

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 2007N-0229]

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Certifier L. CLAWSON
DDM

Agency Information Collection Activities; Proposed Collection; Comment Request; Medical Devices: Current Good Manufacturing Practice Quality System Regulations

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing an opportunity for public comment on the proposed collection of certain information by the agency. Under the Paperwork Reduction Act of 1995 (the PRA), Federal agencies are required to publish notice in the **Federal Register** concerning each proposed collection of information, including each proposed extension of an existing information collection, and to allow 60 days for public comment in response to the notice. This notice solicits comments on recordkeeping requirements related to the medical devices current good manufacturing practice (CGMP) quality system (QS) regulation (CGMP/QS regulation).

DATES: Submit written or electronic comments on the collection of information by *[insert date 60 days after date of publication in the **Federal Register**]*.

ADDRESSES: Submit electronic comments on the collection of information to: <http://www.fda.gov/dockets/ecomments>. Submit written comments on the collection of information to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD

20852. All comments should be identified with the docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT: Denver Presley, Jr., Office of the Chief Information Officer (HFA-250), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-1472.

SUPPLEMENTARY INFORMATION: Under the PRA (44 U.S.C. 3501-3520), Federal agencies must obtain approval from the Office of Management and Budget (OMB) for each collection of information they conduct or sponsor. "Collection of information" is defined in 44 U.S.C. 3502(3) and 5 CFR 1320.3(c) and includes agency requests or requirements that members of the public submit reports, keep records, or provide information to a third party. Section 3506(c)(2)(A) of the PRA (44 U.S.C. 3506(c)(2)(A)) requires Federal agencies to provide a 60-day notice in the **Federal Register** concerning each proposed collection of information, including each proposed extension of an existing collection of information, before submitting the collection to OMB for approval. To comply with this requirement, FDA is publishing notice of the proposed collection of information set forth in this document.

With respect to the following collection of information, FDA invites comments on these topics: (1) Whether the proposed collection of information is necessary for the proper performance of FDA's functions, including whether the information will have practical utility; (2) the accuracy of FDA's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) ways to minimize the burden of the collection of information on respondents, including through

the use of automated collection techniques, when appropriate, and other forms of information technology.

Medical Devices: Current Good Manufacturing Practice Quality System Regulations--21 CFR Part 820 (OMB Control Number 0910-0073)—Extension

Under section 520(f) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 360j(f)), the Secretary of the Department of Health and Human Services (the Secretary) has the authority to prescribe regulations requiring that the methods used in, and the facilities and controls used for, the manufacture, pre-production design validation (including a process to assess the performance of a device but not including an evaluation of the safety and effectiveness of a device), packing, storage, and installation of a device conform to CGMP, as described in such regulations, to assure that the device will be safe and effective and otherwise in compliance with the act.

The CGMP/QS regulation implementing authority provided by this statutory provision is found under part 820 (21 CFR part 820) and sets forth basic CGMP requirements governing the design, manufacture, packing, labeling, storage, installation, and servicing of all finished medical devices intended for human use. The authority for this regulation is covered under sections 501, 502, 510, 513, 514, 515, 518, 519, 520, 522, 701, 704, 801, and 803 of the act (21 U.S.C. 351, 352, 360, 360c, 360d, 360e, 360h, 360i, 360j, 360l, 371, 374, 381, and 383). The CGMP/QS regulation includes requirements for purchasing and service controls, clarifies recordkeeping requirements for device failure and complaint investigations, clarifies requirements for verifying/validating production processes and process or product changes, and clarifies requirements for product acceptance activities quality data evaluations and corrections of nonconforming product/quality problems.

Requirements are compatible with specifications in the international standards “ISO 9001: Quality Systems Model for Quality Assurance in Design/ Development, Production, Installation, and Servicing.” The CGMP/QS information collections will assist FDA inspections of manufacturers for compliance with quality system requirements encompassing design, production, installation, and servicing processes.

Section 820.20(a) through (e) requires management with executive responsibility to establish, maintain, and/or review the following topics: (1) The quality policy; (2) the organizational structure; (3) the quality plan; and (4) the quality system procedures of the organization.

Section 820.22 requires the conduct and documentation of quality system audits and reaudits.

Section 820.25(b) requires the establishment of procedures to identify training needs and documentation of such training.

Section 820.30(a)(1) and (b) through (j), requires in respective order, the establishment, maintenance, and/or documentation of the following topics: (1) Procedures to control design of class III and class II devices, and certain class I devices as listed therein; (2) plans for design and development activities and updates; (3) procedures identifying, documenting, and approving design input requirements; (4) procedures defining design output, including acceptance criteria, and documentation of approved records; (5) procedures for formal review of design results and documentation of results in the design history file (DHF); (6) procedures for verifying device design and documentation of results and approvals in the DHF; (7) procedures for validating device design, including documentation of results in the DHF; (8) procedures for translating device design into production specifications; (9) procedures for documenting,

verifying validating approved design changes before implementation of changes; and (10) the records and references constituting the DHF for each type of device.

Section 820.40 requires manufacturers to establish and maintain procedures controlling approval and distribution of required documents and document changes.

Section 820.40(a) and (b) requires the establishment and maintenance of procedures for the review, approval, issuance and documentation of required records (documents) and changes to those records.

Section 820.50(a)(1), (a)(2), (a)(3), and (b) requires the establishment and maintenance of procedures and requirements to ensure service and product quality, records of acceptable suppliers, and purchasing data describing specified requirements for products and services.

Sections 820.60 and 820.65 require, respectively, the establishment and maintenance of procedures for identifying all products from receipt to distribution and for using control numbers to track surgical implants and life-sustaining or supporting devices and their components.

Section 820.70(a)(1) through (a)(5), (b) through (e), (g)(1) through (g)(3), (h), and (i) requires the establishment, maintenance, and/or documentation of the following topics: (1) Process control procedures; (2) procedures for verifying or validating changes to specification, method, process, or procedure; (3) procedures to control environmental conditions and inspection result records; (4) requirements for personnel hygiene; (5) procedures for preventing contamination of equipment and products; (6) equipment adjustment, cleaning and maintenance schedules; (7) equipment inspection records; (8) equipment tolerance postings; procedures for utilizing manufacturing materials expected

to have an adverse effect on product quality; and (9) validation protocols and validation records for computer software and software changes.

Sections 820.72(a), (b)(1), and (b)(2) and 820.75(a) through (c) require, respectively, the establishment, maintenance, and/or documentation of the following topics: (1) Equipment calibration and inspection procedures; (2) national, international or in-house calibration standards; (3) records that identify calibrated equipment and next calibration dates; (4) validation procedures and validation results for processes not verifiable by inspections and tests; (5) procedures for keeping validated processes within specified limits; (6) records for monitoring and controlling validated processes; and (7) records of the results of revalidation where necessitated by process changes or deviations.

Sections 820.80(a) through (e) and 820.86, respectively, require the establishment, maintenance, and/or documentation of the following topics: (1) Procedures for incoming acceptance by inspection, test, or other verification; (2) procedures for ensuring that in-process products meet specified requirements and the control of product until inspection and tests are completed; (3) procedures for, and records that show, incoming acceptance or rejection is conducted by inspections, tests or other verifications; (4) procedures for, and records that show, finished devices meet acceptance criteria and are not distributed until device master record (DMR) activities are completed; (5) records in the device history record (DHR) showing acceptance dates, results, and equipment used; and (6) the acceptance/rejection identification of products from receipt to installation and servicing.

Sections 820.90(a), (b)(1), and (b)(2) and 820.100 require, respectively, the establishment, maintenance and/or documentation of the following topics: (1)

Procedures for identifying, recording, evaluating and disposing of nonconforming product; (2) procedures for reviewing and recording concessions made for, and disposition of, nonconforming product; (3) procedures for reworking products, evaluating possible adverse rework effect and recording results in the DHR; (4) procedures and requirements for corrective and preventive actions, including analysis, investigation, identification and review of data, records, causes and results; and (5) records for all corrective and preventive action activities.

Section 820.100(a)(1) through (a)(7) states that procedures and requirements shall be established and maintained for corrective/preventive actions, including the following: (1) Analysis of data from process, work, quality, servicing records; investigation of nonconformance causes; (2) identification of corrections and their effectiveness; (3) recording of changes made; and (4) appropriate distribution and managerial review of corrective and preventive action information.

Section 820.120 states that manufacturers shall establish/maintain procedures to control labeling storage/application; and examination/release for storage and use, and document those procedures.

Sections 820.120(b) and (d), 820.130, 820.140, 820.150(a) and (b), 820.160(a) and (b), and 820.170(a) and (b), respectively, require the establishment, maintenance, and/or documentation of following topics: (1) Procedures for controlling and recording the storage, examination, release and use of labeling; (2) the filing of labels/labeling used in the DHR; (3) procedures for controlling product storage areas and receipt/dispatch authorizations; (4) procedures controlling the release of products for distribution; (5) distribution records that identify consignee, product, date and control numbers; and (6)

instructions, inspection and test procedures that are made available, and the recording of results for devices requiring installation.

Sections 820.180(b) and (c), 820.181(a) through (e), 820.184(a) through (f), and 820.186 require, respectively, the maintenance of records: (1) That are retained at prescribed site(s), made readily available and accessible to FDA and retained for the device's life expectancy or for 2 years; (2) that are contained or referenced in a DMR consisting of device, process, quality assurance, packaging and labeling, and installation, maintenance, and servicing specifications and procedures; (3) that are contained in a DHR and demonstrate the manufacture of each unit, lot, or batch of product in conformance with DMR and regulatory requirements, include manufacturing and distribution dates, quantities, acceptance documents, labels and labeling, control numbers; and (4) that are contained in a quality system record (QSR), consisting of references, documents, procedures, and activities not specific to particular devices.

Sections 820.198(a) through (c) and 820.200(a) through (d), respectively, require the establishment, maintenance, and/or documentation of the following topics: (1) Complaint files and procedures for receiving, reviewing and evaluating complaints; (2) complaint investigation records identifying the device, complainant, and relationship of the device to the incident; (3) complaint records that are reasonably accessible to the manufacturing site or at prescribed sites; (4) procedures for performing and verifying that device servicing requirements are met and that service reports involving complaints are processed as complaints; and (5) service reports that record the device, service activity, and test and inspection data.

Section 820.250 requires the establishment and maintenance of procedures to identify valid statistical techniques necessary to verify process and product acceptability; and sampling plans, when used, which are written and based on valid statistical rationale; and procedures for ensuring adequate sampling methods.

The CGMP/QS regulation amends and revises the CGMP requirements for medical devices set out under part 820. The regulation adds design and purchasing controls; modifies previous critical device requirements; revises previous validation and other requirements; and harmonizes device CGMP requirements with QS specifications in the international standard “ISO 9001: Quality Systems Model for Quality Assurance in Design/Development, Production, Installation, and Servicing.” The rule does not apply to manufacturers of components or parts of finished devices, nor to manufacturers of human blood and blood components subject to 21 CFR part 606. With respect to devices classified in class I, design control requirements apply only to class I devices listed in § 820.30(a)(2) of the regulation. The rule imposes burden upon: (1) Finished device manufacturer firms, which are subject to all recordkeeping requirements; (2) finished device contract manufacturers; specification developers; and (3) repacker, relabelers, and contract sterilizer firms, which are subject only to requirements applicable to their activities. In addition, remanufacturers of hospital single-use devices (SUDs) will now be considered to have the same requirements as manufacturers in regard to this regulation. The establishment, maintenance and/or documentation of procedures, records, and data required by this regulation will assist FDA in determining whether firms are in compliance with CGMP requirements, which are intended to ensure that devices meet their design, production, labeling,

installation, and servicing specifications and, thus are safe, effective and suitable for their intended purpose. In particular, compliance with CGMP design control requirements should decrease the number of design-related device failures that have resulted in deaths and serious injuries.

The CGMP/QS regulation applies to approximately 8,963 respondents. These recordkeepers consist of 8,945 original respondents and an estimated 18 hospitals that remanufacture or reuse SUDs. They include manufacturers, subject to all requirements and contract manufacturers, specification developers, repackers, relabelers, and contract sterilizers, subject only to requirements applicable to their activities. Hospital remanufacturers of SUDs are now defined to be manufacturers under guidelines issued by FDA's Center for Devices and Radiological Health (CDRH), Office of Surveillance and Biometrics. Respondents to this collection have no reporting activities, but must make required records available for review or copying during FDA inspection. The regulation contains additional recordkeeping requirements in such areas as design control, purchasing, installation, and information relating to the remanufacture of SUDs. The estimates for this burden are derived from those incremental tasks that were determined when the new CGMP/QS regulation became final as well as those carry-over requirements. The carry-over requirements are based on decisions made by the agency on July 16, 1992, under OMB clearance submission 0910-0073, which still provides valid baseline data.

FDA estimates respondents will have a total annual recordkeeping burden of approximately 3,076,370 hours. This figure also consists of approximately 143,052 hours spent on a startup basis by 650 new firms.

FDA estimates the burden for this collection of information as follows:

TABLE 1.—ESTIMATED ANNUAL RECORDKEEPING BURDEN¹

21 CFR Section	No. of Recordkeepers	Annual Frequency per Record-keeping	Total Annual Hours	Hours per Record	Total Hours
820.20(a)	8,963	1	8,963	6.58	58,977
820.20(b)	8,963	1	8,963	4.43	39,706
820.20(c)	8,963	1	8,963	6.17	55,302
820.20(d)	8,963	1	8,963	9.89	88,644
820.20(e)	8,963	1	8,963	9.89	88,644
820.22	8,963	1	8,963	32.72	293,269
820.25(b)	8,963	1	8,963	12.68	113,651
820.30(a)(1)	8,963	1	8,963	1.75	15,685
820.30(b)	8,963	1	8,963	5.95	53,330
820.30(c)	8,963	1	8,963	1.75	15,685
820.30(d)	8,963	1	8,963	1.75	15,685
820.30(e)	8,963	1	8,963	23.39	209,645
820.30(f)	8,963	1	8,963	37.42	335,395
820.30(g)	8,963	1	8,963	37.42	335,395
820.30(h)	8,963	1	8,963	3.34	29,936
820.30(i)	8,963	1	8,963	17.26	154,701
820.30(j)	8,963	1	8,963	2.64	23,662
820.40	8,963	1	8,963	8.91	79,860
820.40(a) and (b)	8,963	1	8,963	2.04	18,285
820.50(a)(1) through (a)(3)	8,963	1	8,963	21.90	196,290
820.50(b)	8,963	1	8,963	6.02	53,957
820.6	8,963	1	8,963	0.32	2,868
820.65	8,963	1	8,963	0.67	6,005
820.70(a)(1) through (a)(5)	8,963	1	8,963	1.85	16,582
820.70(b) and (c)	8,963	1	8,963	1.85	16,582
820.70(d)	8,963	1	8,963	2.87	25,724
820.70(e)	8,963	1	8,963	1.85	16,582
820.70(g)(1) through (g)(3)	8,963	1	8,963	1.43	12,817
820.70(h)	8,963	1	8,963	1.85	16,582
820.70(i)	8,963	1	8,963	7.50	67,223
820.72(a)	8,963	1	8,963	4.92	44,098
820.72(b)(1) and (b)(2)	8,963	1	8,963	1.43	12,817
820.75(a)	8,963	1	8,963	2.69	24,110
820.75(b)	8,963	1	8,963	1.02	9,142
820.75(c)	8,963	1	8,963	1.11	9,949
820.80(a) through (e)	8,963	1	8,963	4.80	43,022
820.86	8,963	1	8,963	0.79	7,081
820.90(a)	8,963	1	8,963	4.95	44,367
820.90(b)(1) and (b)(2)	8,963	1	8,963	4.95	44,367
820.100 (a)(1) through (a)(7)	8,963	1	8,963	12.48	111,858

TABLE 1.—ESTIMATED ANNUAL RECORDKEEPING BURDEN¹—Continued

21 CFR Section	No. of Recordkeepers	Annual Frequency per Record-keeping	Total Annual Hours	Hours per Record	Total Hours
820.100(b)	8,963	1	8,963	1.28	11,473
820.120(b)	8,963	1	8,963	0.45	4,033
820.120(d)	8,963	1	8,963	0.45	4,033
820.130	8,963	1	8,963	0.45	4,033
820.140	8,963	1	8,963	6.34	56,825
820.150(a) and (b)	8,963	1	8,963	5.67	50,820
820.160(a) and (b)	8,963	1	8,963	0.67	6,005
820.170(a) and (b)	8,963	1	8,963	1.50	13,445
820.180(b) and (c)	8,963	1	8,963	1.50	13,445
820.181(a) through (e)	8,963	1	8,963	1.21	10,845
820.184(a) through (f)	8,963	1	8,963	1.41	12,638
820.186	8,963	1	8,963	0.40	3,585
820.198(a) through (c)	8,963	1	8,963	4.94	44,277
820.200(a) and (d)	8,963	1	8,963	2.61	23,393
820.25	8,963	1	8,963	0.67	6,005
Totals					3,072,337

¹ There are no capital costs or operating and maintenance costs associated with this collection of information.

Burden (labor) hour and cost estimates were originally developed under FDA contract by Eastern Research Group, Inc. (ERG), in 1996 when the CGMP/QS regulation became final. These figures are still accurate. Additional factors considered in deriving estimates included the following:

- Establishment Type: Query has been made of CDRH's registration/listing databank and has counted 8,963 domestic firms subject to CGMPs. In addition, hospitals that reuse or remanufacture devices are now considered manufacturers under new FDA guidance. After investigations of many hospitals and the changes in enforcements of FDA's requirements for hospitals, the number of reuse or remanufactures of single-use medical devices have decreased from the estimated 66 to an estimated 18 hospitals. Because the total number of registered firms is not static, the number of respondents will fluctuate from year to year resulting in slight changes to the overall burden.

Currently, there are 8,963 firms subject to the CGMPs; an increase from the last renewal of 8,254.

- **Potentially Affected Establishments:** Except for manufacturers, not every type of firm is subject to every CGMP/QS requirement. For example, all are subject to FDA's quality policy regulations (§ 820.20(a)), document control regulations (§ 820.40), and other requirements, whereas only manufacturers and specification developers are subject to FDA's design controls regulations (§ 820.30). The type of firm subject to each requirement was identified by ERG.

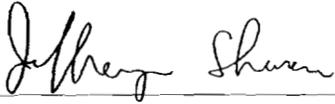
FDA estimates the burden hours (and costs) based on the last approved renewal for this information collection.

FDA estimates that some 650 "new" establishments (marketing devices for the first time) will expend some 143,052 "development" hours on a one-time startup basis to develop records and procedures for the CGMP/QS regulation.

FDA estimates that annual labor hours are apportioned as follows: (1) 40 percent goes to requirements dealing with manufacturing specifications, process controls, and the DHR; (2) 20 percent goes to requirements dealing with components and acceptance activities; (3) 25 percent goes to requirements dealing with equipment, records (the DMR and QSR), complaint investigations, labeling/packaging and reprocessing/investigating product nonconformance; and 15 percent goes to quality audit, traceability, handling, distribution, statistical, and other requirements.

Dated: JUN 28 2007

June 28, 2007.



Jeffrey Shuren,
Assistant Commissioner for Policy.

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