

TYMPANOSTOMY TUBES
Submission Guidance for a 510(k)
Premarket Notification

This document is intended to provide guidance in the preparation of a regulatory submission. It does not bind the FDA or the regulated industry in any manner.

Ear, Nose, and Throat Devices Branch
Division of Reproductive, Abdominal, Ear, Nose, and Throat, and Radiological Devices
Office of Device Evaluation

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While this guidance document represents a final document, comments and suggestions may be submitted at any time for Agency consideration by writing to Harry R. Sauberman, P.E., Chief, ENT Devices Branch, HFZ-470, DRAERD, ODE, Food and Drug Administration, 9200 Corporate Boulevard, Rockville, Maryland 20850. For questions regarding the use or interpretation of this guidance, contact Eric Mann at 240-276-4242 or eric.mann@fda.hhs.gov.

U.S DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration
Center for Devices and Radiological Health

INTRODUCTION

This document outlines the information to be submitted in a 510(k) premarket notification for tympanostomy tubes used in otological procedures. Tympanostomy tubes are described in the FDA regulations under 21 CFR 874.3880(a). The primary reference for the information required to be in a premarket notification (510(k)) for a medical device is 21 CFR 807.87. The purpose of this regulation is to define the documented information necessary to determine substantial equivalence to a legally marketed device. Substantial equivalence is to be established with respect to, but not limited to, intended use, design, materials, performance, safety, effectiveness, labeling, and other applicable characteristics.

This document complements 21 CFR 807.87 and other FDA Guidance documents for the preparation and review of 510(k) submissions. It does not supersede those publications, but provides additional clarification on what is necessary before the FDA can clear a device for marketing. It describes the information needed to evaluate a 510(k) premarket notification for a tympanostomy tube. Appendix I contains a tabular checklist of the required information that can be used in checking the completeness of the documentation in a 510(k) submission. As advances are made in the design and manufacture of medical devices, and changes occur in implementation of Congressional legislation, these review criteria will be re-evaluated and revised as necessary.

For devices that differ significantly from those already in the market, FDA may require additional information specific to those differences. For a device with a different design, material, or intended use from devices already in the market, and the difference could significantly affect the safety and effectiveness of the device, the 510(k) should include appropriate supporting information. The information should include clinical data or other valid scientific studies that demonstrate that these differences do not affect safety or effectiveness, as described in 21 CFR 807.87(f).

One example of a device with a different indication for use and different material is the antimicrobial tympanostomy tube. Appendix II describes additional information to be submitted in a 510(k) premarket notification for the antimicrobial tympanostomy tube.

Copies of the ODE Bluebook Memo Guidances listed in this document may be obtained from the Center for Devices and Radiological Health's (CDRH) Division of Small Manufacturers Assistance (DSMA) at (800) 638-2041 or (301) 443-6597.

I. Device Identification

A. Device Name

Provide the trade name, proprietary name, and classification name of the device.

B. Predicate Device Name

Identify the legally marketed devices to which the new device will be compared. Be as specific as possible, i.e., proprietary and common name, manufacturer, model number, 510(k) reference number, pre-Amendment status, etc. Include a tabbed section with product literature (description, specifications and labeling, etc.) for the predicate device.

II. Administrative Information

Provide the following information about the applicant:

Establishment Registration number
Contact Person and Title
Telephone number and FAX number

Date and sign the premarket notification. Include a table of contents and a listing of tabs and appendices. Number the pages sequentially.

III. Classification: Class II (Special Controls)

Give the CFR classification regulation number for the device, as well as its classification:

<u>Device</u>	<u>Class</u>	<u>21CFR Ref</u>	<u>ProCode</u>
Tympanostomy Tube	II	§874.3880	77ETD

IV. § 514 Special Controls

Special Controls under §514 of the Act have not been developed for these devices. Reference is made in later sections of this guide to voluntary industry standards.

V. Information Required for Substantial Equivalence Determination

The following sections describe the information needed to determine substantial equivalence to a legally marketed device. Additional information may be required depending on the individual design and function of the device. When preparing your 510(k), please use the checklist in appendix I. If your device has antimicrobial properties, additional guidance is provided in appendix II.

A. Intended Use

Clearly state the proposed clinical indications and intended use of the device. They must be consistent with the design of the device and with proposed labeling. Clinical indications and intended use should be reflected in laboratory and clinical study design and must be supported by the results. An acceptable generic intended use statement for conventional tympanostomy tubes is given below:

A device that is intended to be implanted for ventilation or drainage of the middle ear.

A description of indications for use that are consistent with the above intended use is as follows:

A tympanostomy tube is placed in an incision (myringotomy) usually made in the anterior-superior quadrant of the tympanic membrane. The primary purpose of the device is to ventilate the middle ear, allowing air to enter and thus facilitate the drainage of fluids through the Eustachian tube into the pharynx. A secondary purpose is to provide an alternate route for the exit of middle ear fluid. The principal benefit of myringotomy with insertion of tympanostomy tubes is to keep the middle ear clear of effusion. Other benefits are the restoration of hearing and the aeration of the middle ear to prevent or reverse atelectasis of the tympanic membrane. Removal of middle ear effusion permits normal transmission of sound across the middle ear to the inner ear.

An example of an acceptable intended use statement for tympanostomy tubes with antimicrobial properties is the following:

A device that is intended to be implanted for ventilation of the middle ear and to reduce the incidence of recurrent postoperative middle ear infections in patients with otitis media.

B. Device Description

1. Schematics and Diagrams

Provide a physical description, in the form of a labeled diagram, photograph, schematic, etc., of each tympanostomy tube to be marketed. The physical description should include the dimensional specifications (i.e., lumen diameter, inner flange diameter, inter-flange distance, etc.) of the tympanostomy tube. The labeled diagram, photograph, schematic, etc., should address the name and function of all parts of the device.

2. Materials

Provide an exact identification of all materials and colorants (inks, dyes, markings, radiopaque materials, etc.) used to fabricate the tympanostomy tube. Provide the results of biocompatibility testing performed on these materials and colorants or a certification stating that the material formulation and colorants used are identical to those used in a specified, legally marketed device with a similar intended use, and are identically processed and sterilized.

For additional information on biocompatibility, please refer to the Blue Book Memorandum G95-1, "Use of International Standard ISO-10993, 'Biological Evaluation of Medical Devices Part 1: Evaluation and Testing'," available from the Division of Small Manufacturers Assistance. Tympanostomy tubes are considered to be permanent (greater than 30 days) implant devices, contacting tissue/bone.

C. Sterility Information.

Provide complete information regarding tympanostomy tubes that are sold sterile and include the sterilization method; sterilization cycle validation method; packaging materials and a description of the packaging to ensure sterility is maintained; sterility assurance level (SAL); and radiation dose or the maximum levels of residuals of ethylene oxide, ethylene chlorohydrin, and ethylene glycol which remain on the device, whichever is applicable. Guidance on sterility issues is provided in ODE Bluebook Memo K90-1 "510(k) Sterility Review Guidance (2/12/90)." If the device is labeled as pyrogen free or non-pyrogenic, provide a description of the method used to make that determination (LAL or rabbit test). If the device is sold and labeled non-sterile, provide instructions on sterilization.

D. Labeling

Provide proposed labeling sufficient to describe the tympanostomy tube, its intended use, and the directions for use. Labeling should include a specific intended use statement and any warnings, contraindications, or limitations clearly displayed as described in 21 CFR 807.87(e). The intended use statement should include specific indications for use, clinical setting, a defined target population, etc. The label of the device packaging must bear the caution statement as outlined in 21 CFR 801.109(b)(1): "CAUTION: Federal law restricts this device to sale by or on the order of a physician."

Guidance on labeling issues is described in ODE Bluebook Memo G91-1 "Device Labeling Guidance (3/8/91)."

The following is a typical list of warnings and indications for use of legally marketed tympanostomy tubes. You may wish to modify this list based on particular characteristics of your device related to material, design, or construction.

1. *Indications for Use*

- chronic or recurrent otitis media with persistent effusion (OME)
- recurrent acute otitis media
- acute otitis media with complications
- Eustachian tube dysfunction resulting in one or more of the following: significant and symptomatic hearing loss, otalgia, vertigo, and tinnitus
- hearing loss resulting from bilateral chronic middle ear effusion

2. *Warnings*

Post-operative complications - It is often difficult to determine if complications occurring after insertion of tympanostomy tubes are due to the tubes or are due to sequelae of the intrinsic disease. Occasionally tympanostomy tubes may contribute to a number of post-operative complications including

- * secondary infection accompanied by otorrhea through the tube

- * permanent perforations
- * dislocation of the tube into the middle ear cavity
- * tympanosclerosis
- * localized or diffuse membrane atrophy

VI. Summary of Equivalence

To permit an equivalence determination, the indications for use and all of the device characteristics and performance data presented in the premarket notification should be compared with a legally marketed device. This includes devices in commercial distribution prior to May 28, 1976, the enactment date of the Medical Devices Amendments, and any new class II devices introduced subsequently via 510(k). A comparison includes similarities and differences between the new device and the device to which it is compared. The new tympanostomy tube should be compared to a legally marketed device with respect to the following: indications for use, design type (including lumen diameter, inner flange diameter, and inter-flange distance), patient contacting materials, performance, and, if applicable, types of coatings, amount/concentration of coating(s), tube coating process, and target population with a justification for any new population cited.

VII. Changes in Intended Use and Technological Characteristics

For a device with technological characteristics that are different from the predicate device, and those differences could significantly affect the safety or effectiveness of the device, or for a device with an intended use different from that of the predicate device, the 510(k) should include the following:

- (1) appropriate supporting data to show that the manufacturer has considered the consequences and effects that the new technology or different use might have on the safety and effectiveness of the device, as described in 21 CFR 807.87(g)
- (2) supporting documentation including clinical or other valid scientific studies which demonstrate that the differences do not affect safety or effectiveness, as described in 21 CFR 807.87(f).

Companies with claims for tympanostomy tubes other than drainage and ventilation of the middle ear should submit bench testing and clinical data to demonstrate safety and effectiveness of the new claim (e.g., "impedes water entry to the middle ear while bathing or swimming", "bacteriostatic", "resists bacterial attachment").

The description of the tympanostomy tube should include any significant changes or modifications from the predicate device that could affect safety, effectiveness, or intended use. Provide any bench, animal, clinical, functional, in vitro, and/or any other testing data to support marketing claims and to show that changes do not affect safety and effectiveness, as compared to the predicate.

VIII. Other Information

A. 510(k) Summary or Statement

The Safe Medical Devices Act of 1990 (SMDA) requires all persons submitting a premarket notification to include either (1) a summary of safety and effectiveness information upon which an equivalence determination could be based (510(k) Summary) or (2) a statement that safety and effectiveness information will be made available to interested persons upon request (510(k) Statement). Safety and effectiveness information refers to information in the premarket notification, including adverse safety and effectiveness information, that is relevant to an assessment of substantial equivalence. The information could be descriptive information about the new and predicate device(s), or performance or clinical testing information. If a 510(k) statement is submitted, the statement must use the exact wording provided in 21 CFR §807.93, "Content and format of a 510(k) statement".

B. Truthful and Accurate Statement

Provide a statement that the submitter believes, to the best of his knowledge, that all data and information submitted in the premarket notification are truthful and accurate and that no material fact has been omitted as described in 21 CFR 807.87(j).

APPENDIX I

510(k) Checklist for Tympanostomy Tubes

510(k) Number _____

Device Name _____

		<u>Present</u>		<u>Needed</u>	
		<u>Yes</u>	<u>No</u>	<u>Yes</u>	<u>No</u>
1.	Administrative information				
a.	Classification name - Tympanostomy Tube	___	___	___	___
b.	Sponsor/manufacturer name and address	___	___	___	___
c.	Procode/Classification - ETD 77, Class II (§ 874.3880)	___	___	___	___
d.	Establishment registration number, or a statement that it has been requested	___	___	___	___
2.	Reason for the 510(k) submission (new device or a modification to an existing device)	___	___	___	___
3.	Intended use of the device	___	___	___	___
4.	Device description				
a.	Description of the materials used	___	___	___	___
b.	If a coating or colorant is used, a list of the precise formulation(s) and the requirements for the coatings	___	___	___	___
c.	Device dimensions including inner diameter, inter-flange diameter, and inter-flange width	___	___	___	___
d.	Description of any special design or features	___	___	___	___
e.	Diagrams, drawings and/or photographs of the device	___	___	___	___
f.	List of the range of sizes/models proposed for marketing	___	___	___	___

5. Proposed labeling, instructions for use, advertisements
(per the "Device Labeling Guidance," Blue Book Memo G91-1)

a.	Intended use with specific indications, i.e., clinical setting, defined target population, etc.	___	___	___	___
b.	Warnings, contraindications, or limitations (21 CFR §807.87(e))	___	___	___	___
c.	Prescription device statement (21 CFR 801.109)	___	___	___	___
d.	Labeled for disposable/single use only	___	___	___	___
e.	Labeled as sterile with expiration date.	___	___	___	___
f.	Types of coatings	___	___	___	___
g.	If antimicrobial agent is used as a coating, a characterization of the microbial and its activity	___	___	___	___
h.	Advertisements or promotional literature	___	___	___	___

6. Biocompatibility

For all materials used to fabricate the tympanostomy tube provide either:

a.	Evidence that the same formulations of these materials are used in another, similar legally marketed device (provide the device name, manufacturer, and (if possible) 510(k) number); OR	___	___	___	___
b.	The results of the following biocompatibility tests on the finished device (this is the minimum level of required testing for a device implanted in bone/tissue for more than 30 days):				
	(1) Implantation	___	___	___	___
	(2) Cytotoxicity	___	___	___	___
	(3) Genotoxicity, and	___	___	___	___
	(4) Sensitization	___	___	___	___

7. Sterility information (if the device is labeled or otherwise represented to be sterile)

a.	The method of sterilization	___	___	___	___
b.	The method used to validate the sterilization cycle	___	___	___	___
c.	The sterility assurance level (SAL) achieved by the sterilization cycle	___	___	___	___
d.	The levels of the residues of ethylene oxide, ethylene chlorohydrin, and ethylene glycol on the device (for ethylene oxide sterilization)	___	___	___	___
e.	The radiation level (in megarads) used (for radiation sterilization)	___	___	___	___
f.	A description of the packaging material used to ensure the sterility of the device	___	___	___	___
g.	The method used to determine that the device is pyrogen free (if pyrogen free claim will be made)	___	___	___	___

8. Comparison to legally marketed tympanostomy tubes

a.	Name/manufacturer of predicate device	—	—	—	—
b.	510(k) number (if known) of the predicate device (or statement that the predicate is pre-Amendment)	—	—	—	—
c.	Labeling of predicate device	—	—	—	—
d.	Intended use of the predicate device	—	—	—	—
e.	Diagrams/photographs of predicate device	—	—	—	—
f.	A comparison of the similarities/differences between the 510(k) device and the predicate device (in tabular format) including design, physical description, patient-contacting materials, performance, and, if applicable, types of coating, amount/concentration of coating(s), tube coating process, and target population	—	—	—	—

9. Modified Devices (for a device that has undergone a change or modification that could significantly affect safety or effectiveness, or for a device to be marketed for a new or different indication for use)

a.	Rationale for modification with supporting documentation	—	—	—	—
b.	Description of significant changes and modifications affecting safety, effectiveness, or intended use.	—	—	—	—
c.	Data to support marketing claims (bench, clinical, functional, <u>in vitro</u> , etc.	—	—	—	—

- 10. **Truthful and accurate statement**
(signed and in accordance with 21 CFR 807.87(j)) _____
- 11. **510(k) Summary or 510(k) Statement** (per 21 CFR 807.92 and 807.93) _____
- 12. **Indications for use statement** _____

For more information contact:

Ear, Nose, and Throat Devices Branch
Division of Reproductive, Abdominal, Ear, Nose and
Throat, and Radiological Devices
Office of Device Evaluation
Center for Devices and Radiological Health
(301) 594-2080

APPENDIX II

510(k) Supporting Information for ANTIMICROBIAL TYMPANOSTOMY TUBES

Device Description

Provide the precise formulation of the antimicrobial with acceptable tolerances. Also provide the calculations for derivation of the final concentration of the antimicrobial on the device and anticipated change in concentration over time of use and anticipated change in effectiveness. State the requirements for the antimicrobial and describe how the manufacturing process meets those requirements (e.g., uniformity of coating, bonding, material impregnation, polymer/antimicrobial mixture, etc.). The final device specifications for the antimicrobial should be based upon the sterilized, packaged device.

Performance Data

Any changes or modifications to the antimicrobial used in the predicate device, including change in antimicrobial or formulation, concentration, or bonding process, requires performance data to substantiate claims of safety and effectiveness. Provide bench, animal, clinical, functional, in vitro, and/or any other testing data to demonstrate equivalence to the predicate.

Functional and performance data for the antimicrobial component used as a coating or integrated into the device material, should demonstrate that the antimicrobial is effective in reducing the incidence of relevant nosocomial infections and that it is safe. The data set should provide chemistry, pharmacology, microbiology, engineering, preclinical, and clinical information including the following:

1. For an antimicrobial different from the predicate antimicrobial, provide results from a randomized, controlled clinical study to
 - a. demonstrate a clinically and statistically significant decrease in the rate of post-operative otorrhea and at least comparable safety as compared to a legally marketed conventional tympanostomy tube, and/or clinically and statistically similar safety and effectiveness compared to an antimicrobial tube;

- b. quantify the decrease in the rate of post-operative otorrhea during the period until extrusion or surgical removal of the tube; and
- c. obtain data to support any additional claims, including reprocessing.

Clinical information should also include patient history of otitis media and all medications taken.

- 2. Provide in vitro test data characterizing the spectrum and degree of activity of the antimicrobial against all clinically important microorganisms (note: microorganisms should be clinical isolates, i.e., specimens derived from actual patient cultures). These microorganisms include *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Branhamella catarrhalis*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Diplococcus pneumoniae*, and *Pseudomonas aeruginosa*.

The test sample should include the finished form of the device. If additional microorganisms are tested, provide justification with supportive literature.

- 3. Provide elution profile information to simulate and evaluate the release of the antimicrobial when exposed to body fluids.
- 4. Provide an assessment of whether the antimicrobial concentration selected to elicit the desired prophylactic effect against clinically appropriate microorganism is optimal.
- 5. Provide shelf life/expiration date testing data to demonstrate the effect of storage, adverse shipping conditions, and reprocessing (these effects should be reflected in labeling).
- 6. Provide a detailed analysis of the potential for adverse effects such as the risk of infections.
- 7. Provide information on the pharmacological and metabolic profile of the antimicrobial.
- 8. Provide the results from toxicity testing to assess the local and systemic effects of exposure to the antimicrobial.

Labeling

When the device contains an antimicrobial, include a statement on the label indicating that the antimicrobial is an active agent (i.e., it has a prophylactic intended use, and is not present as a preservative). It is recommended that the labeling also include a section which characterizes the antimicrobial and its activity. For example, include the following information:

1. the chemical name and formulation of the antimicrobial and the amount/concentration in the device;
2. information characterizing the pharmacology and toxicology of the antimicrobial including metabolism and excretion information;
3. a statement, if appropriate, to indicate the potential for hypersensitivity or allergic reaction of patients to the antimicrobial selected (e.g., a statement that history of hyper-sensitivity reaction to the antimicrobial agent is a contraindication for use of this tympanostomy tube);
4. the spectrum of activity of the antimicrobial and how that spectrum relates to the type of organisms commonly associated with post-operative otorrhea;
5. the mechanism of action of the antimicrobial as it relates to the device (e.g., microbial growth is inhibited by surface contact with the device, or the antimicrobial is eluted by contact with body fluids to provide a local antimicrobial effect); and
6. a summary of the clinical results on which the antimicrobial claims are based.

Device Materials and Biocompatibility

If the antimicrobial agent that is used on the device is the subject of an approved new drug application (NDA), or over-the-counter (OTC) monograph, then provide a reference to those documents. This may limit the amount of information needed for the antimicrobial agent. Identify any differences between the approved drug product and the antimicrobial agent used in the device (e.g., intended use, dosage, route of administration, formulation, concentration) and discuss their impact on the safety and effectiveness of the antimicrobial tympanostomy tube. Significant differences may require additional data. If the antimicrobial agent is not related to an NDA or OTC monograph whatsoever, or there is insufficient scientific and clinical literature on the antimicrobial agent for this specified use, then it is possible that information comparable to that required for an NDA may be required. Guidance for an NDA or OTC drug may be obtained from the Center for Drug Evaluation and Research's (CDER) Division of Anti-Infective Drug Products at (301) 443-4310.