

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 878

[Docket No. 2006N-0109]

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Certifier	D. Hawkins

General and Plastic Surgery Devices; Reclassification of the Topical Oxygen Chamber for Extremities

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is proposing to reclassify the topical oxygen chamber for extremities (TOCE) from class III (premarket approval) into class II (special controls). The device is intended to surround a patient's limb and apply humidified oxygen to aid healing of chronic skin ulcers such as bedsores. Elsewhere in this issue of the **Federal Register**, FDA is publishing a notice of availability of the draft guidance document that the agency proposes to use as a special control for the device.

DATES: Submit written or electronic comments by *[insert date 90 days after date of publication in the **Federal Register**]*. See section VIII of this document for the proposed effective date of a final rule based on this proposed rule.

ADDRESSES: You may submit comments, identified by Docket No. 2006N-0109, by any of the following methods:

Electronic Submissions

Submit electronic comments in the following ways:

- Federal eRulemaking Portal: <http://www.regulations.gov>. Follow the instructions for submitting comments.

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- Agency Web site: <http://www.fda.gov/dockets/ecomments>. Follow the instructions for submitting comments on the agency Web site.

Written Submissions

Submit written submissions in the following ways:

- FAX: 301-827-6870.
- Mail/Hand delivery/Courier [For paper, disk, or CD-ROM submissions]:

Division of Dockets Management (HFA-305), Food and Drug Administration,
5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

To ensure more timely processing of comments, FDA is no longer accepting comments submitted to the agency by e-mail. FDA encourages you to continue to submit electronic comments by using the Federal eRulemaking Portal or the agency Web site, as described in the *Electronic Submissions* portion of this paragraph.

Instructions: All submissions received must include the agency name and Docket No(s). and Regulatory Information Number (RIN) (if a RIN number has been assigned) for this rulemaking. All comments received may be posted without change to <http://www.fda.gov/ohrms/dockets/default.htm>, including any personal information provided. For detailed instructions on submitting comments and additional information on the rulemaking process, see the “Comments” heading of the **SUPPLEMENTARY INFORMATION** section of this document.

Docket: For access to the docket to read background documents or comments received, go to <http://www.fda.gov/ohrms/dockets/default.htm> and insert the docket number(s), found in brackets in the heading of this document, into the “Search” box and follow the prompts and/or go to the Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Charles N. Durfor, Center for Devices and Radiological Health (HFZ-410), Food and Drug Administration, 9200 Corporate Blvd., Rockville, MD 20850, 301-594-3090, ext. 134.

SUPPLEMENTARY INFORMATION:

I. Background

A. Regulatory Authorities

The Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 301 *et seq.*), as amended by (among other amendments) the Medical Device Amendments of 1976 (the 1976 amendments) (Public Law 94-295) and the Safe Medical Devices Act (SMDA) (Public Law 101-629) established a comprehensive system for the regulation of medical devices intended for human use. Section 513 of the act (21 U.S.C. 360c) established three categories (classes) of devices, depending on the regulatory controls needed to provide reasonable assurance of their safety and effectiveness. The three categories of devices are class I (general controls), class II (special controls), and class III (premarket approval).

Under section 513 of the act, devices that were in commercial distribution before May 28, 1976 (the date of enactment of the 1976 amendments), generally referred to as preamendments devices, are classified after FDA has taken the following steps: (1) Received a recommendation from a device classification panel (an FDA advisory committee); (2) published the panel's recommendation for comment, along with a proposed regulation classifying the device; and (3) published a final regulation classifying the device. FDA has classified most preamendments devices under these procedures.

Devices that were not in commercial distribution prior to May 28, 1976, generally referred to as postamendments devices, are classified automatically by statute (section 513(f) of the act) into class III without any FDA rulemaking

process. Postamendments devices require premarket approval, unless FDA issues an order finding the device to be substantially equivalent, in accordance with section 513(i) of the act, to a predicate device that does not require premarket approval. The agency determines whether new devices are substantially equivalent to predicate devices by means of premarket notification procedures in section 510(k) of the act (21 U.S.C. 360(k)) and 21 CFR part 807) of the regulations.

A preamendments device that has been classified into class III may be marketed, by means of premarket notification procedures, without submission of a premarket approval application (PMA) until FDA issues a final regulation under section 515(b) of the act (21 U.S.C. 360e(b)) requiring premarket approval.

In 1990, the SMDA added section 515(i) to the act. This section requires FDA to issue an order to manufacturers of preamendments class III devices for which no final regulation requiring the submission of PMAs has been issued to submit to the agency a summary of, and a citation to, any information known or otherwise available to them respecting such devices, including adverse safety and effectiveness information that has not been submitted under section 519 of the act (21 U.S.C. 360i). Section 519 of the act requires manufacturers, importers, and device user facilities to submit adverse event reports of certain device-related events and reports of certain corrective actions taken. Section 515(i) of the act also directs FDA to either revise the classification of the device into class I or class II or require the device to remain in class III and establish a schedule for the issuance of a rule requiring the submission of PMAs for those devices.

In the **Federal Register** of May 6, 1994 (59 FR 23731), FDA announced the availability of a document setting forth its strategy for implementing the provisions of the SMDA that require FDA to review the classification of preamendments class III devices. Under this plan, the agency divided preamendments class III devices into the following three groups: Group 1 devices are devices that FDA believes raise significant questions of safety and/or effectiveness, but are no longer used or are in very limited use; group 2 devices are devices that FDA believes have a high potential for being reclassified into class II; and group 3 devices are devices that FDA believes are not likely candidates for reclassification.

In the **Federal Register** of August 14, 1995 (60 FR 41986), FDA published an order for Group 2 preamendment class III devices, including the TOCE, requiring the submission of safety and effectiveness information in accordance with the preamendments class III strategy to implement section 515(i) of the act (515(i) summary). The order describes in detail the format for submitting the type of information required by section 515(i) of the act so that the information submitted would clearly support reclassification or indicate that the device should be retained in class III. This order was updated in the **Federal Register** of June 13, 1997 (62 FR 32355).

Reclassification of classified preamendments devices is governed by section 513(e) of the act. This section provides that FDA may, by rulemaking, reclassify a device based upon "new information." The reclassification can be initiated by FDA or by the petition of an interested person. The term "new information," as used in section 513(e) of the act, includes information developed as a result of a re-evaluation of the data before the agency when the device was originally classified, as well as information not presented, not

available, or not developed at that time. (See, e.g., *Holland Rantos v. United States Department of Health, Education, and Welfare*, 587 F.2d 1173, 1174 n.1 (D.C. Cir. 1978); *Upjohn v. Finch*, 422 F.2d 944 (6th Cir. 1970); *Bell v. Goddard*, 366 F.2d 177 (7th Cir. 1966).)

Re-evaluation of the data previously before the agency is an appropriate basis for subsequent regulatory action where the reevaluation is made in light of changes in “medical science.” (See *Upjohn v. Finch*, supra, 422 F.2d at 951.) However, regardless of whether data before the agency are past or new data, the “new information” upon which reclassification under section 513(e) of the act is based must consist of “valid scientific evidence,” as defined in section 513(a)(3) of the act and 21 CFR 860.7(c)(2). FDA relies upon “valid scientific evidence” in the classification process to determine the level of regulation for devices. For the purpose of reclassification, the valid scientific evidence upon which the agency relies must be publicly available. Publicly available information excludes trade secret and/or confidential commercial information, e.g., the contents of a pending PMA. (See section 520(c) of the act (21 U.S.C. 360j(c)).)

B. Device Description

The TOCE is currently identified as a device intended to surround hermetically a patient’s limb and apply humidified oxygen topically at a pressure slightly greater than atmospheric pressure to aid healing of chronic skin ulcers or bed sores.

C. Regulatory History of the Device

In 1988, the agency issued a final rule classifying this device into class III (53 FR 23856, June 24, 1988). In the preamble to the classification final rule, FDA cited two documents that found little scientific evidence to support

the safety and effectiveness of the device. FDA stated that there was a potential for widespread use of the device in the treatment of skin sores in the elderly and infirm. FDA concluded that the device presented a potential unreasonable risk of illness or injury to these patients if there were not adequate data to assure its safety and effectiveness. In addition, FDA found that the device was purported or represented to be for a use, the treatment of decubitus ulcers, that was of substantial importance in preventing impairment of human health. Accordingly, the agency classified the device into class III.

In August 1997, in response to FDA's order for the submission of information on the TOCE, two manufacturers submitted 515(i) summaries of safety and effectiveness information to the agency for the TOCE (Refs. 1 and 2). These 515(i) summaries recommended that the device be reclassified into class II and provided information to assist FDA in reclassifying the device. FDA referred the 515(i) submissions to the General and Plastic Surgery Devices Panel (GPS Panel) for their recommendation on the requested reclassification.

At a public meeting on November 17, 1998, the GPS Panel recommended that the device be retained in class III (Ref. 3). The GPS Panel based their recommendation on the information in the 515(i) submissions of safety and effectiveness information; the information provided by FDA; testimony presented at the meeting by manufacturers of the device, a physician user of the device, and FDA; and the Panel's deliberations at the meeting.

The GPS Panel believed that the effectiveness of the TOCE remained unestablished. The Panel also concluded that special controls, in addition to general controls, were insufficient to provide a reasonable assurance of the safety and effectiveness of the device and that there was insufficient information, primarily a lack of effectiveness information, to establish special

controls. Accordingly, the GPS panel recommended premarket approval to provide reasonable assurance of the device's effectiveness. The Panel recommended that the call for premarket approval be of low priority to allow manufacturers of the device sufficient time to conduct studies that would establish the effectiveness of the device.

II. Proposed Rule

As discussed in more detail in the following paragraph, FDA is proposing to reclassify the TOCE from class III to class II (special controls). FDA believes that new information now exists to establish special controls, that, in addition to the general controls, will provide a reasonable assurance of the safety and effectiveness of this device.

In addition, FDA is proposing minor revisions to the device description (see 21 CFR 878.5650) intended to more accurately describe this device type. FDA is proposing to remove the term hermetically and to clarify that bedsores are chronic skin ulcers. FDA proposes to identify the TOCE as follows: A topical oxygen chamber for extremities is a device that is intended to surround a patient's limb and apply humidified oxygen topically at a pressure slightly greater than atmospheric pressure to aid healing of chronic skin ulcers such as bedsores.

III. Risks to Health

After considering the information in the 515(i) submissions for the two devices, the GPS Panel's recommendation, the published literature, and Medical Device Reports, FDA has evaluated the risks to health associated with use of the TOCE and determined that the following risks to health are associated with its use.

A. Infection

If the device cannot be sterilized, an infection can occur. FDA also notes that some TOCEs are for single patient use and some are for multiple patient use. If a TOCE for multiple patient use cannot be adequately sterilized between use in multiple patients, there is a high potential for transmission of infection between patients because these patients are already immunologically compromised.

B. Fire and Explosion

The risk of fire and explosion is common to all devices that are used in an atmosphere of pure oxygen.

C. Local Tissue Damage

The therapeutic topical oxygen pressure range, which is only slightly above atmospheric pressure, is very narrow and is critical to maintain. Excessive topical oxygen pressure (higher than 22 millimeters of mercury) can occlude local arterial circulation, decreasing local tissue circulation, which could cause local tissue damage.

D. Adverse Tissue Reaction

Adverse tissue reaction is a risk common to all devices that contact compromised skin. Incompatible materials or impurities in the materials may increase the severity of a local tissue reaction or cause a system tissue reaction.

E. Electrical Shock

Electrical shock is also a risk common to electrical devices that contact compromised skin.

IV. Summary of the Reasons for the Reclassification

FDA believes that the TOCE should be reclassified into class II because special controls, in addition to general controls, can be established to provide reasonable assurance of the safety and effectiveness of the device. In addition, there is now experience in the clinical community and adequate effectiveness information sufficient to establish special controls to provide such assurance.

V. Summary of the Data Upon Which the Reclassification is Based

New information has become available since the 1998 GPS Panel meeting on the clinical effectiveness of the device. Specifically, three recent studies (two prospective and one retrospective) report safe use and adequate healing of wounds using the TOCE. Two studies compared standard wound care with TOCE treatment for gangrenous or necrotic wounds (Refs. 4 and 5), and the third study evaluated the clinical effectiveness of TOCE treatment of chronic ulcers, post-surgical wounds, and acute trauma-induced wounds (Ref. 6). These three studies demonstrated adequate healing for an acceptable number of wounds. Investigators reported no complications related to TOCE use in these three studies.

VI. Special Controls

FDA believes that the draft guidance document entitled "Class II Special Controls Guidance: Topical Oxygen Chamber for Extremities" (draft special controls guidance document), in addition to general controls, can be an adequate special control to address the risks to health associated with the use of the TOCE device described in section III of this document. FDA agrees with the GPS Panel that in 1998 the effectiveness of the TOCE was not established. FDA now believes that the new information cited previously (Refs. 4 to 6) provides sufficient supporting evidence regarding effectiveness. Thus, the agency now believes that the draft special controls guidance document, which

incorporates voluntary consensus standards, device performance testing, and labeling, addresses the GPS Panel's concerns. Elsewhere in this issue of the **Federal Register**, FDA is publishing a notice of availability of the draft guidance document that the agency intends to use as the special control for this device.

The draft special controls guidance document contains specific recommendations for device performance testing and other information that should be included in a premarket notification (510(k)) submission. For example, the draft special controls guidance document addresses the following issues: sterility, fire and explosion control, oxygen pressure control, biocompatibility, electrical safety testing, and labeling. In the following table 1, FDA has identified the risks to health associated with the use of the device in the first column and the recommended mitigation measures identified in the draft special controls guidance document in the second column. These recommendations will also help ensure that the device has appropriate performance characteristics and labeling for its use. Following the effective date of any final reclassification rule based on this proposal, any firm submitting a 510(k) submission for this device will need to address the issues covered in the draft special controls guidance document. However, the firm need only show that its device meets the recommendations of the draft special controls guidance document or in some other way provides equivalent assurances of safety and effectiveness.

TABLE 1

Identified Risk	Recommended Mitigation Measures
Infection	Section 7: Sterility Section 12: Clinical Studies Section 13: Labeling
Fire and Explosion	Section 8: Fire and Explosion Control Section 13: Labeling

TABLE 1—Continued

Identified Risk	Recommended Mitigation Measures
Local Tissue Damage	Section 9: Oxygen Pressure Control Section 13: Labeling
Adverse Tissue Reaction	Section 10: Biocompatibility
Electrical Shock	Section 11: Electrical Safety Testing Section 13: Labeling

VII. FDA's Findings

As discussed previously, FDA believes the TOCE should be reclassified into II because special controls, in addition to general controls, provide reasonable assurance of the safety and effectiveness of the devices, and there is sufficient information to establish special controls to provide such assurance. FDA, therefore, is proposing to reclassify the device into class II and establish the draft class II special controls guidance document as a special control for the device.

Section 510(m) of the act provides that a class II device may be exempted from the premarket notification requirements under section 510(k) of the act, if the agency determines that premarket notification is not necessary to provide reasonable assurance of the safety and effectiveness of the device. For this type of device, FDA has determined that premarket notification is necessary to provide reasonable assurance of safety and effectiveness and, therefore, the device is not exempt from the premarket notification requirements. FDA review of performance characteristics will provide reasonable assurance that acceptable levels of performance for both safety and effectiveness are addressed before marketing clearance. Thus, persons who intend to market this device must submit to FDA a 510(k) submission containing information on the TOCE and receive a substantial equivalence determination from the agency before marketing the device.

VIII. Proposed Effective Date

FDA proposes that any final regulation based on this proposal become effective 30 days after its date of publication in the **Federal Register**.

IX. Environmental Impact

The agency has determined under 21 CFR 25.34(b) that this proposed reclassification action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

X. Analysis of Impacts

FDA has examined the impacts of the proposed rule under Executive Order 12866 and the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act of 1995 (Public Law 104–4). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). The agency believes that this proposed rule is not a significant regulatory action as defined by the Executive order.

The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. Reclassification of this device from class III to class II will relieve all manufacturers of the device of the cost of complying with the premarket approval requirements of section 515 of the act. Because reclassification will reduce the regulatory costs with respect to this device, the agency certifies that the proposed rule will not have a significant economic impact on a substantial number of small entities.

Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that agencies prepare a written statement, which includes an assessment of anticipated costs and benefits, before proposing "any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of \$100,000,000 or more (adjusted annually for inflation) in any one year." The current threshold after adjustment for inflation is \$115 million, using the most current (2003) Implicit Price Deflator for the Gross Domestic Product. FDA does not expect this proposed rule to result in any 1-year expenditure that would meet or exceed this amount.

XI. Federalism

FDA has analyzed this proposed rule in accordance with the principles set forth in Executive Order 13132. FDA has determined that the proposed rule, if finalized, would not contain policies that would have substantial direct effects on the States, on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of government. Accordingly, the agency tentatively concludes that the proposed rule does not contain policies that have federalism implications as defined in the Executive order and, consequently, a federalism summary impact statement has not been prepared.

XII. Paperwork Reduction Act of 1995

FDA tentatively concludes that this proposed rule contains no collections of information. Therefore, clearance by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (the PRA) (44 U.S.C. 3501–3520) is not required.

FDA also tentatively concludes that the draft special controls guidance document does not contain new information collection provisions that are

subject to review and clearance by OMB under the PRA. Elsewhere in this issue of the **Federal Register**, FDA is publishing a notice announcing the availability of the draft guidance document entitled "Class II Special Controls Guidance: Topical Oxygen Chamber for Extremities"; the notice contains an analysis of the paperwork burden for the draft guidance.

XIII. Comments

Interested persons may submit to the Division of Dockets Management Branch (see **ADDRESSES**) written or electronic comments regarding this document. Submit a single copy of electronic comments or two paper copies of any mailed comments, except that individuals may submit one paper copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

XIV. References

The following references have been placed on display in the Division of dockets management (see **ADDRESSES**) and may be seen by interested persons between 9 a.m. and 4 p.m. Monday through Friday.

1. 515(i) Submission submitted by Gaymar Industries, Inc., Orchard Park, NY, dated August 4, 1997, received August 11, 1997.
2. 515(i) Submission submitted by Stephen's Medical Inc./Wound Cure, Inc., Northbrook, IL, dated August 11, 1997, received August 12, 1997.
3. General and Plastic Surgery Devices Panel, Transcript, November 17, 1998, pages 120-201.
4. Heng, M.C.Y., J. Harker, V.B. Bardakjian, and H. Ayvazian, "Enhanced Healing and Cost-Effectiveness of Low Pressure Oxygen Therapy in Healing Necrotic Wounds: A feasibility study of technology transfer," *Ostomy Wound Management*, 46: 52-60, 2000.

5. Heng, M.C.Y., J. Harker, G. Csathy, C. Marshall, J. Brazier, S. Socorro, and E.P. Gomez, "Angiogenesis in Necrotic Ulcers Treated with Hyperbaric Oxygen," *Ostomy Wound Management*, 46: 18–32, 2000.

6. Kalliainen, L.K., G.M. Gordillo, R. Schlanger, and C.K. Sen, "Topical oxygen as an adjunct to wound healing: a clinical case series," *Pathophysiology* 9: 81–87, 2003.

List of Subjects in 21 CFR Part 878

Medical devices.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, it is proposed that 21 CFR part 878 be amended as follows:

Part 878—GENERAL AND PLASTIC SURGERY DEVICES

1. The authority citation for 21 CFR part 878 continues to read as follows:

Authority: 21 U.S.C. 351, 360, 360c, 360e, 360j, 371.

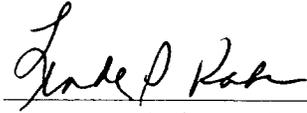
2. Section 878.5650 is revised in Subpart F to read as follows:

§878.5650 Topical oxygen chamber for extremities.

(a) *Identification.* A topical oxygen chamber for extremities is a device that is intended to surround a patient's limb and apply humidified oxygen topically at a pressure slightly greater than atmospheric pressure to aid healing of chronic skin ulcers such as bedsores.

(b) *Classification*. Class II (special controls). The special control for the device is FDA's "Class II Special Controls Guidance: Topical Oxygen Chamber for Extremities." See § 878.1(e) for the availability of this guidance document.

Dated: 3/27/06
March 27, 2006.



Linda S. Kahan,
Deputy Director,
Center for Devices and Radiological Health.

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