1200 G Street NW, Suite 400
Washington, DC 20005-3814
Tel. 202 783 8700
Fax: 202 783 8750
www.AdvaMed.org

AdvaMed
Advanced Medical Technology Association

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Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. 02N-0445—FDA Regulation of Combination Products

Dear Sir or Madam:

AdvaMed respectfully submits these comments to the Food and Drug Administration ("FDA") in response to an October 28, 2002 *Federal Register* notice requesting comments on the assignment, premarket review, and postmarket regulation of combination products.[1/] These comments incorporate and supplement AdvaMed's oral testimony at FDA's November 25, 2002 public hearing to discuss issues important to the future regulation of combination products.

AdvaMed, the Advanced Medical Technology Association, represents more than 1,100 innovators and manufacturers of medical devices, diagnostic products and medical information systems. Its members produce nearly 90 percent of the $68 billion in health technology products consumed yearly in the United States and nearly 50 percent of the $159 billion purchased around the world annually. AdvaMed's members develop these innovative combination technologies and therefore FDA's regulation of combination products is important to AdvaMed members, particularly small companies, whose efforts may not come to fruition if subjected to onerous regulation.

In the October 28 notice, the FDA raised several questions concerning the assignment, premarket review, and postmarket regulation of combination products, intended to assist the Agency in improving the regulation of this category of products. Provided below are AdvaMed's responses and recommendations to each of those questions.

1/ 67 *Fed. Reg.* 65801 (Oct. 28, 2002).

I. Question 1: What types of guiding scientific and policy principles should FDA use in its revisions to the existing Intercenter Agreements that allocate review responsibility for human medical products?

Question 2: What factors should FDA consider in determining the primary mode of action of a combination product? In instances where the primary mode of action of the combination product cannot be determined with certainty, what other factors should the agency consider in assigning primary jurisdiction? Is there a hierarchy among these additional factors that should be considered in order to ensure adequate review and regulation (e.g., which component presents greater safety questions)?

A. Any Interpretation of Primary Mode of Action Must Be Consistent with the Federal Food, Drug, and Cosmetic Act, FDA Regulations, FDA Policy Pronouncements, and Precedents

The FDA has grouped questions 1 and 2 in its notice, and, in turn, AdvaMed has consolidated its responses to these two questions, which it believes are interrelated. Assignment of review responsibility under the Intercenter Agreements is based on a product's primary mode of action, as prescribed by the Federal Food, Drug, and Cosmetic Act ("FFDCA"), and FDA's consistent application of that law over many years. While scientific and policy factors properly play a role in jurisdictional deliberations, these factors must be applied within the context of statutory instruction.

The FFDCA directs the analysis to the composite product, by requiring the FDA to "determine the primary mode of action of the combination product."[2/] FDA regulations and policy documents similarly focus on the action of the combined product.[3/] From this statutory mandate and over a decade of Agency application of this law, two fundamental interpretational standards have emerged. First, it is clear from FDA's policy pronouncements and precedents that the Agency looks to the combined product (i.e., the product as a whole and not the relative contribution of each constituent component, as suggested in a May 2002 *Federal Register*

2/ Section 503(g) of the FFDCA, 21 U.S.C. § 353(g) (emphasis added). Neither the legislative history of this provision, enacted as part of the Safe Medical Devices Act of 1990, nor any other provision of the FFDCA, provides any additional explanation or discussion of "primary mode of action."

3/ See 21 C.F.R. § 3.4 ("the agency shall determine the primary mode of action of the product") (emphasis added); 56 *Fed Reg.* 58754, 58754 (Nov. 21, 1991) ("[t]he designation is to be made based upon a determination of the 'primary mode of action' of the combination product") (emphasis added).

notice[4/]), to assess the primary mode of action. Second, FDA guidance and precedents also establish that the term "mode of action" has been interpreted not as "mechanism of action," but, rather, as the primary intended function of the combined product. The Intercenter Agreements, which have been in use for over a decade, also direct industry to look to the intended function of the combined product. The Intercenter Agreement between the Center for Drug Evaluation and Research ("CDER") and the Center for Devices and Radiological Health ("CDRH"), for example, states that "[a]n implant, including an injectable material placed in the body for primarily a structural purpose[,] even though such an implant may be absorbed or metabolized by the body after it has achieved its primary purpose[ ] will be regulated as a device by [the Center for Devices and Radiological Health] CDRH."[5/] The Center for Biologics Evaluation and Research ("CBER") similarly has employed this "primary function" approach to interpreting "primary mode of action" in its policy documents, stating that tissue-based products that have a "physical action," whether it is diagnostic or therapeutic, "are regulated as devices by CDRH."[6/]

Agency precedents likewise provide clear and consistent guidance on the FDA's historical interpretation of "primary mode of action." As recommended by a former Counsel to CDER and speaker at the November 25, 2002 public hearing, AdvaMed believes the Agency should review and consider the large body of prior decisions on "primary mode of action," in order to "articulate the principles that drove those decisions."[7/] A review of these precedents confirms that: (1) FDA consistently has interpreted "primary mode of action" based on primary intended function of the combined product; and (2) combination products that have primarily a structural, physical, repair, or reconstruction purpose, have been regulated by CDRH under device authorities. Examples include: drug-eluting stents; antibiotic-filled cement; spinal fusion products containing biomaterials; skin replacement products containing extracellular components; surgical or barrier drapes coated or impregnated with antimicrobial drugs; cardiac pacemaker leads with steroid-coated tips; condoms, diaphragms, or cervical caps with contraceptives or antimicrobial (including virucidal) agents; percutaneous cuffs (e.g., for catheter or orthopedic pins) coated/impregnated with antimicrobial agents; urinary and vascular catheters coated/impregnated with antimicrobial agents; dental prophylaxis pastes with drug components; and dental devices containing fluoride.

B. Any Change in FDA's Historical Interpretation or Application of its Laws and Regulations Requires Notice-and-Comment Rulemaking

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4/ See 67 *Fed. Reg.* 34722, 34722 ("[I]n order to determine a combination product's primary mode of action the agency must be able to identify how the product acts on the body and . . . determine the relative contribution of each of its component parts.")

5/ FDA, Intercenter Agreement between the Center for Drug Evaluation and the Center for Devices and Radiological Health (Oct. 31, 1991)(emphasis added).

6/ FDA, Proposed Approach to Regulation of Cellular and Tissue-Based Products (Feb. 28, 1997).

7/ See Presentation by David Fox, Esq., Hogan & Hartson, LLP, FDA Public Hearing on: FDA Regulation of Combination Products (Nov. 25, 2002).

A number of recommendations were provided at FDA's November 25 public hearing and in written comments to the Agency regarding the criteria that should apply in determining "primary mode of action" of a combination product. The recommended criteria included: (1) method of use (e.g., how product is used by a surgeon); (2) whether the product has a local, regional, or systemic effect; (3) which component of the product presents the greatest risk (e.g., the drug or the device component); (4) primary mode of therapeutic action; (5) whether one component serves only as a vehicle to deliver a therapeutic; (6) where "like" products are regulated; (7) what feature of the product predominates or represents the innovation; and (8) which Center has the best clinical skills and expertise to assist sponsor with clinical trial design issues.

These proposals, as applied, provide a reasonable basis for determining which Center should review a combination product, only to the extent that they are consistent with the statutory mandate. New legislation would be required, for example, if the Agency determined to implement criteria that effectively displace the "primary mode of action" standard. AdvaMed notes in this regard that Congress does not support such legislative change. As the Agency is aware, under Section 204 of the Medical Device User Fee and Modernization Act ("MDUFMA"), Congress called for the existing standard of assigning jurisdiction of combination products to be maintained.[8/]

Further, even when new refinements to criteria for determining "primary mode of action" are not seen as inconsistent, and, thus, requiring new legislation, any new interpretation of the statutory and regulatory standard that represents a substantive change from past practices must be implemented consistent with administrative law principles. For example, to the extent that any new interpretation of "primary mode of action" would cause a shift in jurisdiction for certain combination products, such a change would have the force and effect of a substantive rule, requiring formal notice-and-comment rulemaking.[9/]

Pursuant to administrative law precedents and principles, any significant change in an agency's historical interpretation of its regulations that has been relied upon by the regulated industry, must proceed through notice-and-comment rulemaking, particularly where the change could have a substantial impact on such industry. Several federal cases decided over the last few years uphold this principle. In 1999, the U.S. Court of Appeals for the D.C. Circuit held that, "[w]hen an agency has given its regulation a definitive interpretation, and later significantly revises that interpretation, the agency has in effect amended its rule, something it may not accomplish

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8/ See H.R. Rep. No. 107-728, at 39 (2002). This legislative report on the recently enacted Medical Device User Fee and Modernization Act ("MDUFMA") (which included provisions establishing the new Office of Combination Products) states that "[t]he existing criteria in 503(g)(1) for determining a product's primary mode of action and assigning a product to an agency center with primary jurisdiction shall apply."

9/ 5 U.S.C. § 553.

without notice-and-comment.[10/] A similar conclusion was reached by the Court of Appeals for the Fifth Circuit, which held that the Department of Interior's attempt to change its interpretation of its regulation on use of FERC tariff rates in a policy letter, must proceed through notice-and-comment rulemaking.[11/] Although, in that case, the initial Department action was simply an interpretive policy, the subsequent change in interpretation was deemed "a new substantive rule . . . [that] the agency is obliged, under the APA, to submit for notice and comment."[12/]

An important and central theme to these rulings is the courts' concern with the substantial effect that a change in interpretation would have on the regulated industry.[13/] This also is AdvaMed's primary concern with any new or revised interpretation of "primary mode of action." Companies with combination products regulated as devices based on the two interpretive factors—primary intended function and composite product—have oriented their operations around this historical system for classification. Any change in this system that could result in a shift in jurisdiction for certain FDA-regulated products (e.g., from CDRH to CDER or CBER), would have a substantial impact on affected companies. Companies typically orient their systems, personnel, development strategies, compliance programs, and marketing apparatus, based on their products' regulatory classification, and any change in that status could require a substantial investment of funds to reorient, and, more fundamentally, could change these companies' entire structure and framework for doing business. Speakers at both the June 24 public hearing on tissue-based cellular wound products and the November 25 public hearing on combination products stated that such a reorientation could have profound adverse consequences for small, start-up companies.[14/]

Another theme that emerges from these cases is that courts have not required that an agency's initial interpretation of its regulation be in the form of a written document, in order for it to be

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10/ Alaska Professional Hunters Association v. Federal Aviation Administration, 177 F.3d 1030, 1034 (D.C. Cir. 1999). See also Paralyzed Veterans of America v. D.C. Arena, 117 F.3d 579, 586 (D.C. Cir. 1997) (stating that "[o]nce an agency gives its regulation an interpretation, it can only change that interpretation as it would formally modify the regulation itself: through the process of notice and comment rulemaking").

11/ Shell Offshore Inc. v. Babbitt, 238 F.3d 622, 630 (5th Cir. 2001).

12/ Id.

13/ See Shell Offshore Inc. v. Babbitt, 238 F.3d 622, 630 (5th Cir. 2001) (noting that the departure from the Department's long practice "substantially affected the regulated industry"); National Family Planning and Reproductive Health Association v. Sullivan, 979 F.2d 227 (D.C. Cir. 1992) (concluding that an agency action is a "substantive rule," if it does not merely interpret a regulation, but "produces . . . significant effects on private interests").

14/ See Presentation by Barbara D. Boyan, Ph.D., American Academy of Orthopaedic Surgeons, FDA Public Hearing on: FDA Regulation of Combination Products (Nov. 25, 2002); Presentation by Ron Warren, then Executive Director of Regulatory Affairs, Advanced Tissue Sciences, FDA Public Hearing on: Combination Products Containing Live Cellular Components (June 24, 2002).

considered definitive.[15/] In this case, the Agency's interpretation of "primary mode of action" has been illustrated in multiple forms: written guidance, policy documents, and precedent decisions. Thus, the Agency has established a definitive interpretation of "primary mode of action" by its actions as well as its written documents.

Thus, given the substantial consequences to its members from any reinterpretation, and because clear and consistent interpretations have been relied upon over the years, AdvaMed believes that formal notice-and-comment processes are legally required, if FDA is interested in further defining or clarifying the primary mode of action standard.[16/]

C. Equitable Factors To Be Considered in Determining "Primary Mode of Action"

As a related question, the Agency has asked what factors should be considered in assigning primary jurisdiction, in instances where the "primary mode of action" of a combination cannot be, or is not easily, determined. AdvaMed recommends that, in such cases, the Agency give significant consideration to whether the same product is already approved or cleared by a particular Center for a different use. Consistency of regulation with respect to product development strategies, and premarket development and testing programs, is important to all companies, and can be critical to many small companies. Development and maintenance of multiple premarket review systems for the same core technology, requires a substantial investment of additional resources, time, and personnel, that will hinder future product development for many companies, and could be so burdensome as to destroy core businesses for others.[17/]

The theme of fostering technologies and public health advancements also should be considered. Many combinations currently regulated as devices represent important improvements in patient care. These products have benefited from regulatory mechanisms unique to the device premarket review structure, including early collaboration meetings, 100-day meetings, and modular reviews (mechanisms available to each and every Class III product); least burdensome review principles;

15/ See Alaska Professional Hunters Association v. Federal Aviation Administration, 177 F.3d 1030, 1034-35 (D.C. Cir. 1999); Shell Offshore Inc. v. Babbitt, 238 F.3d 622, 630 (5th Cir. 2001). Alaska Professional Hunters involved reliance of Alaskan guide pilots on verbal advice given by the FAA's Alaska Region over a number of years, that certain regulations dealing with commercial pilots did not govern the guide pilots.

16/ The new legislation provides certain specified procedures for revising agreements, guidances, and practices, but those specified procedures are to be used in the context of ensuring consistency with the requirements of new Subsection 503(g)(4). "Primary mode of action" authority is separately addressed under Section 503(g)(1). Consequently, Subsection 503(g)(4) has no relation to, and does nothing to alter, FDA's notice-and-comment requirements for further defining or clarifying "primary mode of action."

17/ See Presentation of Barbara D. Boyan, Ph.D., American Academy of Orthopaedic Surgeons, FDA Public Hearing on: FDA Regulation of Combination Products (Nov. 25, 2002) (noting that two companies facing a changing set of regulatory requirements recently filed for bankruptcy).

and humanitarian device exemption ("HDE") initiatives. Tissue-engineered skin replacement products, for example, have been granted humanitarian device approval for the treatment of epidermolysis bullosis, a rare skin disorder that can cause hand and other deformities. Additionally, a bone graft substitute containing a bone morphogenetic protein has been granted humanitarian device approval as an alternative to autograft in recalcitrant long bone nonunions. This HDE authority, which allows marketing of certain devices intended for rare conditions based primarily on safety data, is unique to device law.[18/] AdvaMed believes that the HDE and other device initiatives have had an important and positive effect on product innovation and the advancement of public health, without any adverse impact on safety. Accordingly, in those instances where "primary mode of action" is otherwise unclear, and companies believe that a device assignment would serve to foster and advance their technologies, deference should be given to this important principle.[19/]

II. Question 3: What are the general scientific and policy principles that should be followed in selecting the premarket regulatory authorities to be applied to combination products? Is one premarket mechanism (e.g., premarket approval (PMA), premarket notification (510(k)), new drug application (NDA), or biologic licensing application (BLA)) more suitable than another for regulating combination products?

The FDA's October 28, 2002 *Federal Register* notice states that, while the FFDCA requires that "the primary mode of action determine which FDA center would be responsible for premarket review," the Act does not address which authorities should be used to review the combination product. This statement, and FDA's "question 3" suggests that there is flexibility in assigning premarket authorities for combination products—that, for example, FDA could require an NDA to be filed when the primary mode of action of a combination product is that of a device. AdvaMed respectfully disagrees with this interpretation.

First, in contrast to single-entity products, the combination product laws are very clear on premarket authority. In contrast to single-entity products, the statute states that, if the primary mode of action is that of a device, "the persons charged with premarket review of devices shall have primary jurisdiction."[20/] In AdvaMed's view, this provision requires the use of device authorities, because it would be illogical and inconsistent with the plain meaning of congressional intent, to conclude that the law assigns jurisdiction to "persons charged with premarket review of devices," in order that drug or biologic authorities could be applied.

18/ Section 520(m) of the FFDCA, 21 U.S.C. § 360j(m).

19/ This approach is consistent with Section 563 of the FFDCA, which permits companies to recommend a classification for their product, which recommendation shall be binding, unless ruled on by the FDA within 60 days. Section 563 of the FFDCA, 21 U.S.C. § 360bbb-2.

20/ Section 503(g)(1)(B) of the FFDCA, 21 U.S.C. § 353(g)(1)(B).

Further, Congress has recently advised FDA to exercise caution and careful deliberation when considering the use of device authorities by other Centers. Specifically, the recently enacted MDUFMA requires the FDA to study the use of premarket device authority by other Centers, in response to the *in vitro* diagnostic ("IVD") industry's concerns regarding the Center for Biologics' application of device authorities to IVDs. Under Section 205 of MDUFMA, the Agency must prepare a report to Congress on the timeliness and effectiveness of device premarket reviews by Centers other than CDRH, and present findings on the times required to review original submissions and supplements, the times required to review manufacturers' replies to submissions, and the times to approve or clear devices.[21/] The FDA is required to include in this report a specific recommendation "on whether responsibility for regulatory [IVDs] should be reassigned to those persons within the [FDA] who are primarily charged with regulating ... devices."[22/]

Industry concerns with use of device authorities by other Centers were further affirmed recently, when the Agency published a self-assessment report on combinations in October. In that report, the Agency offered the following example of other Centers' perspective on device premarket review laws:

> [The Report states that] "[s]ome CBER and CDER participants mistakenly suggest that CDRH does not require effectiveness data, and that the PMA process [is] required only for the first device of a kind ([that is,] the second of a kind could be regulated under the 510(k) process)."[23/]

These types of comments raise understandable misgivings concerning use of device authorities by Centers other than CDRH.

III. Question 4: Recognizing the need to ensure product safety and effectiveness, what criteria should FDA use to determine whether a single application or separate applications for the individual components would be most appropriate for regulation of a combination product? Should the need to apply a mixed regulatory approach [e.g., device postmarketing reporting for the combination product, with drug current good manufacturing practices (CGMPs) applicable to the drug component only] influence whether one application or two are most appropriate?

21/ Medical Device User Fee and Modernization Act, Pub. L. No. 107-250, § 205 (2002).

22/ Id.

23/ FDA, Office of the Ombudsman, Combination Products Program, Regulation of Combination Products: FDA Employee Perspectives (Oct. 2002), at 8.

AdvaMed members believe that in the majority of situations, a single filing for a combination product would be the most appropriate. We recognize that section 3.4 of FDA's regulations grants the Agency authority to require separate applications for combination products.[24/] However, in the majority of cases, separate applications are not advantageous, either for FDA or for the sponsor and should not represent the typical submission path. Instead, FDA should establish that separate filings are allowed at the option of the sponsor. This is a theme that was expressed by other speakers at the November 25 public hearing, including representatives of pharmaceutical as well as device companies.[25/] AdvaMed members' consensus view is that the Agency should not require two separate applications without the sponsor's agreement, but that the parties should be permitted to agree on separate applications.

AdvaMed's specific recommendations outlining this concept are as follows:

1. In order to avoid redundant reviews and excessive regulation, only one filing should be required in the vast majority of cases. AdvaMed believes that, as the consult process continues to be regularized, improved, and held accountable, there should be fewer and fewer mandated separate applications.

2. Under certain select circumstances, a company at its option might consider a separate filing as useful for regulatory and/or business/marketing reasons. Factors include: (a) where two different companies, for example, a drug company and a device company, are involved in the manufacture of combination components; (b) where components are expected to have separate distribution and use/reuse patterns; (c) where primary jurisdiction for the combination has been given to a Center other than CDRH, and the device component is capable of being separately defined and reviewed; and/or (d) where there has been a clearly established device review pathway with predicate devices. Examples include: drug delivery pumps, infusion catheters, nebulizers, jet injectors, insulin pens, and laser activated drug delivery systems. In these circumstances, AdvaMed believes that separate filings may be appropriate. The option of dual filings, however, must be left up to the sponsor.

The Agency also has asked whether the need to apply two different postmarket approaches to a combination product (e.g., device Quality System Regulation requirements for the device component, and drug current good manufacturing practices to the drug component) should influence a decision on whether one or two applications are appropriate. Consistent with its

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24/ 21 C.F.R. § 3.4(b). "[t]he designation of one agency component as having primary jurisdiction for the premarket review and regulation of a combination product does not preclude ... in appropriate cases, the requirement by FDA of separate applications."

25/ See Presentation by Dr. Owen Fields, Wyeth Pharmaceuticals, Inc., FDA Public Hearing on Regulation of Combination Products (Nov. 25, 2002); presentation by David Fox, Esq., Hogan & Hartson LLP, FDA Public Hearing on: FDA Regulation of Combination Products (Nov. 25, 2002).

general recommendation set forth above, AdvaMed believes that application of a mixture of postmarket authorities should not be the determining factor for whether more than one application is required. At their option, however, companies should be permitted to use this as a contributing reason to request dual submissions.

IV. Question 5: What scientific and policy principles should be followed in determining the appropriate manufacturing and quality system regulatory authorities (e.g., Current Good Manufacturing Practice versus Quality System Regulation) applicable to combination products?

Question 6: What scientific and policy principles should be followed in determining the appropriate adverse event reporting requirements (e.g., the drugs and biologics adverse event reporting system, Medical Device Reporting) to be applied to a combination product?

As with jurisdictional assignments, legal principles also bear on a determination of appropriate postmarket controls. MDUFMA, the new device law, requires that the FDA "ensure the consistency and appropriateness of postmarket regulation of like products subject to the same statutory requirements."[26/] In implementing this new law, AdvaMed believes that postmarket decisions should be based first and primarily on appropriateness, and, secondarily, on consistency of "like products."

In AdvaMed's view, the concept of "like products" should be interpreted narrowly, because the same manufacture and postmarket reporting requirements may not be appropriate for every combination product within a category. For example, drug-eluting stents and antibiotic-filled cement should not be considered "like products" for which the same postmarket analysis is appropriate. Additionally, the product category of delivery systems used to augment specific drug therapies will have many subcategories of "like products," each requiring separate evaluation concerning appropriate postmarket approaches.

FDA is not limited by statutory constraints in determining the postmarket obligations of a combination product, as it is in determining premarket authorities.[27/] Accordingly, in ensuring the "appropriateness" of postmarket obligations, AdvaMed recommends that the Agency consider a variety of factual, equitable, and policy factors, including the following:

26/ Medical Device User Fee and Modernization Act, Pub. L. No. 107-250, § 204 (2002). See also H.R. Rep. No. 107-728, at 40 (2002) ("[b]y using the word 'consistent,' the Committee intends that like products will be treated in a like fashion").

27/ See Section 503(g)(2) of the FFDCA, 21 U.S.C. § 353(g)(2) (addressing only premarket authorities, by stating that, "[I]f . . . the primary mode of action is that of . . . a device, the persons charged with premarket review shall have primary jurisdiction")(emphasis added).

- The proposed marketing structure for a combination (i.e., whether the two components of a combination will be sold by different entities and have different distribution and use/reuse schemes).[28/]

- The quality systems and postmarket reporting schemes already in place at a sponsoring entity. While this should not be the most important determinant, it should be a factor, particularly when decisions on appropriate postmarket requirements are difficult.

- Whether specific postmarket authorities (e.g., design controls in the device Quality System Regulation, reporting of malfunctions under the device Medical Device Reporting system), would be useful in defining a single or hybrid postmarket regulatory regime.[29/]

The framework for determining appropriateness, thus should be flexible enough to consider these factors, but overarching any decision, should be the avoidance of redundancies and over-regulation.

Finally, one of the issues discussed at the November 25 hearing, that is critical to many of AdvaMed's members, is that decisions on postmarket regulation of combination products should be made early.[30/] An early understanding of postmarket obligations is important not only for those companies that have sought requests for designation, but also for those that have pursued informal Center assignments for their products. Not until these obligations are defined, can companies begin to develop, establish, and rely on a predictable set of postmarket systems and procedures.

V. What other comments do you have concerning other issues related to FDA regulation of combination products?

AdvaMed's members are gratified that the new Office of Combination Products has now been established, and that this Office will report directly to the Office of the Commissioner. As the

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28/ For example, the drugs used in drug-eluting cardiovascular stents are sold by a different entity than the stent manufacturer, and have a different distribution scheme (i.e., the same drug is sold for multiple purposes). Consequently, although the FDA assigned primary review responsibility to CDRH, the drug component is subject to human drug current Good Manufacturing Practices. See U.S. Food and Drug Administration, Jurisdictional Update: Drug-Eluting Cardiovascular Stents at <http://www.fda.gov/oc/ombudsman/stents.html>.

29/ See Presentation by Michael Gross, Ph.D., Aventis Behring, FDA Public Hearing on: FDA Regulation of Combination Products (Nov. 25, 2002) ("the design control process is a useful process in managing quality assurance and change control issues . . .; "[w]ith respect to adverse event reporting, . . . we need to establish conventions that make sense" and that avoid both underreporting and overreporting).

30/ See Presentation of Barbara D. Boyan, Ph.D., American Academy of Orthopaedic Surgeons, FDA Public Hearing on: FDA Regulation of Combination Products (Nov. 25, 2002).

Office begins to undertake its new responsibilities, AdvaMed's final recommendation is that the staff of this Office be sufficiently strong and deep, to enable it to meaningfully review the diverse and complex scientific/clinical issues that arise with combination technologies. This Office also should have regular and meaningful support from the Office of the Commissioner, to facilitate difficult jurisdictional decisions and reduce the potential for Center politics influencing jurisdictional outcomes.

We appreciate the opportunity to comment on these issues.

Sincerely,

Janet Trunzo
Vice President
Technology and Regulatory Affairs