above between 9 a.m. and 4 p.m., Monday through Friday.

III. Electronic Access

An electronic version of this draft guidance also is available via Internet using the World Wide Web (WWW) (connect to cdrh home page at http://www.fda.gov/cdrh/ode/usgudode.pdf).

Dated: June 4, 1997.

Joseph A. Levitt,

Deputy Director for Regulations Policy, Center for Devices and Radiological Health.

[FR Doc. 97–15452 Filed 6–12–97; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 97D–0211]

Guidance for Industry on Nonsterile Semisolid Dosage Forms (SUPAC-SS) for Chemistry, Manufacturing, and Controls; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a guidance document entitled ''Guidance for Industry: Nonsterile Semisolid Dosage Forms; Scale-Up and Postapproval Changes: Chemistry, Manufacturing, and Controls; In Vitro Release Testing and In Vivo Bioequivalence Documentation.'' The purpose of this guidance document is to provide insight and recommendations to pharmaceutical sponsors of new drug applications (NDA's), abbreviated new drug applications (ANDA's), and abbreviated antibiotic drug applications (AADA's) who intend to change the components or composition, the manufacturing (process and equipment), the scale-up/scale-down of manufacture, and/or the site of manufacture of a semisolid formulation during the postapproval period. This guidance document addresses nonsterile semisolid preparations (e.g., creams, gels, lotions, and ointments) intended for topical routes of administration. This guidance document represents the agency's current thinking on scale-up and postapproval changes for nonsterile semisolid (SUPAC-SS) dosage forms regulated by the Center for Drug Evaluation and Research (CDER).

DATES: Written comments may be submitted at any time.

ADDRESSES: Submit written requests for single copies of ''Guidance for Industry: Nonsterile Semisolid Dosage Forms; Scale-Up and Postapproval Changes: Chemistry, Manufacturing, and Controls; In Vitro Release Testing and In Vivo Bioequivalence Documentation'' to the Drug Information Branch (HFD–210), Center for Drug Evaluation and Research, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857. Send one self-addressed adhesive label to assist that office in processing your requests. Submit written comments on the guidance document to the Dockets Management Branch (HFA–305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1–23, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: Vinod P. Shah, Center for Drug Evaluation and Research (HFD–350), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–594–5635.

SUPPLEMENTARY INFORMATION: FDA is announcing the availability of a guidance document entitled ''Guidance for Industry: Nonsterile Semisolid Dosage Forms; Scale-Up and Postapproval Changes: Chemistry, Manufacturing, and Controls; In Vitro Release Testing and In Vivo Bioequivalence Documentation.'' The purpose of this guidance document is to provide insight and recommendations to pharmaceutical sponsors of NDA's, ANDA's, and AADA's who intend to change: (1) The components or composition; (2) the manufacturing (process and equipment); (3) the scale-up/scale-down of manufacture; and/or (4) the site of manufacture of a semisolid formulation during the postapproval period. This guidance document addresses nonsterile semisolid preparations (e.g., creams, gels, lotions, and ointments) intended for topical routes of administration. The guidance document defines the following: (1) Levels of change; (2) recommended chemistry, manufacturing, and controls (CMC) tests to support each level of change; (3) recommended in vitro release tests and/or in vivo bioequivalence tests to support each level of change; and (4) documentation to support the change.

This guidance document represents the agency's current thinking on scale-up and postapproval changes for nonsterile semisolid dosage forms regulated by CDER. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirement of the applicable statute, regulations, or both.

Interested persons may, at any time, submit written comments on the guidance document to the Dockets Management Branch (address above). Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. The guidance document and received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

An electronic version of this guidance document is also available on the Internet using the World Wide Web (http://www.fda.gov/cder/guidance.htm).

Dated: June 5, 1997.

William K. Hubbard,

Associate Commissioner for Policy Coordination.

[FR Doc. 97–15451 Filed 6–12–97; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 94N–0418]

Order for Certain Class III Devices; Submission of Safety and Effectiveness Information; Group 3

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is revising the schedule for submission of summaries and citations for 4 devices included in the order requiring manufacturers of 27 class III devices (Group 3) to submit to FDA a summary of, and a citation to, all information known or otherwise available to them respecting such devices, including adverse safety or effectiveness information concerning the devices which has not been submitted under the Federal Food, Drug, and Cosmetic Act (the act). In response to comments received on the August 14, 1995, order and in order to facilitate the review process, FDA is grouping four cardiovascular devices with related uses together and is changing the date by which summaries and citations are to be submitted to February 14, 1998. The agency is deferring the due date for one gastroenterology-urological device also until February 14, 1998. As a reminder to device manufacturers, FDA is also

reprinting the due dates for all other devices listed in the August 14, 1995, order.

DATES: Summaries and citations must be submitted by the dates listed below.

ADDRESSES: Submit summaries and citations to the Documents Mail Center (HFZ–401), Food and Drug Administration, Center for Devices and Radiological Health, 9200 Corporate Blvd., Rockville, MD 20850.

FOR FURTHER INFORMATION CONTACT: Doreen M. Melling, Center for Devices and Radiological Health (HFZ–402), Food and Drug Administration, 9200 Corporate Blvd., Rockville, MD 20850, 301–594–2186.

SUPPLEMENTARY INFORMATION:

I. Background

Section 513 of the act (21 U.S.C. 360c) requires the classification of medical devices into one of three classes: Class I (general controls), class II (special controls), and class III (premarket approval). Generally, devices that were on the market before May 28, 1976, the date of enactment of the Medical Device Amendments of 1976 (the amendments) (Pub. L. 94–295), and devices marketed on or after that date that are substantially equivalent to such devices, have been classified by FDA. This notice refers to both the class III devices that were on the market before May 28, 1976, and the substantially equivalent devices that were marketed on or after that date, as ''preamendment devices''.

Section 515(b) of the act (21 U.S.C. 360e(b)) establishes the requirement that a preamendments device that FDA has classified into class III is subject to premarket approval. However, the submission of a premarket approval application (PMA), or a notice of completion of a product development protocol (PDP), is not required until 90 days after FDA issues a final rule requiring premarket approval for the device, or 30 months after final classification of the device, whichever is later. Also such a device is exempt from the investigational device exemption (IDE) regulations (21 CFR part 812) until the date stipulated by FDA in the final rule requiring the submission of a PMA for that device. If a PMA or a notice of completion of a PDP is not filed by the later of the two dates, commercial distribution of the device is required to cease. The device may, however, be distributed for investigational use if the manufacturer, importer, or other sponsor of the device complies with the IDE regulations.

To date, FDA has issued final rules requiring the submission of PMA's for 52 preamendment class III devices. Additionally, FDA has issued proposed rules for 12 other devices. There are 68 remaining preamendment class III devices for which FDA has not yet initiated any action requiring the submission of PMA's. The original number of approximately 140 preamendment class III devices can be accounted for by past reclassification actions.

The Safe Medical Devices Act of 1990 (the SMDA) (Pub. L. 101–629) changed the definition of class II devices from those for which a performance standard is necessary to provide reasonable assurance of safety and effectiveness to those for which there is sufficient information to establish special controls to provide such assurance. Special controls include performance standards, postmarket surveillance, patient registries, guidelines (including guidelines for the submission of clinical data in premarket notification submissions in accordance with section 510(k) of the act (21 U.S.C. 360(k)), recommendations, and other appropriate actions the agency deems necessary to provide such assurance. Thus, the SMDA modified the definition of class II devices to permit reliance on special controls, rather than performance standards alone, to provide reasonable assurance of safety and effectiveness.

The SMDA also added new section 515(i) to the act. This section requires FDA to order manufacturers of preamendment class III devices for which no final regulation requiring the submission of a PMA 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 which has not been submitted under section 519 of the act (21 U.S.C. 360i). Section 519 of the act requires manufacturers, importers, or distributors to maintain records and to report information that reasonably suggests that one of its marketed devices may have caused or contributed to a death or serious injury, or that a malfunction of the device is likely to cause death or serious injury on recurrence. Section 515(i) of the act also directs FDA to publish a regulation before December 1, 1995, for each device subject to section 515(i) of the act, either revising the classification of the device into class I or class II or requiring the device to remain in class III. Finally, section 515(i) of the act requires that, within 12 months after publication of a regulation retaining a device in class III, FDA is to establish a schedule for the issuance of a rule requiring the submission of PMA's for the device.

In the **Federal Register** of May 6, 1994 (59 FR 23731), FDA announced its strategy for addressing the 116 remaining preamendment class III devices. In this notice, FDA made available a document setting forth its strategy for implementing the provisions of the SMDA that require FDA to review the classification of certain class III devices, and either reclassify the devices into class I or class II or retain them in class III. Under this plan, the agency divided the universe of preamendment class III devices into 3 groups. Group 1 devices are devices that FDA believes raise significant questions of safety and/or effectiveness, but are no longer used or are very limited in use. Group 2 devices are devices that FDA believes have a high potential for being reclassified into class II. Group 3 devices are devices that FDA believes are currently in commercial distribution and are not likely candidates for reclassification. There are a total of 43, 31, and 42 (15 high priority) devices in Groups 1, 2, and 3, respectively.

In the May 6, 1994, notice, FDA announced its intention to call for the submission of PMA's for the 15 highest priority devices in Group 3, and for all Group 1 devices. The final rule requiring the filing of a PMA or a notice of completion of a PDP for 41 class III devices (Group 1 devices) was published in the **Federal Register** on September 27, 1996 (61 FR 50704). In the May 6, 1994, notice, the agency also announced its intention to issue an order under section 515(i) of the act for the remaining Group 3 devices and all of the Group 2 devices.

In the **Federal Register** of August 14, 1995 (60 FR 41984), FDA issued an order requiring manufacturers of the 27 devices in Group 3 to submit a summary of, and citation to, all safety and effectiveness information known or otherwise available to them respecting such devices, including adverse safety and effectiveness information concerning the devices which had not been submitted under section 519 of the act. In this notice, FDA is grouping devices with related uses together and is revising the date by which summaries and citations are to be submitted. Thus, the summaries for the membrane lung for long term pulmonary support (originally due by August 14, 1996), the arterial embolization device (originally due by August 14, 1996), the cardiopulmonary bypass defoamer (originally due by February 14, 1997), the sorbent hemoperfusion system (originally due by August 14, 1997), and the artificial embolization device

(originally due by August 14, 1997), are now due by February 14, 1998. Based upon the information submitted in response to this order, FDA will issue a proposed regulation for each device either proposing its reclassification into class I or class II or retaining the device in class III. The due dates for summaries and citations for the other group 3 devices remain the same and are listed below.

II. Statutory Authority and Enforcement

In addition to the provisions of section 515(i) of the SMDA described in section I of this document, this order is issued under section 519 of the act, as implemented by § 860.7(g)(2) (21 CFR 860.7(g)(2)). This regulation authorizes FDA to require reports or other information bearing on the classification of a device. Section 519 of the act also requires the reporting of any death or serious injury caused by a device or by its malfunction.

Failure to comply with this order is a prohibited act under section 301(q) of the act (21 U.S.C. 331(q)), and the agency will use its enforcement powers to deter noncompliance. Violations under section 301 of the act may be subject to seizure or injunction under sections 302(a) and 304(a) of the act (21 U.S.C. 332(a) and 334(a)). In addition, violations under section 301 of the act may be subject to civil penalties under section 303(f) of the act (21 U.S.C. 333(f)) and criminal prosecution under section 303(a) of the act.

III. Order

The agency is hereby issuing this revised order under sections 515(i) and 519 of the act and § 860.7(g)(1) of the regulations. Under the order, the required information shall be submitted by the dates listed below so that FDA may begin promptly the process established by section 515(i) of the act to either revise or sustain the current classification of these devices. The five devices listed with a February 14, 1998, deadline are the devices whose due date is being revised. The remaining due dates are reprinted here from the August 14, 1995, order as a reminder to device manufacturers.

A. Deadlines for Submissions of Information

For the following seven devices, the required information was to be submitted by August 14, 1996:

1. § 868.2450 *Lung water monitor.*
2. § 868.2500 *Cutaneous oxygen monitor.*
3. § 870.1025 *Arrhythmia detector and alarm.*
4. § 870.3375 *Cardiovascular intravascular filter.*
5. § 874.3400 *Tinnitus masker.*
6. § 884.5940 *Powered vaginal muscle stimulator for therapeutic use.*
7. § 890.3890 *Stair-climbing wheelchair.*

For the following eight devices, the required information was to be submitted by February 14, 1997:

8. § 870.3610 *Implantable pacemaker pulse generator.*
9. § 870.3700 *Pacemaker programmers.*
10. § 870.3800 *Annuloplasty ring.*
11. § 870.5225 *External counter-pulsating device.*
12. § 870.5550 *External transcutaneous cardiac pacemaker (noninvasive).*
13. § 886.3400 *Keratoprosthesis.*
14. § 874.3930 *Tympanostomy tube with semipermeable membrane.*
15. § 874.5350 *Suction antichoke device.*

For the following seven devices, the required information shall be submitted by August 14, 1997:

16. § 870.3450 *Vascular graft prosthesis of less than 6 millimeters diameter.*
17. § 870.3535 *Intra-aortic balloon and control system.*
18. § 870.3600 *External pacemaker pulse generator.*
19. § 874.5370 *Tongs antichoke device.*
20. § 876.5955 *Peritoneo-venous shunt.*
21. § 882.1790 *Ocular plethysmograph.*
22. § 882.5860 *Implanted neuromuscular stimulator.*

For the following five devices, the required information shall be submitted by February 14, 1998:

23. § 868.5610 *Membrane lung for long-term pulmonary support.* (Originally due by August 14, 1996.)[1]
24. § 870.3300 *Arterial embolization device.* (Originally due by August 14, 1996.)[1]
25. § 870.4230 *Cardiopulmonary bypass defoamer.* (Originally due by February 14, 1997.)[1]
26. § 876.5870 *Sorbent hemoperfusion system.* (Originally due by August 14, 1997.)[1]
27. § 882.5950 *Artificial embolization device.* (Originally due by August 14, 1997.)[1]

[1] Revised due date

B. Required Contents of Submissions

By the dates listed above, all manufacturers currently marketing preamendments class III devices subject to this order shall provide a summary or, and citation to, any information known or otherwise available to them respecting the devices, including adverse safety and effectiveness data that has not been submitted under section 519 of the act. FDA suggests that it may be in the best interest of submitters to summarize the information submitted under section 519 of the act to facilitate FDA's decisionmaking, even though such information is not required.

The information should be submitted in one of the two following formats depending on whether the applicant is aware of any information which would support the reclassification of the device into class I (general controls) or class II (special controls). Information that would support the reclassification of the device must consist of adequate, valid scientific evidence showing that general controls alone (class I), or general controls and special controls (class II) will provide a reasonable assurance of the safety and effectiveness of the device.

For manufacturers who are not aware of any information that would support the reclassification of their device into class I or class II, the information provided should be submitted in the following format:

1. *Indications for Use.* A general description of the disease or condition to be diagnosed, treated, cured, mitigated, or prevented, including a description of the patient population for which the device is intended.

2. *Device Description.* An explanation of how the device functions, significant physical and performance characteristics of the device, and basic scientific concepts that form the basis for the device.

3. *Other Device Labeling.* Other device labeling that includes contraindications, warnings and precautions and/or promotional materials.

4. *Risks.* A summary of all adverse safety and effectiveness information and identification of the risks presented by the device as well as any mechanisms or procedures that will control the risk.

5. *Alternative Practices and Procedures.* A description of alternative practices or procedures for diagnosing, treating, preventing, curing, or mitigating the disease or condition for which the device is intended.

6. *Summary of Preclinical and Clinical Data.* The summary of preclinical and clinical data should include the conclusions drawn from the studies which support the safety and effectiveness of the device as well as special controls, if any, that address the adverse effects of the device on health. The summary should include a brief description of the objective of the

studies, the experimental design, how the data were collected and analyzed, and a brief description of the results of the studies, whether positive, negative, or inconclusive. The summary of the clinical study(ies) should also include a discussion of the subject inclusion and exclusion criteria, the study population, reasons for patient discontinuations, and results of statistical analyses.

7. *Bibliography*. A copy of the key references, a brief summary of the salient features of each key reference, and a brief discussion of why the reference is relevant to an evaluation of the safety and effectiveness evaluation of the device.

Manufacturers who are aware of information that would support the reclassification of their device into class I or class II may either submit information using the format described below or may submit a formal reclassification petition, which should include the information described below in addition to the information required under 21 CFR 860.123.

1. *Identification*. A brief narrative identification of the device. This identification should be specific enough to distinguish a particular device from a generic type of device. Where appropriate, this identification should include a listing of the materials, and the component parts, and a description of the intended use of the device.

2. *Risks to Health*. An identification of the risks to health should be provided. This section should summarize all adverse safety and effectiveness information, which have not been submitted under section 519 of the act, particularly the most significant. The mechanisms or procedures which will control the risk should be described. A list of the general hazards associated with the device and a bibliography with copies of the referenced material should be provided.

3. *Recommendation*. A statement whether the manufacturer believes the device should be reclassified into class I or class II.

4. *Summary of Reasons for Recommendation*. Each manufacturer should include a summary of the reasons for requesting reclassification of its device and an explanation of why it believes the device meets the statutory criteria for reclassification into class I or class II. Each manufacturer should also identify the special controls that it believes would be sufficient to provide reasonable assurance of the safety and effectiveness of its device if it believes the device should be reclassified into class II.

5. *Summary of Valid Scientific Evidence on Which the Recommendation Is Based*. Manufacturers are advised that, when considering a formal reclassification petition, FDA will rely only upon valid scientific evidence to determine that there is a reasonable assurance of the safety and effectiveness of the device, if regulated by general controls alone (class I) or by general controls and special controls (class II). Valid scientific evidence consists of evidence from well-controlled investigations, partially controlled studies, studies and objective trials without matched controls, well-documented case histories conducted by qualified experts, and reports of significant human experience with a marketed device, from which it can fairly and responsibly be concluded by qualified experts that there is reasonable assurance of the safety and effectiveness of a device under its conditions of use. The evidence required may vary according to the characteristics of the device, its conditions of use, the existence and adequacy of warnings and other restrictions, and the extent of experience with its use. Isolated case reports, random experience, reports lacking sufficient details to permit scientific evaluation, and unsubstantiated opinions are not regarded as valid scientific evidence to show safety or effectiveness (see § 860.7(c)(2)).

According to § 860.7(d)(1), there is reasonable assurance that a device is safe when it can be determined, based upon valid scientific evidence, that the probable benefits to health from use of the device for its intended uses and conditions of use, when accompanied by adequate directions and warnings against unsafe use, outweigh any probable risks. The valid scientific evidence used to determine the safety of a device shall adequately demonstrate the absence of unreasonable risk of illness or injury associated with the use of the device for its intended uses and conditions for use. Moreover, under § 860.7(e)(1), there is reasonable assurance that a device is effective when it can be determined, based upon valid scientific evidence, that in a significant portion of the target population, the use of the device for its intended uses and conditions of use, when accompanied by adequate directions for use and warnings against unsafe use, will provide clinically significant results.

Manufacturers submitting a formal reclassification petition may wish to request two petitions as examples of successful reclassification petitions. Magnetic Resonance Imaging devices, docket Nos. 87P–0214/CP–1 through CP–13, and Nd:YAG Laser for posterior capsulotomy devices, docket no. 86P–0083, were both reclassified from class III to class II subsequent to the submission of reclassification petitions. Both petitions are available upon submission of a Freedom of Information request to the Dockets Management Branch (HFA–305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1–23, Rockville, MD 20850.

IV. Submission of Required Information

The summary of, and citation to, any information required by the act must be submitted by the dates listed above to the Document Mail Center (address above).

Dated: May 30, 1997.

Joseph A. Levitt,

Deputy Director for Regulations Policy, Center for Devices and Radiological Health.

[FR Doc. 97–15449 Filed 6–12–97; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 94N–0417]

Order for Certain Class III Devices; Submission of Safety and Effectiveness Information; Group 2

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is revising the schedule for submission of summaries and citations for 3 devices included in the order requiring manufacturers of 31 class III devices (Group 2) to submit to FDA a summary of, and a citation to, all information known or otherwise available to them respecting such devices, including adverse safety or effectiveness information concerning the devices that have not been submitted under the Federal Food, Drug, and Cosmetic Act (the act). In response to comments received on the August 14, 1995, order and in order to facilitate the review process, FDA is grouping three cardiovascular devices with related uses together and is changing the date by which summaries and citations are to be submitted for them to February 14, 1998. As a reminder to device manufacturers, FDA is also reprinting the due dates for all other devices listed in the August 14, 1995, order.

DATES: Summaries and citations must be submitted by the dates listed below.