Medical Devices; Exception from General Requirements for Informed Consent
RIN 0910-AC25
SUPPORTING STATEMENT 0910-0586 Revision

A. JUSTIFICATION

1. Circumstances Making the Collection of Information Necessary

Abstract

The final rule amends FDA's informed consent regulation to provide an exception to the general requirement to obtain informed consent from the subject of an investigation involving an unapproved or not cleared in vitro diagnostic device intended to identify a chemical, biological, radiological, or nuclear agent. This regulation was issued under the statutory authority provided in section 520(g)(3)(D) of the Federal Food Drug and Cosmetic Act, which outlines the criteria under which an exemption from informed consent may be permissible. It amends 21 CFR 50.23, to add paragraph (e). Section 50.23(e)(1) and (e)(2), require the investigator and an independent licensed physician to make the determination and certify in writing certain facts concerning the need for use of the investigational in vitro diagnostic device without informed consent. The investigator would submit this written certification to the institutional review board (IRB) and FDA Section 50.23(e)(3). Section 50.23(e)(4) provides that an investigator must disclose the investigational status of the device and what is known about the performance characteristics of the device at the time test results are reported to the subject's health care provider and public health authorities.

The information collection requirements in § 50.23 (e)(1),(e)(2), and (e)(4) in the interim final rule have been approved under OMB control number 0910-0586. The

information collection requirement in § 50.23 (e)(3) (submitting the certifications to the IRB) was considered part of the burden for § 50.23 (e)(1) and (2).

This final rule makes one change to the regulatory requirements established by the interim final rule. This change requires the investigator to submit the documentation required in § 50.23 (e)(1) and (2) to FDA, in addition to the reviewing IRB. The documentation the investigator must submit to FDA is identical to the documentation the investigator must submit to the IRB.

FDA is seeking OMB approval for one change in § 50.23 (e)(3), requiring the written documentation to be submitted to FDA.

This information is not related to the American Recovery and Reinvestment Act of 2009 (ARRA).

2. Purpose and Use of the Information Collection

FDA is requiring this information disclosure in order to assure that exceptions to the informed consent requirement occur only in cases in which the investigator may not obtain informed consent in sufficient time to protect the health of the subject.

The prospective respondents are investigators who are using investigational in vitro diagnostic devices intended to identify a chemical, biological, radiological, or nuclear agent. These investigators may be private sector laboratory directors and physicians who have their own business or are affiliated with business entities such as hospitals or device manufacturers. Respondents may also include investigators affiliated with federal or local government institutions such as public health laboratories and state health departments.

3. Use of Improved Information Technology and Burden Reduction

Respondents can use any appropriate technology to develop, maintain, and/or disseminate the required certification information. Use of computers and word processors has greatly reduced the time needed to compile, submit, and maintain the required documents. FDA estimates that 98% of the respondents will use electronic means to fulfill the agency's requirement.

4. Efforts to Identify Duplication and Use of Similar Information

The Food and Drug Administration is the only agency charged with the responsibility of regulating the investigation of in vitro diagnostic manufacture devices that are not approved or cleared for introduction into interstate commerce. Therefore, no similar information is available that can be used or modified for the purpose described.

5. Impact on Small Businesses or Other Small Entities

The FDA has established a Division of Small Manufacturers International and Consumer Assistance (DSMICA). DSMICA provides technical and nonfinancial assistance through a comprehensive program, which includes seminars and educational conferences, informational materials and use of a toll-free number which may be used by firms that require information or assistance. Additional Center for Devices and Radiological Health staff are available for consultation on request. The percentage of respondents that may be considered small business is estimated to be 20%.

6. Consequences of Collecting the Information Less Frequently

Data will be submitted occasionally. FDA requires a certification within five days of each use of investigational in vitro diagnostic device subject to this rule without obtaining

informed consent in order to assure adequate protection for subjects of such investigations.

7. Special Circumstances Relating to the Guidelines of 5 CFR 1320.5

This collection of information is consistent with 5 CFR 1320.5.

8. Comments in Response to the Federal Register Notice and Efforts to Consult Outside Agency

FDA published the Interim Final Rule in the FEDERAL REGISTER of 06/07/2006 (71 FR 32827) The agency received comments on the interim final rule from nine different entities, however only three were PRA related.. Comments were received from four individual consumers, two from consumer groups, and one each from a health professional, a health professional group, and a local government. Below is a summary of the PRA related comments.

(Comment 1) Two comments noted that the interim final rule has no provisions to prevent abuse.

(Response) FDA disagrees that the rule has no provisions to prevent abuse. The rule requires that the investigator and an independent physician each make specific determinations and that an IRB review these determinations. The determinations that the investigator and independent physician must make require careful consideration related to the use of the device and are intended to prevent abuse. However, FDA does agree that the interim rule could have included an additional measure to prevent abuse of the exception; specifically, the interim rule could have required that an investigator's documentation be submitted to the agency, not just to the reviewing IRB. Although FDA relies on IRBs to adequately monitor the procedures set forth by the rule, the agency recognizes that the interim final rule did not provide a mechanism for FDA to track the use of this exception from the general requirements for informed consent. Therefore, FDA is adding a requirement that the investigator submit to the FDA the

documentation required in § 50.23(e)(1) or (e)(2) (21 CFR 50.23 (e)(1) or (e)(2)) within 5 working days after the use of the device, in addition to submitting this information to the IRB within the same time frame.

(Comment 2) One comment stated that the notification obligations of the investigator described in the interim final rule are too complex, stating it should be sufficient to have a certification by the laboratory director declaring that the investigational test was performed in accordance with the rule and to send to the subject a copy of the notice sent to the IRB. The comment also noted that the concurrence of an independent physician adds no value.

(Response) The agency believes that the notification obligations of the investigator described in this rule, which are similar to the obligations described in other exceptions from the general requirements of informed consent under § 50.23, are needed because they are intended to provide added human subject protections and to prevent abuses. Moreover, concurrence of an independent physician is mandated by section 520(g)(3)(D) of the FD&C Act.

(Comment 3) One comment requested that FDA consider extending the number of days allowed for submitting the written certification for the exception. (Under the rule the investigator has 5 working days after the use of the investigational device to submit the investigator's determinations and those of the independent physician to the IRB.)

(Response) FDA disagrees with this comment. The requirement that the investigator's determinations and those of the independent physician be submitted to the IRB within 5 working days, which is similar to the obligations described in other exceptions from the general requirements of informed consent under § 50.23, are intended to assure prompt action by the IRB, as needed.

9. Explanation of Any Payment or Gift to Respondents

The regulation does not provide any payment or gift to respondents.

10. Assurance of Confidentiality Provided to Respondents

Under the Freedom of Information Act (FOIA) (5 U.S.C. 552), the public has broad access to government documents. FDA will make the fullest possible disclosure of records to the public, consistent with the rights of individuals to privacy, the property rights of persons in trade and confidential commercial or financial information. All records and other information submitted to FDA are releasable under 21 CFR Part 20. However, FOIA provides certain exemptions from mandatory public disclosures of government records (5 U.S.C. 522(b)(1-9). One such exemption, personnel, medical, and similar files, disclosure of which would constitute a clearly unwarranted invasion of personal privacy applies to patient information that may be included in the information collection provisions of this rule.

11. Justification for Sensitive Questions

The information required does not include questions about sexual behavior, attitude, religious beliefs, or any other matters, which are commonly considered private or sensitive in nature.

12. Estimates of Hour Burden Including Annualized Hourly Costs

12 a. Estimates of Annualized Burden Estimate

From its knowledge of the in vitro diagnostic device investigations, FDA estimates that there are approximately 150 laboratory directors or physicians who could perform this type of testing and, as investigators, are required to comply with information collection

and recordkeeping. FDA estimates that there are approximately 450 naturally occurring cases of this type each year. Based on its knowledge of similar types of submissions, FDA estimates that it will take about .25 hour to prepare each written documentation to be submitted to FDA as required by § 50.23(e)(3).

This final rule also refers to previously approved collections of information found in FDA regulations. The collections of information in 50.23(e)(1-2) and (e)(4) have been approved under OMB control number 0910-0586.

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

Table 1. Estimated Annual Reporting Burden[1]

21 CFR Part	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response (in hours)	Total hours	Total Operating and Maintenance Costs
50.23(e)(3) [2]	150	3	450	0.25	113	$100

[1]There are no capital costs associated with this collection of information.

12 b. Annualized Cost Burden Estimate

Type of Respondent	Total Burden Hours	Hourly Wage Rate	Total Respondent Costs
Laboratory Director	113	$75.00	$8,475.00

13. **Estimate of Other Total Annual Costs to Respondents and/or Recordkeepers**

The operating and maintenance costs of $100 is for copying and mailing information to the FDA.

14. Annualized Cost to the Federal Government

There are no anticipated costs to the Federal Government, since this information need not be submitted to the FDA. Inspections of clinical investigators may include reviews of

certification statements required by this rule, will be conducted under the auspices of the bioresearch monitoring program.

15. Explanation for Program Changes or Adjustments

FDA is making one change to the interim final rule, in response to comments that the rule did not protect against misuse of this limited exception from informed consent requirements. In response to those concerns, FDA is adding one new requirement (amending the regulation) that investigators also send the documentation required in paragraph (e)(1) or (e)(2) to FDA, not just to the reviewing IRB. FDA has created this exception to help ensure that individuals who may have been exposed to a chemical, biological, radiological, or nuclear agent are able to benefit from the timely use of the most appropriate diagnostic devices, including those that are investigational. The final rule will add 150 respondents, 450 total annual responses, and 113 burden hours.

16. Plans for Tabulation and Publication and Project Time Schedule

FDA does not intend to publish the results of this information collection.

17. Reason(s) Display of OMB Expiration Date is Inappropriate

Currently, CDRH is not requesting an exemption for display of the OMB expiration date.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

Currently, CDRH is not requesting an exemption to Certification for the Paperwork Reduction Act Submissions.