FDA Categorization of Investigational Device Exemption (IDE) Devices to Assist the Centers for Medicare and Medicaid Services (CMS) with Coverage Decisions

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Draft Guidance for Sponsors, Clinical Investigators, Industry, Institutional Review Boards and Food and Drug Administration Staff

DRAFT GUIDANCE

This draft guidance document is being distributed for comment purposes only.

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You should submit comments and suggestions regarding this draft document within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Identify all comments with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions about this document, contact Program Operations Staff at 301-796-5640, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, rm. 1522, Silver Spring, MD 20993-0002, 301-796-5640. For questions regarding this document as applied to devices regulated by CBER, contact the Office of Communication, Outreach and Development in CBER at 1-800-835-4709 or 240-402-8010 or ocod@fda.hhs.gov.

When final, this guidance will supersede IDE Guidance Memorandum #95-2 “Implementation of

the FDA/HCFA Interagency Agreement Regarding Reimbursement Categorization of Investigational Devices" issued on September 15, 1995.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health

Center for Biologics Evaluation and Research

Preface

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Table of Contents

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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff or Office responsible for this guidance as listed on the title page.

I. Introduction

This guidance modifies the Food and Drug Administration's (FDA's or the Agency's) current policy on categorizing investigational device exemption (IDE) devices which assists the Centers for Medicare & Medicaid Services (CMS) in determining whether or not an IDE device should be covered (reimbursed) by CMS.

On December 2, 2015, FDA's Center for Devices and Radiological Health (CDRH) and CMS's Coverage and Analysis Group (CAG) executed a Memorandum of Understanding (MOU) to

streamline and facilitate the efficient categorization of investigational medical devices in order to support CMS's ability to make Medicare coverage (reimbursement) determinations for those investigational devices under 42 C.F.R. 405 Subpart B. The MOU noted the need for FDA and CMS to revise their shared understanding regarding categorization. This guidance document is intended to implement the MOU by further explaining the framework that FDA (both CDRH and the Center for Biologics Evaluation and Research [CBER]) intends to follow for such decisions. The MOU will take effect June 2, 2016 (6 months following signature from both FDA and CMS, as stated in the MOU). The framework in this guidance will represent the Agency's current thinking on categorization upon publication of an FDA final guidance.

II. Background

1995 Final Rule and FDA-HCFA Interagency Agreement

In September 1995, the Health Care Financing Administration (now known as CMS) published a final rule and entered into an Interagency Agreement (IA) with FDA regarding reimbursement categorization of investigational devices. 60 Federal Register (FR) 48417 (September 19, 1995). The rule established that certain devices with an IDE approved by FDA (and certain services related to those devices) may be covered under Medicare, and set forth the process by which FDA would assist CMS in identifying such devices. FDA would assign a device with an FDA approved IDE to one of two categories: Experimental/Investigational (Category A) devices or Non-experimental/Investigational (Category B) devices based on the level of risk the device presented to patients. The IA set forth criteria, agreed upon by CMS and FDA, that FDA would use to categorize devices. The categorization would then be used by CMS as part of its determination of whether or not items and services met the requirements for Medicare coverage under Section 1862(a)(1)(A) of the Social Security Act (the "reasonable and necessary" clause). That is, to be eligible to be covered (e.g., to have a benefit category determination) under Medicare, the device must be reasonable and necessary for the diagnosis or treatment of an illness or injury, or to improve the functioning of a malformed body member.[1]

Under the 1995 CMS final rule, Category A devices were devices believed to be in class III for which "absolute risk" of the device type had not yet been established. That is, initial questions of safety and effectiveness had not been resolved and FDA was unsure whether the device type could be safe and effective. The IA contained two sub-categories which provided criteria indicating that a given device met this standard and should be placed into Category A: those devices for which no marketing application had been approved through the premarket approval (PMA) process for any indication for use and devices that would otherwise be a Category B, but

[1] Implementation of the FDA/HCFA Interagency Agreement Regarding Reimbursement Categorization of Investigational Devices, Att. A Interagency Agreement, Att. B Criteria for Categorization of Investigational Devices, & Att. C List. #D95-2 (IDE Guidance Memorandum #95-2, Sept. 15, 1995).

had undergone significant modification for a new indication or use. An example of a significant modification may be the addition of a drug onto a legally marketed device.

Under the 1995 CMS final rule, Category B devices were those devices believed to be in Class I or II, or devices believed to be in Class III for which the incremental risk was the primary risk in question. That is, underlying questions of safety and effectiveness of that device type had been resolved or it was known that the device type could be safe and effective because, for example, other manufacturers had obtained FDA approval for that device type. The IA identified six sub-categories of investigational devices that were of a device type for which the underlying questions of safety and effectiveness had been resolved and thus should be placed in Category B. Under the IA, Category B devices included those that were under investigation to demonstrate substantial equivalence to a predicate device (legally marketed device) through the 510(k) process or devices comparable to a PMA-approved device. Category B also included situations in which it was known that the device type could be safe and effective because, for example, other manufacturers had obtained FDA approval for that device type. Several examples of Category A and B devices can be found later in this document.

Importantly, CMS and FDA both recognized that experience in categorizing devices might require changes to the Interagency Agreement.[2]

2013 Amendment to 42 CFR 405 Subpart B

In 2013, CMS published a final rule in the Federal Register (FR), 78 FR 74230, 74809 (Dec. 10, 2013), that, among other things, modified the definitions for Category A and Category B. These definitions can be found in the Code of Federal Regulations (CFR) at 42 CFR 405.201:

Category A (Experimental)
42 CFR 405.201(b): "…a device for which 'absolute risk' of the device type has not been established (that is, initial questions of safety and effectiveness have not been resolved) and the FDA is unsure whether the device type can be safe and effective."

Category B (Nonexperimental/investigational)
42 CFR 405.201(b): "…a device for which the incremental risk is the primary risk in question (that is, initial questions of safety and effectiveness of that device type have been resolved), or it is known that the device type can be safe and effective because, for example, other manufacturers have obtained FDA premarket approval or clearance for that device type."

CMS uses FDA's categorization determination in evaluating whether or not an IDE device receives Medicare coverage. Medicare may make payment for an investigational device and routine care items and services furnished in an FDA-approved Category B (Nonexperimental/Investigational) IDE study if CMS (or its designated entity) determines prior to the submission of the first related claim that the Medicare coverage IDE study criteria in 42

[2] The Interagency Agreement was published as an addendum to the final rule in 1995. The FR noted that: "As experience is gained in the categorization process, this addendum may be modified." 60 FR at 48419.

CFR 405.212 are met.[3] Medicare may cover only routine care items and services furnished in an FDA-approved Category A (Experimental) IDE study, but not the device itself if CMS (or its designated entity) determines that Medicare coverage IDE study criteria in 42 CFR 405.212 are met.[4] In other words, Medicare cannot cover device expenses for studies that FDA has categorized as Category A (Experimental).

Reasons for Modification of the Previous FDA Policy

In the more than twenty years since the IA was signed, FDA has received a number of IDEs which do not easily fit into any of the eight sub-categories identified in the IA.

In 2013, FDA published a final guidance document entitled "Investigational Device Exemptions (IDEs) for Early Feasibility Medical Device Clinical Studies, Including Certain First in Human (FIH) Studies." This document provides guidance on the development and review of IDE applications for early feasibility studies (EFS) of significant risk devices. EFS are feasibility studies that are very small in size and allow for early clinical evaluation of devices that may not be a final design. They are intended to provide proof of principle and initial clinical study data. Traditional feasibility studies, on the other hand, are completed with a device design that is near-final or final and are commonly used to capture preliminary safety and effectiveness information which may be used to inform a pivotal study design. They are typically larger than EFS. The general term "feasibility studies" may refer to EFS or traditional feasibility studies. Pivotal studies are clinical investigations designed to collect definitive evidence of the safety and effectiveness of a device for a specified intended use, typically in a statistically justified number of subjects. The previous FDA policy regarding reimbursement categorization did not adequately articulate categorization criteria that are relevant to certain feasibility studies, particularly those for devices similar to approved devices but with modifications which raise significant new safety questions. As a result of this and the recent increase in EFS submissions subsequent to the publication of the guidance document referenced above, FDA has determined that additional clarification of these categorization criteria is warranted. It is important to note that the CMS category designation is made independent of study type and instead is based on the criteria described in this document.

In addition to the above consideration, there are situations when adequate data are provided to resolve initial questions of safety and effectiveness (e.g., data from a feasibility study becomes available) and, therefore, it is appropriate to change the device category for subsequent studies of the same device from Category A to Category B. In these circumstances, a device that had previously been categorized as experimental could now be considered nonexperimental/investigational. However, the IA did not describe a pathway for changing categorization from Category A to Category B when approving subsequent studies for the same device. In order to outline a mechanism to revisit the categorization of IDE devices when new information is gathered, the previous FDA policy for CMS categorization of IDE devices is being modified.

[3] 42 CFR 405.211(b)
[4] 42 CFR 405.211(a)

Lastly, in its changes to the regulations (42 CFR 405 Subpart B), effective January 1, 2015, CMS added criteria for coverage of IDE studies and changed from local Medicare Administrative Contractor (MAC) review and approval of IDE studies to a centralized review and approval of IDE studies. The change to a centralized IDE review further reinforced the need for CMS and FDA to revisit the policy that FDA used to categorize IDE devices. CMS and FDA recognized the necessity to revise their shared understanding regarding the categorization of IDE devices to help ensure that devices will not be precluded from reimbursement due to an inappropriate reimbursement categorization determination. Rather than amending their 1995 IA, FDA and CMS entered into an MOU on December 2, 2015. It becomes effective on June 2, 2016. The policies and framework in this guidance will represent the Agency's current thinking on categorization upon publication of a final guidance document.

III. FDA Interpretation of Medicare Coverage Categories A and B

After receipt of an IDE application, FDA will determine whether the sponsor has provided enough information to support initiation of the clinical study. An IDE application is "approved" or "approved with conditions" if FDA has determined that the sponsor has provided adequate data to support initiation of a human clinical study, no subject protection concerns preclude initiation of the investigation, and the benefit-risk profile is sufficiently favorable to justify enrollment.[5] FDA intends to use the criteria described below to assign a device to a CMS Category A or B when the IDE is approved or approved with conditions. Please refer to Appendix A for a flowchart depicting the decision making process.

Category A: Experimental

42 CFR 405.201(b): "…a device for which 'absolute risk' of the device types has not been established (that is, initial questions of safety and effectiveness have not been resolved) and the FDA is unsure whether the device type can be safe and effective." FDA intends to consider a device to be in Category A if one or more of the following criteria are met:

- No PMA approval, 510(k) clearance or *de novo* request has been granted for the proposed device or similar devices, and non-clinical and/or clinical data on the proposed device do not resolve initial questions of safety and effectiveness.

- The proposed device has different characteristics compared to a legally marketed device; and information related to the marketed device does not resolve initial questions of safety

[5] For more information on how IDE Decisions are made please refer to the FDA Guidance document "FDA Decisions for Investigational Device Exemption Clinical Investigations."

and effectiveness for the proposed device. Available non-clinical and/or clinical data on the proposed device also do not resolve these questions.

- The proposed device is being studied for a new indication or new intended use for which information from the proposed or similar device related to the previous indication does not resolve initial questions of safety and effectiveness. Available non-clinical and/or clinical data on the proposed device relative to the new indication or intended use also do not resolve these questions.

Category B: Nonexperimental/Investigational

42 CFR 405.201(b): "…a device for which the incremental risk is the primary risk in question (that is, initial questions of safety and effectiveness of that device type have been resolved), or it is known that the device type can be safe and effective because, for example, other manufacturers have obtained FDA premarket approval or clearance for that device type.".

FDA intends to consider a device to be in Category B if one or more of the following criteria are met:

- No PMA approval, 510(k) clearance or *de novo* request has been granted for the proposed device or similar devices; however, available clinical data (e.g., feasibility study data) and/or non-clinical data for the proposed device or a similar device resolve the initial questions of safety and effectiveness.

- The proposed device has similar characteristics compared to a legally marketed device, and information related to the marketed device resolves the initial questions of safety and effectiveness for the proposed device. Additional non-clinical and/or clinical data on the proposed device may have been used in conjunction with the leveraged[6] information to resolve these questions.

- The proposed device is being studied for a new indication or new intended use; however, information from the proposed or similar device related to the previous indication resolves the initial questions of safety and effectiveness. Additional non-clinical and/or clinical data on the proposed device may have been used in conjunction with the leveraged information to resolve these questions.

IV. Considerations When Changing from Category A to B

[6] For purposes of this draft guidance, the term "leveraged" means that data from the legally marketed device are relevant to the proposed device, were determined to be valid scientific evidence, and may be used to help resolve initial questions of safety and effectiveness.

As mentioned previously in this document, there are situations in which non-clinical and/or clinical evaluations provide adequate data to resolve initial questions of safety and effectiveness and, therefore, it is appropriate to change the device category for subsequent studies of the same device from Category A to Category B. For example, a categorization change may be justified when a completed study, in which the device was designated as Category A, has resulted in clinical data that resolve the initial questions of safety and effectiveness. In this case, the device may then be designated as Category B in the subsequent study.

Another situation where a category change may be warranted is when an IDE study receives a staged approval or staged approval with conditions.[7] In a staged approval, FDA may grant IDE approval or approval with conditions for a portion of the intended study cohort, enabling certain outstanding questions to be answered concurrently with enrollment in this cohort. The sponsor will be permitted to expand enrollment once an IDE supplement containing the necessary additional information is submitted to FDA and found to be acceptable. In some cases, the purpose of the initial stage of the clinical study is to resolve initial questions of safety and effectiveness. In this situation the device will be designated as Category A for the initial stage. If adequate data are gathered from the initial stage of the study such that the initial questions of safety and effectiveness have been resolved and the sponsor has been granted expanded enrollment, the category may be changed from Category A to Category B for the device in the expanded study.

FDA will evaluate whether adequate data are present to resolve the initial questions of safety and effectiveness and a categorization decision will be made upon study approval (for a new study), study expansion (for a staged study), or submission of a request to change the category. A request to change the category should be submitted as an IDE supplement. The categorization decision will be included in either the IDE approval letter to the sponsor or a letter to the sponsor in response to a request for category change.

V. Examples

Category A: Experimental

The list below provides examples of when a Category A determination may be appropriate, but it does not represent an exhaustive list of when a device should be classified as Category A.

- A device is completely novel and has no, or limited, previous human use and there are initial questions of safety and effectiveness. There is adequate non-clinical information to support initiation of an early feasibility study that will provide data to inform potential device design or procedural improvements.

- A drug is added to a previously approved or cleared device. While substantial information is known about the previously approved or cleared device, the addition of a

[7] See "FDA Decisions for Investigational Device Exemption Clinical Investigations."

drug has resulted in initial questions of safety and effectiveness that have not yet been resolved.

- An already approved or cleared device is being evaluated for a new intended use or indication wherein the device will be placed in a different anatomical location. The device's technology is unchanged from what was initially approved; however, it is uncertain as to whether the device can be safely placed in the new anatomical location and whether the device can also be effective in the new anatomical location. Therefore, there are inadequate data to resolve the initial questions of safety and effectiveness relative to the new intended use or indication.

- The initial question of safety has been answered with the submission of non-clinical and/or clinical data. There is inadequate evidence to resolve initial questions related to effectiveness; however, the benefit-risk profile supports initiation of a pivotal study.

Category B: Nonexperimental/Investigational

The list below provides examples of when a Category B determination may be appropriate, but it does not represent an exhaustive list of when a device should be classified as Category B.

- The insertion system of an approved device has been modified to improve ease of use for the clinician. Non-clinical test data resolved initial questions of safety and effectiveness related to this change; however, confirmatory clinical information about the device performance is required due to the inherent differences between the non-clinical test environment and the clinical setting. (The non-clinical data and a benefit-risk assessment support initiation of a small feasibility study to resolve this incremental risk and inform the final device design.)

- Adequate data have been gathered from non-clinical testing and the clinical results of a feasibility study such that initial questions of safety and effectiveness have been resolved. A pivotal study will be initiated to provide the primary clinical evidence for the safety and effectiveness of the device in support of a future marketing application.

- A range of device sizes will be included in a clinical study, but data that resolve initial questions of safety and effectiveness have been received on only a subset of the sizes. It is anticipated that the data for the other sizes will also resolve initial questions; therefore, the study will be staged. In this case, the study will start with the initially approved device sizes while additional supportive information is collected on the remaining device sizes. Because the initial questions of safety and effectiveness have been resolved for the initial stage and will be resolved for the additional device sizes prior to expansion of the study, the devices in both the initial stage and expanded study will be designated Category B.

- A new device will be studied for an indication for which substantial safety and effectiveness information exists from other similar device(s) of the same type that are used for the same or similar indication. Non-clinical test data that have been provided

can answer initial questions regarding the anticipated device performance relative to this indication. Because the initial questions of safety and effectiveness have been resolved, a pivotal study to evaluate this new device will be designated Category B.

- A modification has been made to an approved device in order to improve its performance. Non-clinical and clinical data available from the previous version of the device along with additional testing on the modified device resolved initial questions of safety and effectiveness. The purpose of the study will be to gather further data regarding device performance for this modified version of the device.

- New device sizes will be added to a product matrix for an approved device. Initial questions of safety and effectiveness have been resolved based on experience with the approved device, and it is generally understood how the new device sizes will perform. The new device sizes will be studied such that statistical information on safety and effectiveness relevant to these sizes can be gathered.

- An approved device will be evaluated in a new patient population. Non-clinical and clinical data from use in the previous patient population resolved initial questions of safety and effectiveness for the new patient population. The new study to be conducted will provide further data regarding device performance for this new patient population.

- An approved device will be evaluated for a new indication. Data exist on the approved device for another similar indication, and non-clinical data have also been supplied such that the initial questions of safety and effectiveness related to the new indication have been resolved. The new study to be conducted will provide further data regarding device performance for this new indication.

- A new device will be studied for an indication in which there are no other devices of a similar type. However, the non-clinical test data supplied are robust and resolve the initial questions of safety and effectiveness. The study to be conducted will provide further data regarding device performance for this indication.

Change from Category A to Category B

If the device was previously designated as Category A, but the initial questions of safety and effectiveness of the device have since been resolved, it may be appropriate to change the Category from A to B. The list below provides examples of when a change from Category A to Category B may be appropriate, but it does not represent an exhaustive list of when a device may change from Category A to Category B.

- A novel insertion procedure will be used to place an already approved or cleared device and there are initial questions of safety and effectiveness regarding the novel insertion procedure that have not been resolved. In this case, these questions of safety and effectiveness may be answered in a short time frame with a limited number of subjects in the context of a larger clinical study. Therefore, the device will be evaluated in a staged clinical study where the first stage falls under Category A. If the initial questions of

safety and effectiveness are resolved and the study continues, the device may be re-categorized to Category B.

- Adequate data have been gathered on a device from non-clinical testing, the completion of an early feasibility study within the United States (US), as well as a small non-US clinical study such that initial questions of safety and effectiveness have been resolved. Additional data are needed to help inform a pivotal study design; therefore, a traditional feasibility study will be initiated. Although the EFS was originally designated as Category A, adequate data as described above have since been gathered to support a change to Category B for the traditional feasibility study.

- A device is currently being evaluated in a clinical study and has been designated Category A. While the study is being conducted, clinical study results for comparable products became available which resolve initial questions of safety and effectiveness for the device. This information will be used to support a categorization change from Category A to Category B for the device evaluated in the ongoing clinical study.

VI. Conclusions

FDA categorizes IDE devices based on whether available data demonstrate that initial questions of safety and effectiveness have been resolved. This guidance document describes the criteria that will be used to help determine the appropriate category for a device to be studied. This guidance document also describes when it is appropriate to change the device category from Category A to Category B. The categorization of IDE devices is used by CMS as part of its determination of which devices meet the requirements for Medicare coverage under Section 1862 (a)(1)(A) of the Social Security Act (the "reasonable and necessary" clause). IDE device categorization is only part of the information used to determine coverage by CMS. Please refer to the website "Medicare Coverage Related to Investigational Device Exemption (IDE) Studies" for guidance on requesting coverage and for contact information.

VII. Appendix A: Category Decision Flowchart