特別公務員である諮問委員会メンバーに適用される条項の 18 U.S.C.208 (b) (3) によると、特例措置が付与されうるかどうかを評価するための基準は、その人物の参加の必要性が、関与する金銭的利益によって生じる利益相反の可能性を上回るかどうかである。

その人物の参加の必要性が利益相反の可能性を上回るかどうかを明らかにする際は、不適格性を生み出す利益の種類、その金銭的利益に関与する人物とメンバーとの関係、個人の適格性の独自性、不適格な金銭的利益がなく、同様に適格とされた個人を特定することの困難さ、不適格な金銭的利益の金額、不適格な金銭的利益が諮問委員会の措置によって影響されうる程度など、多数の要因が検討されうる。(5 CFR 2640.302 (b) を参照)。

スタッフはすでにステップ 9 で、諮問委員会へ不可欠な専門知識を提供するためにその個人の参加が必要であると判断しているため、ほとんどの場合、その個人はすでに 18 U.S.C.208 (b) (3) で求められたバランス水準を満たしている。

FDA は、アルゴリズムのこの段階まできている (すなわち、ステップ 9 に概説した「不可欠な専門知識」の水準を満たしている) 特別公務員は、ほとんどの場合、18 U.S.C.208 (b) (3) による特例措置にも適切であると考える。しかし、当局は該当するすべての法的条項による特例措置の適格者のみに特例措置が付与されることを確実にするため、18 U.S.C.208 (b) (3) 下で十分に問題を分析する。

その人物の参加の必要性が利益相反の可能性を上回らないとスタッフが結論付けた場合、その個人は特例措置の適格者とはされず、会議に参加することはできない。

そうではなく、その人物の参加の必要性が利益相反の可能性を上回るとスタッフが結論付けた場合、スタッフはステップ 11 に進む。

L. ステップ 10b—その個人が一般公務員である場合、金銭的利益はその職員に求められる信頼性に影響を及ぼしうるほど深刻なものではないか?

一般公務員である諮問委員会メンバーに適用される条項の 18 U.S.C.208 (b) (1) によると、特例措置が付与されうるかどうかを評価するための基準は、メンバーの金銭的利益がその職員に求められる信頼性に影響を及ぼしうると見られるほど深刻なものかどうかである。

メンバーの金銭的利益がその職員に求められる信頼性に影響を及ぼしうると見られるほど大きくないかどうかを明らかにする際には、不適格性を生み出す金銭的利益の種類、その金銭

的利益が関与する人物とメンバーとの関係、不適格な金銭的利益の金額、その問題で職員が果たす役割の特性および重要性、問題の感度、当該事項の職員の参加の必要性など、多数の要因が検討されうる。(5 CFR 2640.301 (b) を参照)。

この基準が満たされていない、すなわちメンバーの金銭的利益がその個人によって提供されるサービスの完全性に影響を及ぼしうると見られるほど大きいとスタッフが判断した場合、その個人は特例措置の適格者とはされず、諮問委員会会議に出席することはできない。

そうではなく、メンバーの金銭的利益がその個人によって提供されるサービスの完全性に影響を及ぼしうると見られるほど大きくないとスタッフが判断した場合、スタッフはステップ11に進む。

M. ステップ11－特例措置の上限と矛盾しない場合に、特例措置は推奨されうる。

ステップ11に至るまでに、特例措置が法的基準およびFDAのより厳格な政策検討事項を満たすという結論を得ている。ステップ11では、その個人に特例措置を推奨することにより、Actのセクション712 (c) (2) (C) の下で出される、現会計年度の特例措置について確立された目標率を超えないかどうかを評価する。該当する特例措置の上限を超えなければ、スタッフはその個人に対する特例措置を推奨することができる。FDAは投票権の無い参加に制限するなど、18 U.S.C.208およびActのセクション712 (c) (2) (C) の下で限られた特例を措置するための裁量を有する。スタッフが特例措置を推奨することを決定した場合は、どのような種類の特例措置（上限の推奨を含む）がFDA当局者への提案として適切かを判断し、FDA当局者はそれをレビューして特例措置を承認するかどうかを決定する[13]。

本人、その配偶者または未成年の子供に不適格な金銭的利益がある場合は、Actのセクション712による特例措置を準備する。このような場合は、18 U.S.C.208をも適用して、208による特例措置を準備する。その個人が一般公務員である場合は、208 (b) (1) による特例措置を推奨する。その個人が特別公務員である場合は、208 (b) (3) による特例措置を推奨する。

本人、その配偶者または未成年の子供に不適格な個人的利益はないが、他の人物または組織（配偶者および未成年の子供以外）の金銭的利益がその個人に帰属する場合、Actのセクション712 (c) (2) (A) は適用されず、スタッフは712による特例措置を準備しない。しかし、こ

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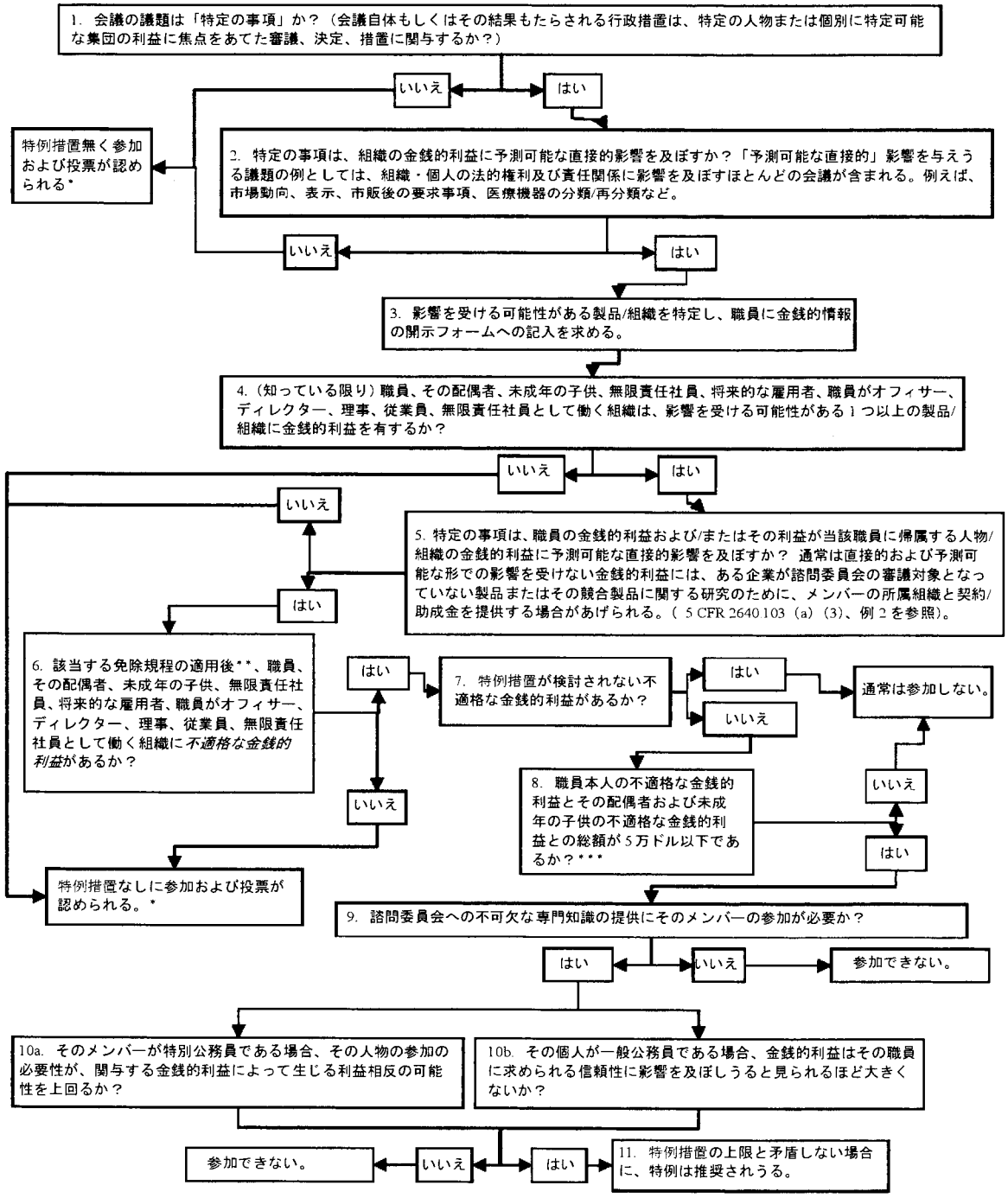
[13] 実際問題として、スタッフはその個人について、該当するすべての法的権限に必要な情報を含む単一の特例を準備する。

のような場合には、18 U.S.C.208 が必ず適用され、208 による特例措置を準備する。その個人が一般公務員である場合は、208（b）（1）による特例措置を推奨する。その個人が特別公務員である場合は、208（b）（3）による特例措置を推奨する。

付録 1



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* 時として、職員は、不適格な金銭的利益ではないが、関連する事実についての知識を持つ妥当な人物に問題の公平性に疑問を抱かせうる金銭的利益または関係を有する。5 CFR 2635.502 を参照。このような問題は、規制基準に基づいて評価し、適切であれば公平性の判定を要請する。

** 該当する免除規程は 5 CFR 2640.201-206 に記載されている。

*** 稀に、職員個人、その配偶者、未成年子供が有する不適格な利害関係の合計がたとえ5万ドル以上であっても、特例措置を検討してもよい場合も稀にある。

Guidance for the Public, FDA Advisory Committee Members, and FDA Staff on Procedures for Determining Conflict of Interest and Eligibility for Participation in FDA Advisory Committees

Additional copies of this guidance are available from:

Office of Consumer and Constituent Relations
Office of the Commissioner
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

http://www/fda/gov/ohrms/dockets

U.S. Department of Health and Human Services
Food and Drug Administration

August 2008

Guidance for the Public, FDA Advisory Committee Members, and FDA Staff on Procedures for Determining Conflict of Interest and Eligibility for Participation in FDA Advisory Committees[1]

This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. INTRODUCTION

This guidance document is intended for FDA staff involved with advisory committee matters, FDA advisory committee members, and the public to help describe the applicable laws, regulations, and policies for determining whether an advisory committee member has a potential conflict of interest and whether participation in an advisory committee meeting is appropriate. FDA plans to develop further staff instructions consistent with this guidance to assist staff in implementing the guidance. This guidance describes FDA's policy in applying the statutory and regulatory requirements found in 18 U.S.C. 208(b), 21 U.S.C. 379d-1, and 5 CFR 2640. This guidance applies to special Government employees (SGEs) and regular Government employees invited to participate in FDA advisory committees subject to the Federal Advisory Committee Act (FACA) (5 U.S.C. App. 2). For purposes of the guidance, we refer to such SGEs and regular Government employees as advisory committee "members."

[1] This guidance has been prepared by the Office of Policy, Planning, and Preparedness in the Office of the Commissioner in conjunction with the Agency's Office of Science in the Office of the Commissioner, Center for Drug Evaluation and Research (CDER), Center for Veterinary Medicine (CVM), Center for Devices and Radiological Health (CDRH), Center for Biologic Evaluation and Research (CBER), and Center for Food Safety and Applied Nutrition (CFSAN).

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances 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.

This guidance document replaces the "FDA Waiver Criteria 2000" guidance document.

II. WHY IS FDA REVISING ITS GUIDANCE ON CONFLICTS OF INTEREST AND PARTICIPATION IN FDA ADVISORY COMMITTEE MEETINGS?

FDA's advisory committees play an essential role in FDA's activities to protect and promote public health through the regulation of human and animal drugs, biological products, medical devices, and foods. FDA's advisory committees provide independent expert advice to the agency on scientific, technical, and policy matters related to the development and evaluation of FDA-regulated products. Advisory committees enhance FDA's ability to protect and promote public health by ensuring FDA has access to such advice in a manner as public as permitted by existing laws and regulations. Although advisory committees provide recommendations to FDA, FDA makes the final decisions.

FDA is committed to strictly adhering to the laws and regulations governing the process for selecting advisory committee members. FDA for many years has screened, prior to each meeting, all potential participants who are SGEs or regular Government employees, to determine whether the potential for a financial conflict of interest exists. Where such a conflict exists, the agency may grant a waiver allowing participation in an advisory committee meeting when statutory criteria are met; for example, when the need for the individual's services outweighs the potential for a conflict of interest created by the financial interest involved (18 U.S.C. 208(b)(3)). However, because FDA's conflict of interest screening process is complex and has been poorly understood, the agency has been criticized in its application of the legal framework. Moreover, while many

conflict of interest laws and regulations apply to advisory committees across the federal government, the public has a particular interest in and high expectations for FDA's process.

FDA administers several laws and regulations that govern conflict of interest determinations -- and the legal landscape has changed in recent years. The current laws set forth different standards for determining whether participation in advisory committee meetings may be permitted. For example, two separate statutes govern whether the SGEs and regular Government employees subject to this guidance are prohibited from participating in advisory committee meetings because of financial interests that may be affected by the work the committee is to perform. First, 18 U.S.C. § 208 prohibits an SGE or regular Government employee with disqualifying financial interests (see 5 CFR 2640.103(b)) from participating in an advisory committee meeting unless a waiver is granted. Under 18 U.S.C. 208, the financial interests of certain persons and organizations are imputed to the employee, and must be considered in addition to his personal financial interests. Second, section 712(c)(2)[2] of the Federal Food, Drug, and Cosmetic Act (the Act), which replaces former 21 U.S.C. § 355(n)(4) and expands its applicability, prohibits advisory committee members from participating in a meeting if they (or any immediate family member) have a disqualifying financial interest, unless a waiver is granted.

Both statutes specify the circumstances under which FDA may grant waivers to permit participation in specific meetings. Section 712 (c)(2)(B) authorizes FDA to grant a waiver (to participate as a voting member or as a non-voting member) if "it is necessary to afford the committee essential expertise." FDA must also apply the provisions of 18 U.S.C. 208(b)(1) or 208(b)(3) to these same advisory committee meetings. The test for a regular Government employee who seeks to participate in an advisory committee meeting is whether the financial interest is "not so substantial as to be deemed likely to affect the integrity of the services which the

[2] Section 712 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 379d-1) was added by the Food and Drug Administration Amendments Act of 2007 (FDAAA), Pub. L. No. 110-85, sec. 701. Section 712 became effective October 1, 2007.

Government may expect" from the employee (18 U.S.C. 208(b)(1)). However, in the case of an SGE seeking to participate in an advisory committee meeting, the test is whether the "need for the individual's services outweighs the potential for a conflict of interest created by the financial interest involved" (18 U.SC. 208(b)(3)). Several regulations promulgated pursuant to 18 U.S.C. 208(b) further explain and delineate the parameters of the statutes and detail certain exemptions to the conflict of interest prohibitions (see 5 CFR Part 2640).

Issued before recent changes in the applicable law under FDAAA (section 712 of the Act), FDA's Waiver Criteria 2000 guidance attempted to address a complex set of variables by setting out a series of tables indicating involvement levels and expected action that FDA advisory committee staff would take. The tables varied depending on the type of interest (e.g., stocks and investments, primary employment, consulting work, contracts and grants, patents/royalties/trademarks, expert witness work, teaching/speaking/writing, contracts/grants for department heads, and institutional directors), level of involvement (low, medium, or high), type of meeting (particular matters involving specific parties or particular matters of general applicability), as well as a number of other factors. In applying the tables, FDA staff also considered enumerated circumstances favoring the use of the member and additional criteria that would exclude a member.

The Waiver Criteria 2000 guidance was an attempt to address comprehensively the multiple variables that can be applied in reaching a determination about an individual advisory committee member. However, because of its complexity and discretionary elements, Centers and offices sometimes found it difficult to achieve consistent results that the public could readily understand.

Most recently, Congress enacted section 701 of FDAAA (section 712 of the Act), which, in addition to establishing a new conflict of interest prohibition and standard for assessing waivers, encourages FDA to focus efforts on recruitment of advisory committee members with fewer potential conflicts of interest and caps the numbers of waivers that the agency may grant in a given year. Section 712(c)(2)(C) requires that FDA reduce

the rate of waivers the agency issues each year (total number of waivers issued per total number of members attending advisory committee meetings) by 5 percent, beginning with fiscal year 2008. By 2012, the agency may issue waivers at a maximum rate of 75 percent of the rate issued in 2007.

As part of FDA's recent internal assessment of its advisory committee process, the agency has targeted its assessment of potential conflicts of interest and granting of waivers as an area that needs improvement. This guidance incorporates the changes in the applicable law made by FDAAA and greatly simplifies and streamlines the process by which we determine meeting participation. FDA intends that this guidance increase the transparency, clarity, and consistency of the advisory committee process and enhance public trust in this important function.

III. WHAT ARE THE GOALS AND PRINCIPLES OF THIS GUIDANCE?

This guidance sets out a clear, streamlined approach for considering who may participate in an advisory committee meeting. As a policy matter, FDA is choosing to implement a more stringent policy for considering eligibility for participation than is required under the current legal framework. Under this approach, participation of members with potential conflicts of interest generally would occur under narrow circumstances where the potential conflict is minimal and the member's expertise is necessary to afford the committee essential expertise. The principal tool in considering advisory committee participation is a flowchart, or algorithm, that sets out the questions and considerations to address in a step-wise manner. This algorithm is discussed in detail in Part IV of this guidance, and is attached as Appendix 1.

The algorithm consolidates the various standards and tests found in the applicable statutes into a series of straightforward steps that generally apply to all meetings, regardless of the subject matter or type of meeting and irrespective of the type of financial interest(s) held by the member. This unified, simpler approach will

improve consistency within the agency in considering advisory committee participation and will provide greater clarity to the public regarding how FDA selects members.

FDA's policy for evaluating whether a waiver should be issued is more stringent than the Waiver Criteria 2000 Guidance (that this guidance replaces) in four major ways. First, FDA intends to apply a stricter policy with respect to granting waivers for those whose personal financial interests and those of their immediate family exceed certain levels. Under this guidance, if an individual or her spouse or minor child has disqualifying financial interests whose combined value exceeds $50,000, she generally would not participate in the meeting, regardless of the need for her expertise.

Second, FDA does not intend to issue a waiver in certain circumstances where the agency has determined that the conflict of interest is significant. These circumstances are enumerated and described in Section H (Step 7) of this guidance.

Third, FDA will apply a more stringent test to all waivers than is contemplated by some of the laws that the agency administers. FDA is choosing to limit the waivers the agency grants and harmonize our implementation of the various statutory provisions by applying a stricter test than would be required in some cases. Although 18 U.S.C. 208(b)(3) authorizes the agency to grant a waiver to an SGE where a balancing test is met -- "the need for the individual's services outweighs the potential for a conflict of interest created by the financial interest involved"-- FDA will also apply to all waivers for SGEs the generally stricter standard established by section 712 (c)(2)(B) of the Act, requiring a showing that the waiver "is necessary to afford the committee essential expertise." Similarly, for regular Government employees, where the test under 18 U.S.C. 208(b)(1) is whether the "financial interest is not so substantial as to be deemed likely to affect the integrity of the services provided by that individual," FDA will also require a showing of essential expertise. In order to meet the "essential expertise" standard, the agency will conduct a needs analysis -- recommending in most cases that

staff document their search for an equally qualified expert with few or no conflicts of interest. An expanded search for unconflicted, qualified experts is consistent with FDAAA's focus on recruitment of advisory committee members with no conflicts of interest and may assist in minimizing the numbers of waivers needed.

Fourth, as discussed in Section II, FDA will limit the number of waivers the agency grants each year, in accordance with section 712(c)(2)(C) of the Act. By applying the $50,000 limit for personal financial interests and the strict "essential expertise" test, FDA intends that the agency will meet the waiver limits incorporated in FDAAA. However, the agency intends to further limit numbers of waivers if necessary to assure that the FDAAA waiver caps are met, even if an employee's personal financial interests are at or below $50,000, and the "essential expertise" test is met.

IV. HOW DOES THE ALGORITHM OPERATE?

A. Introduction

This part of the guidance discusses each step in the algorithm. The algorithm consists of ten steps, and we will discuss each step sequentially.

B. Step 1 – Is the Subject Matter of the Meeting a "Particular Matter?"

The first step is to ask, "Will the meeting itself or a governmental action of which it is a part involve a 'particular matter'?" The term "particular matter" includes only matters that involve deliberation, decision, or action that is focused upon the interests of specific persons, or a discrete and identifiable class of persons. It does not cover consideration or adoption of broad policy options directed to the interests of a large and diverse group of persons such as actions that will affect all companies or the economy in general (5 CFR 2640.103(a)(1)). While most FDA advisory committee meeting topics will involve "particular matters," some

topics are so wide-ranging in nature and could potentially affect such a large number of persons or organizations, that they would not be considered a "particular matter."

When an FDA advisory committee meeting is educational in purpose and the agency is not seeking advice on a regulatory decision or action, it may not meet the definition of "particular matter." For example, a meeting of FDA's Risk Communication Advisory Committee was determined not to involve a "particular matter" because the meeting focused on a broad discussion of hypothetical communication problems and the pros and cons of different components of a draft template for press releases about recalls of all FDA-regulated products. The discussion pertained to such a large number of firms and organizations that it would not be considered to have an effect on a discrete and identifiable class.

Other examples of FDA advisory committee meeting topics that are not "particular matters" include:

- The agenda topic is devoted to committee member training on advisory committee practices and procedures.
- The agenda topic is devoted to general scientific presentations and discussions exclusive of particular products or guidance for a class of products. For example, a presentation solely on methodology for analyzing statistical data may be a general scientific presentation.
- The agenda topic is devoted to a review of intramural research, where the research would have no impact on an outside financial interest.

If the answer to this question is "no," no further inquiry is necessary to determine whether there is a conflict of interest. All members may fully participate[3] in the meeting.

If your answer to the question is "yes," then proceed to step 2.

[3] Full participation includes voting.

C. Step 2 – Will the particular matter have a direct and predictable effect on the financial interest(s) of any organization?

Under step 2, the question is, "Will the meeting have a direct and predictable effect on the financial interests of any organization?" This step is intended to provide an early opportunity for the agency to determine, before meeting-specific conflict of interest screening, whether the meeting is of the type that would not have a direct and predictable effect on any financial interest that could be anticipated. In order to determine that there is no direct and predictable effect on any potential financial interest, the meeting topic and any anticipated FDA actions as a result of the advisory committee's advice would need to be well understood. In many cases, staff will be unable to conclude at this stage that the meeting topic will not have a direct and predictable effect on any potential financial interest and will need to proceed to Step 3 and subsequent steps. Nevertheless, in proceeding through the subsequent steps in this guidance, staff will analyze reported financial interests and may determine for an individual that the outcome of the meeting will not have a direct and predictable effect on his or her reported interest(s).

Under 5 CFR 2640.103(a)(3)(i), a particular matter will have a "direct" effect on a financial interest if there is a close causal link between any decision or action to be taken in the matter and any expected effect of the matter on the financial interest. An effect may be direct even though it does not occur immediately. A particular matter will not have a direct effect on a financial interest, however, if the chain of causation is attenuated or is contingent upon the occurrence of events that are speculative or that are independent of, and unrelated to, the matter. A particular matter will have a "predictable" effect if there is a real, as opposed to a speculative, possibility that the matter will affect the financial interest. It is not necessary, however, that the magnitude of the gain or loss be known, and the dollar amount of the gain or loss is immaterial (5 CFR 2640.103(a)(3)(ii)).

For example, a meeting that will affect the legal rights or responsibilities of a known organization or organizations, such as most potential advisory committee recommendations pertaining to marketing status, labeling, post-marketing requirements, and device classification or reclassification, would ordinarily have a "direct and predictable effect" on financial interests. In some cases, however, the meeting topic will be so general that to determine any effect on any organization's financial interests would be speculative. In these cases, it may be concluded that the particular matter will not have a direct and predictable effect on the financial interests of any organization.

If the answer to this question is "no," no further inquiry is necessary to determine whether there is a conflict of interest, and all members may fully participate in the meeting.

If the answer to this question is "yes," or staff cannot determine at this stage that the meeting topic will not have a direct and predictable effect on any potential financial interest, proceed to step 3.

D. Step 3 – Identify Potentially Affected Products/Organizations and Request that the Employee Complete the Financial Disclosure Form

Once it is determined that the meeting will likely have a direct and predictable effect on the financial interests of an organization or organizations, staff will need to identify potentially affected products and/or organizations and request that the member complete FDA Form 3410, a financial disclosure form.[4]

Potentially affected organizations generally include companies or entities that could be affected by the outcome of the advisory committee proceedings and any FDA decision based on the committee's recommendations. For example, the sponsor of a new drug application that is being presented to an advisory

[4] Note that for some meetings, the agency may determine that a complete and efficient review of potential conflicts of interest may be accomplished by reviewing OGE Form 450, which requires the employee to list all financial interests in a broad range of areas. If review of a current OGE Form 450 is conducted, it can replace the more specific review under FDA Form 3410.