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

A. JUSTIFICATION

1. Circumstances Making the Collection of Information Necessary

The interim 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. For the exception to apply, it would be necessary for 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). When reporting the test results to the subject's physician and possibly to the appropriate public health authorities, the investigator must disclose the investigational status of the in vitro diagnostic device to the subject or the subject's legally authorized representative and that the investigational test was used on the subject's specimen.

Section 50.23(e)(1) and (e)(2) – Third Party Disclosure

Section 50.23(e)(1) provides an exception to the general rule that informed consent is required for the use of an in vitro investigational device for the purpose of preparing for and responding to a chemical, biological, radiological, or nuclear terrorism event or other public health emergency, if the investigator and an independent licensed physician make the determination and later certify in writing that (1) There is a life-threatening situation necessitating the use of the investigational device, (2) obtaining informed consent from the subject is not feasible because there was no need to predict the need to use the investigational device when the specimen was collected and there is not sufficient time to obtain consent from the subject or the subject's legal representative, and (3) no satisfactory alternative device is available. These determinations must be made before the device is used and the written certifications must be made within 5 working days after the use of the device. If use of the device is necessary to protect the life of the subject and there is not sufficient time to obtain the determination of the independent licensed physician in advance of using the investigational device, § 50.23(e)(2) provides that the certification must be made within 5 working days of use of the device without obtaining informed consent. In either case, the certifications must be submitted to the IRB within 5 working days of the use of the device.

Section 50.23(e)(4) – Third Party Disclosure

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 investigator must provide the IRB with the information required by § 50.25 and the procedures that will be used to provide this information to each subject or the subject's legally authorized representative.

2. Purpose and Use of the Information

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

3. Use of Information Technology and Burden Reduction

Investigators may 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.

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.

6. Consequences of Collecting the Information Less Frequently

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.

There are no technical and legal obstacles to the collection of this information. Firms are free to use any available technology to simplify the gathering of information.

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

In a Federal Register of June 7, 2006 (71 FR 32827), FDA requested public comment on the information collection requirements in the interim final rule.

OMB approved this collection of information under the emergency processing provisions of the Paperwork Reduction Act and assigned OMB control number 0910-0586. With this approval, OMB informed the FDA that the preamble and solicitation of public comment by this interim final rule, served as the 60 day notice for the 3 year extension of this information collection FDA received 10

comments on this interim final rule, three of which related to information collection requirements. The other comments on the rule will be addressed in the preamble to the final rule. FDA expects to publish the final rule in 2009.

One comment suggested that the requirement that a laboratory certify to an IRB that the testing was done in a life-threatening situation and that have already been pre-determined by FDA and provide the basis for exemption. FDA disagrees. The certification requirement ensures that the laboratory documents for the IRB that it is complying with the requirements of the regulation. The comment also stated that the concurrence of an independent physician, which will occur post-testing, adds no value to the certification. FDA also disagrees with this point: the information is necessary because it provides confirmation from an independent source that the regulations are being followed. This provision is found in other FDA regulations and is an important additional protection to the subjects in these trials. Lastly, the comment stated that providing the subject with consent information is of no value because at that time the subject can not choose whether to have the specimen tested since the test has already been performed. According to the comment, sending the subject a copy of the notice to the IRB should be sufficient. While the comment correctly states that subjects can not give informed consent after the test has been performed, providing subjects with this information demonstrates respect for the individual (one of the core principles in the Belmont Report and an important component of human subject protection) by fully informing them of the circumstances of the trial. It would not be appropriate to send the subject the information provided to the IRB because the type of information the IRB usually receives would not fully inform the subject about the trial; the IRB document is typically written in technical language that is likely to be less understandable to subjects.

Another comment requested that section 50.32(e)(4) explicitly require investigators to notify the jurisdictional public health authority upon suspicion of need for testing for a chemical, biological, radiological, or nuclear agent with the investigational device; and further that the language should reinforce that investigators must provide test results to the jurisdictional public health authority in accordance with State and/or Federal law. This comment falls out of the scope of the questions posed in the Federal Register Notice and this type of reporting to public health authorities is beyond FDA's purview.

The last comment encouraged FDA to consider increasing the length of time in which the written certification for the exception is required to be submitted, with the goal of easing the reporting burden. The certification is required to be submitted within 5 working days of the use of the investigational device. FDA believes that the 5-day reporting period is important because it helps ensure that IRBs will receive timely notice of instances in which this rule is used. In addition, the 5-day reporting period appears in other FDA human subject protection regulations that address other exceptions to the general requirement of obtaining informed consent and the agency believes that it is important to maintain consistency within its regulations wherever possible.

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 Respondent

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

From its knowledge of the in vitro diagnostic device investigations, FDA estimates that there are approximately 150 laboratories that will perform this type of testing. 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 two hours to prepare each certification required by § 50.23(e)(1) and (2). FDA also estimates that it will take each investigator approximately one hour to make each of the disclosures required by § 50.23(e)(4). The respondents to this collection of information are expected to be clinical laboratories and physicians.

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

Estimated Average Annual Reporting Burden[1]

21 CFR Section	No. of Respondents	Annual Frequency of Responses	Total Annual Responses	Hours per response	Total hours
50.23(e)(1)(2)	150	3	450	2	900
50.23(e)(4)	150	3	450	1	450
Total					1350

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

13. Estimate of Other Total Annual Cost Burden to Respondents or Recordkeepers

Other than the costs lists in item 12 above, there is no other annual cost burden to respondents.

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

The number of laboratories (respondents) was changed (adjusted) to 150 laboratories that perform this type testing. This resulted in an adjustment in the total annual responses from 450 to 900 and an increase (adjustment) in the total burden hours from 900 to 1350 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.

B. Collection of Information Employing Statistical Methods

There are no statistical methods being employed in this collection of information.