DEPARTMENT OF HEALTH AND HUMAN SERVICES

Centers for Disease Control and Prevention

[Program Announcement 99065]

National Institute for Occupational Safety and Health; Research on Young Worker Safety and Health Risks in Construction; Notice of Availability of Funds; Amendment

A notice announcing the availability of Fiscal Year 1999 funds for the Research on Young Worker Safety and Health Risks in Construction was published in the **Federal Register** on April 9, 1999, [Vol. 64 FR No. 68]. The notice is amended as follows:

On page 17392, first column, agency docket number should be changed to read [Program Announcement 99065].

On page 17392, third column, paragraph F, first paragraph, line 7, fourth word should read ''99065''.

On page 17392, third column, paragraph F, second paragraph, line 8, fourth word should read ''99065''.

On page 17393, third column, paragraph J, second paragraph, line 7, second word should read ''99065''.

Dated: April 13, 1999.

Diane D. Porter,

Acting Director, National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention (CDC).

[FR Doc. 99–9740 Filed 4–16–99; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 98N–1110]

Agency Information Collection Activities; Submission for OMB Review; Comment Request; CGMP Regulations for Finished Pharmaceuticals

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

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

DATES: Submit written comments on the collection of information by May 19, 1999.

ADDRESSES: Submit written comments on the collection of information to the Office of Information and Regulatory Affairs, OMB, New Executive Office Bldg., 725 17th St. NW., rm. 10235, Washington, DC 20503, Attn: Desk Officer for FDA.

FOR FURTHER INFORMATION CONTACT: Karen L. Nelson, Office of Information Resources Management (HFA–250), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–1482.

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

CGMP Regulations for Finished Pharmaceuticals—21 CFR Parts 210 and 211 (OMB Control Number 0910–0139)—Reinstatement

Under section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 351(a)(2)(B)), a drug is adulterated if the methods used in, or the facilities or controls used for, its manufacture, processing, packing, or holding do not conform to or are not operated or administered in conformity with current good manufacturing practices (CGMP's) to ensure that such drug meets the requirements of the act as to safety and has the identity and strength, and meets the quality and purity characteristics, which it purports or is represented to possess.

FDA has the authority under section 701(a) of the act (21 U.S.C. 371(a)) to issue regulations for the efficient enforcement of the act regarding CGMP procedures for manufacturing, processing, and holding drugs and drug products. The CGMP regulations help ensure that drug products meet the statutory requirements for safety and have their purported or represented their purported or represented identity, strength, quality, and purity characteristics. The information collection requirements in the CGMP regulations provide FDA with the necessary information to perform its duty to protect public health and safety.

Although CGMP must be current in the industry, a practice need not be widely prevalent providing such practice is both feasible and valuable in ensuring drug quality. CGMP requirements establish accountability in the manufacturing and processing of drug products, provide for meaningful FDA inspections, and enable manufacturers to improve the quality of drug products over time. The recordkeeping requirements also serve preventive and remedial purposes and provide crucial information if it is necessary to recall a drug product.

The general requirements for recordkeeping under part 211 (21 part 211) are set forth in § 211.180. Any production, control, or distribution record associated with a batch and required to be maintained in compliance with part 211 must be retained for at least 1 year after the expiration date of the batch and, for certain OTC drugs, 3 years after distribution of the batch (§ 211.180(a)). Records for all components, drug product containers, closures, and labeling are required to be maintained for at least 1 year after the expiration date and 3 years for certain OTC products (§ 211.180(b)).

All part 211 records must be readily available for authorized inspections during the retention period (§ 211.180(c)), and such records may be retained either as original records or as true copies (§ 211.180(d)). In addition, 21 CFR 11.2(a) provides that ''For records required to be maintained but not submitted to the agency, persons may use electronic records in lieu of paper records or electronic signatures in lieu of traditional signatures, in whole or in part, provided that the requirements of this part are met.'' To the extent this electronic option is used, the burden of maintaining paper records should be substantially reduced as should any review of such records.

In order to facilitate improvements and corrective actions, records must be maintained so that data can be used for evaluating, at least annually, the quality standards of each drug product to determine the need for changes in drug product specifications or manufacturing or control procedures (§ 211.180(e)). Written procedures for these evaluations are to be established and include provisions for a review of a representative number of batches and, where applicable, records associated with the batch, and provisions for a review of complaints, recalls, returned or salvaged drug products, and investigations conducted under § 211.192 for each drug product.

Written procedures, referred to here as standard operating procedures (SOP's), are required for many part 211 records. The current SOP requirements were initially provided in a final rule published in the **Federal Register** of September 29, 1978 (43 FR 45014), and are now an integral and familiar part of the drug manufacturing process. The major paperwork impact of SOP's results from their creation. Thereafter, SOP's need to be periodically updated. A combined estimate is provided in

Table 1 of this document for routine maintenance of SOP's. Estimates for specific recordkeeping requirements are listed individually.

The 25 SOP's provisions under part 211 in the combined maintenance estimate include: (1) § 211.22(d) (responsibilities and procedures of the quality control unit); (2) § 211.56(b) (sanitation procedures); (3) § 211.56(c) (use of suitable rodenticides, insecticides, fungicides, fumigating agents, and cleaning and sanitizing agents; (4) § 211.67(b) (cleaning and maintenance of equipment); (5) § 211.68(a) (proper performance of automatic, mechanical, and electronic equipment); (6) § 211.80(a) (receipt, identification, storage, handling, sampling, testing, approval or rejection of components and drug product containers or closures); (7) § 211.94(d) (standards or specifications, methods of testing, and methods of remove pyrogenic properties for drug product container and closures); (8) § 211.100(a) (production and process control; (9) § 211.110(a) (sampling and testing of in-process materials and drug products); (10) § 211.113(a)(prevention of objectionable microorganisms in drug products not required to be sterile); (11) § 211.113(b) (prevention of microbiological contamination of drug products purporting to be sterile, including validation of any sterilization process); (12) § 211.115(a) (system for reprocessing batches that do not conform to standards or specifications, to insure that reprocessed batches conform with all established standards, specifications, and characteristics); (13) § 211.122(a) (receipt, identification, storage, handling, sampling, examination and/or testing of labeling and packaging materials); (14) § 211.125(f) (control procedures for the issuance of labeling); (15) § 211.130 (packaging and label operations, prevention of mixup and cross contamination, identification and handling of filed drug product containers that are set aside and held in unlabeled condition, identification of the drug product with a lot or control number that permits determination of the history of the manufacture and control of the batch); (16) § 211.142 (warehousing); (17) § 211.150 (distribution of drug products); (18) § 211.160 (laboratory controls); (19) § 211.165(c) (testing and release for distribution); (20) § 211.166(a) (stability testing); (21) § 211.167 (special testing requirements); (22) § 211.180(f) (notification of responsible officials of investigations, recalls, reports of inspectional observations, and any regulatory actions relating to good manufacturing practice); (23) § 211.198(a) (written and oral complaint procedures, including quality control unit review of any complaint involving specifications failures, and serious and unexpected adverse drug experiences); (24) § 211.204 (holding, testing, and reprocessing of returned drug products); and (25) § 211.208 (drug product salvaging).

The following burden estimates for routine maintenance and for specific recordkeeping requirements are based on FDA's institutional experience regarding creation and review of such procedures and similar recordkeeping requirements, and data provided by the Eastern Research Group (ERG), which is a consulting group hired by FDA's economics staff to prepare an economic analysis of the potential economic impact of the May 3, 1996 (61 FR 20104), proposed rule. ERG prepared a report for FDA that estimated the recordkeeping burden for the proposed rule entitled ''Current Good Manufacturing Practice; Proposed Amendment of Certain Requirements for Finished Pharmaceuticals'' (61 FR 20104). This report provided information on the current number of establishments affected by FDA's recordkeeping requirements and the agency has relied on these figures to estimate the number of establishments affected by part 211 recordkeeping provisions. ERG estimated that there are 1,077 establishments involved in pharmaceutical preparations, diagnostic substances, and biological products; 948 repackers or relabelers; and 2,159 medical gas establishments for a total estimate of 4,184 recordkeepers subject to CGMP recordkeeping requirements. ERG used a variety of sources to obtain its estimates including reports from the Department of Commerce and FDA's registration files. The ERG report is available at the Dockets Management Branch (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852, under Docket No. 95N–0362.

ERG also provided estimates on the burden involved in creating SOP's. While most of the CGMP provisions covered in this document were created many years ago, there will be some existing firms expanding into new manufacturing areas and start-up firms that will need to create SOP's. FDA is assuming that approximately 100 firms will have to create up to 25 SOP's for a total of 2,500 records, and the agency estimates that it will take 20 hours per recordkeeper to create 25 new SOP's for a total of 50,000 hours as a one-time burden. Annual SOP's maintenance is estimated to involve 1 hour annually per SOP, totaling 25 hours annually per recordkeeper.

The proposed rule revising part 211 CGMP requirements of May 3, 1996, would require additional SOP's. Cost estimates for those additional SOP's were included in the proposed rule, but are not included here. Any comments on those estimates will be evaluated in any final rule based on that proposal.

In the **Federal Register** of December 24, 1998 (63 FR 71291), the agency requested comments on the proposed collections of information. One comment was received from a pharmaceutical trade association. The comment said that the agency's estimates of paperwork needed to comply with the CGMP regulations were far too low. The comment based its conclusion on : (1) An informal poll of seven pharmaceutical firms; (2) the assertion that the agency had not considered the records that are required by several specific sections of the regulations; (3) the added recordkeeping attendant to agency guidances; and (4) the premise that part 11 (21 CFR part 11) (electronic records; electronic signatures) imposed costs that do not offset savings of electronic recordkeeping.

The agency has carefully considered the comment and concludes that the agency's estimates of the CGMP paperwork are reasonable and correct. The agency's estimates are based upon not only the ERG report, but its extensive experience with a broad spectrum of industry, including small and large firms, makers of generic and innovator drug products, and repackers. FDA believes these estimates reflect a more accurate characterization of the industry than the comment suggests. FDA's estimates are based on information received from large and small pharmaceutical firms. The numbers in the burden chart reflect an average of all firms involved in the review process.

With respect to the comment that FDA had not considered several sections of the regulations, the agency believes there may have been some misunderstanding on the part of comments. In fact, all sections of the regulations were considered, including those which the comments stated ''were ignored.'' Part of the misunderstanding is likely due to the fact that sections the comments considered to be ''ignored'' were those that contained no paperwork and therefore were not factored into the final analysis.

With respect to recordkeeping that is referenced in agency guidance documents, where a guidance document

addresses recordkeeping requirements that are already codified, the guidance documents themselves create no new paperwork burdens. However, the agency acknowledges that, on occasion, the information collection contained in guidance documents is beyond the scope of the regulation. FDA recognizes the need to ensure all potentially new paperwork burdens are identified, and that public comment is sought accordingly.

Regarding electronic recordkeeping, the agency fully met its obligations under the paperwork reduction act in developing and issuing part 11 and received no objections to the rule with respect to paperwork reduction. In fact, extensive discussions were held with industry throughout the development of the rule. FDA believes that the benefits of electronic recordkeeping, especially with regard to paperwork reduction, far outweigh the costs of compliance with part 11 to ensure that the electronic records are trustworthy, reliable, and compatible with FDA's mandate to protect and promote public health.

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

TABLE 1.—ESTIMATED ANNUAL RECORDKEEPING BURDEN[1]

21 CFR Section	No. of Recordkeepers	Annual Frequency per Recordkeeping	Total Annual Records	Hours per Recordkeeper	Total Hours
SOP Maintenance (See previous list of 25 SOP's)	4,184	1	4,184	25	104,600
One-time Burden (New Start-up SOP's)[2]	100	25	2,500	20	50,000
211.34	4,184	.25	1,046	.5	523
211.67(c)	4,184	50	209,200	.25	52,300
211.68	4,184	2	8,368	1	8,368
211.68(a)	4,184	10	41,840	.5	20,920
211.68(b)	4,184	5	20,920	.25	5,230
211.72	4,184	.25	1,046	1	1,046
211.80(d)	4,184	.25	1,046	.1	105
211.100(b)	4,184	3	12,552	2	25,104
211.105(b)	4,184	.25	1,046	.25	262
211.122(c)	4,184	50	209,200	.25	52,300
211.130(e)	4,184	50	209,200	.25	52,300
211.132(c)	1,698	20	33,960	.5	16,980
211.132(d)	1,698	.2	340	.5	170
211.137	4,184	5	20,920	.5	10,460
2111.160(a)	4,184	2	8,368	1	8,368
211.165(e)	4,184	1	4,184	1	4,184
211.166(c)	4,184	2	8,368	.5	4,184
211.173	1,077	1	1,077	.25	269
211.180(e)	4,184	.2	837	.25	209
211.180(f)	4,184	.2	837	1	837
211.182	4,184	2	8,368	.25	2,092
211.184	4,184	3	12,552	.5	6,276
211.186	4,184	10	41,840	2	83,680
211.188	4,184	25	104,600	2	209,200
211.192	4,184	2	8,368	1	8,368
211.194	4,184	25	104,600	.5	52,300
211.196	4,184	25	104,600	.25	26,150
211.198	4,184	5	20,920	1	20,920
211.204	4,184	10	41,840	.5	20,920
Total					848,625

[1] There are no capital costs or operating and maintenance costs associated with this collection of information.
[2] This is a one-time burden.

Dated: April 12, 1999.

William K. Hubbard,

Acting Deputy Commissioner for Policy.

[FR Doc. 99–9636 Filed 4–16–99; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 99F–0804]

Rohm and Haas Co.; Filing of Food Additive Petition

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing that Rohm and Haas Co. has filed a petition proposing that the food additive regulations be amended to provide for the safe use of 4,5-dichloro-2-n-octyl-3(2H)-isothiazolone as a preservative and slimicide in the manufacture of paper and paperboard in contact with food.

FOR FURTHER INFORMATION CONTACT: Hortense S. Macon, Center for Food Safety and Applied Nutrition (HFS–206), Food and Drug Administration, 200 C St. SW., Washington, DC 20204, 202–418–3086.

SUPPLEMENTARY INFORMATION: Under the Federal Food, Drug, and Cosmetic Act (sec. 409(b)(5)(21 U.S.C. 348(b)(5), notice is given that a food additive petition (FAP 9B4645) has been filed by Rohm and Haas Co., 100 Independence