Contains Nonbinding Recommendations

Bundling Multiple Devices or Multiple Indications in a Single Submission

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Guidance for Industry and Food and Drug Administration Staff

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This document supersedes Bundling Multiple Devices or Multiple Indications in a Single Submission issued November 26, 2003.

For questions about this document regarding CDRH-regulated devices, contact the 510(k) Program at (301) 796-5640, or by email to 510k_program@fda.hhs.gov. For devices reviewed by the Office of In Vitro Diagnostics and Radiological Health (OIR), contact DPOM at (301) 796-5640, or by email to 510k_program@fda.hhs.gov.

For questions about this document regarding CBER-regulated devices, contact the Office of Communication, Outreach, and Development (OCOD) at 1-800-835-4709 or 240-402-8010.

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

Public Comment

You may submit electronic comments and suggestions at any time for Agency consideration to http://www.regulations.gov . Submit written comments to the Dockets Management Staff, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD 20852. Identify all comments with the docket number FDA-2003-D-0376. Comments may not be acted upon by the Agency until the document is next revised or updated.

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CDRH

Additional copies are available from the Internet. You may also send an e-mail request to CDRH-Guidance@fda.hhs.gov to receive a copy of the guidance. Please use the document number 1215 to identify the guidance you are requesting.

CBER

Additional copies are available from the Center for Biologics Evaluation and Research (CBER), Office of Communication, Outreach, and Development (OCOD), 10903 New Hampshire Ave., WO71, Room 3128, Silver Spring, MD 20903, or by calling 1-800-835-4709 or 240-402-8010, by email, ocod@fda.hhs.gov, or from the Internet at http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

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Bundling Multiple Devices or Multiple Indications in a Single Submission

Guidance for Industry and Food and Drug Administration Staff

This guidance represents 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

A. Background

The Medical Device User Fee and Modernization Act of 2002 (MDUFMA), P.L. 107-250, amended the Federal Food, Drug, and Cosmetic Act (the act) by authorizing FDA to collect user fees for certain premarket submissions received on or after October 1, 2002. A letter from the Secretary of Health and Human Services to Congress that accompanies the user fee legislation sets forth performance goals and policy and procedural provisions. One of these provisions is entitled, "Bundling Policy," and states that FDA will consider, in consultation with its stakeholders, when bundling multiple devices in a single submission may be appropriate.

Prior to MDUFMA, submitting separate applications for devices that could have been bundled in a single submission, or bundling of devices that should have been submitted in separate applications, was primarily an administrative issue related to the efficiency of the review process. Under MDUFMA, bundling within a single premarket submission takes on additional importance because of the fees that are now associated with premarket submissions as well as the performance goals that the agency has committed to meet. This guidance is intended to assist industry and FDA staff in understanding when bundling may be appropriate. This guidance will be used by both the Center for Devices

and Radiological Health (CDRH) and the Center for Biologics Evaluation and Research (CBER) when reviewing bundled premarket submissions.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidance documents describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word should in Agency guidances means that something is suggested or recommended, but not required.

B. Consultation with Stakeholders

As discussed above, FDA has committed to considering the issue of bundling in consultation with its stakeholders. In developing this guidance, the Agency has considered comments on bundling that were submitted to the Public Docket on MDUFMA Implementation, Docket No. 02N-0534. FDA also received comments on the topic before and after issuing the guidance entitled, "Assessing User Fees: PMA Supplement Definitions, Modular PMA Fees, BLA and Efficacy Supplement Definitions, Bundling Multiple Devices in a Single Application, and Fees for Combination Products; Guidance for Industry and FDA."[1] In that guidance, FDA asked for comments on bundling in general as well as specific comments on the concepts presented in the document.

Most of the comments supported the concept of bundling, and some stakeholders provided examples of when bundling should be considered appropriate. FDA included many of these examples in this document. One stakeholder expressed concern that the practice of bundling was not well known and asked that the agency clearly identify "criteria" for both industry and FDA staff. The agency has attempted to be as specific as possible in defining when bundling should be appropriate. Because not all situations can be anticipated, there may be bundling issues that are not addressed in this guidance. Finally, one commentor was concerned that the misuse of bundling could lead to higher user fees in subsequent years. FDA believes that the concepts and examples of when bundling should be appropriate that are provided in this document will help to alleviate that concern.

The agency recognizes that bundling is a complicated topic and continues to invite comments. In addition, the agency intends to include "bundling" as a topic for discussion at future stakeholder meetings.

[1] This guidance can be found at https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089726.htm.

C. The Least Burdensome Approach

We believe we should consider the least burdensome approach in all areas of medical device regulation. This guidance reflects our careful review of the relevant scientific and legal requirements and what we believe is the least burdensome way for you to comply with those requirements. However, if you believe that an alternative approach would be less burdensome, please contact us so we can consider your point of view. You may send your written comments to the contact person listed in the preface to this guidance or to the CDRH or CBER Ombudsman. Comprehensive information on CDRH's Ombudsman, including ways to contact him, can be found on the Internet at https://www.fda.gov/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cdrh/cdrhombudsman/default.htm. CBER's Ombudsman can be reached at (301) 827-0379.

II. Frequently Asked Questions on Bundling of Multiple Devices or Multiple Indications in a Single Submission

A. Overview of Bundling

(1) What is "bundling"?

Bundling refers to the inclusion of multiple devices or multiple indications for use for a device in a single premarket submission, including products subject to the device and biologics license application (BLA) authorities, for purposes of review and user fee payment. In CBER, the term may also include the designation of separate submissions as one premarket submission for review and user fee payment. Multiple devices may include different models within a generic type of device[2] or devices that are of differing generic types.

Under current review practices, CDRH and CBER have accepted submissions in which multiple devices or indications for use were bundled when the devices or indications presented issues that could be addressed during one review.[3] An applicant is not required to bundle multiple devices or indications, but may choose to do so when

[2] Generic type of device is defined in 21 CFR § 860.3(i) as "a grouping of devices that do not differ significantly in purpose, design, materials, energy source, function, or any other feature related to safety and effectiveness, and for which similar regulatory controls are sufficient to provide reasonable assurance of safety and effectiveness."

[3] The classification letter for a bundled submission generally will identify the classification regulation for the device with the highest regulatory class within the bundle (e.g., if the submission bundles a Class I device and a Class II device, the letter will refer to the Class II classification). This letter does not impose any additional regulatory requirements on devices within the bundle beyond those associated with their individual classification. Unless devices within the bundle are subject to their own classification regulations, they are subject to the regulatory requirements applicable to the device with which they are intended to be used.

appropriate. Each device or indication in a bundled submission must satisfy the applicable statutory and regulatory premarket requirements.

Prior to MDUFMA, bundling was primarily an administrative issue. The Agency's primary consideration in determining what devices, or indications for use, could be bundled in one premarket submission was the Agency's ability to conduct efficient reviews and render timely decisions. The total review time for an application in which multiple devices presenting disparate scientific and regulatory issues were bundled was determined by the device that took the longest time to review.

(2) What effect does MDUFMA have on bundling?

Under MDUFMA, bundling within a single premarket submission takes on additional importance because of the fees[4] that are now associated with certain submissions as well as the performance goals that the agency has committed to meet.[5] According to the new law, there is one user fee per submission. In addition, as specified in the Secretary's letter to Congress, the agency has committed to improving its premarket review times by meeting both cycle and decision goals for 510(k)s and PMAs. Thus, if devices or indications for use are bundled when they should have been submitted in separate applications, the user fee revenues for that year will be affected and subsequent fees for all regulatory submissions
may require adjustment. Premarket review times may also suffer if devices or indications are bundled inappropriately.

Appropriate bundling, however, will help ensure that user fees revenues are not adversely affected and that the agency meets its cycle and decision goals. The agency is providing this guidance to help its own staff and industry determine when it may be appropriate to bundle multiple devices or indications for use in a single submission.

(3) What are the general bundling principles applicants should follow?

The general principles are:

- Bundling is appropriate for devices that present scientific and regulatory issues that can most efficiently be addressed during one review. In determining whether it can review a bundled submission during the course of one review, FDA may consider whether: (i) the supporting data are similar; (ii) primarily one review division/group will be involved; and (iii) the devices or indications for use are similar.

[4] For fiscal year 2004, see http://www.fda.gov/OHRMS/DOCKETS/98fr/03-19655.htm or http://www.fda.gov/OHRMS/DOCKETS/98fr/03-19655.pdf.
[5] The performance goals can be found at https://www.fda.gov/forindustry/userfees/medicaldeviceuserfee/default.htm.

- FDA should not "cull out" a device or an indication for use from a premarket submission for the purpose of collecting additional user fees.

- Applicants should not inappropriately combine devices in a premarket submission for the purpose of avoiding user fees.

B. Bundling of Specific Types of Devices or Indications for Use

(4) Can I bundle multiple devices within a generic device type in a single510(k) or PMA submission?

You generally may bundle multiple devices within the same generic device type for both 510(k)s and PMAs. You should consider whether the devices have similar indications, rely on similar data, and/or whether primarily one review division/group will review the devices. If the devices have these characteristics in common, bundling is typically appropriate.

Examples include:

- Bundling of catheters or single lumen hypodermic needles with various dimensions and configurations in a single 510(k) submission.

- Bundling of soft contact lenses of various materials and lens designs in a single 510(k) submission when the lens designs and indications for use of each lens material are generally the same. (This example may also illustrate the bundling of "changes" discussed following question 10 below.)

- Bundling of class I (or II) spinal implants made of multiple metallic alloys (stainless steel and titanium versions) into one 510(k) submission, if the indications for use are generally the same for the two materials.

- Bundling of several sizes of aortic heart valves in a single PMA submission.

(5) Can I bundle differing generic device types in a single 510(k) submission?

In some cases, you may bundle differing generic device types in a single 510(k) submission. In determining whether bundling differing generic device types in a single 510(k) is appropriate, you should consider the general principles outlined above and also whether the bundled devices are used together during a therapeutic or diagnostic

procedure. You generally may bundle the devices if one device is an accessory to another. Examples of differing generic device types that may be bundled include a device with its ancillary components or peripherals, and devices generally included in convenience kits and device systems.

(6) Can I bundle differing generic device types in a single PMA submission?

Generally, you should not bundle differing generic device types in a single PMA submission because of the substantially different pre-clinical and clinical data needed to support each of the devices.

(7) Can I bundle multiple indications for use for a device in one 510(k)?

In many cases, you may bundle multiple related indications for use in a single 510(k) submission. An example is a spinal implant system intended for both anterior and posterior spinal fixation for fracture, scoliosis, tumor, and grade 3 and 4 spondylolisthesis.

If one of the indications for use is new (i.e., a use that has not been cleared), the applicant should consider submitting a separate 510(k) for the new use because it will likely include clinical data and the review may take longer than the review for the other indications for use. Additionally, devices with different indications for use in multiple medical specialties, which would require reviews by different divisions, should have separate submissions.

(8) Can I bundle multiple indications for use for a device in one PMA?

You generally should not bundle multiple indications for use in one PMA because each indication is usually supported by a clinical study that requires significant review resources. Bundling multiple indications in one PMA might be appropriate, however, if much of the data needed to support approval of the indications would be the same (e.g., the same clinical data). For example, CDRH has permitted bundling of multiple indications for use in a single PMA for cardiac ablation catheters when all the indications were supported by the same clinical data.[6]

[6] Please refer to the guidance entitled, "Cardiac Ablation Catheters Generic Arrhythmia Indications for Use; Guidance for Industry," which may be found on CDRH's website at: https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm072860.htm.

(9) Can I bundle a 510(k) device with a PMA device in a single submission?

You generally should not bundle PMA and 510(k) devices in a PMA. There are some exceptions, however, for devices that are used together in a single procedure or that are part of a system. In those instances, bundling the PMA and 510(k) devices in a single PMA submission might be appropriate. For instance, if a Class II special surgical instrument is used to implant a Class III device subject to premarket approval, such as a pacing lead, it may be appropriate to bundle both devices in a PMA. Additionally, a digital mammography system is frequently bundled with its printer. If a 510(k) device and a PMA device are bundled in a single submission, the PMA user fee and review timeframe will apply.

(10) Can I bundle changes that affect multiple devices of the same or differing generic types?

You may submit one application when a change affects multiple devices of the same or differing generic types if the impact of the change on each of the devices can be efficiently assessed during one review. You should consider the complexity of device design, technological characteristics, and the modifications/changes being made to the existing devices.

Examples of when bundling might be appropriate for changes affecting multiple devices of the same generic type include:

- Bundling a change from one polyethelene (material) in various hip acetabular cups to another highly crosslinked polyethelene (material) in a single 510(k) submission.

- Bundling when a contact lens manufacturer proposes the addition of a color additive to a line of its contact lenses (i.e., lenses of differing materials and/or configurations), where the color additive has been listed or certified for that use.

- Bundling a change to a pacemaker programmer where the programmer is used for several types of pacemakers. Even though the change would affect several PMAs, only one PMA submission need be made.

Examples of when bundling might be appropriate for changes affecting multiple devices of
differing generic types include:

- Bundling in a single 510(k) submission a change that involves the addition of a heparin coating to various cardiopulmonary bypass devices, such as an arterial line blood filter and pump tubing.

- Bundling in a single PMA submission changes that involve a manufacturing facility or a manufacturing process where the same equipment and closely related processes are used for all the devices in the submission. For example, if a manufacturer makes a material for two products using the same equipment and closely related processes, one PMA supplement may be submitted in support of the process change affecting both products.

- Bundling in a single PMA submission changes in sterilization (e.g., a change from ethylene oxide sterilization to radiation sterilization or a change in sterilization release method), where the scientific evidence provided is valid for all devices referenced.

- Bundling certain labeling changes in either a 510(k) or PMA submission. For example, a labeling change to multiple devices of differing generic types may be bundled in a single 510(k) or PMA submission when the labeling change involves a change to the packaging of the devices, such as new instructions for opening the package.

A change that affects multiple devices that are reviewed by different divisions may be appropriate for bundling if the change can be reviewed during one review. For example, a software change to a stimulator that has gastric and neural indications could be bundled even though the original PMAs were reviewed by different divisions.

Finally, there are some instances when you may bundle a change that affects a device that has both a 510(k) and a PMA indication. For example, it may be appropriate to bundle a software change to a lithotripter that has a 510(k) indication (kidney stones) and a PMA indication (tennis elbow) if the change can be assessed during one review.

(11) Can I bundle reprocessed single-use devices (SUDs) in a single submission?

MDUFMA amended the act to provide new regulatory requirements for reprocessed SUDs
(MDUFMA § 302). One of these requirements is the submission of validation data in 510(k)s for certain reprocessed SUDs. The validation data submitted must demonstrate that these SUDs will remain substantially equivalent to their predicate devices after the maximum number of times the device is reprocessed as intended by the person submitting the
premarket notification (MDUFMA § 302(b), the act § 510(o)). The validation data to be submitted include cleaning, sterilization, and functional performance data.

Although some aspects of the validation process may be common to various reprocessed SUDs (e.g., SUDs of the same generic type), the designs of these SUDs may be unique (e.g., different original equipment manufacturers (OEMs)). If the SUDs are within the same generic type and have the same OEM, the validation data may apply equally to each of the SUDs, and a single 510(k) would likely be appropriate. If the SUDs were produced by different OEMs, however, the reprocessor should explain how the submitted

data apply to all the devices in the submission and only bundle those SUDs that can be reviewed together.

In addition, reprocessors generally should not bundle differing generic device types in one submission because different data requirements will typically apply. For example, a reprocessor should not bundle catheters and compression limb sleeves in a single 510(k).

For additional information on MDUFMA's validation data requirements for reprocessed SUDs requiring 510(k) clearance, please refer to the guidance entitled, "Medical Device User Fee and Modernization Act of 2002, Validation Data in Premarket Notification Submissions [510(k)s] for Reprocessed Single-Use Medical Devices."[7]

MDUFMA also requires the submission of validation data for reprocessed SUDs subject to PMA requirements. The data must demonstrate that the reasonable assurance of the safety and effectiveness of the reprocessed SUD will remain after the maximum number of times the device is reprocessed as intended by the person making the premarket submission
(MDUFMA § 302(c)(2)), the act § 515(c)(2)). The validation data and other data required to support the premarket submission or, in this case, a "premarket report," requires significant review. Thus, it may be inappropriate to bundle reprocessed SUDs across multiple OEMs because the design, etc., of each of the SUDs may be unique and require significant review resources. If, however, multiple individual submissions would contain substantially the same pre-clinical and clinical information, then it may be appropriate to submit a single premarket report for these reprocessed SUDs across multiple OEMs. The reprocessor may contact the relevant review division to discuss whether bundling in a specific situation might be appropriate.

B. In Vitro Diagnostic Devices

(12) Are there specific considerations for in vitro diagnostic devices?

Yes. For in vitro diagnostic devices, FDA recommends that you consider the points below. If, after reading this guidance, you are still unsure as to whether it is appropriate to bundle, we encourage you to discuss the issue with the responsible review division.

Multiple Analytes

You generally may bundle in a single submission multiple analytes or instruments when the same analytical and clinical data can be used for all the analytes/instruments

[7] This guidance may be found on CDRH's website at: https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm071434.htm

referenced. You should not bundle multiple analytes, or across test panels or profiles, if they present disparate scientific and clinical issues.

Examples of panels that could be bundled into one submission include:

(1) Certain population specific respiratory viruses measured simultaneously in one system (e.g., Flu A/B and RSV)

(2) Drugs of abuse (cocaine, THC, opiates, methamphetamine, and amphetamine) panel

Submissions for antimicrobial susceptibility testing (AST) systems should include only one drug, and one method of reading or inoculation. However, you may bundle gram-negative and gram positive claims (if the same methods of reading and inoculation are used for both).

For any type of premarket submission, assayed controls and/or calibrators may be bundled with an assay. Also, controls or calibrators used for multiple assays (and/or multiple platforms) may be bundled to cover their use in all of the assays.

Multiple Reagents

You may bundle multiple reagents that are intended to be used together to obtain a profile (e.g., to obtain a donor or patient blood group phenotype, or a cardiac panel (troponin, CK MB, and myoglobin)) into a single submission. Whereas a single reagent could be submitted as a single submission, there are situations where multiple reagents have many commonalities, and the additional information to support each of the reagents is minor and does not require substantial review resources. These multiple reagents may be bundled. Reagents generally should not be bundled if the reagents require separate preclinical data, clinical data, or separate statistical analyses of such data sets that would preclude efficient review of the submission. Although CBER accepts separate submissions for individual reagents, CBER would consider the applicant's designation of these separate submissions meeting the above criteria as a bundle for purposes of review and user fee payment.

Multiple Intended Uses

You generally should not bundle multiple intended uses of a single test system (or indications for use such as professional and over-the-counter (OTC) use), because it is unlikely that such multiple uses would be supported by the same data sets.

There may be cases, however, when you could bundle different intended uses. For example, you may not bundle assays intended for the detection of Neisseria menigitidis, and Neisseria gonorrhoea, but you may bundle a combination assay in which N. gonorrhoea and Chlamydia trachomatis are measured in a single reaction and when the same clinical trial using the same specimen type and same population are used.

Sample Matrix

Bundling when similar matrices (e.g., serum and plasma) are used generally should be appropriate. You should not bundle dissimilar sample matrices (e.g., hair and/or saliva with serum and/or plasma), because the information for review would be expected to be substantially different. For example, a Helicobacter pylori assay indicated for use with serum, plasma, and/or finger-stick capillary blood may be bundled. However, a H. pylori breath test, a saliva test, or a stool antigen may not be bundled with a H. pylori assay using plasma or serum.

Replacement Reagent

The replacement reagent policy entitled, "Data for Commercialization of Original Equipment Manufacturer, Secondary and Generic Reagents for Automatic Analyzers" (see www.fda.gov/cdrh/ode/odecl950.html) will continue to apply and those associated changes may be made without incurring a fee.

In Vitro Diagnostic Devices Regulated by CBER

As with devices reviewed by CDRH, some devices reviewed at CBER are marketed as 510(k) products, while others are marketed as PMA products. These products are subject to the procedures discussed in this document. Instruments used to test the blood supply are regulated as either 510(k) devices or PMA devices. Reagents and test kits used to test the blood supply are regulated as licensed biological products. When the reagents and instruments can be used together and significant portions of multiple individual submissions would contain the same information, you may bundle the submission for the different articles, even though one article is regulated under the device authorities and the other under the BLA authorities. The BLA user fee and review time would apply when making such a submission. Please identify the submissions to be bundled in the cover letter submitted with the applications.

In cases involving a BLA or efficacy supplement where one submission in a bundle is delaying approval of the others, CBER may discuss mechanisms for "de-linking" the problem submission so that the others can be finalized. The remaining portion of the bundle would be handled at a later date and the labeling would be revised to include the additional reagent. These cases primarily involve immunohematology reagents. For example, ABO/Rh blood grouping reagents that use the same clinical data set and the same labeling can be considered for bundling. If the ABO reagents are ready for approval, but the Anti-D reagent has a few issues remaining, CBER would consider allowing the applicant to revise the labeling to delete the references to Anti-D and approve only the ABO reagents. Upon subsequent approval of the Anti-D reagent, the labeling could be revised to include the references to Anti-D.

C. Bundling Procedures

(13) How do I bundle multiple devices or indications for use in a single submission?

FDA recommends the following when:

- **Bundling in a 510(k) the same or differing generic device types or multiple indications for use for a single device**

As is true for any 510(k), you must provide all the information required by 21 CFR § 807.87. Therefore, the submission should include the appropriate supporting information for each of the different devices or indications for use. You should also include an "Indications for Use" form for each device in the submission, if individual devices will have differing indications for use.

- **Bundling in one 510(k) a change that affects more than one previously cleared device**

When submitting one 510(k) for a change that affects multiple devices, you should refer to the other previously cleared 510(k)s. Like all 510(k)s, the 510(k) must provide all the information required under 21 CFR § 807.87. You should also provide updated Indications for Use forms that address all the devices in the submission, if individual devices will have differing indications for use.

- **Bundling in one PMA multiple devices of the same generic device type or multiple indications for use for a single device**

When bundling devices of the same generic type in a PMA, you should ensure that you provide all the information required by 21 CFR § 814.20 to support approval for each of the devices, including labeling that addresses all of the devices.

As stated earlier in this guidance, bundling multiple indications for use in one PMA is generally not appropriate. If, however, much of the data needed to support approval of the devices would be the same (e.g., clinical data), you may submit one PMA for multiple indications. You should ensure that the supporting information and the labeling address all the indications.

- **Bundling in one PMA supplement a change that affects multiple PMAs**

When bundling a change(s) that affects more than one PMA, you may submit all the required information to support approval of the modification, including any associated labeling changes that result from the modification, in one PMA supplement. In the cover letter for the supplement, you should identify the other affected PMA(s).

If the affected PMAs are reviewed by different divisions, you may still be able to bundle the change(s) in one PMA supplement. In this situation, you should submit a complete

copy of the supplement to each PMA, so that each division has its own copy. The same cover letter should be used for each copy and should clearly indicate that the same change(s) is being made to each of the affected PMA(s). The cover letter should identify all of the affected PMA(s).

- **Bundling a change that affects a device with 510(k) and PMA indications**

When submitting a change to a device that affects both a previously cleared 510(k) and an approved PMA, you should submit a PMA supplement and reference the cleared 510(k). In this situation, the PMA review time and user fee would apply for the submission.

- **Bundling a 510(k) device and a PMA device in one PMA**

As stated above, in general, a 510(k) device should not be bundled with a PMA device. If, however, you have devices that are used together in a procedure or that are part of a system, bundling may be appropriate. In such a case, the PMA should include all the information needed to support both approval and clearance of the devices when used as indicated. As above, the PMA review time and user fee would apply for the submission.

(14) What will FDA do if devices or indications are bundled inappropriately?

If a submission includes a device or indication that should not be bundled because it presents disparate scientific/clinical or regulatory issues (from the other devices or indications in the submission), the agency will notify the applicant in writing and request that the applicant withdraw the device or indication from the bundled submission. Upon issuance of this letter, the application will be placed on hold. The applicant may resubmit the device or indication for use in a separate submission, withdraw the device or indication for use (the review of the rest of the submission will continue), withdraw the entire application, or appeal the decision. See related information in question 15.

(15) How can I appeal an FDA determination that it is not appropriate to bundle a device or indication for use in a single application?

You should refer to 21 CFR § 10.75, which outlines the framework for internal review of decisions. Additionally, FDA intends to provide specific recommendations and procedures regarding appeals related to user fees in a future guidance document. While the appeal is under review, the submission will remain on hold (to ensure appropriate review of the submission and efficient use of resources).

(16) Can I add more devices or indications for use to a submission once the review of that submission has begun?

FDA strongly recommends that bundling occur before the application is submitted to the agency.

(17) Can I withdraw a device or indication for use from my premarket submission, for example, because the review of that device or indication for use is slowing down the review of the others?

Yes. Submitters may withdraw a device(s) (or indication for use) from a bundled submission for any reason. You may resubmit the device(s) or indication for use in a new application. Resubmission of a premarket submission for a withdrawn device or indication for use will require payment of the fee applicable to the type of submission.

(18) How can I get information on the appropriateness of bundling certain devices or indications for use before submitting a marketing application?

The persons listed below can assist you with general bundling questions. For specific questions about bundling certain types of devices or indications for use, you should contact the branch chief in the appropriate review division.

Program Operations Staff
ODE/OIR, CDRH
(301) 796-5640or by email: 510k_program@fda.hhs.gov

For devices reviewed by CBER, contact the Office of Communication, Outreach and Development at 1-800-335-4709 or 240-402-8010