Letter of Authorization:
510(k)/PMA Right of Reference Guidance and Template

ICTR Navigator
April 26, 2013
Version 1.0
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2.0 Abbreviations

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<td>510(k)</td>
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<td>CDRH</td>
<td>Center for Devices and Radiologic Health</td>
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<td>CFR</td>
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<td>FDA</td>
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<td>IDE</td>
<td>Investigational Device Exemption</td>
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3.0 Definitions

**510(k)**

A 510(k) is a premarket submission made to FDA to demonstrate that a medical device to be marketed is at least as safe and effective (also called ‘substantially equivalent’) as a legally marketed device that is not subject to PMA.

**Pre-Market Approval (PMA)**

Per the FDA website, ‘premarket approval (PMA) is the FDA process of scientific and regulatory review to evaluate the safety and effectiveness of Class III medical devices. Class III devices are those that support or sustain human life, are of substantial importance in preventing impairment of human health, or which present a potential, unreasonable risk of illness or injury.’

**Agent or representative**

Agent or representative means any person who is appointed by a 510(k) holder to serve as the contact for the holder.

**Authorized Party**

The authorized party in this case is the Sponsor-Investigator or Applicant whose IDE submission references the 510(k) application.
Holder

Holder means the person or company that owns the 510(k) being referenced.

Letter of authorization

A letter of authorization is a written statement by the 510(k) holder or representative permitting FDA to refer to information in their 510(k) application in support of another person's (authorized party) IDE submission.

Right of reference

Right of reference or use means the authority to rely upon, and otherwise use, an investigation for the purpose of obtaining approval of an application, including the ability to make available the underlying raw data from the investigation for FDA audit, if necessary. (21 CFR 314.2(b)(8))

Sponsor-Investigator

The sponsor-investigator is someone who is both 1) responsible for initiating the studies conducted with the investigational agent and 2) who conducts the studies. (21 CFR 312.3(b))

4.0 Overview of Device Research and Letters of Authorization (LOA)

4.1 Overview of Device Research

Medical devices being used in clinical investigations are handled differently depending on whether they are deemed “significant risk” or “non-significant risk.” A significant risk device is defined as a medical device that:

(1) is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;

(2) is for use in supporting or sustaining human life and represents a potential for serious risk to the health, safety, or welfare of a subject;

(3) is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or

(4) otherwise presents a potential for serious risk to a subject.

Significant risk devices require submission of Investigational Device Exemption (IDE) applications to the FDA and are subject to specific oversight and reporting guidelines (See 21 CFR 812).
4.2 IDEs and Letters of Authorization

If an investigator is proposing a human subjects research project involving the use of a legally marketed device in a manner which is inconsistent with the FDA approved labeling, the investigator should approach the manufacturer and request a letter of authorization to the marketing application (i.e. 510(k) or PMA) submitted to FDA for the device. If granted, this letter of authorization will give the investigator permission to reference manufacturing and design controls data contained in the manufacturer’s marketing application in support of his or her IDE, thus significantly decreasing the amount of work required to prepare the IDE submission.

4.2.1 510 (k) Application

Per the FDA site, anyone wishing ‘to market in the U.S., a Class I, II, or III device intended for human use, for which a Premarket Approval (PMA) is not required, must submit a 510(k) to FDA unless the device is exempt from 510(k) requirements.

There is no 510(k) form, however, 21 CFR 807 Subpart E describes requirements for a 510(k) submission. Before marketing a device, each submitter must receive an order, in the form of a letter, from FDA which finds the device to be substantially equivalent (SE) and states that the device can be marketed in the U.S. This order "clears" the device for commercial distribution.

A 510(k) is a premarket submission made to FDA to demonstrate that the device to be marketed is at least as safe and effective, that is, substantially equivalent, to a legally marketed device (21 CFR 807.92(a)(3)) that is not subject to Pre-Market Approval (PMA). Submitters must compare their device to one or more similar legally marketed devices and make and support their substantial equivalency claims.’

4.2.2 Pre-Market Approval

Per the FDA, “premarket approval (PMA) is the FDA process of scientific and regulatory review to evaluate the safety and effectiveness of Class III medical devices. Class III devices are those that support or sustain human life, are of substantial importance in preventing impairment of human health, or which present a potential, unreasonable risk of illness or injury. Due to the level of risk associated with Class III devices, FDA has determined that general and special controls alone are insufficient to assure the safety and effectiveness of class III devices. Therefore, these devices require a premarket approval (PMA) application under section 515 of the FD&C Act in order to obtain marketing clearance.”

4.3 Nomenclature

In the US, the Letter of Authorization is very commonly referred to as a “Right of Reference” letter. A Letter of Authorization grants the Authorized Party (i.e. the IDE Sponsor-Investigator) the right to incorporate the information contained within the 510(k) or PMA submission into their IDE or other application by reference.
4.4 **LOA Process**

5.0 **Number of Copies to be submitted**

The Authorized party (i.e. sponsor-investigator) should include a copy of the 510(k) or PMA Letter of Authorization in the IDE application and reference same in the appropriate application sections. (See ICTR DDRS IDE guidance and template)

6.0 **Hyperlinks**

All hyperlinks included in this document are operational as of the date of this version. If any non-functional hyperlinks are identified, please contact the ICTR Research Navigator via the contact information below so that the links may be updated.

7.0 **Questions and Additional Information Contacts**

For questions relating to any of the information presented or use of the template, please contact the ICTR Research Navigators at ICTR_Navigators@jhmi.edu or via telephone at 410-614-5383.

Investigators may also direct comments or questions regarding 510(k) and PMA letters of authorization the Division of Small Manufacturers, International and Consumer Assistance (DSMICA) at CDRH via email or telephone.

**Email:** dsmica@fda.hhs.gov or industry.devices@fda.hhs.gov

**Telephone:** 1-800-638-2041 or 301-796-7100

8.0 **LOA Request Example**

Please see an example of an LOA request on the following page. This is the recommended language for investigators to use to request a letter of authorization for their IDE from the device manufacturer.
Subject: [Insert: Letter of Authorization Request]

Dear [Insert: Name of contact with the 510(k) or PMA Holder],

I am emailing to request a Letter of Authorization permitting the FDA to access [Insert: 510(k) or PMA Holder’s name] [Insert: 510(k) OR PMA] No. [Insert 510(k) OR PMA number] for [Insert: device name] for my [Insert: pre-IDE OR IDE] submission to the FDA for the protocol entitled, “[Insert: protocol title OR IDE submission title].” I do not yet have an IDE number as this is a [Insert: pre-IDE submission OR IDE application that has not yet been submitted for review.] Please do not hesitate to contact me for any questions or concerns regarding this request. Thank you in advance for your support of this endeavor.

Sincerely,

[Insert: Name Sponsor-investigator]
9.0 LOA Template

Please see an LOA template on the following page. The following is a letter template that a manufacturer may use to grant the investigator authorization to reference their 510(k) or PMA.
[Place on 510(k) or PMA Holder letterhead]

Date: [Insert date that the authorization is issued]

510(k) or PMA#: [Enter number and delete unneeded header]

Holder: [Enter the Name of 510(k) or PMA Holder]

Device Trade Name: [Enter the Device Trade Name as it appears on the original 510(k) clearance or PMA approval]

Letter of Authorization for: [Enter the name of the device being referenced]

Dear Sir/Madam:

This letter authorizes Dr. [Insert: Authorized Party’s name] to incorporate by reference the manufacturing and design control data for the [Insert: device name] previously submitted by [Insert: Holder’s name] in [Insert: 510(k) OR PMA] No. [Insert 510(k) OR PMA number] into [Insert: his/her] [Insert: pre-IDE submission OR IDE application]. This authorization is in support of Dr. [Insert: Authorized Party’s name]’s [Insert: pre-IDE submission entitled, ‘[Insert: Application title]’ and subsequent Investigational Device Exemption Application OR Insert: Investigational Device Exemption Application entitled, ‘[Insert: Application title]’ and subsequent supplements thereto] involving the use of [Insert: product name].

Dr. [Insert: Authorized Party’s name]’s full contact information is:

[Insert Authorized Party’s name and credentials]
[Insert Authorized Party’s full title]
[Insert Authorized Party’s institutional address]
[Insert Authorized Party’s institutional email address]
[Insert Authorized Party’s office telephone]

Thank you for your assistance with this matter.

Sincerely,

Signature of Responsible Official
Name of Responsible Official
Responsible Official’s Title
Responsible Official’s Company i.e. Holder or Agent
Responsible Official’s Telephone number
Responsible Official’s Fax number
Responsible Official’s e-mail address