Medical Devices

In Vitro Diagnostic Devices: Guidance for the Preparation of 510(k) Submissions

NOTE: On October 26, 2002, the President signed the Medical Device User Fee and Modernization Act (MDUFMA) of 2002. Under this new law, you must pay a fee before FDA will review your Premarket Notification 510(k). Please see "Premarket Notification 510(k) Review Fees" for details on submitting user fees.

Please see "Medical Device User Fee and Modernization Act (MDUFMA)" for further information on the Medical Device User Fee and Modernization Act.

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Office of Health and Industry Programs

CENTER FOR
DEVICES AND
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CDRH

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration
Center for Devices and Radiological Health
Rockville, Maryland 20850

Contents

FOREWORD

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA), develops and implements national programs to protect the public health in the fields of medical devices and radiological health. These programs are intended to assure the safety, effectiveness, and proper labeling of medical devices, to control unnecessary human exposure to potentially hazardous ionizing and non-ionizing radiation, and to assure the safe, efficacious use of such radiation.

The Center publishes the results of its work in scientific journals and in its own technical reports. These reports disseminate results of CDRH and contractor projects. They are sold by the Government Printing Office and/or the National Technical Information Service.

We welcome your comments and requests for further information.

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Contents

PREFACE

The Medical Device Amendments of 1976 mandated the establishment of "an identifiable office to provide technical and other nonfinancial assistance to small manufacturers of medical devices to assist them in complying with the requirements of the Federal Food, Drug, and Cosmetic Act." The Division of Small Manufacturers Assistance (DSMA) in the Office of Health and Industry Programs (OHIP) was established to meet this requirement. DSMA develops educational materials and sponsors workshops and conferences to provide firms with firsthand working knowledge of medical device requirements and compliance policies.

This manual covers premarket notification [510(k)] submission requirements and overviews the basic regulatory requirements that all manufacturers and importers must consider when they plan to market in vitro diagnostic medical devices including medical device convenience kits, trays or packs.

I would like to express my appreciation to members of the Division of Clinical Laboratory Devices (DCLD) in the Office of Device Evaluation (ODE) for valuable assistance in the development of this document. I also want to thank Althea Barcome of my staff who provided editorial assistance.

For further information, please contact the appropriate office within the Center for Devices and Radiological Health (CDRH) or call DSMA at 800-638-2041, 301-443-6597 or FAX 301-443-8818. Comments on this manual and other DSMA activities are always welcome.

John Stigi
Director
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Contents

ABSTRACT

Bracey, A., Associate Director for Biotechnology (Project Officer), Division of Small Manufacturers Assistance, Office of Health and Industry Programs. In Vitro Diagnostic Devices: Guidance for the Preparation of 510(k) Submissions. HHS Publication FDA 97-4224 (pp. 127).

This manual covers premarket notification requirements for medical devices. It contains guidance of significance to manufacturers and importers of medical devices. This manual incorporates changes required by the Safe Medical Devices Act of 1990 and the Medical Device Amendments of 1992.

This is a manual used in the Division of Small Manufacturers Assistance (DSMA) medical device workshops.

CONTENTS

Contents

1 INTRODUCTION

Chapter 1 Contents

BACKGROUND

The premarket notification provisions, [Section 510(k)]of the 1976 Medical Device Amendments (the Amendments) to the Food, Drug, and Cosmetic (FD&C) Act as amended by the Safe medical Devices Act of 1990 is intended to serve as a screening mechanism to allow for marketing of medical devices with a reasonable assurance of safety and effectiveness. The 510(k) requirement also assures that manufacturers of medical devices do not intentionally or unintentionally circumvent the automatic classification of "new" devices into regulatory Class III, which requires premarket approval by the Food and Drug Administration (FDA). Additionally, the 510(k) provision is intended to facilitate the marketing of in

vitro diagnostic devices that were already on the market before the Amendments were passed on May 28, 1976 preamendment devices). The 510(k) provision requires the manufacturer intending to introduce a new or significantly modified in vitro diagnostic device into the United States (U.S.) market to notify FDA at least 90 days prior to marketing and obtain a marketing clearance letter from FDA. Procedures required by the FDA for premarket notification are included in Title 21, Part 807 of the Code of Federal Regulations, Subpart E (21 CFR 807.87). Additional guidance has been provided in the publication, FDA 95-4158, *Premarket Notification: 510(k) Regulatory Requirements for Medical Devices,* available from the Division of Small Manufacturers Assistance (DSMA).

A "new in vitro diagnostic device," i.e., an in vitro diagnostic device intended for commercial distribution in the U.S. after May 28, 1976 that is not substantially equivalent to a preamendment in vitro diagnostic device or another in vitro diagnostic device subsequently reclassified from Class III to Class II or I, will be automatically classified into Class III and will require an approved Premarket Approval Application (PMA) before it may be marketed.

It cannot be overemphasized that the 510(k) requirement is based on the premise that the notification and subsequent review will enable the FDA to provide reasonable assurance that "new" in vitro diagnostic devices will not be marketed until they comply with premarket approval requirements or are reclassified into Class I or II.

Because of the wide variation in design, methodology and type of in vitro diagnostic devices (IVDD), the range of scientific disciplines involved (e.g., chemistry, microbiology, immunology, hematology, toxicology, pathology) and the rapidly emerging and advancing technologies (e.g., hybridoma, DNA probes, computerization, and nucleic acid amplification), more definitive guidance is needed regarding complying with the regulatory requirements for these devices. This publication on premarket notification 510(k) preparation is intended to assist both manufacturers and FDA reviewers. The manufacturer submitting a 510(k) will be better informed about specific types of information that must be included in a 510(k) application, as well as information not needed. The FDA reviewers of 510(k) applications for in vitro diagnostic devices will receive information identified by them as pertinent to rendering a decision to clear the device for marketing, thus increasing the efficiency of the process.

The 510(k) regulations specify categories for which information should be included. On January 2, 1996 FDA specified another category of information required in a 510(k) submission, "Indications for Use." Nine of these are addressed in the initial notification and the remaining two allow for additional information requested by the FDA reviewer and information needed for notifications based upon significant device modifications. The information that requires interpretative judgment is the focus of this publication, namely the information to show substantial equivalence.

A general model for all in vitro diagnostic devices is provided in Chapter 2, as well as "product class models" that apply to specific categories of in vitro diagnostic devices, i.e., clinical chemistry/toxicology, clinical microbiology/immunology, and clinical hematology/pathology.

Chapter 1 Contents

510(k) REGULATIONS

Section 510(k) requires registered manufacturers of in vitro diagnostic products who plan to begin marketing such products to report at least 90 days before marketing and obtain a marketing clearance letter from FDA. Section 510(k) applies to postamendment medical devices; i.e., devices placed into commercial distribution after May 28, 1976, the date on which the Amendments were enacted.

The implementing regulation for section 510(k) is 21 CFR 807, Subpart E. This regulation sets forth the following information.

When a Premarket Notification is Required

- A device is being introduced into the market for the first time.
- A new device or product line is being introduced that may already be marketed by another manufacturer.
- A device currently in (or being reintroduced into) commercial distribution is about to be significantly changed or modified.

or

- There is a change in the intended use of a device.

When a Device is Exempt from the Premarket Notification Requirement

- The device is not made available in finished form for commercial distribution and is not offered through labeling or advertising by the manufacturer, importer, or distributor, and the device meets one of the following conditions:

    1. it is intended for use by a specific patient, identified by the attending physician or dentist (or other specially qualified person); or
    2. it is intended solely for use by a specific physician or dentist (or other specially qualified person) and is not generally available to, or generally used by, other physicians or dentists (or other specially qualified persons).

- A distributor (or repackager) places a device into commercial distribution for the first time under their own name, and does not change any other labeling, provided that: (1) the device was in commercial distribution prior to May 28, 1976, or (2) a premarket notification was filed by another person.

or

- Many Class I in vitro diagnostic devices exempt from the requirements of premarket notification in accordance with section 513(d)(2)(A) of the FD&C Act. FDA exempted 108 generic types of Class I in vitro diagnostic devices. (see Appendix J). The classification regulations excluding exemptions for in vitro diagnostic devices, 21 CFR Parts 862, 864, and 866 may be obtained by accessing the Government Printing Office home page on the World Wide Web at http://www.gpoaccess.gov/cfr/index.html, or by contacting the Division of Small Manufacturers Assistance at (800) 638-2041, (301) 443-6597 or by FAX at (301) 443-8818. In vitro diagnostic devices labeled "For Research Use Only (RUO)" or "Investigational Use Only (IUO)" are not intended to be used for obtaining test results from human specimens for the diagnosis, treatment, or management of patients and are not subject to premarket notification.

Information Required in a Premarket Notification

- The in vitro diagnostic product name, including the trade or proprietary name, the common or usual name, and the classification name of the device.
- The establishment registration number, if applicable, of the owner or operator submitting the 510(k) submission.
- The class in which the in vitro diagnostic product was placed under section 513 of the FD&C Act, if known, its appropriate panel, or, if the owner or operator determines that the device has not been classified under such section, a statement of that determination and the basis for the determination that the in vitro diagnostic product is not so classified.
- Action taken to comply with the requirements of the FD&C Act under section 513(B) Special Controls (Class II devices), or under section 514 Performance Standards. No special controls or performance standards have been issued by the FDA for in vitro diagnostic devices, thus indicate not applicable for this item.

- Proposed labels, labeling and advertisements sufficient to describe the in vitro diagnostic product, its intended use, and directions for use. Where applicable, photographs or engineering drawings should be supplied.
- A statement indicating that the device is similar to and/or different from other in vitro diagnostic products of comparable type in commercial distribution in the U.S., accompanied by data to support the statement.
- A 510(k) submission for a significantly modified in vitro diagnostic product, i.e., new usage, new methodology (DNA) probe, monoclinal antibody) must include appropriate supporting data to show the consequences and effects of such change on the safety and effectiveness of the in vitro diagnostic product.
- A 510(k) summary of the safety and effectiveness data upon which the substantial equivalence determination is based; or a statement that the 510(k) safety and effectiveness information supporting the FDA finding of substantial equivalence will be made available to any person within 30 days of a written request.
- A Class III certification and summary is required for submissions claiming substantial equivalence to a device which has been classified into Class III under section 513(b) of the Act. The 510(k) submitter shall certify that a reasonable search of all information known or otherwise available about the Class III device and other similar legally marketed devices has been conducted. Also, a summary of the types of safety and effectiveness problems associated with the type of devices being compared and a citation to the information upon which the summary is based is required.
- A statement that the submitter believes, to the best of their knowledge, that all data and information submitted in the premarket notification are truthful and accurate and that no material fact has been omitted.
- Any additional information regarding the in vitro diagnostic product requested that is necessary for the FDA to make a substantial equivalency determination. A request for additional information will advise the 510(k) submitter that there is insufficient information contained in the original 510(k) submission for a substantial equivalent determination to be made. In this situation the 510(k) submitter may: (a) submit the requested data or a new 510(k) containing the requested information, or (b) submit a PMA application in accordance with section 515 of the FD&C Act. If the additional information is not submitted within 30 days following the date of the request, the FDA may consider the 510(k) to be withdrawn.
- All 510(k) submissions must have clearly defined "Indications for Use."

Application Address - Applications should be sent to the following address by a method such as registered mail which provides you proof of delivery:

Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Office of Device Evaluation
Food and Drug Administration
9200 Corporate Blvd.
Rockville, Maryland 20850 USA

Chapter 1 Contents

FACTORS CONSIDERED BY FDA 510(k) REVIEWERS

These factors are reflected in the following questions used by FDA reviewers in determining substantial equivalency:

- Does the in vitro diagnostic device have the same intended use as a currently marketed device (sometimes referred to as a "predicate device"), e.g., glucose test, CPK isoenzyme?
- Does the in vitro diagnostic device have the same technological characteristics, e.g., RIA, antigen/antibody?
- If new technological features are present, e.g., DNA probe, monoclinal antibody, do they raise new questions regarding safety and effectiveness?
- What type of data are needed to substantiate a substantial equivalency claim?

Additionally, the following questions will be used by FDA reviewers to assess whether an in vitro diagnostic device that includes technological changes is substantially equivalent to a predicate device.

- Does the in vitro diagnostic device pose the same type of questions about safety and effectiveness as the predicate device?
- Are there accepted scientific methods for assessing the impact of technological changes on safety and effectiveness, e.g., accuracy, specificity, sensitivity, precision?

For more information on preparing a 510(k) application, please see Chapter 2.

Chapter 1 Contents

THIRDPARTY REVIEW PILOT PROGRAM

Background

On April 3, 1996, FDA announced in the Federal Register (61 FR 14789) that it would begin a 2year, voluntary pilot program on August 1, 1996, to test the feasibility of using thirdparty reviews to improve the efficiency of the agency's review of 510(k)s for selected low and moderate risk medical devices.

The April 3rd notice announced the availability of a list of 251 types of devices that are included in the pilot program. These include 221 Class I devices that are not already exempt from 510(k), and 30 Class II devices. The 221 Class I devices and 6 of the Class II devices were immediately eligible for thirdparty review upon commencement of the pilot program; the 24 remaining Class II devices are to be phasedin during the first year of the pilot program as FDA makes devicespecific review guidance available. For information on eligible IVDDs, please refer to Appendix P.

On April 15, 1996, FDA held an information session for more than 200 organizations and individuals who had expressed an interest in being prospective third parties on the recognition process. Recognition applications were submitted by 37 prospective third parties by the June 3, 1996 deadline set forth in the April 3, 1996 FR notice. These applications were reviewed by a ThirdParty Review Recognition Board established by FDA, and on July 11, 1996, FDA made publicly available a list of seven recognized third parties and the devices they are eligible to review (see Appendix P). On July 2223, 1996, FDA conducted an intensive training program for the seven recognized third parties, which was attended by approximately 40 thirdparty personnel.

Under the pilot program, persons who are required to submit 510(k)s for the eligible devices may contract with an FDArecognized thirdparty review organization and submit a 510(k) directly to the third party, in lieu of FDA. Persons who do not wish to participate in the pilot may continue to submit 510(k)s directly to FDA. The third party applies FDA's 510(k) review criteria and submits its documented review and recommendation on the substantial equivalence of the device to FDA. FDA checks the review and issues a decision letter. FDA has established a 30day performance goal for its issuance of final decisions based on thirdparty reviews.

If the piloted approach is successful, it will: (1) provide manufacturers of eligible devices an alternative review process that may yield more rapid marketing clearance decisions; and (2) enable FDA to target its scientific review resources at higherrisk devices while maintaining confidence in the review by third parties of low and moderate risk devices.

FDA will continually monitor the pilot program and will conduct an evaluation during the second year to determine if the pilot program should be continued.

How to Obtain Additional Information on the Third Party Review Program

Additional information about FDA's thirdparty review pilot program may be obtained from either of the CDRH Document Retrieval Systems described below.

CDRH FactsOnDemand This automated system allows anyone with a touchtone telephone and a fax machine to obtain CDRH information 24 hours a day, 7 days a week, by calling 8008990381 or 3018270111. At the first voice prompt press 1 on your telephone keypad (to select DSMA Facts), at the second voice prompt press 2 (to select documents), and enter the Document Number from the table below. Then follow the remaining voice prompts to complete your request. Callers can request one document per telephone call. The requested document will be sent to your fax machine, so please be prepared to provide your fax number when prompted.

Document #	Description
1258	April 3, 1996 Federal Register Notice
3258	Lists of Devices for Third Party Review
4258	List of Recognized Third Party Review Organizations.

World Wide Web FDA/CDRH maintains an entry on the World Wide Web allowing easy access to information that may be downloaded to a personal computer. Updated on a regular basis, the CDRH Home Page contains a variety of information on the thirdparty review pilot program, including the documents listed in the above table. To access this information, go to the Third-Party Review Information page.

For further information on CDRH Document Retrieval Systems, refer to Appendix D.

Contents

2 GENERAL 510(k) DATA ELEMENTS

The following chapter contains general information required in a premarket submission [510(k)] submission for in vitro diagnostic devices.

Chapter 2 Contents

1.0 IN VITRO DIAGNOSTIC PRODUCT NAME

The name is to include:

- trade or proprietary name,
- common or usual name, and
- classification name when available or ascertainable.

Classification names for in vitro diagnostic devices (IVDD) appear in classification regulations for: (1) hematology and pathology devices (21 CFR 864), (2) microbiology and immunology devices (21 CFR 866), and (3) clinical chemistry and clinical toxicology devices (21 CFR 862), as well as in the CDRH publication, FDA 95-4246, *Classification Names for Medical Devices and In Vitro Diagnostic Products*. In addition, classification names can be obtained from the Product Code Classification Database by accessing the CDRH Homepage on the World Wide Web.

Chapter 2 Contents

2.0 ESTABLISHMENT REGISTRATION

Include the establishment registration number, if any, of the owner or operator submitting the 510(k) submission. If you are in the process of registering your establishment, so indicate.

Chapter 2 Contents

3.0 CLASSIFICATION INFORMATION

Indicate regulatory class (if known), i.e., Class I, II or III and the identity of the classification panel that reviewed similar preamendment in vitro diagnostics. Use the 5 character alphanumeric product code from the CDRH publication on classification names mentioned above.

Chapter 2 Contents

4.0 COMPLIANCE WITH SPECIAL CONTROLS OR PERFORMANCE STANDARDS

If a special control or a mandatory performance standard is established, the 510(k) submission must include information that demonstrates compliance. At the time of this publication, no special controls under Section 513 or performance standard under Section 514 were issued for in vitro diagnostic products.

Chapter 2 Contents

5.0 PROPOSED LABELS, LABELING, AND ADVERTISEMENT

Include draft copies of labeling that are prepared in accordance with the FDA labeling requirements for in vitro diagnostic products, 21 CFR 809.10.

Chapter 2 Contents

6.0 INFORMATION AND DATA SUPPORTIVE OF SUBSTANTIAL EQUIVALENCY CLAIM

The following information should be considered in submitting data in support of a substantial equivalency claim:

- Be sure
    1. a similar in vitro diagnostic device was marketed prior to May 28, 1976, or
    2. a similar in vitro diagnostic product is currently being marketed legally in the U.S.
- Provide the identity of the similar in vitro diagnostic product, if any.
- Include performance claims made for your product, e.g., accuracy, precision, sensitivity, specificity, etc.
- State intended use of all test results.
- State what methodology was used in performing tests.
- Indicate what reagents and materials comprise your product.
- Specify the type of in vitro diagnostic device your product is, e.g., control, calibrator, finished component, reagent, instrument.

Chapter 2 Contents

7.0 SIGNIFICANT CHANGE OR MODIFICATION

When a change or modification is made to an in vitro diagnostic product that could significantly affect its safety and effectiveness or there is a major change or modification of the intended use of test results, the 510(k) submission must include appropriate supporting data. Such data must show the correlation between changes and the safety and effectiveness of the in vitro diagnostic device.

Chapter 2 Contents

8.0 SUMMARY OR STATEMENT

The Safe Medical Devices Act (SMDA) of 1990 requires that a person submitting a premarket notification 510(k) to FDA must also include either:

1. a summary of the 510(k) safety and effectiveness information upon which the substantial equivalence determination is based; or
2. a statement as required in 21 CFR 807.93 that the 510(k) safety and effectiveness information supporting the FDA finding of substantial equivalence will be made available by your firm to any person within 30 days of a written request.

Definition - A 510(k) summary means a summary, submitted under section 513(i) of the FD&C Act, of the safety and effectiveness information contained in a premarket notification submission upon which a determination of substantial equivalence can be based. The statement in the format presented below is the same as the definition of the statement. Summary and statement are defined in 21 CFR 807.3 (*Federal Register*, Vol. 59, No. 239, pg. 64295).

Requests for Summaries or Statements- If a manufacturer or other applicant provides a summary with the 510(k) submission to satisfy the conditions in (1) above, requests by individuals for copies of the 510(k) summary will be furnished by FDA. Per §807.95(d), FDA will make a 510(k) summary of the safety and effectiveness data available to the public within 30 days of the issuance of a determination that the device is substantially equivalent to another device. Recent 510(k) summaries can be obtained from the CDRH Home Page.

If a manufacturer or other person submitting a 510(k) chooses to provide a statement to satisfy the conditions in (2) above, written requests by any individual for a copy of the 510(k) safety and effectiveness information should be fulfilled by the statement certifier within 30 days of receipt of the request. FDA will publish the name of certifiers on the list of premarket notification submissions for which substantial equivalence determinations have been made [§807.93(b)].

The choice between the above summary and statement should be made before the 510(k) is submitted.

Requirements for a Summary - If you choose to meet the conditions for a summary, then a summary must be submitted with your 510(k) application and clearly marked as such in order for FDA to begin its review of a 510(k) submission. A complete and correct summary as described below must be submitted in order for FDA to complete its review of a 510(k) submission. As required by §807.92(a), FDA will accept summaries and amendments thereto until FDA issues a determination of substantial equivalence. Amendments may be needed because of changes in regulations, policies, and standards, or deficiencies in the 510(k) or summary as originally submitted. Deficiencies in the original 510(k) and summary submission may delay the review process; and significant deficiencies in the original 510(k) submission may cause your submission to be rejected by FDA.

Please make a copy of the following to use as a checklist and check off each item to make sure the summary you have prepared is adequate and complete. This checklist paraphrases the requirements of 21 CFR 807.92 before completing your summary.

1. The summary is a separate section of the submission, beginning on a new page and ending on a page not shared with any other part of the premarket notification submission [§807.92(c)].
2. The summary contains, on the first page preferably on your letterhead paper, the submitter's name, address, phone and fax numbers, name of contact person, and date the summary was prepared [§807.92(a)(1)].
3. The summary also contains the following title and two sentences on the first page:

    510(k) SUMMARY

    "This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92."

    "The assigned 510(k) number is: _____ ." (applicant leave blank)

4. The summary includes the name of the device, including the trade or proprietary name if applicable, the common or usual name, and the classification name, if known [§807.92(a)(2)].
5. The summary identifies the legally marketed device to which your firm is claiming equivalence [§807.92(a)(3)].
6. The summary includes a description of the device [§807.92.(a)(4)].
7. The summary describes the intended use of the device [§807.92(a)(5)].
8. Per §807.92(a)(6), the 510(k) summary contains a summary of the technological characteristics of your device compared to the

predicate device. If your device has different technological characteristics from the predicate device, the 510(k)summary contains a summary of how the technological characteristics of your device compare to a legally marketed device to which you are claiming equivalence.

9. If the determination of substantial equivalence is also based on an assessment of performance data, the summary includes a brief discussion of the nonclinical tests and how their results support a determination of substantial equivalence [§807.92(b)(1)].

10. If the determination of substantial equivalence is also based on an assessment of performance data, the summary includes a brief discussion of clinical tests and how their results support a determination of substantial equivalence [§807.92(b)(2)].

    Clinical data is not needed for most devices cleared by the 510(k) process.

11. The summary includes the conclusions drawn from the nonclinical and clinical tests in (b1) and (b2) [§807.92(b)(3)]. (See steps 9 and 10 above.)
12. Per §807.92(d), the summary includes any other information reasonably deemed necessary by FDA. Such requests will be made directly to the applicant or the requirements will be published in guidance documents such as this document. Additional information requested by FDA during review of the 510(k) may include additional safety and effectiveness information which may necessitate an update of your summary if requested by FDA.

Please make sure you have included all of the information listed above and verify that the following criteria have been met.

- The summary includes only information that is also covered in the body of the 510(k).
- The summary does not contain any puffery or unsubstantiated labeling claims.
- The summary does not contain any raw data, i.e., contains only summary data.
- The summary does not contain any trade secret or confidential commercial information.
- The summary does not contain any patient identification information.

In instances where a 510(k) submitter provides a 510(k) summary of the safety and effectiveness information upon which the substantial equivalence determination is based with the 510(k) submission to FDA, written requests by individuals for copies of the 510(k) summary will be furnished by FDA through the Freedom of Information (FOI) process within 30 days after determining that the device is substantially equivalent to another device.

Requirements for a Statement - For persons who choose to submit to FDA a statement with the 510(k), the specific statement shown below must be submitted with the 510(k) in order for FDA to begin the review process. The statement should be on a separate letterhead page, clearly identified as "510(k) Statement," and must include the specific language beginning with "I certify...," shown in the following sample as required by 21 CFR 807.93:

510(k) STATEMENT
(As required by 21 CFR 807.93)

"I certify that in my capacity as (*the position held in company by the person required to submit the premarket notification, preferably the official correspondent*) of (*company name*), I will make available all information included in this premarket notification on safety and effectiveness within 30 days of request by any person if the device described in the premarket notification is determined to be substantially equivalent. The information I agree to make available will be a duplicate of the premarket notification submission, including any adverse safety and effectiveness information, but excluding all patient identifiers, and trade secret and confidential information, as defined in 21 CFR 20.61.

_____
(Signature of certifier)

_____
(Typed Name)

_____
(Date)

_____
* (Premarket Notification [510(k)] Number)

* For a new submission, leave the space for the 510(k) number blank. You will receive your 510(k) number in your 510(k) acknowledgment letter. The 510(k) document control number begins with the letter K followed by 6 digits.

Make a copy of your complete 510(k) including your signed statement for your records. Submit the complete original 510(k) including the statement and a complete copy of the 510(k) including the statement to FDA.

If you have already submitted a 510(k) without a summary or statement and the 510(k) is still pending, then you must submit a summary or statement to complete the 510(k). You must put the 510(k) document control number on such a summary or statement in order for FDA to append it to the correct 510(k) application.

Chapter 2 Contents

9.0 CLASS III CERTIFICATION AND SUMMARY

A 510(k) submitted for a Class III device not requiring premarket approval must include a Class III certification and summary. Class III summary means: a summary of the types of safety and effectiveness problems associated with the type of device being compared and a citation to the information upon which the summary is based. The summary must be comprehensive and describe the problems to which the type of device is susceptible and the causes of such problem. [807.3(q)]

The certification should be signed by the certifier -- not a consultant to the 510(k) submitter, clearly identified as "Class III Certification and Summary", and listed in the table of contents. Attach the summary of problem data, bibliography or other citations upon which the summary is based, to the certification statement. The language to be used in the certification statement is shown below.

CLASS III CERTIFICATION AND SUMMARY
(As required by 21 CFR 807.94])

I certify that, in my capacity as (*the position held in company*) of *(company name*) that I have conducted a reasonable search of all information known or otherwise available about the types and causes of safety and/or effectiveness problems that have been reported for the (*device name*). I further certify that I am aware of the types of problems to which the (*device name*) is susceptible and that, to the best of my knowledge, the following summary of the types and causes of safety and/or effectiveness problems about the (*device name)*is complete and accurate.

(Attach the summary of problem data, bibliography or other citations upon which the summary is based.)

_____
(Signature of Certifier)

_____
(Typed Name)

_____
(Date)

_____
*(Premarket Notification [510(k)] Number)

*For a new submission, leave the space for the 510(k) number blank. You will receive your 510(k) number in your 510(k) acknowledgment letter. The 510(k) document control number begins with the letter K followed by 6 digits.

Chapter 2 Contents

10.0 TRUTHFUL AND ACCURATE STATEMENT

All 510(k) submitters must include a statement certifying that all information submitted in the 510(k) is truthful and accurate and that no material fact has been omitted. The statement may be in the 510(k) cover letter or may be on a separate page identified in the table of contents.

PREMARKET NOTIFICATION
TRUTHFUL AND ACCURATE STATEMENT
[As required by 21 CFR 807.87(j)]

I certify that, in my capacity as (*the position held in company*) of *(company name)*, I believe to the best of my knowledge, that all data and information submitted in the premarket notification are truthful and accurate and that no material fact has been omitted.

_____
(Signature of Certifier)

_____
(Typed Name)

_____
(Date)

_____
*(Premarket Notification [510(k)] Number)

*For a new submission, leave the space for the 510(k) number blank. You will receive your 510(k) number in your 510(k) acknowledgment letter. Document control numbers begin with the letter K followed by 6 digits.

The truthful and accurate statement must be signed by a responsible person of the firm required to submit the premarket notification -- not a consultant for the 510(k) submitter.

Chapter 2 Contents

11.0 ADDITIONAL INFORMATION

In the event that additional information is needed for the evaluation of a 510(k) submission, a request from FDA will be made informing the submitter to (a) provide the requested information, or (b) submit a new 510(k) notification containing the requested information. If requested information is not submitted within 30 days following the date of request, the 510(k) may be considered withdrawn unless an extension has been requested and granted.

Chapter 2 Contents

12.0 INDICATIONS FOR USE STATEMENT

The Office of Device Evaluation (ODE) has developed the attached optional form to assist them with instituting the requirement for all original 510(k)s received by ODE on or after 1/2/96.

The requirement is for all 510(k) submissions to have clearly defined "Indications for Use". These indications will be attached by ODE to any substantial equivalence (SE) letter to define what the device is cleared for.

No 510(k) submitted on or after 1/2/96 will be cleared for marketing by ODE without the inclusion of the indications for use information, which will be attached to an SE letter.

INDICATIONS FOR USE STATEMENT

510(k) Number (if known): K_____

Device Name: _____

Indications For Use: _____

(PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NEEDED)

_____

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use	OR	Over-The-Counter Use
(Per 21 CFR 801.109)		(Optional Format 1-2-96)

Application Address - Premarket notification [510(k)] applications should be sent to the following address by a method such as registered mail which provides you proof of delivery.

Document Mail Center (HFZ-401)
ODE\Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Boulevard
Rockville, Maryland 20850 USA

FDA Requests Additional Information - After you submit your application, if FDA requests additional information by telephone, FAX, or letter, you should:

- either submit the information within 30 days, or request an extension for submitting information and state the time needed to submit;
- include any information needed to update the summary, if your submission contains a summary;
- identify the additional information with your company name and 510(k) number; and
- state where the information should be included in your application, such as by topic, section and/or page numbers.

Specific Standards and Guidance - The Office of Device Evaluation (ODE) in FDA has developed guidance documents for generic categories of in vitro diagnostic devices that indicate requirements for 510(k) submissions. More information regarding these documents and how to access them can be found in Appendix D. Where a specific guidance document exists for your device, it should always be used in preparation of the 510(k).

If the in vitro diagnostic device complies with any voluntary standards, identify the standard and the requirement that your in vitro diagnostic device meets, as well as that of the predicate device.

510(k) Acceptance for Review - ODE receives approximately 6,000 premarket notification [510(k)] submissions per year. Many of these submissions have been found over the years to be deficient in important information. As a means of employing resources more effectively, the CDRH has developed and implemented a refuse to accept policy to ensure that 510(k)s meet a minimum threshold of acceptability. (See Appendix G.)

Expedited Review - The FDA believes it is in the interest of the public health to review 510(k)s for certain devices in an expedited manner. Expedited review will generally be considered when a device offers a potential for meaningful benefit as compared to existing alternatives (diagnostic) or when the new device promises to provide a revolutionary advance over currently available devices. Granting of expedited review status means that the 510(k) will receive priority review before other pending 510(k)'s. (See Appendix M.)

Home Use In Vitro Diagnostic Devices - In vitro diagnostic devices intended to be used outside the traditional laboratory environment, by persons unlikely to have received training in their use have been on the increase over the past decade. Because of the increasing trend in the use of these types of devices, and the increasing number of 510(k) submissions, the need for uniformity in the criteria for testing and evaluation emerged. In order to provide issuance, these types of devices were regulated in consistent fashion and that consumers/users are provided with safe and effective products, i.e., accurate, reliable, and useful. See *Points to Consider Regarding Labeling and Premarket Submissions for Home Use In Vitro Diagnostic Devices* in Appendix C.

Chapter 2 Contents

13.0 PRODUCT CLASS 510(k) MODELS

The following section provides an outline of information needed in submitting 510(k) applications for in vitro diagnostic devices for specific areas of discipline.

Clinical Chemistry/Toxicology

Similarities and/or differences

- Methodology, e.g., radio immunological assay (RIA)
- Analyze and/or test objective
- Specimen type, e.g., urine, blood, serum
- Product type, e.g., calibrator, control, kit, instrument, reagent
- Intended use
- Similar in vitro diagnostic device on U.S. market
- Data on performance, e.g., accuracy, specificity, sensitivity, precision
- Use of diagrams to illustrate similarities

Labeling (21 CFR 809.10)

- Include draft or copies of
  - Package insert
  - Vial label
  - Kit box label
- Name and intended use of test
- Summary and explanation of test
- Chemical and biological principles of test procedure
- Reagents
- Specimen collection, preparation, analysis and storage
- Assay procedure
- Equipment and materials required
- Test results interpretation
- Limitations of the test procedure
- Specific performance characteristics
- Selected bibliography

Substantial equivalence rationale discussion

Example:

This device is an in vitro diagnostic product intended for the measurement of _____ concentration in human serum. The principle of the test relies upon the competitive binding of an antigen with its specific antibody. The ability to monitor this reaction in order to candidate specific analyses is widely recognized and has gained widespread acceptance in the development of radioimmunoassay (RIA) and enzyme immunoassay (EIA).

The EIA in vitro diagnostic products already on the U.S. market include the following:

1.)
2.)
3.)

Several in vitro diagnostic products are commercially available for the analysis of _____ using either RIA or EIA methodologies.

The RIA kits for the measurement of _____ are distributed by the following companies:

1.)
2.)
3.)

Clinical Microbiology / Immunology

Similarities and / or differences

- Methodology, e.g., immunofluorescence, latex agglutination
- Analyze and/or test objective, e.g., rheumatoid factor
- Comparison data (parallel testing)
- Source of material, e.g., bovine serum
- Intended use of test result
- Type of test, e.g., quantitative, qualitative

Labeling

- Intended use (include clinical application or purpose of test)
- Principle of test
- Material required but not supplied
- Specimen collection and preparation
- Sample record sheet
- Data record sheet
- Precautions
- Interpretation of results
- Limitation of procedure
- Quality control
- Performance characteristics, e.g., precision, sensitivity (detection level)
- Expected values
- References

Substantial equivalence rationale discussion

Example:

This _____ test is substantially equivalent in principle and clinical performance to the currently marketed _____ test for the detection of _____. (See _____ product insert-addendum _____.) Similarities between the procedures and the _____ test kits are described as follows:

1. Both assays employ the _____ organisms.
2. Both tests are indirect immunofluorescent techniques.
3. Both tests require _____ in the analytical process.

Please refer to the draft product insert (Addendum _____) for a detailed description of the [510(k) subject] test kit.

Clinical Hematology / Pathology

Similarities and / or differences

- Methodology
- Instrument system
    - Principles of operation
    - Operating procedures
- Test Objective
- Comparison data (e.g., charts, graphs)
- Reasons for similarities or differences
    - Specimen type
    - Specimen preparation
    - Detection system, e.g., optical
    - Specimen collection
    - Methodology
- Conformance with voluntary standards

Labeling

- Include draft or copies of
    - Outside container label
    - Package insert
    - Vial label
    - Labeling for comparative product
- Name and intended use of test
- Summary and explanation of test
- Hematological or pathological principles of test procedure, e.g., cell morphology, dye absorption
- Reagent characterization, i.e., source (e.g., rabbit brain)
- Limitations of procedure
- Specimen collection, preparation, analysis and storage
- Performance specifications
- Selected bibliography

Substantial equivalence rationale discussion

Example:

The in vitro diagnostic device presented in this 510(k) submission (Exhibit A _____) is substantially equivalent to the _____ manufactured by _____ (Exhibit B).

Both in vitro diagnostic test systems are based upon the _____, and subsequent detection or observation of _____. The following performance characteristic included in table I is illustrative of performance comparability. (Include a table delineating this information.)

Contents

APPENDIXES