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1.0 TABLE OF CONTENTS

1.1 Revision History Table

Revision	Date	Author	Description and Location of Change(s)
01	9/01/2004	J. Rogers	Initial Release

2.0 PURPOSE/INTRODUCTION

FDA regulations require a new, complete 510(k) premarket notification submission for device modifications to a device that is currently in commercial distribution, or is being reintroducing into commercial distribution, and that is about to be significantly changed or modified, where those modifications could significantly affect the safety or effectiveness of the device. In addition FDA regulations require a new 510(k) if the device is to be marketed for a new or different indication for use.

Examples of significant changes or modifications that generally require a 510(k) submission include…

- Sterilization method
- Structural material
- Manufacturing method
- Operating parameters or conditions for use
- Patient or user safety features
- Sterile barrier packaging material
- Stability or expiration claims
- Design
- Materials
- Energy source
- Chemical composition
- Intended Use

It is not FDA's intent that a 510(k) must be submitted for every modification. FDA believes that the manufacturer is best qualified to determine when modifications could significantly affect safety or effectiveness.

EVERY modification to the device should, however, be reviewed by appropriate personnel to determine if it affects safety or effectiveness. To avoid "design creep," the changed device should be compared to the most recently 510(k)-cleared device, or the preamendments device. If a 510(k) submission is required, the 510(k) should identify or "roll up," all previous changes that did not necessitate a 510(k) submission, and the change that triggered the 510(k) should be identified.

If the modification is not significant, the decision, and the supporting rationale, shall be documented and added to the device's Design History FIle (DHF). In addition, design changes must be formally documented according to the Company's Document Controls/Configuration Management procedures, and added to the Device Master Record (DMR).

The problem is that the phrase "could significantly affect the safety or effectiveness of the device" and adjectives "major" and "significant" can sometimes lead to subjective interpretations. This procedure is provides guidance to the Company to evaluate device modifications and assists in determining whether those changes require a new 510(k) premarket notification submission. Modifications addressed in this procedure include…

- Labeling changes
- Technology or performance specifications changes
- Materials changes

Because many simultaneous changes may be considered in the evolution of device design, each type of change should be assessed individually, and collectively with other changes made since the last 510(k) clearance. An "any or nothing" approach should be taken in assessing design changes; in other words, if any aspect of the design change requires a 510(k) submission, then the decision is binding.

This procedure consists of four flowcharts to assist Company personnel through the logic determination of whether or not to submit a 510(k) submission for a change to an existing device. The flowcharts include logical breakouts for each type of design change.

The procedure additionally provides a means to document the rationale substantiating the 510(k) / NO 510(k) decision.

In certain circumstances, the proposed change is not addressed by this procedure or flowchart. Company personnel should consult their regulatory professionals, as well as device-specific guidance document(s) for additional advice and guidance.

2.1 Background/Introduction

Each person who intends to market Class I, II and some III devices intended for human use in the U.S. must submit a 510(k) premarket notification submission (or "510(k)") to FDA at least 90 days before marketing unless the device is exempt from 510(k) requirements.

A 510(k) is intended to demonstrate that the device to be marketed is as safe and effective, ("substantially equivalent"), as one or more legally marketed, similar device(s) that is/are not subject to premarket approval (PMA). A legally marketed device is a device that…

- Was legally marketed prior to May 28, 1976 (preamendments device)
- Has been reclassified from Class III to Class II or I,
- Has been found to be substantially equivalent to such a device through the 510(k) process, or one established through Evaluation of Automatic Class III Definition.

The legally marketed device(s) to which equivalence is drawn is the "predicate device(s)."

A 510(k) includes a comparison of the new device to the predicate device(s). To support the substantial equivalency claims, the 510(k) must include descriptive data and, when necessary, supporting performance, bench, and/or clinical data.

A device is substantially equivalent to a predicate device, if, in comparison to a predicate device, it has…

- The same intended use as the predicate device; and
- The same technological characteristics as the predicate device; or
- Different technological characteristics, that do not raise new questions of safety and effectiveness,
- Been demonstrated that the device is as safe and effective as the legally marketed device.

Substantial equivalence is established with respect to…

- Intended use
- Design
- Energy used or delivered
- Materials
- Performance

- Safety
- Effectiveness
- Labeling
- Biocompatibility
- Standards
- Other applicable characteristics

Until the submitter of the 510(k) receives an order from FDA in which FDA determines that the new device is substantially equivalent to the predicate device,the new device may not be advertised, promoted, marketed, or commercially distributed within the U.S. The substantially equivalent determination is usually made within 90 days and is based upon the information contained within the 510(k) submission document.

If FDA determines that a device is not substantially equivalent, another 510(k) with new data, may be resubmitted, or a reclassification petition may be filed, or a premarket approval application (PMA) may be submitted.

2.2 Who Must Submit a 510(k)

The following four categories of parties must submit a 510(k) to the FDA:

- Domestic manufacturers introducing a device to the U.S. market…

  Finished device manufacturers have to submit a 510(k) if they assemble a device according to their own specifications and market it in the U.S. However, manufacturers of device components are not required to submit a 510(k) unless those components are promoted for sale to an end-user as replacement parts. Also, contract manufacturers, those firms assembling devices on contract according to someone else's specifications, are not required to submit a 510(k).

- Specification developers introducing a device to the U.S. market…

  FDA views specification developers almost the same as manufacturers. These are persons who develop specifications for a finished device, but have it manufactured under contract by another firm or entity. Again, the specification developer submits the 510(k), not the contract manufacturer.

- Repackers or relabelers who make labeling changes, or whose operations significantly affect the device.

  Repackagers or relabelers may be required to submit a premarket notification if they significantly change the labeling (e.g., modifying manuals, deleting or adding warnings, contraindications, etc.) or otherwise altering any condition of the device. Most repackagers or relabelers are not required to submit a 510(k).

- Foreign manufacturers/exporters or U.S. representatives of foreign manufacturers/ exporters introducing a device to the U.S. market.

2.3 When Is a 510(k) Required

A 510(k) is required when…

- If the device was not marketed by the Company before May 28, 1976.
- A different intended use is proposed for a device which is already in commercial distribution. Intended use is indicated by claims made for a device in labeling or advertising.
- There is a change or modification to a device which is already in commercial distribution, if that change could significantly affect its safety or effectiveness.

The burden is on you to decide whether or not a modification could significantly affect safety or effectiveness. Whatever your conclusion, make a record which should be reflected in your device master record and change control records, required under the medical device good manufacturing practices. Then, if you're challenged, you will be able to document that in good faith you evaluated the change.

2.4 When is a 510(k) Not Required

A 510(k) is not required…

- If unfinished devices, or components to be used in the assembling of devices, are sold to another firm for further processing. However, if those components or devices are to be sold directly to end-users as replacement parts, then a 510(k) is required.
- If the new device is not being marketed or commercially distributed. A 510(k) is not a prerequisite to development, testing, evaluation (including clinical evaluation) of a device.

  Note that clinical testing and evaluation of a medical device (clinical studies, or clinical trials), must be in accordance with FDA's Investigational Device Exemption (IDE) regulations.
- If the Company distributes other company's domestically manufactured devices. A label such as "Distributed by ABC Firm" may be placed on the device or its labeling, and the device sold to end-users.
- If the Company is a repackager or a relabeler, provided that the existing labeling or condition of the device is not significantly changed.
- If the device was legally in commercial distribution before May 28, 1976, unless it has been modified or there has been a change in its intended use.
- If the Company is an importer of a foreign-manufactured medical device, provided that…
  - The foreign manufacturer has submitted a 510(k) submission for the device and has received marketing clearance, or
  - An importer has submitted a 510(k) submission for the device and has received marketing clearance on behalf of the foreign manufacturer and has received marketing clearance.

    If one importer submits a 510(k) on behalf of the foreign manufacturer, all other importers of that device, imported from the same foreign manufacturer, are not required to submit a 510(k) for that device.
- If the device is exempted from the 510(k) submission requirement by FDA regulations.

3.0 REFERENCE DOCUMENTS

3.1 Company-External References

3.1.1 Prescriptive References

- 21CFR807 Establishment Registration and Device Listing for Manufacturers and Importers of Devices
- 21CRF 807 E Premarket Notification Procedures

3.1.2 Guidance References

- **See** FORM 1.1.4 GLOSSARY AND LIST OF REFERENCES

3.2 Company-Internal References

- FORM 1.1.3 QUALITY MATRIX: REGULATIONS - SOPS - GUIDES - FORMS - PERSONNEL - FLOWCHART
- FORM 1.1.4 GLOSSARY AND LIST OF REFERENCES
- FORM 5.6.1 510(k) DECISION TREE
- — Device Master Record (DMR)
- — Design History File (DHF)

4.0 TOOLS, CONSUMABLES, SUPPLIES

The following tools, consumables, and supplies are required in order to perform the process instructions defined within this SOP:

- N/A

5.0 DEFINITIONS

N/A

6.0 ABBREVIATIONS AND ACRONYMS

Except as previously defined, the following non-standard abbreviations and acronyms are used in this document:

N/A

7.0 PROCEDURE

STEP	ACTION	RESPONSIBILITY
7.1	Identify the Type of Design Change	
7.1.1	Using the flowchart in Section §8.1 Flowchart #1: Types of Design Changes, identify the type(s) of design change. Is the design change due to a recall or corrective action? If YES, consult Company Regulatory Affairs for guidance and assistance.	Responsible Engineer, Regulatory Affairs
7.1.2	Is the design change a labeling change? If YES, use the flowchart in 8.2 Flowchart #2: Labeling Changes.	Responsible Engineer
7.1.3	Is the design change a technology or performance specification change? If YES, use the flowchart in 8.3 Flowchart #3: Technology or Performance Changes.	Responsible Engineer
7.1.4	Is the design change a materials change? If YES, use the flowchart in 8.4 Flowchart #4: Materials Change.	Responsible Engineer
7.1.5	Is the design change another type of change? If YES, consult Company Regulatory Affairs for guidance and assistance.	Responsible Engineer, Regulatory Affairs
7.1.6	Annotate Flowchart #1: Types of Design Changes.	Responsible Engineer
7.1.7	It is not sufficient to merely document the decision-making process. Documentation supporting and justifying each decision, as appropriate, shall be attached to the FORM 5.6.1 510(k) DECISION TREE.	Responsible Engineer
7.1.8	Record the determination on FORM 5.6.1 510(k) DECISION TREE.	Responsible Engineer
7.1.9	Attach a copy of the completed ECR/ECO to the FORM 5.6.1 510(k) DECISION TREE.	Responsible Engineer
7.1.10	Design changes must be formally documented according to the Company's Document Controls/Configuration Management procedures, and added to the Device Master Record (DMR).	Responsible Engineer, Document Controls/ Configuration Mangement

STEP	ACTION	RESPONSIBILITY
7.2	Labeling Changes	
7.2.1	Does the change affect the indications for use? "Indications for Use" identifies the target population in which sufficient scientific evidence has demonstrated that the device as labeled will provide clinically significant results, and an unreasonable risk of illness or injury associated with the use of the device is not present. Generally, most changes in indications for use will require a 510(k) submission. Any expansion of indications for use will require a 510(k) submission (e.g., revising an indication for use from adult use to include pediatrics). However, a change that limits use to within the currently cleared indications for use (e.g., further limiting the patient population by age or weight, etc.) does not require a 510(k) submission. More difficult is the expansion of indications for use to closely related populations. If the expansion is to a population with similar demographics, diagnosis, prognosis, comorbidity and potential for complications as the original, then a 510(k) is generally not required. The change to the indications for use should be evaluated to determine if it raises new issues of safety or effectiveness, additional risks, expansion to a new and distinguishable patient populations, etc. The "intended use" of the device is different from "indications for use," and includes a general description of the diseases or conditions that the device will diagnose, treat, prevent, cure, or mitigate, including a description, where appropriate, of the patient population for which the device is intended. Two common labeling changes that impact intended use and would generally require submission of a 510(k) are… ● reuse of devices previously labeled "single use only" ● changes from prescription to over the counter (OTC) **CONSULT COMPANY REGULATORY AFFAIRS FOR ASSISTANCE**	Responsible Engineer, Regulatory Affairs
7.2.2	Is it a change in warnings or precautions? Events that result in changes of this type are usually reported to FDA under the Medical Device Reporting regulation (MDR) 21 CFR Part 803, and 510(k) submissions are generally not required.	Responsible Engineer

STEP	ACTION	RESPONSIBILITY
7.2.3	Does the change add a new contraindication? While all changes in the labeled contraindications for device use should be reviewed by the agency, CDRH recognizes that, in general, The addition of a contraindication based upon new information is important to public health and should be implemented immediately. The Company is required to notify existing users of their device as expediently as possible. Finally, the new labeling is required to be submitted to FDA as part of a new 510(k), and prominently labeled "change being effected". The Company may continue to market the device with the modified labeling, unless otherwise notified by FDA.	Responsible Engineer
7.2.4	Does the change delete a contraindication? Deleting a contraindication usually requires the submission of a 510(k), because this type of labeling change typically expands the indications for use. Such a 510(k) submission must be submitted prior to effecting the change. Device labeling often includes contraindications that would more appropriately be warnings or precautions. Labeling changes that delete/revise contraindications under such circumstances can be made without the need for a 510(k).	Responsible Engineer
7.2.5	Is the labeling being revised for clarity to ensure safer or more effective use? Most labeling changes result from attempts to clarify instructions to make the device easier, safer, or more effective to use. Generally, these labeling changes do not require a 510(k) submission.	Responsible Engineer
7.2.6	Annotate Flowchart #2: Labeling Changes.	Responsible Engineer
7.2.7	Documentation supporting and justifying each decision, as appropriate, shall be attached to the FORM 5.6.1 510(k) DECISION TREE.	Responsible Engineer

STEP	ACTION	RESPONSIBILITY
7.3	Technology, Engineering and Performance Changes	
7.3.1	Is it a control mechanism change? Almost all changes in the control mechanism for a device raise questions of safety and effectiveness, and normally requires the submission of a new 510(k). An obvious example of a control mechanism change that would raise new questions of safety and effectiveness, and that would require a 510(k) submission, is the change from analog to digital control of a medical device. While the change to digital control can markedly improve device performance specifications and effectiveness, the integration of a digital control into a previously all analog system is complex and usually undertaken only as part of a major redesign of a product.	Responsible Engineer
7.3.2	Is it an operating principle change? Similar to a control mechanism change, almost all changes in operating principle for a device raise questions of safety and effectiveness, and normally requires the submission of a new 510(k). For example, an operating principle change would be changing the image reconstruction algorithm used in a computed tomography x-ray system from simple back-projection to a more radiation-efficient method. Both bench testing and a clinical study would be necessary to support a finding of substantial equivalence for the new device. Operating principle changes may also be accompanied by significant changes in labeling and by a need for operator retraining to assure continued safe and effective operation. Minor changes to the algorithm that can easily be validated by the Company may not necessarily require the submission of a 510(k).	Responsible Engineer

STEP	ACTION	RESPONSIBILITY
7.3.3	Is it a change in energy type? Almost all changes in the energy type for a device raise questions of safety and effectiveness, potentially expands the indications for use, and normally requires the submission of a new 510(k). For example, changing from AC to battery power is usually part of a redesign to improve a device's portability, such that can be used under different environmental conditions than the original device. Such a change would normally be accompanied by significant labeling changes, including a new or expanded indication for use. Minor changes, such as changing from a 3V to a 9V supply, or from lead-acid to NiCad batteries may not necessarily require the submission of a 510(k).	Responsible Engineer
7.3.4	Is it a change in environmental specifications? See 7.3.11 below.	Responsible Engineer
7.3.5	Is it a change in performance specifications? See 7.3.11 below.	Responsible Engineer
7.3.6	Is it a change in ergonomics of the patient/user interface? See 7.3.11 below.	Responsible Engineer
7.3.7	Is it a change in dimensional specifications? See 7.3.11 below.	Responsible Engineer
7.3.8	Is it a change in software or firmware? See 7.3.11 below.	Responsible Engineer
7.3.9	Is there a change in packaging or expiration dating? Generally, changes in device packaging or changes in the expiration date for use of a device do not result in the need for a new 510(k). However, if new methods or protocols are used to support expanded package integrity or shelf-life claims, a new 510(k) is generally required.	Responsible Engineer
7.3.10	Has there been a change in sterilization? Changes in sterilization have the potential for affecting the safety or effectiveness of the device and must be carefully assessed.	Reference Information

STEP	ACTION	RESPONSIBILITY
7.3.10.1	Has there been a change in performance specification of the device as a result of the change in sterilization? Changes in the method of sterilization have the potential for changing performance characteristics of a device.If a change is made in sterilization methods, the important properties/specifications of the device and integrity of device materials remains unaffected. These types of changes tend to raise additional questions of safety and effectiveness, and a new 510(k) is generally required. Similarly, has there been a change in the sterility assurance level attained as a result of the change in sterilization? Changes in sterilization processes which result in a lower sterility assurance level (SAL) must be critically assessed to ensure that device safety or effectiveness is not compromised by the new level. In general, reductions in SAL automatically trigger 510(k) submissions unless the SAL remains above 10^{-6}.	Responsible Engineer
7.3.11	The types of changes identified in 7.3.4 through 7.3.8 are frequently called design changes or engineering changes. They encompass everything from the routine specification changes necessary to maintain or improve device performance as a result of feedback from users, field or plant personnel, etc., up to and including significant product redesign. The major difficulty lies in determining which of these changes is significant enough to trigger the need for a 510(k). Steps 7.3.11.1 through 7.3.11.3 can assist in this determination.	Reference Information

STEP	ACTION	RESPONSIBILITY
7.3.11.1	Does the change affect the indications for use? As with an explicit labeling change, if the change affects the indications for use, i.e., if it creates an implied new indication for use, a new 510(k) is generally required. For example, consider changing the length of a surgical scissor from 10 to 30cm so that the modified device can be used in laparoscopic procedures. The original indication for use was for open surgical procedures, while the new indication for use would be for closed, endoscopically-controlled procedures. Note that even though surgical scissors are exempt from the requirement to submit a 510(k) by regulation,design changes must still be evaluated to ensure that the change does not affect the device's classification or exemption status. **CONSULT COMPANY REGULATORY AFFAIRS FOR ASSISTANCE**	Responsible Engineer, Regulatory Affairs
7.3.11.2	Are clinical data necessary to evaluate safety and effectiveness for purposes of determining substantial equivalence? When a Company recognizes that clinical data are needed because bench testing or simulations are not sufficient to assess safety and effectiveness and, thus, to establish the substantial equivalence of a new design, a 510(k) is generally required. **CONSULT COMPANY REGULATORY AFFAIRS FOR ASSISTANCE**	Responsible Engineer, Regulatory Affairs
7.3.11.3	Do results of design validation raise new issues of safety and effectiveness? All changes to device design will require some level of design validation to assure that the device continues to perform as intended. The successful application of routine design validation activities will logically result in manufacturers documenting their efforts and proceeding with the design change, i.e., assuring that no issues of safety or effectiveness are raised. Occasionally, however, design validation activities produce unexpected results or otherwise prove to be inadequate to validate the design change. In these cases, questions of safety and effectiveness may be associated with the design change, and a new 510(k) is generally required. **CONSULT COMPANY REGULATORY AFFAIRS FOR ASSISTANCE**	Responsible Engineer, Regulatory Affairs

STEP	ACTION	RESPONSIBILITY
7.3.12	Annotate Flowchart #3: Technology or Performance Changes.	Responsible Engineer
7.3.13	Documentation supporting and justifying each decision, as appropriate, shall be attached to the FORM 5.6.1 510(k) DECISION TREE.	Responsible Engineer
7.4	Materials Changes	
	Changes to materials may have other collateral changes to the device, including labeling changes (e.g., delete a contraindication, addition of a new warning, etc.), or technology/engineering/performance specificagion changes (e.g., reduction in the strength of the device). These collateral changes should be evaluated first, prior to evaluating materials changes as a direct requirement for a new 510(k) submission.	Reference Information
7.4.1	Is there a change in the type of material from which the device is manufactured?	Responsible Engineer
7.4.2	Is there a change in the material formulation? These changes are within a single generic material type that can affect the chemistry, metallurgy, stability, or other property of the material. However, these changes do not include changes in processing aids, catalysts, residual contaminants, or manufacturing aids that are not intended to be part of the material. For example, a material formulation changes from AISI Type 316 stainless steel to AISI type 400 stainless steel.	Responsible Engineer
7.4.3	Is the device an implant? Implant devices are those described in the "permanent contact" category of ISO 10993-1, Section 5.1.4 and 5.2.21	Responsible Engineer

STEP	ACTION	RESPONSIBILITY
7.4.3.1	(Since the device is an implant) Will the material of the affected part of the implant be likely to contact body tissues or fluids? Changes in materials that contact body tissues or fluids may critically affect the device's safety or effectiveness, either because of potentially new interactions of the device material on the body or because of the body's environmental effects on the new material in the device. A new 510(k) submission is automatically required for a material change in implant material where the material contacts tissue (including bone tissue) or body fluid. Changes in materials of an implant that are NOT intended to contact body tissues or fluids generally do not require a 510(k) submission, (e.g., changes in material type to the interior materials of an implantable electric stimulator which sealed from ingress of body fluids or tissues).	Responsible Engineer
7.4.3.2	Is there a change in performance specifications? A change in material is made to purposefully alter the performance specifications of a device. Sometimes, however, changes in materials can inadvertently affect the performance of a device, in which case a new 510(k) may be required. In either situation, see 7.3 Technology, Engineering and Performance Changes for assistance and guidance to determine whether a 510(k) is necessary.	Responsible Engineer
7.4.4	Will the material of the affected part of the (non-implant) device be likely to contact body tissues or fluids in vivo? Non-implant devices include both "limited exposure" and "prolonged exposure" devices, as described in ISO 10993-1: Biological Evaluation of Medical Devices, Part 1: Evaluation and Testing. Examples of prolonged exposure devices that might contact in vivo fluids or tissues include parenteral feeding cathetes, rwound drains, infusion catheters sutures, etc.	Responsible Engineer

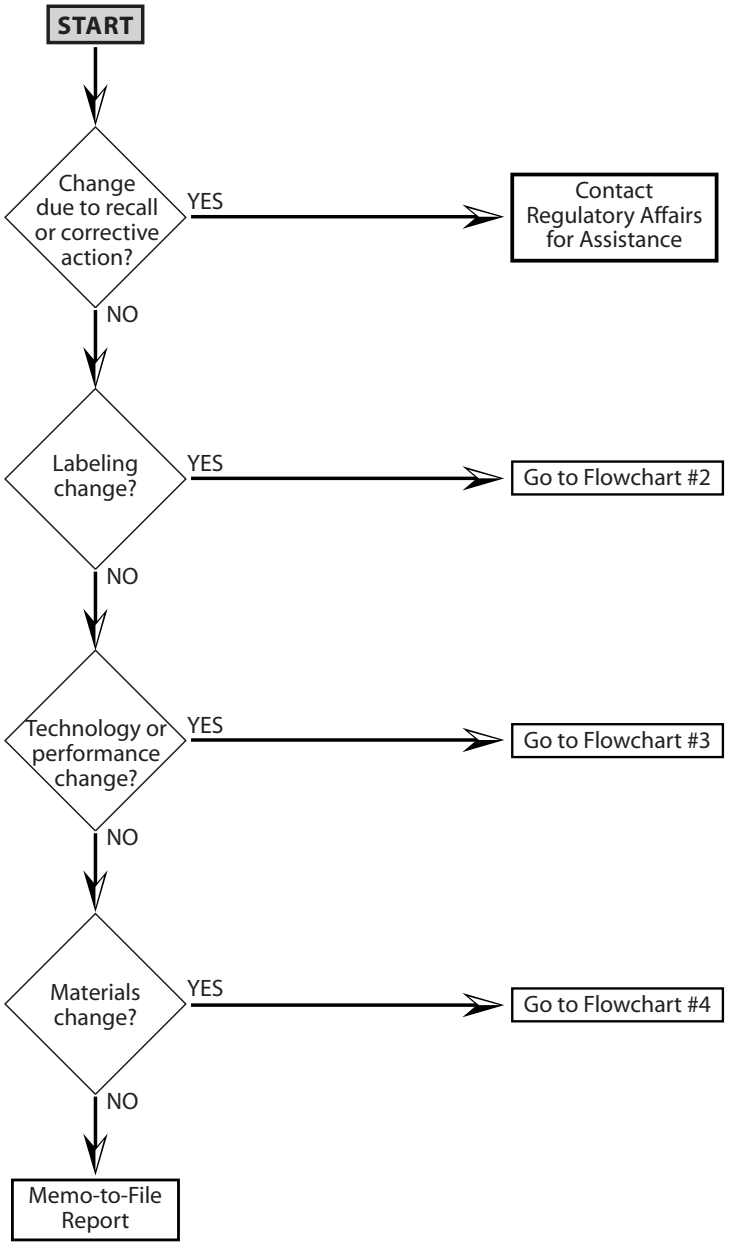
STEP	ACTION	RESPONSIBILITY
7.4.4.1	(Since the material is likely to contact in vivo body tissues or fluids) Consider the requirements of ISO 10993-1; is additional testing required? A 510(k) may not be needed if the Company has satisfactory results from the testing indicated by ISO 10993-1 for the material in question and for the material's intended use. Thus is much clearer for materials such as metal alloys, in which the physical and chemical descriptions for a particular formulation are exact. For materials such as polymers or ceramics, the characterization of the formulation may be less exact. In addition, there may not be a good correspondence between the material formulation for which the testing results are well established, as compared to the material formulation intended for use with the device. Generally, for polymer or ceramic materials, additional testing according to ISO10993-1 is probably necessary. If such additional testing is required, then a 510(k) is usually also required.	Responsible Engineer
7.4.5	(Since the device is an implant and the materials are not likely to contact blood or body fluids in vivo) Is there a change in performance specifications? A change in material is made to purposefully alter the performance specifications of a device. Sometimes, however, changes in materials can inadvertently affect the performance of a device, in which case a new 510(k) may be required. In either situation, see 7.3 Technology, Engineering and Performance Changes for assistance and guidance to determine whether a 510(k) is necessary.	Responsible Engineer
7.4.6	Is there a change in the vendor of the raw material from which the device is manufactured? FDA Quality System Regulations (QSR) and 510(k) regulations require the Company to purchase materials from approved suppliers according to a material specification, which documents the required performace specifications of the raw materials.	Responsible Engineer

STEP	ACTION	RESPONSIBILITY
7.4.6.1	Is the new material being supplied according to a material specification? If the material is being supplied to the device manufacturer's specification, then a 510(k) is generally not required. HOWEVER, if the new material does not have an associated material specification, then a 510(k) submission is automatically required.	Responsible Engineer
7.4.7	Annotate Flowchart #4: Materials Change.	Responsible Engineer
7.4.8	Documentation supporting and justifying each decision, as appropriate, shall be attached to the FORM 5.6.1 510(k) DECISION TREE.	Responsible Engineer

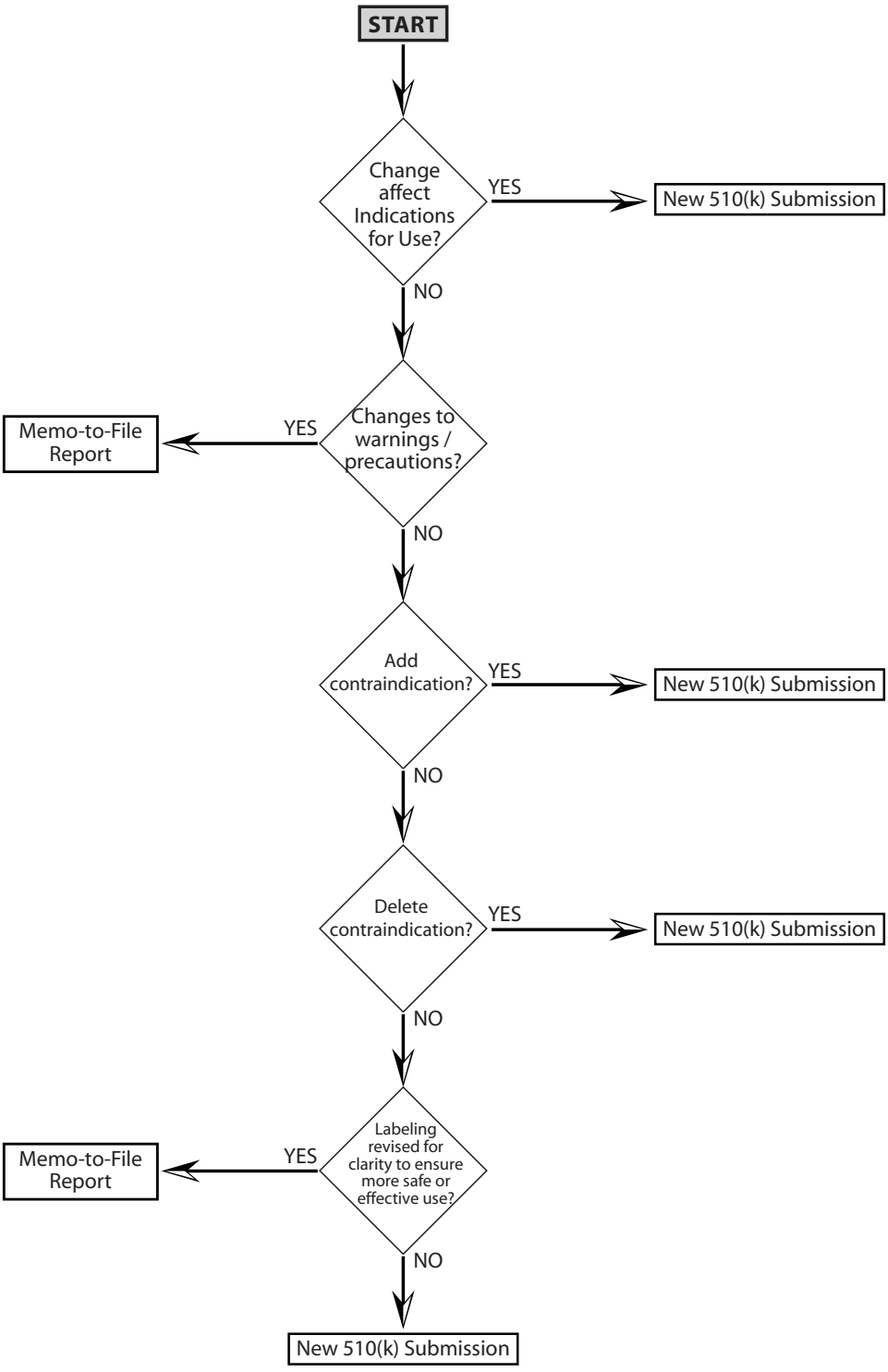
8.0 Appendices

- Flowchart #1: Types of Design Changes
- Flowchart #2: Labeling Changes
- Flowchart #3: Technology or Performance Changes
- Flowchart #4: Materials Change

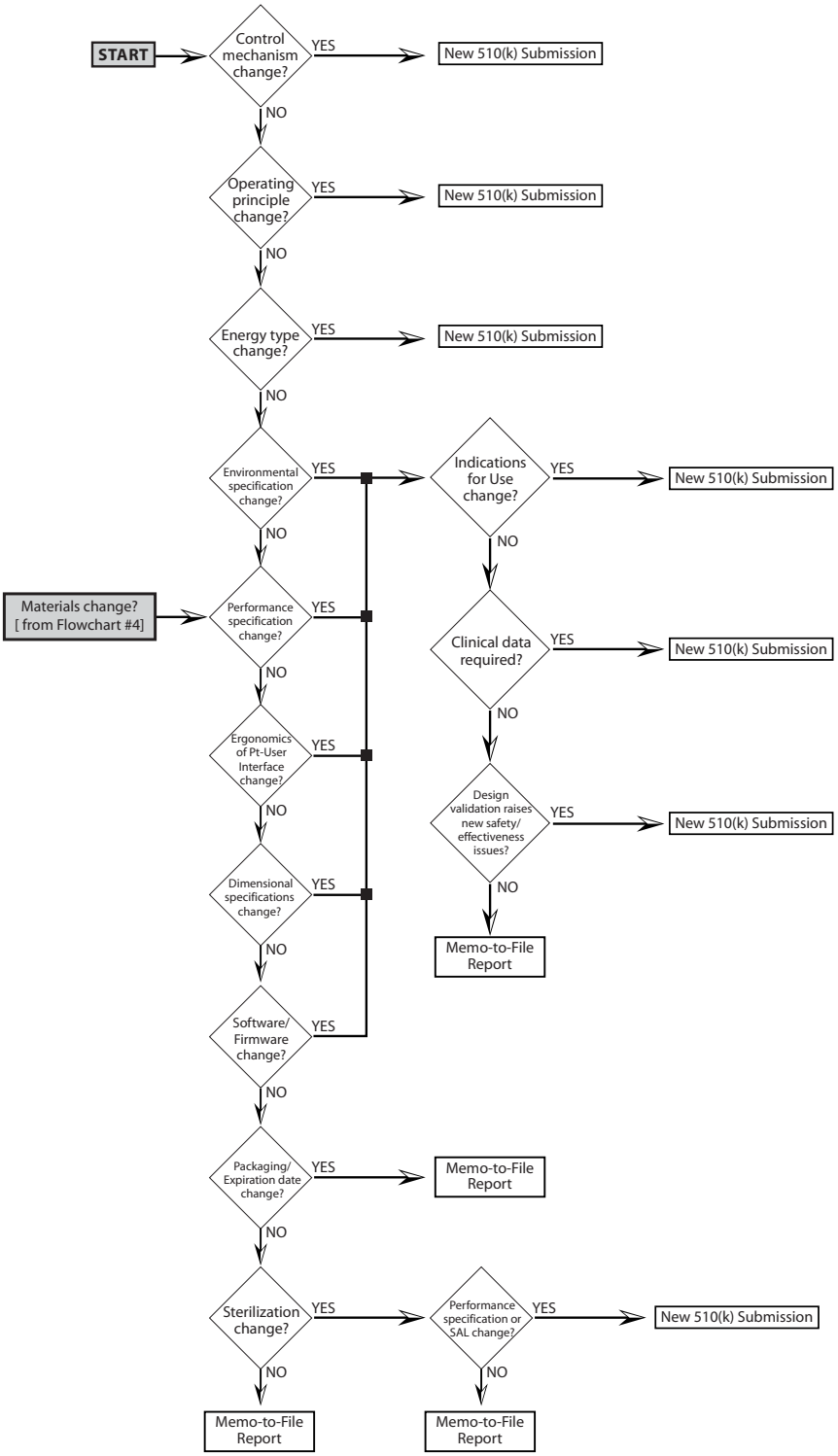
8.1 Flowchart #1: Types of Design Changes



8.2 Flowchart #2: Labeling Changes



8.3 Flowchart #3: Technology or Performance Changes



8.4 Flowchart #4: Materials Change