

van Assendelft said that a standard for an MCV calibrator could not be written at that time because there were so many questions as to methods or methodology used in arriving at "a" value for MCV.

10. One comment stated that the reference provided, when correctly interpreted, were either not relevant to the issue of calibrators for cell indices, or not condemnatory of such calibrators.

FDA agrees that the references provided did not justify the proposed classification into class III. The final regulation classifies these calibrators into class II.

11. FDA received one comment agreeing with the proposed classification into class III.

On November 19, 1979, FDA held a public meeting of the Hematology Section of the Clinical Chemistry and Hematology Devices Panel to consider the comments received on the proposal to classify calibrators for cell indices into class III. At that meeting, a representative of Coulter Electronics Inc., presented his view that calibrators for cell indices should be classified into class II, rather than class III as proposed. A representative of Diagnostic Technology stated that classification into class III is appropriate, and that the cell size, shape, concentration, and other pertinent characteristics of calibrators for cell indices should be determined directly by classical reference methods, and that assay values for calibrators must be verifiable by manual methods prior to use. After considering the comments and additional testimony, the Section concluded that sufficient information exists to develop a performance standard for calibrators for cell indices and recommended that these devices be placed in class II rather than class III, as proposed.

Based upon the comments, the additional information and data submitted on this device, and the Section's recommendation, FDA has changed the classification of calibrators for cell indices in the final rule to class II rather than class III as proposed. The agency believes that the references submitted by one comment (Refs. 1 and 2) demonstrate that a reference methodology exists for the measurement of the cell indices that can serve as the basis for the development of a performance standard. Accordingly, the final regulation is changed to classify the device into class II. For the reasons stated in the general provisions for hematology and pathology devices published elsewhere in this issue of the Federal Register, FDA does not believe that it is necessary to issue a new proposal concerning this decision.

Persons who disagree with classifying calibrators for cell indices into class II may petition for reclassification of the device under Subpart C of Part 860 of the classification procedure regulation. Accordingly, the proposed regulation is being adopted with the changes noted.

On April 28, 1978, the agency terminated all of the device classification panels and reestablished them with the same functions, but with new names and with a new structure. FDA published notices of these changes in the Federal Register of May 19, 1978 (43 FR 21666, 21667, and 21668) and May 26, 1978 (43 FR 22672 and 22673). Further information regarding the device advisory committees and a list of their new names may be found in the preamble to the general provisions, published elsewhere in this issue of the Federal Register.

References

1. Gilmer, P. R. et al., "Calibration Methods for Automated Hematology Instruments," *American Journal of Clinical Pathology*, 68(1): 185-190, 1977.
2. Crosland-Taylor, P. J. et al., "Draft Protocol for Testing Calibration and Quality Control Material Used with Automatic Blood-counting Apparatus," *Clinical Laboratory Hematology*, 1:61-64, 1979.

Therefore, under the Federal Food, Drug, and Cosmetic Act (secs. 513, 701(a), 52 Stat. 1055, 90 Stat. 540-546 (21 U.S.C. 360c, 371(a))) and under authority delegated to him (21 CFR 5.1), the Commissioner of Food and Drugs is amending Part 864 in Subpart I by adding new § 864.8150, to read as follows:

§ 864.8150 Calibrator for cell indices.

(a) *Identification.* A calibrator for cell indices is a device that approximates whole blood or certain blood cells and that is used to set an instrument intended to measure mean cell volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC), or other cell indices. It is a suspension of particles or cells whose size, shape, concentration, and other characteristics have been precisely and accurately determined.

(b) *Classification.* Class II (performance standards).

Effective date. This regulation shall be effective October 14, 1980.

(Secs. 513, 701(a), 52 Stat. 1055, 90 Stat. 540-546 (21 U.S.C. 360c, 371(a)))

Dated: August 15, 1980.

William F. Randolph,
Acting Associate Commissioner for
Regulatory Affairs.

[FR Doc. 80-27371 Filed 9-11-80; 8:45 am]

BILLING CODE 4110-03-M

21 CFR Part 864

[Docket No. 78N-1910]

Classification of Calibrators for Hemoglobin or Hematocrit Measurement

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is issuing a final rule classifying calibrators for hemoglobin or hematocrit measurement into class II (performance standards). The effect of classifying a device into class II is to provide for the future development of one or more performance standards to assure the safety and effectiveness of the device. This action is being taken under the Medical Device Amendments of 1976.

EFFECTIVE DATE: October 14, 1980.

FOR FURTHER INFORMATION CONTACT: Kaiser Aziz, Bureau of Medical Devices (HFK-440), Food and Drug Administration, 8757 Georgia Ave., Silver Spring, MD 20910, 301-427-7550.

SUPPLEMENTARY INFORMATION: FDA published in the Federal Register of September 11, 1979 (44 FR 52950), a proposed regulation explaining the development of the proposed regulations classifying hematology and pathology devices, the medical device classification procedures, and the activities of the Hematology and Pathology Device Section of the Clinical Chemistry and Hematology Devices Panel (formerly the Hematology Device Classification Panel and the Pathology Device Classification Panel). FDA also published in that issue of the Federal Register (44 FR 53033) a proposed regulation to classify calibrators for hemoglobin and hematocrit measurement into class II (performance standards). A period of 60 days was provided for interested persons to submit written comments to FDA.

The following is a summary of the comments received on the proposal and the agency's response to them:

1. One comment objected to the identification of calibrators for hemoglobin or hematocrit measurement as materials whose "characteristics have been carefully determined". The comment suggested that the manner in which the characteristics are

determined is irrelevant and should be deleted. Discussion of this sort is more appropriate to the standards development process and at that time precision and accuracy will be considered rather than care.

FDA agrees that the calibrator material characteristics should be precisely and accurately determined rather than carefully determined. Accordingly, the identification has been modified to reflect this emphasis. FDA also agrees that the manner in which the characteristics are determined is appropriate to the standards development process.

2. One manufacturer agreed with the proposed classification into class II but stated that the Panel had not provided reasoning to prove that the labeling requirements and general controls are not adequate to control these products. The comment recommended that safety and effectiveness can be adequately insured by general controls (class I), including compliance with labeling and GMP's, until a standard is promulgated in final form.

FDA disagrees with this comment. The Panel recommended classification into class II because of the need to specify acceptable ranges for the precision and accuracy of these devices. General controls alone, including labeling requirements of 21 CFR 809.10, will not specify these ranges. FDA acknowledges, however, that until a standard is promulgated in final form, these devices will be regulated under general controls.

3. One comment suggested that the Panel had not solicited or considered information from industry sources on the state-of-the-art regarding these products.

FDA disagrees with this comment. The Panel meeting during which calibrators were discussed was announced in advance in the Federal Register. Manufacturers of calibrators were present at that meeting, made presentations, participated in the discussions, and they were also represented by the Panel's industry representative. Accordingly, the proposed regulation is being adopted with changes noted.

On April 28, 1978, the agency terminated all of the device classification panels and reestablished them with the same functions, but with new names and with a new structure. FDA published notices of these changes in the Federal Register of May 19, 1978 (43 FR 21666, 21667, and 21668) and May 26, 1978 (43 FR 22672 and 22673). Further information regarding the device advisory committees and a list of their new names may be found in the

preamble to the general provisions, published elsewhere in this issue of the Federal Register.

Therefore, under the Federal Food, Drug, and Cosmetic Act (secs. 513, 701(a), 52 Stat. 1055, 90 Stat. 540-546 (21 U.S.C. 360c, 371(a))) and under authority delegated to him (21 CFR 5.1), the Commissioner of Food and Drugs is amending Part 864 in Subpart I by adding new § 864.8165, to read as follows:

§ 864.8165 Calibrator for hemoglobin or hematocrit measurement.

(a) *Identification.* A calibrator for hemoglobin or hematocrit measurement is a device that approximates whole blood, red blood cells, or a hemoglobin derivative and that is used to set instruments intended to measure hemoglobin, the hematocrit, or both. It is a material whose characteristics have been precisely and accurately determined.

(b) *Classification.* Class II (performance standards).

Effective date. This regulation shall be effective October 14, 1980.

(Secs. 513, 701(a), 52 Stat. 1055, 90 Stat. 540-546 (21 U.S.C. 360c, 371(a)))

Dated: August 15, 1980.

William F. Randolph,

Acting Associate Commissioner for Regulatory Affairs.

[FR Doc. 80-27372 Filed 9-11-80; 8:45 am]

BILLING CODE 4110-03-M

21 CFR Part 864

[Docket No. 78N-1911]

Classification of Calibrators for Platelet Counting

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

SUMMARY: The Food and Drug Administration (FDA) is issuing a final rule classifying calibrators for platelet counting into class II (performance standards). The effect of classifying a device into class II is to provide for the future development of one or more performance standards to assure the safety and effectiveness of the device. This action is being taken under the Medical Device Amendments of 1976.

EFFECTIVE DATE: October 14, 1980.

FOR FURTHER INFORMATION CONTACT: Kaiser Aziz, Bureau of Medical Devices (HFK-440), Food and Drug Administration, 8757 Georgia Ave., Silver Spring, MD 20910, 301-427-7550.

SUPPLEMENTARY INFORMATION: FDA published in the Federal Register of September 11, 1979 (44 FR 52950), a

proposed regulation explaining the development of the proposed regulations classifying hematology and pathology devices, the medical device classification procedures, and the activities of the Hematology and Pathology Device Section of the Clinical Chemistry and Hematology Devices Panel (formerly the Hematology Device Classification Panel and the Pathology Device Classification Panel). FDA also published in that issue of the Federal Register (44 FR 53034) a proposed regulation to classify calibrators for platelet counting into class III (premarket approval). A period of 60 days was provided for interested persons to submit written comments to FDA.

The following is a summary of the comments received on the proposal and the agency's response to them:

1. One comment objected to the use of the word "fixed" in the identification, because its meaning is not sufficiently precise to be understood in this context.

FDA agrees with this comment. The identification has been modified to delete the term "fixed."

2. One comment objected to the statement that calibrators are materials whose "characteristics have been carefully determined". The comment suggested that precision and accuracy are more appropriate than care.

FDA agrees with this comment. The identification has been modified to emphasize precision and accuracy rather than care.

3. Two comments suggested further distinctions between different kinds of platelet calibrators. One comment suggested dividing these devices into whole blood calibrators and platelet-rich plasma calibrators. The comment suggested that platelet-rich plasma calibrators have been shown to be effective and should be placed in class II. Instruments that make platelet counts on whole blood samples must be calibrated with platelet-rich plasma calibrators. Another comment suggested a distinction between numerical calibration and size or threshold calibration, noting that both forms of calibration are required for accurate platelet counting.

FDA agrees that these distinctions are important. FDA believes that numerical and size calibration were indicated in the proposed identification. However, the identification has been modified to include whole blood calibrators. As discussed below, FDA has concluded that all calibrators for platelet counting, including platelet-rich plasma calibrators, will be classified into class II.

4. Two comments objected to the statement that no calibration material has sufficient stability or reproducibility to serve as a calibrator for platelet counting. A reference (Ref. 1) was presented documenting the stability, accuracy, and reproducibility of calibration materials.

FDA agrees that there are materials with sufficient stability and reproducibility to serve as platelet calibrators.

5. Two comments objected to the statement that technology has not advanced to the stage that a true numerical value can be assigned to a material to be used as a platelet calibrator. The comments suggested that presently there are a number of methods by which platelet concentration may be measured, including an International Committee on Standards in Hematology (ICSH) proposed reference method (Ref. 2) for counting chamber hemacytometry. One comment noted that most of these methods do not require the use of calibrators and thus could be suitable reference methods. One comment noted that "the difficulties in platelet counting" referred to should not disqualify a technique of scientific measurement.

FDA agrees that methodologies exist whereby sufficiently accurate and precise numerical values may be assigned to calibration materials for platelet counting.

6. Two comments disagreed with the agency position that general controls or performance standards would not provide reasonable assurance of the safety and effectiveness of these devices. One comment stated that the benefits of the class III classification would not be available for 30 months. The comments suggested that the good manufacturing practices and labeling requirements as presently enforced by FDA would not be enhanced by requiring premarket approval.

FDA does not agree that general controls would ensure the safety and effectiveness of these devices. Acceptable ranges for the precision, accuracy, and stability of these products must be established by a performance standard. FDA does acknowledge that it would be 30 months before any benefits could be derived from the premarket approval process. In any event, the final regulation classifies the device into class II rather than class III as proposed.

7. One comment suggested that FDA had applied too broad an interpretation of the Federal Food, Drug, and Cosmetic Act regarding the use of premarket approval (class III) for ensuring safety and effectiveness. The comment suggested that the intent of the act is to

use class III controls to protect the public against direct life-threatening hazards, and that platelet calibrators do not constitute such a threat.

FDA disagrees with the comment's interpretation of the act. The act specifies that devices that are "of substantial importance in preventing the impairment of human health" may, in FDA's discretion, be classified into class III. Further discussion of the classification of this device can be found in the agency response to comment number 11.

8. One comment stated that the reference in the proposed regulation (Ref. 1) to the lack of stability and reproducibility of platelet calibrators is no longer valid and should be deleted. It was suggested that those Panel members who concurred with this opinion be required to provide scientific evidence in support of their concurrence.

FDA agrees that the reference in the proposed regulation to the lack of stability and reproducibility of the device is no longer valid.

9. One comment suggested that there are a number of factors that could cause an inaccurate platelet count and if the platelet calibrator is to be placed into class III, then the other components of the platelet counting system should also be considered for class III.

FDA agrees that the platelet calibrator is but one of the components of the platelet counting system. However, its importance in establishing the accuracy of the platelet count should not be minimized. Under the final regulation, the platelet calibrator is classified into class II.

10. One comment noted that the error in the platelet count mentioned in Reference 2 of the proposed regulation was an isolated instance and is not typical of the performance of these devices.

FDA presented this reference as an example of the sort of error that could result from the use of a calibration material.

11. One comment objected to classifying calibrators for platelet counting into class III. The comment stated that sufficient information exists to establish performance standards that will ensure the safety and effectiveness of the device.

FDA agrees with the comment and is publishing a final regulation classifying the device into class II.

On November 19, 1979, FDA held a public meeting of the Hematology Devices Section of the Clinical Chemistry and Hematology Devices Panel. At the meeting, a representative of an industry group presented the view that calibrators for platelet counting

should be classified into class II rather than class III as proposed.

Based on the comments, the presentation and additional information reviewed by the Section, and the Section's recommendation that the device be classified into class II, FDA has concluded that sufficient information exists to establish a performance standard for the device and is classifying the device into class II rather than class III as proposed.

For the reasons stated in the general provisions for hematology or pathology devices published elsewhere in this issue of the Federal Register, FDA does not believe that it is necessary to issue a new proposal concerning this decision. Persons who disagree with classifying calibrators for platelet counting into class II may petition for reclassification of the device under Subpart C of Part 860 of the classification procedure regulation. Accordingly, the proposed regulation is being adopted with the changes noted.

On April 28, 1978, the agency terminated all of the device classification panels and reestablished them with the same functions, but with new names and with a new structure. FDA published notices of these changes in the Federal Register of May 19, 1978 (43 FR 21666, 21667, and 21668) and May 26, 1978 (43 FR 22672 and 22673). Further information regarding the device advisory committees and a list of their new names may be found in the preamble to the general provisions, published elsewhere in this issue of the Federal Register.

List of References

1. Ross, D. W., L. Aysone, and M. Gulley, "Automated Platelet Counts: Accuracy, Precision, Range," Presented at Joint ASCP/CAP Meeting, Las Vegas, NE, October 29, 1979.
2. Proposed ICSH Reference Method for Counting Chamber Hemocytometry, "Presented at Meeting of ICSH Expert Panel on Blood Cell Sizing, Berlin, September 3-5, 1979.

Therefore, under the Federal Food, Drug, and Cosmetic Act (secs. 513, 701(a), 52 Stat. 1055, 90 Stat. 540-546 (21 U.S.C. 360c, 371(a))) and under authority delegated to him (21 CFR 5.1), the Commissioner of Food and Drugs is amending Part 864 in Subpart I by adding new § 864.8175, to read as follows:

§ 864.8175 Calibrator for platelet counting.

(a) *Identification.* A calibrator for platelet counting is a device that resembles platelets in plasma or whole blood and that is used to set a platelet counting instrument. It is a suspension

of particles or cells whose size, shape concentration, and other characteristics have been precisely and accurately determined.

(b) *Classification.* Class II (performance standards).

Effective date. This regulation shall be effective October 14, 1980.

(Secs. 513, 701(a), 52 Stat. 1055, 90 Stat. 540-546 (21 U.S.C. 360c, 371(a)))

Dated: August 15, 1980.

William F. Randolph,
Acting Associate Commissioner for
Regulatory Affairs.

[FR Doc. 80-27373 Filed 9-11-80; 8:45 am]

BILLING CODE 4110-03-M

21 CFR Part 864

[Docket No. 78N-1912]

Classification of Calibrators for Red Cell and White Cell Counting

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is issuing a final rule classifying calibrators for red cell and white cell counting into class II (performance standards). The effect of classifying a device into class II is to provide for the future development of one or more performance standards to assure the safety and effectiveness of the device. This action is being taken under the Medical Device Amendments of 1976.

EFFECTIVE DATE: October 14, 1980.

FOR FURTHER INFORMATION CONTACT: Kaiser Aziz, Bureau of Medical Devices (HFK-440), Food and Drug Administration, 8757 Georgia Ave., Silver Spring, MD 20910, 301-427-7550.

SUPPLEMENTARY INFORMATION: FDA published in the *Federal Register* of September 11, 1979 (44 FR 52950), a proposed regulation explaining the development of the proposed regulations classifying hematology and pathology devices, the medical device classification procedures, and the activities of the Hematology and Pathology Device Section of the Clinical Chemistry and Hematology Devices Panel (formerly the Hematology Device Classification Panel and the Pathology Device Classification Panel). FDA also published in that issue of the *Federal Register* (44 FR 53035) a proposed regulation to classify calibrators for red cell and white cell counting into class II (performance standards). A period of 60 days was provided for interested persons to submit written comments to FDA.

The following is a summary of the comments received on the proposal and the agency's response to them:

1. One comment objected to the identification of calibrators for red and white cell counting as materials whose "characteristics have been carefully determined." The comment suggested that a discussion of the manner in which the characteristics are determined is irrelevant and should be deleted. Discussion of this sort is more appropriate to the standards development process and at that time precision and accuracy will be considered rather than care.

FDA agrees that the materials' characteristics should be precisely and accurately determined, rather than carefully determined. Accordingly, the identification has been modified to reflect this emphasis. FDA also agrees that a discussion of the manner in which the characteristics are determined is appropriate to the standards development process.

2. One comment noted that the technology for assigning a true value to red cell and white cell calibrators was developed in the absence of a standard. The comment stated that the Panel had not presented any evidence of hazards which are attendant to the use of such products. The comment also stated that the Panel should present evidence to show that current labeling and GMP requirements are not adequate to ensure the safety and effectiveness of these products. The comment recommended that the controls of class I are adequate to ensure the safety and effectiveness of these products until a standard is promulgated in final form.

FDA disagrees with this comment. The Panel presented the risk of misdiagnosis and inappropriate therapy due to inaccurate data from an improperly calibrated cell counting instrument. The Panel also stated that a performance standard prescribing acceptable ranges for the accuracy and precision of these devices would be sufficient to ensure their safety and effectiveness. Current labeling and GMP requirements would not specify these acceptable ranges. Therefore, a performance standard is necessary. FDA acknowledges that until a performance standard is promulgated in final form, these calibrators will be regulated under general controls.

3. FDA received one comment supporting the proposed classification into class II and recommending that the assay of the calibrator be verifiable by a second methodology to ensure the safety and effectiveness of the calibrator prior to its usage in the laboratory.

Accordingly, the proposed regulation is being adopted with the changes noted.

On April 28, 1978, the agency terminated all of the device classification panels and reestablished them with the same functions, but with new names and with a new structure. FDA published notices of these changes in the *Federal Register* of May 19, 1978 (43 FR 21666, 21667, and 21668) and May 26, 1978 (43 FR 22672 and 22673). Further information regarding the device advisory committees and a list of their new names may be found in the preamble to the general provisions, published elsewhere in this issue of the *Federal Register*.

Therefore, under the Federal Food, Drug, and Cosmetic Act (secs. 513, 701(a), 52 Stat. 1055, 90 Stat. 540-546 (21 U.S.C. 360c, 371(a))) and under authority delegated to him (21 CFR 5.1), the Commissioner of Food and Drugs is amending Part 864 in Subpart I by adding new § 864.8185, to read as follows:

§ 864.8185 Calibrator for red cell and white cell counting.

(a) *Identification.* A calibrator for red cell and white cell counting is a device that resembles red or white blood cells and that is used to set instruments intended to count red cells, white cells, or both. It is a suspension of particles or cells whose size, shape, concentration, and other characteristics have been precisely and accurately determined.

(b) *Classification.* Class II (performance standards).

Effective date. This regulation shall be effective October 14, 1980.

(Secs. 513, 701(a), 52 Stat. 1055, 90 Stat. 540-546 (21 U.S.C. 360c, 371(a)))

Dated: August 15, 1980.

William F. Randolph,
Acting Associate Commissioner for
Regulatory Affairs.

[FR Doc. 80-27374 Filed 9-11-80; 8:45 am]

BILLING CODE 4110-03-M

21 CFR Part 864

[Docket No. 78N-1913]

Classification of Blood Cell Diluents

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is issuing a final rule classifying blood cell diluents into class I (general controls). The effect of classifying a device into class I is to require that the device meet only the general controls applicable to all devices. This action is being taken under