminated during recovery

- **PC -**-** PROCESSING AND PROCESS CONTROLS**
  - **PC-01-** Processing
    - **PC-01-01** - HCT/P contaminated, potentially contaminated, or cross-contaminated during processing
    - **PC-01-02** - HCT/Ps from more than one donor were pooled during manufacturing
Product Codes

Importance of familiarizing yourself with these codes as well

- Two types of Product Codes:
  - Blood product codes
    [Website](http://www.fda.gov/cber/biodev/bldcode.htm)
  - Non-Blood product codes
    [Website](http://www.fda.gov/cber/biodev/nbldcode.htm)
Product Codes

HCT / Ps

*Reporting encouraged, but not required for these products

- JH01 – Fascia
- JH02 – Cartilage
- JH03 – Bone
- JH04 – Ligament
- JH05 – Tendon
- JH06 – Vascular Graft
- KH01 – Semen *
- KH02 – Oocyte *
- KH03 – Embryo *
- LH01 – Cornea
- LH02 – Sclera
- LH03 – Whole Eye
- LH04 – Limbal graft

- MH01 – Umbilical Cord
- MH02 – Peripheral Blood Stem Cells
- MH03 – Bone marrow stem cells
- MH04 – Donor Leukocytes
- MH05 – Tendon
- MH06 – Vascular Graft

- OH01 – Skin
- OH02 – Heart Valve
- OH03 – Dura Mater
- OH04 – Pericardium
- OH05 – Amniotic membrane
- OH06 – Nerve
- OH07 – Parathyroid tissue
- OH08 – Placenta
- OH09 – Spinal cord
- OH10 – Testicular tissue
- OH11 – Trachea
- TA01 – Autologous Cultured Chondrocytes
REPORT FORM #42 Deviation Management

Type of Occurrence: 

Date of Occurrence: Date Form Completed: 

Tech(s) Involved: 

Patient Name: Medical Record Number: 

Brief Description: 

Corrective Action – short term: 

Corrective Action – long term: 

Follow-up: Date: Initials: 

Physician notified: Date: Time: 

Physician response: 

Laboratory and/or Medical Director notified: YES NO 

Signature of Tech Completing Form: Date: 

Medical or Laboratory Director Analysis: 

- Component not compromised, no risk to recipient 
- Report as Adverse Event at monthly TQM meeting 
- Report to FDA as Biological Product Deviation. Code: 

Medical or Laboratory Director Comments: 

Signature of Medical or Laboratory Director: Date: 

Laboratory or Medical Director Signature: Date:
BPD Reporting

Paper Form


Electronic Form

http://www.fda.gov/cber/biodev/biodevsub.htm
Mock Reporting Exercise

- Took an event that occurred prior to the May 25th deadline
- Wrote it up as a BPD on the FDA form, recommended
  - Practise filling out the form
  - Information needed to complete form
  - Familiarity with the codes
Adverse Event Reporting

21 CFR 1271.350(a)

Must initiate an investigation of any adverse reaction involving a communicable disease.

Must report using MedWatch form if:

- fatal
- life-threatening
- results in permanent impairment
- medical or surgical intervention
Comparison of Reporting

Adverse Event Reporting
- 15 days from receipt of info
- Reported by facility that made HCT/P available for distribution
- FDA form 3500A

BPD Reporting
- 45 days from receipt of info
- Reported by manufacturer
- FDA Form 3486
Examples

- Infusion of product that subsequent tests prove to be contaminated
- Failure of testing lab to demonstrate sterility of product
- Infusion of a contaminated product due to medical exception
Examples

- Mislabeling of product due to transcription error that does NOT result in a transmission of communicable disease
- An adverse reaction to infusion that is considered an anticipated or expected event according to a defined SOP.
Exception

- BPDs and AEs that occur with NMDP products are NOT reportable to the FDA. They are 351 products under the NMDP’s IND for HPC-As, TC-Ts are voluntarily reported to the FDA.

- Report events to your NMDP coordinator in Search and Transplant at the NMDP who will in turn report it to the FDA.

- NMDP Contact for questions is Fran Rabe in Quality Systems and Management Services Dept; frabe@nmdp.org,
Conclusions

Remember that BPD under GTPs refers to the *transmission* of communicable disease from biological products (*distributed* products)

Use the FDA Website for clarification and reporting as it has full instructions and lots of information