

§ 660.25

(Information collection requirements approved by the Office of Management and Budget under control number 0910-0209)

**§ 660.25 Potency tests without reference preparations.**

Products for which Reference Blood Grouping Reagents are not available shall be tested for potency by a method approved by the Director, Center for Biologics Evaluation and Research (HFN-830), Food and Drug Administration, 8800 Rockville Pike, Bethesda, MD 20892.

(a) *Potency requirements.* Blood Grouping Reagents recommended for the test tube methods, including the indirect antiglobulin tests, shall have the following potency titer values, unless other values are approved by the Director, Center for Biologics Evaluation and Research (HFN-830), Food and Drug Administration, 8800 Rockville Pike, Bethesda, MD 20892.

(1) For Anti-K, Anti-k̄, Anti-Jk<sup>a</sup>, Anti-Fy<sup>a</sup>, Anti-C<sup>w</sup>, at least 1+ reaction with a 1:8 dilution of the reagent.

(2) For Anti-S, Anti-s̄, Anti-P<sub>1</sub>, Anti-M, Anti-I, Anti-e (saline), Anti-c̄ (saline), and Anti-A<sub>1</sub>, at least 1+ reaction with a 1:4 dilution of the reagent.

(3) For Anti-U, Anti-Kp<sup>a</sup>, Anti-Kp<sup>b</sup>, Anti-Js<sup>a</sup>, Anti-Js<sup>b</sup>, Anti-Fy<sup>b</sup>, Anti-N, Anti-Le<sup>a</sup>, Anti-Le<sup>b</sup>, Anti-Lu<sup>a</sup>, Anti-Lu<sup>b</sup>, Anti-Di<sup>a</sup>, Anti-Mg, Anti-Jk<sup>b</sup>, Anti-Cob, Anti-Wr<sup>a</sup>, and Anti-Xg<sup>a</sup>, at least 2+ reaction with undiluted reagent.

(b) *Products recommended for slide tests or microplate techniques.* Blood Grouping Reagent recommended for slide test methods or microplate techniques shall produce clearly positive macroscopic results when both undiluted reagent and reagent diluted with an equal volume of diluent are tested by all methods recommended in the manufacturer's package insert using red blood cells showing heterozygous or diminished expression of the corresponding antigen. The dilution shall be made with an equal volume of compatible serum or approved diluent.

(c) *Products recommended for use in an automated system.* The manufacturer of Blood Grouping Reagent that is recommended for use in an automated system shall demonstrate that its product when used both undiluted and diluted with an equal volume of diluent satisfactorily performs when tested with

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cells representing heterozygous or diminished expression of the corresponding antigen.

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**§ 660.26 Specificity tests and avidity tests.**

Specificity and avidity tests shall be performed using test procedures approved by the Director, Center for Biologics Evaluation and Research (HFN-830), Food and Drug Administration, 8800 Rockville Pike, Bethesda, MD 20892.

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**§ 660.28 Labeling.**

In addition to the applicable labeling requirements of §§ 610.62 through 610.65 and § 809.10, and in lieu of the requirements in §§ 610.60 and 610.61, the following requirements shall be met:

(a) *Final container label—(1) Color coding.* The final container label of all Blood Grouping Reagents shall be completely white, except that all or a portion of the final container label of the following Blood Grouping Reagents may be color coded with the specified color which shall be a visual match to a specific color sample designated by the Director, Center for Biologics Evaluation and Research (HFN-830), Food and Drug Administration, 8800 Rockville Pike, Bethesda, MD 20892. Printing on all final container labels shall be in solid black. A logo or company name may be placed on the final container label; however, the logo or company name shall be located along the bottom or end of the label, outside the main panel.

| Blood grouping reagent                                  | Color of label paper |
|---|----------------------|
| Anti-A .....  | Blue.                |
| Anti-B .....  | Yellow.              |
| Slide and rapid tube test blood grouping reagents only: |                      |
| Anti-C .....  | Pink.                |
| Anti-D .....  | Gray.                |
| Anti-E .....  | Brown.               |
| Anti-CDE .....  | Orange.              |
| Anti-c̄ .....   | Lavender.            |

|                        |                      |
|------------------------|----------------------|
| Blood grouping reagent | Color of label paper |
| Anti-e .....           | Green.               |

(2) *Required information.* The proper name "Blood Grouping Reagent" need not appear on the final container label provided the final container is distributed in a package and the package label bears the proper name. The final container label shall bear the following information:

- (i) Name of the antibody or antibodies present as set forth in paragraph (d) of this section.
- (ii) Name, address (including ZIP code), and license number of the manufacturer.
- (iii) Lot number, including subplot designations.
- (iv) Expiration date.
- (v) Source of product if other than human plasma or serum.
- (vi) Test method(s) recommended.
- (vii) Recommended storage temperature in degrees Celsius.
- (viii) Volume of product if a liquid, or equivalent volume for a dried product if it is to be reconstituted.
- (ix) If a dried product, to remind users to record the reconstitution date on the label, the statement "RECONSTITUTION DATE \_\_\_\_\_. EXPIRES 1 YEAR AFTER RECONSTITUTION DATE."

(3) *Lettering size.* The type size for the specificity of the antibody designation on the labels of a final container with a capacity of less than 5 milliliters shall be not less than 12 point. The type size for the specificity of the antibody designations on the label of a container with a capacity of 5 milliliters or more shall be not less than 18 point.

(4) *Visual inspection.* When the label has been affixed to the final container, a sufficient area of the container shall remain uncovered for its full length or no less than 5 millimeters of the lower circumference to permit inspection of the contents. The label on a final product container for antibodies Anti-c, Anti-k, or Anti-s shall display a bar immediately over the specificity letter used in the name, i.e., Anti-ċ, Anti-k̄, or Anti-š.

(b) *Package label.* The following information shall appear either on the pack-

age label or on the final container label if it is visible within the package.

- (1) Proper name of the product.
- (2) Name of the antibody or antibodies present as set forth in paragraph (d) of this section.
- (3) Name, address (including ZIP Code), and license number of the manufacturer.
- (4) Lot number, including subplot designations.
- (5) Expiration date.
- (6) Preservative used and its concentration.
- (7) Number of containers, if more than one.
- (8) Volume or equivalent volume for dried products when reconstituted, and precautions for adequate mixing when reconstituting.
- (9) Recommended storage temperature in degrees Celsius.
- (10) Source of the product if other than human serum or plasma.
- (11) Reference to enclosed package insert.
- (12) If a dried product, a statement indicating the period within which the product may be used after reconstitution.
- (13) The statement: "FOR IN VITRO DIAGNOSTIC USE."
- (14) The statement: "MEETS FDA POTENCY REQUIREMENTS."
- (15) If human blood was used in manufacturing the product, the statement: "CAUTION: ALL BLOOD PRODUCTS SHOULD BE TREATED AS POTENTIALLY INFECTIOUS. SOURCE MATERIAL FROM WHICH THIS PRODUCT WAS DERIVED WAS FOUND NEGATIVE WHEN TESTED IN ACCORDANCE WITH CURRENT FDA REQUIRED TESTS. NO KNOWN TEST METHODS CAN OFFER ASSURANCE THAT PRODUCTS DERIVED FROM HUMAN BLOOD WILL NOT TRANSMIT INFECTIOUS AGENTS."
- (16) A statement of an observable indication of an alteration of the product, e.g., turbidity, color change, precipitate, that may indicate possible deterioration of the product.

(c) *Package insert.* Each final container of Blood Grouping Reagent shall be accompanied by a package insert meeting the requirements of §809.10. If two or more final containers requiring identical package inserts are placed in

a single package, only one package insert per package is required.

(d) *Names of antibodies.*

BLOOD GROUP DESIGNATION FOR CONTAINER LABEL

|                      |                      |
|----------------------|----------------------|
| Anti-A               | Anti-Jk <sup>b</sup> |
| Anti-A <sub>1</sub>  | Anti-Js <sup>a</sup> |
| Anti-A, B            | Anti-Js <sup>b</sup> |
| Anti-A and B         | Anti-K               |
| Anti-B               | Anti-k               |
| Anti-C               | Anti-Kp <sup>a</sup> |
| Anti-C <sup>w</sup>  | Anti-Kp <sup>b</sup> |
| Anti- $\bar{c}$      | Anti-Le <sup>a</sup> |
| Anti-CD              | Anti-Le <sup>b</sup> |
| Anti-CDE             | Anti-Lu <sup>a</sup> |
| Anti-Co <sup>b</sup> | Anti-Lu <sup>b</sup> |
| Anti-D               | Anti-M               |
| Anti-DE              | Anti-M <sup>s</sup>  |
| Anti-Di <sup>a</sup> | Anti-N               |
| Anti-E               | Anti-P <sub>1</sub>  |
| Anti-e               | Anti-S               |
| Anti-Fy <sup>a</sup> | Anti- $\bar{s}$      |
| Anti-Fy <sup>b</sup> | Anti-U               |
| Anti-I               | Anti-Wr <sup>a</sup> |
| Anti-Jk <sup>a</sup> | Anti-Xg <sup>a</sup> |

[53 FR 12764, Apr. 19, 1988, as amended at 59 FR 23637, May 6, 1994]

(Information collection requirements approved by the Office of Management and Budget under control number 0910-0209)

**Subpart D—Reagent Red Blood Cells**

SOURCE: 52 FR 37450, Oct. 7, 1987, unless otherwise noted.

**§ 660.30 Reagent Red Blood Cells.**

(a) *Proper name and definition.* The proper name of the product shall be Reagent Red Blood Cells, which shall consist of a preparation of human red blood cells used to detect or identify human blood-group antibodies.

(b) *Source.* Reagent Red Blood Cells shall be prepared from human peripheral blood meeting the criteria of §§ 660.31 and 660.32, or from umbilical cord cells which shall be collected and prepared according to the manufacturer's product license application.

**§ 660.31 Suitability of the donor.**

Donors of peripheral blood for Reagent Red Blood Cells shall meet the criteria for donor suitability under § 640.3 of this chapter, except that paragraphs (b)(5) and (6), (d), and (e) of § 640.3 shall not apply.

**§ 660.32 Collection of source material.**

Blood for Reagent Red Blood Cells from donors of peripheral blood shall be collected as prescribed under § 640.4 of this chapter, except that paragraphs (c), (d), (g), and (h) of § 640.4 shall not apply.

**§ 660.33 Testing of source material.**

Except as provided in this section, a sample of each blood incorporated into the Reagent Red Blood Cell product shall be individually tested, with no fewer than two donor sources of each antibody specificity employed, to confirm the identification of all blood group antigens specified in the labeling as present or absent. The manufacturer shall perform at least one of the required tests for each factor. The Reagent Red Blood Cell product may be tested with a single donor source of antibody specificity if only one source of antibody is available, and the Director, Center for Biologics Evaluation and Research, has approved the use of a single donor source of antiserum. Each of these tests shall be conducted and interpreted independently, and any discrepancy between the results of these two tests shall be resolved by testing with at least one additional antiserum before concluding that the antigen is present or absent. Where fewer than three donor sources of an antibody specificity are available, test discrepancies shall be resolved in accordance with the manufacturer's product license application. Group O Reagent Red Blood Cells used in the detection or identification of unexpected antibodies shall include at least the following common antigens in each lot of the product: D, C, E,  $\bar{c}$ , e, K, k, Fy<sup>a</sup>, Fy<sup>b</sup>, Jk<sup>a</sup>, Jk<sup>b</sup>, Le<sup>a</sup>, Le<sup>b</sup>, P<sub>1</sub>, M, N, S, and  $\bar{s}$ .

[52 FR 37450, Oct. 7, 1987, as amended at 55 FR 11013, Mar. 26, 1990]

**§ 660.34 Processing.**

(a) *Processing method.* The processing method shall be one that has been shown to yield consistently a product that is capable of detecting, throughout the dating period, alloantibodies corresponding to all required blood group antigens specified in the labeling as present.