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Display Date 6-10-04
Publication Date 6-14-04
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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 2004N–0034]

Agency Information Collection Activities; Submission for Office of Management and Budget Review; Comment Request; Medical Devices; Current Good Manufacturing Practice Quality System Regulation

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing that a proposed collection of information has been submitted to the Office of Management and Budget (OMB) for review and clearance under the Paperwork Reduction Act of 1995.

DATES: Fax written comments on the collection of information by [*insert date 30 days after date of publication in the* **Federal Register**].

ADDRESSES: OMB is still experiencing significant delays in the regular mail, including first class and express mail, and messenger deliveries are not being accepted. To ensure that comments on the information collection are received, OMB recommends that comments be faxed to the Office of Information and Regulatory Affairs, OMB, Attn: Fumie Yokota, Desk Officer for FDA, FAX: 202–395–6974.

FOR FURTHER INFORMATION CONTACT: Peggy Robbins, Office of Management Programs (HFA–250), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–1223.

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SUPPLEMENTARY INFORMATION: In compliance with 44 U.S.C. 3507, FDA has submitted the following proposed collection of information to OMB for review and clearance.

Medical Devices; Current Good Manufacturing Practice (CGMP) Quality System (QS) 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 the authority provided by this statutory provision is found at 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 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 international quality standards, ISO (International Organization for Standardization) 9001 entitled "Quality Systems Model for Quality Assurance in Design/Development, Production, Installation, and Servicing." CGMP/QS information collections will assist FDA inspections of manufacturer 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 these topics: The quality policy, the organizational structure, the quality plan, and 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 the following respective order, the establishment, maintenance, and/or documentation of these 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), and (h) and (i) requires the establishment, maintenance, and/or documentation of these 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) and (b)(1) and (b)(2) and 820.75(a) through (c) require, respectively, the establishment, maintenance, and/or documentation of these 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 these 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), (b)(2), and 820.100 require, respectively, the establishment, maintenance and/or documentation of these 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 these 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 DHRs, demonstrate the manufacture of each unit, lot or batch of product in conformance with DMR and regulatory requirements, and include manufacturing and distribution dates and quantities, acceptance documents, labels and labeling, and 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) and (d), respectively, require the establishment, maintenance and/or documentation of these 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, that are written and based on a 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 at part 820. It adds design and purchasing controls; modifies previous critical device requirements; revises previous validation and other requirements; and harmonizes device CGMP requirements with quality system specifications in the international standard, ISO 9001:1994 entitled "Quality Systems—Model for Quality Assurance in Design, Development Production, Installation and Servicing." The regulation applies neither 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).

The regulation imposes burdens upon finished device manufacturer firms, which are subject to all recordkeeping requirements, and also upon finished device contract manufacturer, specification developer, repacker and relabeler, and contract sterilizer firms, which are subject only to requirements applicable to their activities. Due to modifications to the guidance given for remanufacturers of hospital single-use devices, reusers of hospital single-use devices 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.

If FDA did not impose these recordkeeping requirements, it anticipates that design-related device failures would continue to occur in the same numbers as before and continue to result in a significant number of device recalls and preventable deaths and serious injuries. Moreover, manufacturers would be unable to take advantage of substantial savings attributable to reduced recall costs, improved manufacturing efficiency, and improved access to international markets through compliance with CGMP requirements that are harmonized with international quality system standards.

The CGMP/QS regulation applies to some 8,254 respondents. These recordkeepers consist of 8,188 original respondents and an estimated 66 hospitals which remanufacture or reuse single use medical devices. 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 single use medical devices (SUDs) are now defined to be manufacturers under guidelines issued by FDA's Center for Devices and Radiological Health's (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 single use medical devices. The estimates for 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 control number 0910–0073. This still provides valid baseline data.

FDA estimates respondents will have a total annual recordkeeping burden of approximately 2,833,020 hours. This figure also consists of approximately 143,052 hours spent on a startup basis by 650 new firms. FDA estimates information collection burdens imposed as follows:

TABLE 1.—ESTIMATED ANNUAL RECORDKEEPING BURDEN[1]

CFR Section	Number of Recordkeepers	Annual Frequency of Recordkeeping	Total Annual Hours	Hours per Recordkeeper	Total Hours	Total Operating and Maintenance Cost
820.20(a)	8,254	1	8,254	6.58	54,311	--------
820.20(b)	8,254	1	8,254	4.43	36,565	--------
820.20(c)	8,254	1	8,254	6.17	50,927	--------
820.20(d)	8,254	1	8,254	9.89	81,632	--------
820.20(e)	8,254	1	8,254	9.89	81,632	--------
820.22	8,254	1	8,254	32.72	270,071	--------
820.25(b)	8,254	1	8,254	12.68	104,661	--------
820.30(a)(1)	8,254	1	8,254	1.75	14,445	--------
820.30(b)	8,254	1	8,254	5.95	49,111	--------
820.30(c)	8,254	1	8,254	1.75	14,445	--------
820.30(d)	8,254	1	8,254	1.75	14,445	--------
820.30(e)	8,254	1	8,254	23.39	193,061	--------
820.30(f)	8,254	1	8,254	37.42	308,865	--------
820.30(g)	8,254	1	8,254	37.42	308,865	--------
820.30(h)	8,254	1	8,254	3.34	27,568	--------
820.30(i)	8,254	1	8,254	17.26	142,464	--------
820.30(j)	8,254	1	8,254	2.64	21,791	--------
820.4	8,254	1	8,254	8.91	73,543	--------
820.40(a)-(b)	8,254	1	8,254	2.04	16,838	--------
820.50(a)(1)-(a)(3)	8,254	1	8,254	21.9	180,763	$1,181,925
820.50(b)	8,254	1	8,254	6.02	49,689	--------
820.60	8,254	1	8,254	0.32	2,641	--------
820.65	8,254	1	8,254	0.67	5,530	--------
820.70(a)(1)-(a)(5)	8,254	1	8,254	1.85	15,270	--------

TABLE 1.—ESTIMATED ANNUAL RECORDKEEPING BURDEN[1]—Continued

CFR Section	Number of Recordkeepers	Annual Frequency of Recordkeeping	Total Annual Hours	Hours per Recordkeeper	Total Hours	Total Operating and Maintenance Cost
820.70(b)-(c)	8,254	1	8,254	1.85	15,270	--------
820.70(d)	8,254	1	8,254	2.87	23,689	--------
820.70(e)	8,254	1	8,254	1.85	15,270	--------
820.70(g)(1)-(g)(3)	8,254	1	8,254	1.43	11,803	--------
820.70(h)	8,254	1	8,254	1.85	15,270	--------
820.72(a)	8,254	1	8,254	4.92	40,610	--------
820.70(i)	8,254	1	8,254	7.5	61,905	--------
820.72(b)(1) to (b)(2)	8,254	1	8,254	1.43	11,803	--------
820.75(a)	8,254	1	8,254	2.69	22,203	--------
820.75(b)	8,254	1	8,254	1.02	8,419	--------
820.75(c)	8,254	1	8,254	1.11	9,162	--------
820.80(a)-(e)	8,254	1	8,254	4.8	39,619	--------
820.86	8,254	1	8,254	0.79	6,521	--------
820.90(a)	8,254	1	8,254	4.95	40,857	--------
820.90(b)(1)-(b)(2)	8,254	1	8,254	4.95	40,857	--------
820.100(a)(1)-(a)(7)	8,254	1	8,254	12.48	103,010	--------
820.100(b)	8,254	1	8,254	1.28	10,565	--------
820.120	8,254	1	8,254	0.45	3,714	--------
820.120(b)	8,254	1	8,254	0.45	3,714	--------
820.120(d)	8,254	1	8,254	0.45	3,714	--------
820.130	8,254	1	8,254	0.45	3,714	--------
820.140	8,254	1	8,254	6.34	52,330	--------
820.150(a)-(b)	8,254	1	8,254	5.67	46,800	--------
820.160(a)-(b)	8,254	1	8,254	0.67	5,530	--------
820.170(a)-(b)	8,254	1	8,254	1.5	12,381	--------
820.180(b)-(c)	8,254	1	8,254	1 5	12,381	--------
820.181((a)-(e)	8,254	1	8,254	1.21	9,987	--------
820.184(a)-(f)	8,254	1	8,254	1.41	11,638	--------
820.186	8,254	1	8,254	0.4	3,302	--------
820.198(a)-(c)	8,254	1	8,254	4.94	40,775	--------
820.200(a) and (d)	8,254	1	8,254	2.61	21,543	--------
820.250	8,254	1	8,254	0.67	5,530	--------
Totals					2,283,020	$1,181,925

[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:

• Establishment type: Query has been made of CDRH's registration/listing databank and has counted 8,188 domestic firms subject to CGMPs. In addition, hospitals which reuse or remanufacture devices are now considered manufacturers under new FDA guidance. During the last report, it was estimated that out of the 6,000 hospitals in the United States, one third of them (or 2,000 hospitals) will reuse or remanufacture single use medical devices. 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 2,000 to an estimated 66 hospitals. Thus, the number of manufacturers will increase from 7,229 to 8,188, but the total number of firms subject to CGMPs will decrease from 9,229 to 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 estimated the burden hours (and costs) for the previous CGMP regulation in 1992. That estimate was submitted to OMB on May 4, 1992. It was approved by OMB on July 16, 1992, and expired on June 30, 1995. The methodology used is different than that used by ERG in estimating incremental tasks when the new CGMP/QS became final. Nevertheless, the agency believes its 1992 estimate adequately represents labor hours (and costs) needed to comply with previous CGMP requirements carried over into the new CGMP/

QS regulation. The 1992 estimate used 9,289 respondents (rather than 8,254 respondents), which compensates for differences in methodology.

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: 40 percent goes to requirements dealing with manufacturing specifications, process controls and the DHR; 20 percent goes to requirements dealing with components and acceptance activities; 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 4 2004

June 4, 2004.

Jeffrey Shuren

Jeffrey Shuren,
Assistant Commissioner for Policy.

[FR Doc. 04–????? Filed ??–??–04; 8:45 am]

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