

§ 558.355 Monensin.

(d) (6) The labeling of all formulations containing monensin shall bear the following caution statement: Do not allow horses or other equines access to formulations containing monensin. Ingestion of monensin by equines has been fatal.

(7) The labeling of all premixes and feed supplements (liquid and dry) containing monensin intended for use in cattle shall bear, in addition to the caution statement in paragraph (d)(6) of this section, the following caution statements:

(i) Monensin medicated cattle feed is safe for use in cattle only. Consumption by unapproved species may result in toxic reactions;

(ii) Feeding undiluted or mixing errors resulting in high concentrations of monensin could be fatal to cattle;

(iii) Must be thoroughly mixed in feeds before use;

(iv) Do not feed undiluted;

(v) Do not exceed the levels of monensin recommended in the feeding directions, as reduced average daily gains may result.

(8) The labeling of complete feeds containing monensin intended for use in cattle shall bear the caution statements specified in paragraph (d)(6) and (7) (i) and (v) of this section.

(9) The labeling of premixes containing monensin intended for use in chickens shall bear the caution statements specified in paragraph (d)(6) and (7) (iii) and (iv) of this section.

Effective date, October 29, 1982.

(Sec. 512(i); 82 Stat. 347 (21 U.S.C. 360(i)))

Dated: October 21, 1982.

Gerald B. Guest,

Acting Director, Bureau of Veterinary Medicine.

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21 CFR Parts 600, 610, and 640

[Docket No. 79N-0405]

**Platelet Concentrate (Human);
Additional Standards**

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending the biologics regulations by: (1) eliminating the volume limits required for the shipping, processing, and storage of Platelet Concentrate (Human); (2) requiring that the Rh and ABO blood

group be designated on the label of Platelet Concentrate (Human); and (3) reducing the dating period for Platelet Concentrate (Human) and Single Donor Plasma (Human), Platelet Rich stored at 1° to 6° C from 72 hours to 48 hours from the time of collection of the source blood. These updated regulations, based on recently published scientific studies and experience, reflect an improvement in the safety, purity, potency, and efficacy of Platelet Concentrate (Human).

DATES: Effective November 29, 1982; labeling requirements shall become effective April 29, 1983.

FOR FURTHER INFORMATION CONTACT: T. Rada Proehl, National Center for Drugs and Biologics (HFB-620), Food and Drug Administration, 8800 Rockville Pike, Bethesda, MD 20205, 301-443-1306.

SUPPLEMENTARY INFORMATION: FDA issued additional standards for Platelet Concentrate (Human) on January 29, 1975 (40 FR 4300) under §§ 640.20 through 640.26 (21 CFR 640.20 through 640.26). As a result of significant changes in platelet production since the publication of the additional standards for Platelet Concentrate (Human), FDA published a notice of proposed rulemaking in the Federal Register on January 15, 1980 (45 FR 2852) to amend the biologics regulations specifically by (1) eliminating the volume limits for Platelet Concentrate (Human), (2) requiring that Rh and ABO blood groups be designated on the label for Platelet Concentrate (Human), and (3) reducing the dating period for Platelet Concentrate (Human) and Single Donor Plasma (Human). These changes are discussed below.

A. Elimination of Volume Limits for Platelet Concentrate (Human)

Section 640.24(d) (21 CFR 640.24(d)) previously required that a specified volume of original plasma be used for the resuspension of platelets and that the plasma be stored at a specified temperature in order to maintain a pH of not less than 6.0 during the storage period. The required storage temperature and corresponding volume of resuspension plasma to be used continuously was: 20° to 24° C resuspended in 30 to 50 milliliters of plasma or 1° to 6° C resuspended in 20 to 30 milliliters of plasma. The pH was required to be measured on a sample of platelet concentrate at the selected storage temperature. As stated in the proposal, current manufacturing techniques produce a higher concentration of platelets in each unit of Platelet Concentrate (Human). This change in platelet concentration is

significant because the current upper limit of 50 milliliters for the volume of resuspension plasma for Platelet Concentrate (Human) no longer ensures the maintenance of the required pH of not less than 6.0 during the storage period. Platelet viability is known to be compromised at a pH of less than 6.0. Consequently, the present limits for the volume of resuspension plasma for Platelet Concentrate (Human) do not ensure the quality of the product or encourage the development of techniques that improve the yield of platelets from a unit of source blood. FDA therefore proposed to eliminate the volume limits and to require that the volume of resuspension plasma be determined solely by the maintenance of a pH of not less than 6.0 during the storage period. The proposal did not recommend change of the storage temperatures which continue to be 20° to 24° C or 1° to 6° C with pH measured on a sample of platelet concentrates stored for the maximum dating period at the selected storage temperature. Consistent with the elimination of the volume limits of resuspension plasma in § 640.24(d), FDA also proposed to amend § 640.20(a) (21 CFR 640.20(a)) to revise the wording concerning the volume of resuspension plasma in the definition of Platelet Concentrate (Human). Correspondingly, FDA proposed to eliminate references to the volume limits of the resuspension plasma for Platelet Concentrate (Human) in § 600.15(a) (21 CFR 600.15(a)) and § 640.25(a) (21 CFR 640.25(a)).

B. Requiring Label Designation of ABO and Rh Blood Group

Section 640.26(e) (21 CFR 640.26(e)) previously required the container label for Platelet Concentrate (Human) to bear the blood group designations. Although tests used to identify both the ABO and Rh blood groups are required for the blood from which plasma is separated for the preparation of Platelet Concentrate (Human), the existing labeling requirements were interpreted by many people to apply only to the ABO blood group designation because of its clinical use. The proposal explained that designation of the Rh blood group is important because platelet products are contaminated with significant number of red blood cells which can cause immunization to the Rh antigen. Therefore, FDA proposed to amend § 640.26(e) to specify that the container label for Platelet Concentrate (Human) bear the ABO and Rh blood group designation of the source blood.

C. Reduction of Dating Period

The previous dating period in § 610.53(a) (21 CFR 610.53(a)) for Platelet Concentrate (Human) and Single Donor Plasma (Human), Platelet Rich stored at 20° to 24° C or 1° to 6° C was 72 hours from the time of collection of the source blood. Because published studies demonstrate that platelets stored at 1° to 6° C for 72 hours are substantially and significantly inferior to platelets stored at 20° to 24° C for the same period, FDA proposed to reduce the dating period for Platelet Concentrate (Human) and Single Donor Plasma (Human), Platelet Rich stored at 1° to 6° C from 72 hours to 48 hours from the time of collection of the source blood. Consistent with the reduction in dating period in § 610.53(a), FDA proposed to amend § 640.25(b) (21 CFR 640.25(b)) to specify that quality control testing be performed at the end of the storage period.

Interested persons were given until March 17, 1980 to file written comments regarding the proposal with the agency. Ten comments were received on the proposal. Three comments completely supported the proposed changes. One comment proposed an amendment to 21 CFR 640.24(b) to extend the time from 4 hours to 6 hours for separating platelet concentrate after the collection of the unit of whole blood or plasma. Although this comment is outside the scope of the subject proposed, the agency advises that it is currently considering data and, if appropriate, will propose to amend the regulations using separate rulemaking procedures.

The remainder of the comments received and the agency's responses appear below:

1. One comment stated that proposed § 600.15(a) was confusing because it specified two shipping temperature ranges but did not specify what storage temperatures the shipping temperatures corresponded to. The comment recommended that the two shipping temperature requirements be related to the storage temperature requirements prescribed in § 610.53(a).

The agency agrees with this comment. For clarification, the agency is amending proposed § 600.15(a) to require that the temperature during shipping be between 1° and 10° C, if the label indicates storage between 1° and 6° C, or if the label indicates storage between 20° and 24° C, all reasonable methods to maintain the shipping temperature as close as possible to a range between 20° and 24° C.

2. One comment suggested clarifying proposed § 610.53(a), which prescribes the dating period for Platelet Concentrate (Human) stored at 20° to

24° C or 1° to 6° C. Proposed § 610.53(a) required that the dating period be "48 hours from the time of collection of source blood, provided labeling recommends storage at 1° to 6° C." The comment recommended that the phrase "if shipped and stored" be substituted for the phrase "provided labeling recommends storage." However, the comment did not explain why the suggested clarification was needed.

The agency disagrees with the comment because the shipping and storage temperatures for Platelet Concentrate (Human) are different. According to § 600.15(a), a shipping temperature of 1° to 10° C is permitted for Platelet Concentrate (Human) that is labeled for storage at 1° to 6° C. Under the proposed comment, the shipping temperature for Platelet Concentrate (Human) stored at 1° to 6° C would be limited to 1° to 6° C. This would be inconsistent with § 600.15(a). Accordingly, the comment is rejected.

3. Two comments on proposed § 610.53(a) objected to the proposed reduction in the dating period (expiration date) from 72 hours to 48 hours for Platelet Concentrate (Human) stored at 1° to 6° C. The comments acknowledged published data demonstrating a shortened survival in the long-term stored refrigerated (1° to 6° C) platelets. The comments further stated, however, that the reduction will result in burdens being imposed upon the attending physician, the hemorrhaging patient, and the night blood bank technician in emergency situations because platelets may be unavailable as a result of the reduced dating. The comments stated that the reduced risk of bacterial contamination of the product is an additional factor which should be considered for retaining the current 72-hour dating period for platelets stored at 1° to 6° C. One of the comments proposed a label statement to indicate that platelets stored for 72 hours between 1° and 6° C be permitted for use if the platelets stored at 48 hours are not available.

The agency emphasizes that the dating period established for Platelet Concentrate (Human) or for any biological product as prescribed in § 610.53(a) is "based on data relating to usage, clinical experience or laboratory tests that establish the period beyond which the product cannot be expected beyond reasonable doubt to yield its specific results and retain its safety, purity, and potency provided the product is maintained at the recommended temperatures." According to section 351(d) of the Public Health Service (PHS) Act, licenses are issued to establishments for the manufacture of

products in interstate commerce only if the product meets standards designed to ensure the continued safety, purity, and potency of such products.

As stated in the preamble of the proposal, data available to the agency demonstrate that platelets stored at 1° to 6° C for 72 hours result in a product having inferior clinical efficacy when compared with platelets stored for 72 hours at 20° to 24° C. The approval by the agency of a flexible label statement that permits the use of platelets stored for a period beyond the stated dating period would violate § 610.53(a) of the biologics regulations and section 351(d) of the PHS Act that specifically provides for the continued potency of the product. The agency believes that, as with the dating periods of other drugs, procedures will be developed by hospitals to ensure the availability of sufficient quantities of platelets for emergencies and the efficient use of the product before the expiration date.

Published studies further demonstrate that bacterial contamination is not a limiting factor for platelets stored at 20° to 24° C, if venipuncture technique and donor selection are satisfactory. In fact, Platelet Concentrate (Human) units have been found by some laboratories to contain inherent bactericidal properties which reduce the risk of bacterial growth. The agency advises that the benefit to the patient of a superior platelet product stored at 1° to 6° C for 48 hours compared with storage at 1° to 6° C for 72 hours outweighs the cost, if any, to the manufacturer. For these reasons, therefore, the agency finds no basis for retaining the 72-hour dating period for platelets stored at 1° to 6° C or for permitting the use of a flexible label statement, and the comments are rejected.

4. One comment on proposed § 640.20(a) questioned how Platelet Concentrate (Human) is to be distinguished from Single Donor Plasma (Human), Platelet Rich if the volume limits of resuspension plasma are deleted for Platelet Concentrate (Human), as proposed in § 640.24(d).

The agency advises that with the elimination of the volume limits of resuspension plasma for Platelet Concentrate (Human), the method of preparing Platelet Concentrate (Human) and Single Donor Plasma (Human), Platelet Rich by centrifugal spin continues to be a distinguishing feature between these plasma-derived products. Single Donor Plasma (Human), Platelet Rich is manufactured from the first centrifugal spin of a unit of whole blood. Single Donor Plasma (Human), Platelet Rich is then spun at a different time and

speed to produce Platelet Concentrate (Human). In the process of two centrifugal spins, plasma volume is decreased. Consequently, a significantly smaller volume of plasma should be used to resuspend the platelets in Platelet Concentrate (Human). This volume difference would be reflected on the label of the final product which would indicate the product name Platelet Concentrate (Human) or Single Donor Plasma (Human), Platelet Rich and the actual volume of original plasma that is suspending the platelets for the respective final product. Thus, Single Donor Plasma (Human), Platelet Rich can be distinguished from Platelet Concentrate (Human).

5. One comment suggested replacing the word "suspended" with the word "resuspended" in proposed § 640.20(a) to more accurately describe the processing of Platelet Concentrate (Human) in the original plasma of a single donor.

The agency agrees with this comment because the preparation of Platelet Concentrate (Human) involves the resuspension of platelets in original plasma. The term "resuspension" therefore more accurately describes the preparation of Platelet Concentrate (Human).

The agency is also making one other revision to the definition of Platelet Concentrate (Human). The proposed definition stated that the " . . . platelets [should be] collected from a single donor . . ." The agency has substituted the phrase "one unit of blood" for the proposed phrase "a single donor" to more precisely identify the method of collecting the platelets intended for the preparation of Platelet Concentrate (Human). The phrase "one unit of blood" makes clear that the preparation of Platelet Concentrate (Human) does not involve the pooling of more than one platelet unit collected by plateletpheresis from the single donor. The word and phrase substitutions provide no change in the intent of the proposed definition. Accordingly, the agency has revised § 640.20(a) to define the product as platelets collected from one unit of blood and resuspended in an appropriate volume of original plasma as prescribed in proposed § 640.24(d).

6. One comment recommended that the existing volume requirements of resuspension plasma for Platelet Concentrate (Human) in § 640.24(d) be retained. The comment criticized the FDA internal study identified in the proposal which demonstrated that 21 percent of the Platelet Concentrate (Human) units submitted as prelicensing samples had a pH of less than 6.0. The comment stated that the samples tested

in this study were not representative of the routine preparation of platelet concentrate units because they were prelicensing samples and consequently probably had a greater yield of platelets. The comment further questioned the clinical significance of 21 percent of platelet concentrate units with a pH of less than 6.0 and suboptimal activity. In addition, the comment stated that the original volume of 20 to 30 milliliters for 1° to 6° C storage and 30 to 50 milliliters for 20° to 24° C storage was determined to be adequate for an average yield of platelet concentrate. Therefore, the comment states the belief that the result of eliminating the volume limits of resuspension plasma for Platelet Concentrate (Human) could be the production of a greater yield of platelets that may produce more metabolic end products to drive the pH lower at the end of the dating period.

The agency disagrees with this comment. The agency has no basis for believing the comment's suggestion that platelet yield in the routine preparation of platelet concentrate units by blood establishments is significantly less than the platelet yield in the preparation of units submitted as prelicensing samples. The agency maintains that platelets with a pH of less than 6.0 demonstrate inferior clinical behavior and, therefore, the 21 percent of platelet concentrate units with a pH of less than 6.0 may be clinically significant.

Moreover, the agency does not believe that eliminating the volume units will result in a greater yield of platelets. Each laboratory is required by § 606.100(b) to maintain a Standard Operating Procedure (SOP) in which a volume limit of resuspension plasma, required to maintain the platelet concentrate pH of not less than 6.0, is defined. The resuspension plasma volume established by each laboratory and stated in the SOP should apply to all platelet concentrate units processed by that laboratory and result in a similar yield of platelets for each unit of platelet concentrate prepared by each respective laboratory. Accordingly, the comment is rejected.

7. As a result of staff reviews, the agency discovered that § 640.24(d) did not specify the time when pH shall be measured on a sample of platelet concentrate stored at the selected storage temperature. The agency is therefore amending § 640.24(d) to require that pH be measured on a sample of platelet concentrate which has been stored "for the maximum dating period."

8. One comment on proposed § 640.24(d) expressed concern over an increase in cost of Platelet Concentrate

(Human), if the volume limits were removed. The comment believed that the increase could result because the technologist would not know how much plasma to leave on the platelet units.

The agency advises that the cost of Platelet Concentrate (Human) should not be increased by eliminating the volume requirements. Section 606.100(b) requires each laboratory to have a Standard Operating Procedure (SOP) which includes a description of all steps to be followed in the manufacture and distribution of blood and blood components. The SOP would, therefore, define a procedure to obtain a volume limit of resuspension plasma required to maintain the platelet concentrate pH of not less than 6.0. The SOP would apply to all platelet concentrate units processed by that laboratory and result in no cost increase for the recipient of a platelet unit. Accordingly, the comment is rejected.

9. One comment on proposed § 640.24(d) suggested that due to the availability of several methods to measure pH, a specific pH method for platelet concentrate should be required to promote uniformity.

The agency acknowledges that other methods, in addition to the pH meter, are available to measure pH. However, the agency does not believe it is necessary to recommend a standard pH measuring method for all laboratories as long as the method selected to measure pH of the Platelet Concentrate (Human) after storage accurately measures a pH of not less than 6.0 with a sensitivity to a tenth of a unit. Any method that does not measure pH with a sensitivity to a tenth of a unit is not acceptable. Accordingly, the comment is rejected.

10. As a result of staff reviews, the agency advises that it is necessary to change a proposed word in the first sentence of § 640.25(a) to ensure the performance of an essential step in the procedure for preparing Platelet Concentrate (Human). Two centrifugal spins are required to prepare Platelet Concentrate (Human) from a unit of whole blood. A product known as Single Donor Plasma (Human), Platelet Rich is produced from the first centrifugal spin. Single Donor Plasma (Human), Platelet Rich is then spun at a different time and speed to produce Platelet Concentrate (Human). It is essential to permit the platelet button produced by the second spin to stand undisturbed for a period of time in order to facilitate resuspension. This period of time, determined by each laboratory and stated in each laboratory's Standard Operating Procedure (SOP), is appropriately considered to be a part of processing a

unit of Platelet Concentrate (Human). The proposed first sentence stated that "Immediately after processing, Platelet Concentrate (Human) shall be placed in storage at the selected temperature range". The agency believes that the phrase "Immediately after processing" could be misinterpreted by manufacturers of Platelet Concentrate (Human) to mean that the product should be placed in storage at the selected storage temperature immediately after the second centrifugal spin. In order to ensure that the platelet button is permitted to stand undisturbed for a period of time to facilitate resuspension, the agency is substituting the word "resuspension" for the proposed word "processing".

11. Two comments suggested modifying proposed § 640.25(b) to require that a minimum percentage of platelet concentrate units meet the pH 6.0 limitation in determining the storage volume. One comment suggested that the regulation require that more than 90 percent of units tested at the expiration date, over any 3-month period, have a pH greater than 6.0. In addition, one of the comments further stated that the quality control issue could be avoided by requiring that the pH be above 6.0, as stated in proposed § 640.24(d), on at least "x" percent of samples tested before storage.

The agency rejects these comments. As stated in the preamble of the proposal, units of Platelet Concentrate (Human) with high platelet concentrations are likely to demonstrate a decrease in pH due to inadequate plasma volumes and consequently become clinically ineffective. As a result, the agency proposed to eliminate the plasma volume limits to facilitate use of plasma volumes that will maintain units of Platelet Concentrate (Human) at a pH of not less than 6.0 during the storage period. Accordingly, the agency believes that all units for the quality control testing should reflect a pH of 6.0 or greater. The agency emphasizes that the 4 units required for quality control testing each month from different donors must be tested at the end, rather than at the beginning, of the storage period because it is the pH changes occurring during storage which present the problem. Section 640.25(b)(2) has been amended accordingly. In addition, the agency advises that it is currently reviewing the benefits of quality control testing for Platelet Concentrate (Human) and other biological products as part of the retrospective review of biologics regulations to identify and eliminate

regulations that are burdensome and unnecessary.

12. One comment on proposed § 640.25(b)(2) recommended specifying the temperature at which the pH is measured. The comment stated that if the pH of the same blood sample is measured at 4° C, the pH meter will read approximately 0.4 unit higher than if the sample is measured at 37° C.

The agency recognizes that pH varies with temperature. Through built-in electronic controls, the pH meter can compensate for any variation in temperature reading that occurs when measuring a solution not at room temperature. Accordingly, § 640.25(b)(2) is amended in the final regulation to require that the pH determination be measured at the storage temperature of Platelet Concentrate (Human).

13. One comment on proposed § 640.26(e) objected to the addition of the Rh designation on the label and questioned whether there was any evidence that the absence of the Rh designation on the label has caused a significant clinical problem. The comment further questioned how the pool would be labeled since a number of units of Platelet Concentrate (Human) are pooled before almost all transfusions, resulting in pooling both Rh positive and negative units together.

The agency advises that there have been reports of Rh sensitization in patients receiving Platelet Concentrate (Human) because of significant numbers of red blood cells contaminating the platelet products. The published data, which have been placed on file with the Dockets Management Branch, also support the contention that a recipient may be immunized to an Rh determinant with a total dose of 1 milliliter, or less, of red blood cells. In addition, one commentator who supports the proposal cited personal experience with three patients who became sensitized to the Rh factor by platelet transfusions. As stated in the preamble of the proposal, FDA believes that labeling is an important factor in safely administering blood products and that information regarding the Rh factor in platelet concentrate should be available for the physician. Any difficulty, as suggested by the comment, with labeling the Rh blood group should not occur since the label would specify the Rh blood group in the unit, or in the case of pooling Rh positive and negative units, the number of each Rh blood group used in the pooling process to make the platelet unit. Accordingly, the comment is rejected.

The economic impact of this rule has been reassessed in accordance with

Executive Order 12291. This rule is not a major rule as defined by that order. Specifically, this rule which eliminates the volume limits, reduces the dating period, and specifies that the ABO and Rh blood group be designated on the label for Platelet Concentrate (Human) ensures the production of a safer and more effective product without creating major increases in costs for manufacturers, physicians, or consumers. The assessment for making the determination that this is not a major rule has been placed on file with the Dockets Management Branch.

The requirement for a regulatory flexibility analysis under the Regulatory Flexibility Act does not apply to this final rule because the proposed rule was issued prior to January 1, 1981, and is therefore exempt.

List of Subjects

21 CFR Part 600

Biologics.

21 CFR Part 610

Biologics, Labeling.

21 CFR Part 640

Blood.

Therefore, under the Federal Food, Drug, and Cosmetic Act (secs. 201, 502, 701, 52 Stat. 1041-1042 as amended 1050-1051 as amended, 1055-1058 as amended (21 U.S.C. 321, 352, 371)) and the Public Health Service Act (sec. 351, 58 Stat. 702 as amended (42 U.S.C. 262)) and under authority delegated to the Commissioner of Food and Drug (21 CFR 5.10), Chapter I of Title 21 of the Code of Federal Regulations is amended in Subchapter F as follows:

PART 600—BIOLOGICAL PRODUCTS: GENERAL

1. In Part 600, § 600.15(a) is amended by revising the entry for "Platelet Concentrate (Human)," as follows:

§ 600.15 Temperatures during shipment.

(a) . . .

Platelet Concentrate (Human). Between 1° and 10° C if the label indicates storage between 1° and 6° C, or all reasonable methods to maintain the temperature as close as possible to a range between 20° and 24° C, if the label indicates storage between 20° and 24° C.

PART 610—GENERAL BIOLOGICAL PRODUCTS STANDARDS

2. In Part 610, § 610.53(a) is amended by revising the entries for "Platelet

Concentrate (Human)" and "Single Donor Plasma (Human), Platelet Rich" as follows:

§ 610.53 Dating periods for specific products.

(a) . . .

Platelet Concentrate (Human). (a) 72 hours from time of collection of source blood, provided labeling recommends storage at 20° to 24° C or, (b) 48 hours from time of collection of source blood, provided labeling recommends storage at 1° to 6° C. Section 610.51 does not apply.

Single Donor Plasma (Human), Platelet Rich. (a) 72 hours from time of collection of source blood, provided labeling recommends storage at 20° to 24° C or, (b) 48 hours from time of collection of source blood, provided labeling recommends storage at 1° to 6° C. Section 610.51 does not apply.

PART 640—ADDITIONAL STANDARDS FOR HUMAN BLOOD AND BLOOD PRODUCTS

3. In Part 640:

a. Section 640.20(a) is amended by revising the last sentence to read as follows:

§ 640.20 Platelet concentrate (Human).

(a) . . . The product is defined as platelets collected from one unit of blood and resuspended in an appropriate volume of original plasma, as prescribed in § 640.24(d).

b. Section 640.24 is amended by revising paragraph (d), to read as follows:

§ 640.24 Processing.

(d) The volume of original plasma used for resuspension of the platelets shall be determined by the maintenance of a pH of not less than 6.0 during the storage period. The pH shall be measured on a sample of platelet concentrate which has been stored for the maximum dating period at the selected storage temperature. One of the following storage temperatures shall be used continuously:

- (1) 20° to 24° C.
- (2) 1° to 6° C.

c. Section 640.25 is amended by revising paragraphs (a) and (b), to read as follows:

§ 640.25 General requirements.

(a) *Storage.* Immediately after resuspension. Platelet Concentrate

(Human) shall be placed in storage at the selected temperature range. If stored at 20° to 24° C, a continuous gentle agitation of the platelet concentrate shall be maintained throughout the storage period. Agitation is optional if stored at a temperature between 1° and 6° C.

(b) *Quality control testing.* Each month four units prepared from different donors shall be tested at the end of the storage period as follows:

- (1) Platelet count.
- (2) pH of not less than 6.0 measured at the storage temperature of the unit.
- (3) Measurement of actual plasma volume.
- (4) If the results of the quality control testing indicate that the product does not meet the prescribed requirements, immediate corrective action shall be taken and a record maintained of such action.

d. Section 640.28 is amended by revising paragraph (e), to read as follows:

§ 640.26 Labeling.

(e) The ABO and Rh blood group designations of the source blood.

Effective dates. This regulation becomes effective November 29, 1982. Labeling requirements shall become effective April 29, 1983. On or after April 29, 1983, no person may initially introduce or initially deliver for introduction into interstate commerce any licensed biological product to which the regulations apply, unless the product's labeling complies with the requirements set forth in the regulations.

(Secs. 201, 502, 701, 52 Stat. 1041-1042 as amended, 1050-1051 as amended, 1055-1056 as amended (21 U.S.C. 321, 352, 371); sec. 351, 58 Stat. 702 as amended (42 U.S.C. 262))

Dated: October 7, 1982.

Joseph P. Hile,
Associate Commissioner for Regulatory Affairs.

(FR Doc. 82-39729 Filed 10-28-82; 8:45 am)
BILLING CODE 4180-01-M

21 CFR Part 884

[Docket No. 81P-0306]

**Schmid Laboratories, Inc.;
Reclassification of Condom With
Spermicidal Lubricant**

AGENCY: Food and Drug Administration.
ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is issuing a final

regulation that codifies the reclassification of the condom with spermicidal lubricant (nonoxynol-9) from class III (premarket approval) into class II (performance standards). FDA also is announcing that it issued an order in the form of a letter to a petitioner reclassifying the device. The effect of reclassifying a device into class II is to require that the device meet the general controls applicable to all devices and comply with the requirements of any performance standard applicable to the device. FDA reclassified this device in response to a petition from Schmid Laboratories, Inc., Little Falls, NJ 07424.

EFFECTIVE DATES: The reclassification was effective on August 9, 1982. This rule becomes effective November 29, 1982.

FOR FURTHER INFORMATION CONTACT: Lillian Yin, Bureau of Medical Devices (HFK-470), Food and Drug Administration, 8757 Georgia Ave., Silver Spring, MD 20910, 301-427-7555.

SUPPLEMENTARY INFORMATION: On August 28, 1981, Schmid Laboratories, Inc., Little Falls, NJ 07424, submitted to FDA under section 513(f)(2) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 360c(f)(2)), a petition requesting that a new device with the brand name "Condom with Spermicidal Lubricant (nonoxynol-9)" be reclassified from class III into class II. The device was classified by statute into class III because it was not in commercial distribution before enactment of the Medical Device Amendments of 1976 (Pub. L. 94-295) (see 21 U.S.C. 360c(f)(1)), nor is it substantially equivalent to another device that was in commercial distribution before the date of enactment or to another device that was classified by statute into class III and subsequently reclassified.

FDA referred the petition to the Obstetrics-Gynecology Device Section of the Obstetrics-Gynecology and Radiology Devices Panel (the Section) for a recommendation. On September 28, 1981, the Section reviewed the petition and recommended that FDA reclassify the device into class II, provided the labeling bear the following specific contraceptive effectiveness cautionary provision:

The condom with spermicidal lubricant is a contraceptive which combines a latex condom and a lubricant containing nonoxynol-9, a spermicide. Evidence of added contraceptive effectiveness has not been established with the addition of a spermicidal preparation to the condom.

The recommendation was based on the Section's belief that although general