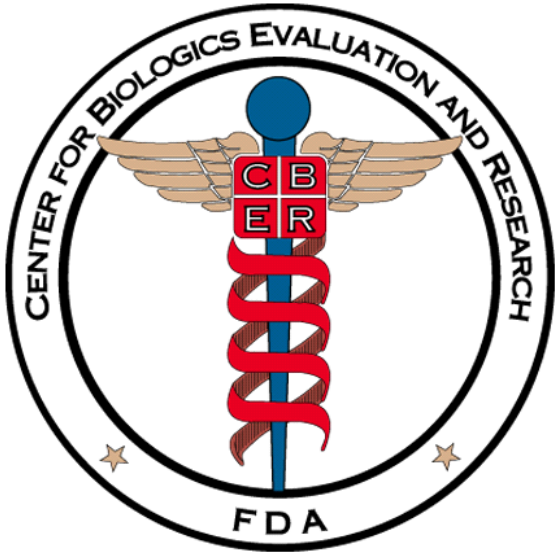

Top Ten Pitfalls With Submissions

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Licensure of Apheresis Blood Products

August 15, 2007

Top Ten Pitfalls With Submissions

1. Donor Informed Consent and applicable SOPs do not include all possible adverse reactions cautioned by device manufacturers
2. Applicable SOPs are not submitted with the application
3. SOPs are incomplete
4. Failure Investigation SOPs are incomplete
5. Quality Control data in submissions missing or inadequate

Top Ten Pitfalls With Submissions

6. Quality Control form incomplete
7. General content problems
8. Comparability protocol content problems and subsequent submissions
9. Label submissions incomplete
10. Platelet product submissions

Top Ten Pitfalls With Submissions

- **Donor Informed Consent and Applicable SOPs Do Not Include all Possible Adverse Reactions cautioned by device manufacturers. For example:**
  - **Anxiety**
  - **Allergic symptoms**
  - **Unusual taste or smell**
  - **Improper operating conditions may cause complications such as: blood loss, hemolysis, air embolism and blood clotting**

Top Ten Pitfalls With Submissions

- **Applicable SOPs are not submitted with the application**
  - **SOPs that have an impact on the manufacture of the components being requested for licensure**

    should be included, such as:
    - **Quality Control SOPs**
    - **Failure Investigation SOPs**
    - **Donor Reaction SOPs**
    - **Approved SOPs that have undergone major revisions**

    - **Note: Previously approved SOPs do not have to be submitted but the firm needs to reference the STN.**

Top Ten Pitfalls With Submissions

- **SOPs are Incomplete:**
  - **SOPs including donor deferral criteria are often lacking pertinent information (such as Red Blood Cell Loss)**
  - **SOPs do not state what to do with Platelets, Pheresis, or Red Blood Cell components that have been flagged for QC by the collection device for possible leukocyte reduction problems (relabel or discard?)**
  - **SOPs for component collection do not contain all of the operation specifications described in the device operators manual such as:**
    - **Type of sample**
    - **Timeframe for performing WBC and platelet counts**
    - **What to do if timeframe for testing is not met.**

Top Ten Pitfalls With Submissions

- **SOPs are Incomplete (continued):**

SOPs Describing Monthly QC Do Not Always Include:

- **Random or representative selection**
- **Time limits for testing [21 CFR 211.111]**
- **Acceptance/rejection criteria [21 CFR 211.165(d)]**
- **Disposition of unsuitable units [21 CFR 211.165(f)]**

Top Ten Pitfalls With Submissions

- **Failure Investigation SOPs often do not**
  - **Include when to initiate a failure investigation/root cause analysis**
  - **Include methods for investigation and correction**

Top Ten Pitfalls With Submissions

- **Quality Control Data in Submissions Missing or Inadequate**
  - **Monthly QC data for Platelets, Pheresis does not always include the required collections per machine type, product type, per site**
  - **Two consecutive months of QC data not submitted with application**
  - **Monthly QC for apheresis Red Blood Cells does not always include fifty units per site with at least one single component included**
  - **The measured total volume is not within the volume limits**

Top Ten Pitfalls With Submissions

- **Monthly QC Data Forms Do not Include all Required Information:**
  - **Facility [21 CFR 211.194(a)(1)]**
  - **Device manufacturer and type [21 CFR 211.194(a)(2)]**
  - **Blood Unit Number [21 CFR 606.140(c)]**
  - **Date of collection [21 CFR 211.194(a)(1)]**
  - **Date of testing [21 CFR 211.194 (a)(7); 606.160 (a)(1)]**
  - **Appropriate collection types (single, double, triple)**

Top Ten Pitfalls With Submission

- **Monthly QC Data Forms Do Not Include All Required Information (Continued)**
  - **Interpretation of results [21 CFR 211.194(a)(6); 606.160 (a)(1); 606.160 (a)(2)(i)]**
  - **Yield [21 CFR 211.103; 211.186(b)(7)]**
  - **Acceptable criteria [21 CFR 211.165(d)]**
  - **Initials [21 CFR 211.194 (a)(7); 606.160 (a)(1)]**
  - **Evidence of review [21 CFR 211.194(a)(8; 211.103)]**
  - **Records of calculations [21 CFR 211.194 (a)(5)]**

  - **Note: If using summary sheets, copies of the raw data should be included**

Top Ten Pitfalls With Submissions

- **General Submission Content Problems**
  - **Form FDA 356h not included**
  - **Cover letter does not accurately or clearly state what the firm is requesting**

Top Ten Pitfalls With Submissions

- **Comparability Protocol Submissions Often Lack:**
  - **Summary of validation including performance/acceptance criteria**
  - **Summary of results**
  - **Description of actions taken if acceptable results are not achieved**
  - **Proposed change in reporting category**
  - **Description of training**
  - **Subsequent submissions do not refer to approved STN**

Top Ten Pitfalls With Submissions

- **Label Submissions Lack:**
  - **A completed Form FDA 2567, “Transmittal of Labels and Circular Form”**
  - **Conformity with Codabar or ISBT Format**

Top Ten Pitfalls With Submissions

- **Product Submission**
  - **Improper Shipment of Products to Department of Hematology**
    - **Temperature is not maintained during shipment**
    - **Products are not received between Monday – Friday**
    - **Products expiring over the week-end**

Summary

- **This is not an all inclusive list of deficiencies that we see in submissions.**
- **In addition to following the CFR, firms should follow the manufacturers operators manuals and package inserts**
- **Submitting a complete application may ensure a comprehensive review in a shorter timeframe.**