Collection of Platelets by Automated Methods Guidance Documents

Background

- FDA guidance provides blood establishments and FDA staff with FDA's current thinking on acceptable ways to comply with regulatory requirements.

- Guidance is intended to help you ensure donor safety and the safety, purity, and potency of the product.

Background

- We consider the recommendations in guidance documents to provide appropriate criteria for a biologics license application or supplement for manufacturing and provides guidance on preparing a manufacturing supplement under Title 21 Code of Federal Regulations 601.12.

Background

- FDA's guidance documents, including guidance discussed today, do not establish legally enforceable responsibilities. Instead, guidances describe the FDA's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in FDA's guidances means that something is suggested or recommended, but not required.

FDA Guidance for Industry

- Guideline for Collection of Platelets, Pheresis, October 1988
- Draft: Guidance for Industry and FDA Review Staff Collection of Platelets by Automated Methods, September 2005
- Issues under current consideration

Donor Selection

- A donor weight
  - Donor weight requirements in the Operators Manual of the instrument must be followed [21 CFR 606.60(a)]

    As stated in the 2005 draft guidance, one issue under consideration at FDA is minimum donor weight of 110 lbs.

Donor Selection

- Platelet Pheresis donors must meet all the donor suitability requirements described in 21 CFR 640.3

Donor Selection

- Additionally FDA recommends:
  - All AIDS related deferral procedures are followed

Donor Selection

FDA recommends (cont):

- Persons who have recently ingested medicines containing aspirin, especially within 36 hours should not donate platelets.

Donor Selection

At the March 2006 BPAC meeting and on the FDA docket, public comments were made on the medication deferrals in the the draft guidance. The issues and data are currently under consideration at FDA.

Donor Selection

FDA recommends (cont):

- The platelet count should be greater than 150,000/uL.
  - Platelet counts obtained after the previous procedure may be used.
  - Donors with platelet counts less than 150,000/uL should be deferred until the count has returned to normal.

Donor Selection

FDA recommends (cont):

- A donor should not undergo more than 2 procedures in a 7 day period with an interval of 48 hours between procedures.
- A donor should not generally undergo a total of more than 24 platelet pheresis procedures during a calendar year.

Donor Selection

The donation frequency and donation intervals from the draft guidance are issues currently under consideration at FDA. Based on comments that were received, we are considering the following issues:

- Collections per year
- Donation interval for doubles and triples
- Minimum post donation target

Donor Selection

FDA recommends (cont):

- Any person who has donated a unit of Whole Blood or who has lost the equivalent amount of whole blood during a platelet pheresis procedure should not serve as a pheresis donor for eight weeks if the extracorporeal volume is greater than 100 mL.

Donor Selection

FDA recommends (cont):

- Maximum total red blood cell loss for one calendar year should not exceed the loss of red blood cells permitted by FDA regulations for Whole Blood collection [21 CFR 640.3]
- Red blood cell loss for pheresis procedures that exceed the frequency limit stated for Whole Blood should be monitored.
- complete and accurate records should be maintained.

Donor Selection

FDA recommends (cont):

- The total volume (excluding anticoagulant) of all products should not exceed 500 mL (600 mL for donors weighing more than 175 lbs). Collection of plasma by-products resulting in a larger total volume will be considered upon receipt of requests.

Donor Selection

FDA recommends (cont):

- The accumulated laboratory data for donors should be monitored by qualified personnel and reviewed every four months by a licensed physician.
- Donors should be questioned about adverse reactions.
- Pheresis instruments employed should be approved [cleared] by CBER.

Informed Consent

FDA recommends (cont):

- Informed consent should be obtained from new donors.
- On subsequent donations a simple consent is adequate.
- Appropriate consent should be obtained by a physician or an allied health person experienced in the procedure to be performed.
- A copy should be offered to the person signing the form.

Informed Consent

FDA recommends (cont):

- The following information should be provided each donor.
  - A description of the procedure
  - A description of the possible adverse effects and side effects of the procedure and solutions and/or drugs the donor will receive.

Informed Consent

FDA recommends (cont):

- A clear opportunity to refuse consent
- A statement that participation is voluntary and that donors may withdraw their consent anytime.
- A statement informing the donor of his/her right to ask questions of and discuss the procedure with a physician.
- A statement that the long term effect of the reduction of lymphocytes is not clear
- A statement that the donor has reviewed and understands the information provided to him/her regarding the spread of AIDS virus by donated blood and plasma.

Collection Protocols

- The equipment shall be observed, standardized and calibrated on a regularly scheduled basis. [21 CFR 606.60]

Collection Protocols

FDA recommends:

- A qualified Physician who is familiar with the procedure should be available to attend the donor within 15 minutes.
- Personnel engaged in platelet pheresis should obtain specialized training for the use of the instruments.

Collection Protocols

FDA recommends (cont):

- During the procedure you should visually inspect the plasma for hemolysis.
- There should be a written procedure for management of a cardiopulmonary emergency which contains steps for contacting physicians, obtaining an emergency rescue squad, and transport of the donor to the hospital.

Processing and Testing

FDA recommends:

- Platelets, Pheresis should be tested as a whole blood donation.
- A hematocrit should be performed on final products containing visibly apparent red blood cells to determine total packed red blood cell volume.
  - If the final product contains more than 2 mL of pRBCs, a sample of donor blood should be attached to the container for compatibility testing.

Processing and Testing

FDA recommends (cont):

- The dating period for Platelets, Pheresis collected with an approved instrument is 24 hours from the termination of the procedure, unless the system used for collection has been specifically approved for longer storage.

Processing and Testing

FDA recommends (cont):

- Platelets Pheresis should be stored at 20 – 24^{o}C

Processing and Testing

FDA recommends (cont):

- During the establishment phase of the procedure the following determinations should be made for each unit:
  - Hematocrit or red blood cell count
  - Platelet count
  - White blood cell count
  - pH
  - Total product volume
  - Sterility test at outdate

  The procedure may be considered established when all operators have been trained and several consecutive procedures yield consistently satisfactory products meeting all requirements.

Processing and Testing

Once the procedure is operating satisfactorily for QC you must:

- Test four units per month at issue for actual plasma volume, pH and platelet count. [21 CFR 640.25]
  - All units must have a pH of not less than 6.0

Processing and Testing

Additionally, we recommend for QC:

- At least 75% of the units tested should contain a minimum of 3.0×10^{11} platelets
- A WBC count should be done if applicable
- The product volume should be determined after sampling.
- The standard operating procedure should contain acceptable limits for instruments.

Processing and Testing

The draft guidance addressed the importance of statistically significant sampling plans for quality control. We received many comments from industry and are considering several issues for the final guidance.

Processing and Testing

FDA recommends (cont):

- The actual platelet yield should be determined on every unit. These data should be a part of the issue records.

Labeling

FDA requires:

- A statement that “This product may transmit infectious agents.”
- The name, address, registration number, and, if a licensed product, the license number of each manufacturer.
- The donor, unit number.
- The expiration date, including the day, month, and year, and, if the dating period for the product is 72 hours or less, the hour of expiration.
- The donor’s ABO and Rh blood groups
- A statement indicating the kind and volume of anticoagulant solution present.

Labeling

FDA Requires:

- The proper name of the product in a prominent position, and modifier(s), if appropriate.
- The appropriate donor classification statement, i.e., "paid donor" or "volunteer donor”
- The volume of the product, accurate to within +/-10 percent; or a volume range within reasonable limits.
- The recommended storage temperature (in degrees Celsius).
- "Rx only."
- "See circular of information for indications, contraindications, cautions, and methods of infusion."
- "Properly identify intended recipient."

Labeling

FDA recommends:

- The instruction circular should include the following specific information in addition to the general requirements for all blood products:
  - Instructions to begin administration as soon as possible but should not exceed 4 hours after entering the container
  - A statement that the actual platelet content is available from the manufacture upon request
  - Instructions to maintain continuous gentle agitation during storage.

Labeling

The instruction circular must also include the following specific information in addition to the general requirements for all blood products:

Instructions to use a filter [21 CFR 606.122(b)]

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