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.

committee and sponsors of drugs that closely compete with the subject drug would all be "potentially affected organizations" for which the financial interest of the SGE or regular Government employee in the organization would need to be considered for potential conflict of interest.

The list of potentially affected products and/or organizations should be transmitted to the member with the FDA Form 3410 so that the member can complete his financial disclosure to the agency, referring to the list.

E. Step 4 -- Does the employee, or persons/organizations whose interests are imputed to him, have a financial interest in one or more of the potentially affected products and/or organizations?

Under Step 4, staff should examine the member's financial disclosure form and determine whether the member or the persons or organizations whose interests are imputed to him have financial interests in the potentially affected products or organizations.[5] The term "financial interest" means the potential for gain or loss to the employee (or persons/organizations whose interests are imputed to him) as a result of governmental action on the particular matter (5 CFR 2640.103(b)). Disqualifying financial interests include only financial interests that are currently held.[6] In general, staff should consider the financial interests (if any) of:

- The member;
- The member's spouse and minor children;
- The member's general partner(s);

[5] In some cases, an advisory committee member will identify a relevant financial interest that is not included in the agency's list of potentially affected products and/or organizations. Staff should include this interest when working through the remaining applicable steps for that member, and add the entity to the list of potentially affected products and/or organizations to consider for other members.

[6] In some cases, an employee will have a financial interest or relationship that, while not a disqualifying financial interest, may cause a reasonable person with knowledge of the relevant facts to question his impartiality in the matter. *See* 5 CFR 2635.502. Such matters should be evaluated under this regulatory standard and, if appropriate, an impartiality determination should be requested.

- Prospective employers of the member[7]; and
- Any organization in which the member serves as an officer, director, trustee, employee, or general partner.

The nature and amount of those financial interests also needs to be determined.

If the member and the persons or organizations whose interests are imputed to him do not have any financial interests in the potentially affected products or organizations, then that individual may fully participate in the meeting.[8] Alternatively, if the member or persons or organizations whose interests are imputed to him has financial interests in the potentially affected products and/or organizations, staff should proceed to step 5.

F. Step 5 – Will the Particular Matter Have a Direct and Predictable Effect on the Financial Interest of the Employee and/or Persons/Organizations Whose Interests are Imputed to Him?

Under Step 5, staff should examine the financial interest(s) that the employee has reported on his financial disclosure form and determine whether the particular matter to be discussed at the meeting will have a direct and predictable effect on any current financial interest of the employee or the financial interest of a person or organization whose interests are imputed to him. Although the question of "direct and predictable effect" has been examined in Step 2 for the effect of the meeting as a whole, here the question is individualized to the particular financial interests held by, or imputed to, the member. For each interest, staff should ask 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, and if there is a real, as opposed to a speculative, possibility that the matter

---

[7] A prospective employer would be anyone with whom the employee has any arrangement concerning future employment or with whom he/she is seeking or negotiating for employment.
[8] See note 6.

will affect the financial interest. For further discussion about the meaning of "direct and predictable effect," refer back to Section IV C of this document.

Financial interests that ordinarily will not be affected in a direct and predictable manner include a grant or contract between an organization and the employee's university to conduct research on a product that is not the subject of the particular matter before the advisory committee or a competitor product (see 5 CFR 2640.103(a)(3), example 2).

If the answer to this question is "no," no further inquiry is necessary to determine whether there is a conflict of interest, and the member may fully participate in the meeting.[9]

If the answer to this question is "yes," you should proceed to Step 6.

G. Step 6 – After Applying Applicable Regulatory Exemptions, Does the Employee or Persons/Organizations Whose Interests are Imputed to Him Have a Disqualifying Financial Interest?

Under Step 6, staff should consider whether regulatory exemptions apply to the financial interests identified under Step 5.

Certain financial interests have been determined by the Director of the Office of Government Ethics to be too remote or too inconsequential to affect the integrity of the services of the Government officers or employees (see 18 U.S.C. 208(b)(2)). The regulations issued by the Office of Government Ethics (OGE) expressly exempt these financial interests from consideration (see 5 CFR 2640.201-206). Likewise, section 712(c)(2)(A) of the Act excludes from consideration those same interests exempted in the OGE regulations.

[9] See note 6.

Staff should consider whether any of the following exemptions apply. For further description of each exemption, see the applicable provision in 5 CFR 2640, Subpart B.

- Diversified mutual funds and unit investment trusts (5 CFR 2640.201(a)).
- Certain sector mutual funds (see 5 CFR 2640.201(b)).
- Certain employee benefit plans (5 CFR 2640.201(c)).
- Certain matters affecting mutual funds and unit investment trusts (5 CFR 2640.201(d)).
- *De minimis* exemptions for interests in securities (5 CFR 2640.202).
- Certain financial interests that may arise for individuals on a leave of absence from an institution of higher education (see 5 CFR 2640.203(b)).
- Certain financial interests that may arise for individuals employed by one campus of a multi-campus State institution of higher education (see 5 CFR 2640.203(c)).
- Certain financial interests that may arise for individuals whose financial interests arise from Federal Government employment or from Social Security or veterans benefits (see 5 CFR 2640.203(d)).
- Certain employment interests of SGEs serving on advisory committees (5 CFR 2640.203(g)).
- Hospital employment and use/prescription of medical products for patients for advisory committee matters concerning medical products (5 CFR 2640.203(i)).
- Certain non-voting representative members of FDA standing technical advisory committees (5 CFR 2640.203(j).

If, after applying the regulatory exemptions, there are no disqualifying financial interests, the member may fully participate in the advisory committee meeting.[10]

If the employee or those persons or organizations whose interests are imputed to him have disqualifying financial interests, staff should proceed to Step 7.

H. Step 7 – Are There Disqualifying Financial Interests For Which a Waiver Would Not Be Considered?

Under Step 7, staff should review the disqualifying financial interests and determine whether any is such a significant conflict of interest that a waiver would not be considered.

The following list includes the disqualifying financial interests that are considered so significant that a waiver would not be issued:

- The SGE or his/her employing institution receives (or is negotiating) a contract, grant, or Cooperative Research and Development Agreement (CRADA) from a firm that is the sponsor of the product application that is the subject of the particular matter involving specific parties to be discussed at the advisory committee meeting, and the SGE is or will be the principal investigator or co-principle investigator on the same product/indication that is the subject of the meeting.
- The SGE or his/her employing institution receives (or is negotiating) a contract, grant, or CRADA from a firm that is the sponsor of a product labeled for the same indication (or, if an investigational product, that has the same indication for use) as the product that is the subject of the particular matter involving specific parties to be discussed at the advisory committee

[10] See note 6.

meeting, and the SGE is or will be the principal investigator or co-principle investigator on the competing product.

- The SGE or his/her employing institution receives (or is negotiating) a contract, grant, or CRADA from a firm that is the sponsor of the product that is the subject of the particular matter involving specific parties to be discussed at the advisory committee meeting, and the SGE is the head of the department that is conducting or will conduct the studies on the same product/indication that is the subject of the meeting, and the SGE:
  - Receives or will receive personnel or salary support; or
  - Designs/will design or advises/will advise on any aspect of the clinical trial(s); or
  - Reviews or will review data or reports from the clinical trial(s).
- The SGE or his/her employing institution receives (or is negotiating) a contract, grant, or CRADA from a firm that is the sponsor of a product labeled for the same indication (or, if an investigational product, that has the same indication for use) as the product that is the subject of the particular matter involving specific parties to be discussed at the advisory committee meeting, and the SGE is the head of the department that is conducting or will conduct the studies on the competing product, and the SGE:
  - Receives or will receive personnel or salary support; or
  - Designs/will design or advises/will advise on any aspect of the clinical trial(s); or
  - Reviews or will review data or reports from the clinical trial(s).

If staff determines that the individual has one or more of the above listed financial interests, the member should not be considered for a waiver and would not participate in the advisory committee meeting.

Alternatively, if the answer to the question is "no," staff should proceed to Step 8.

I. Step 8 – Is the Combined Value of the Employee's Personal Disqualifying Financial Interests and Those of His Spouse and Minor Children $50,000 or Less?

Under Step 8, staff should calculate the total value of the disqualifying financial interests that are his personal interests, those of his spouse, and those of his minor children. Disqualifying financial interests include only financial interests that are currently held. Some examples of an employee's personal financial interests would be stocks or investments that he owns, his primary employment relationship, his consulting work, patents/royalties/trademarks owned by him, his work as an expert witness, and his teaching/speaking/writing work. If the employee's spouse and/or minor children have personal disqualifying interests, these should be included in the total value. In calculating the value of an employee's disqualifying financial interests attributed to a financial interest that extends into the future, such as a contract or employment, staff should include current financial interests over a one year period of time. For example, if the employee has a $100,000 personal consulting contract that covers a five year period of work, he would be deemed to have a financial interest in the consulting contract of $20,000 per year. If the employee's relationship is ongoing but there is no specified dollar amount for future work, staff should calculate the amount of the financial interest over the previous 12 months.

If the combined value of these disqualifying financial interests is greater than $50,000, the member would not ordinarily be considered for a waiver and would not participate in the advisory committee meeting.[11]

If the answer to the question is "yes," staff should proceed to Step 9.[12]

---

[11] In limited cases, FDA may determine that a conflict of interest waiver is appropriate, provided that the relevant statutory and regulatory standards are met. In such cases, the Commissioner of FDA will review the request and make a determination on the appropriateness of a waiver.

J. Step 9 – Is the Individual's Participation Necessary to Afford the Advisory Committee Essential Expertise?

Under Step 9, staff will determine whether a waiver may be considered to permit the member to participate in the advisory committee meeting. As a policy matter, FDA is choosing to limit the waivers the agency grants and harmonize our implementation of the various statutory provisions by applying a more stringent test than would be required in some cases. Before FDA grants a waiver, we will determine that the individual's participation is necessary to afford the advisory committee essential expertise.

As discussed in Section II of this document, FDA must evaluate the potential for conflict of interest, and may grant waivers, under three statutory provisions: section 712(c)(2) of the Act, 18 U.S.C. 208(b)(1), and 18 U.S.C. 208(b)(3). The "essential expertise" test is the standard for granting a waiver under section 712(c)(2)(B) of the Act for a member who has a personal financial interest (or whose spouse or minor child has a financial interest) that could be affected by the advice given with respect to the matter. Because this is generally a stricter test than the balancing test contemplated in 18 U.S.C. 208(b)(3) for an SGE -- whether the "need for the individual's services outweighs the potential for a conflict of interest created by the financial interest involved" – when FDA finds that an SGE qualifies for a waiver under section 712(c)(2)(B) of the Act, the SGE would ordinarily also qualify for a waiver under 18 U.S.C. 208(b)(3).

In order to determine that the employee's participation is necessary to afford the committee essential expertise, staff should perform a needs analysis that demonstrates that the member provides important expertise that may not be feasibly acquired through alternative means. The test does not impose a standard of indispensability or demonstration that it would be impossible for the committee to accomplish its work without

[12] Note that, even if the member has $0 personal and immediate family disqualifying financial interests, staff should still proceed to Step 8, as other imputed financial interests will require evaluation as to whether a waiver may be granted.

the member's expertise; however, it requires more than a showing of inconvenience to the committee or FDA from the loss of the member. To determine whether the "essential expertise" test is met, FDA's judgment may be informed by Office of Government Ethics (OGE) regulations at 5 CFR 2640.302(b) that interpret the requirements for issuing a waiver pursuant to 18 U.S.C. 208(b)(3).

Some factors that may be considered include:

- The uniqueness of the individual's qualifications (5 U.S.C. 2640.302(b)(3));
- The difficulty of locating a similarly qualified individual without a disqualifying financial interest to serve on the committee (5 U.S.C. 2640.302(b)(4));
- The SGE will provide expertise that is necessary to the issues on the agenda and that would otherwise be unavailable. Expertise may ordinarily be considered unavailable if staff has failed to find similar expertise on other standing committees or among existing consultants, and has made reasonable efforts to survey the field;
- For a product-specific meeting, the product in question is studied widely and it would be difficult to find a qualified SGE who was not at least as involved/conflicted with the product or a competing product.

In most cases, staff should document that a search for an equally qualified, less conflicted individual has been conducted and the results of that search.

If staff concludes that the individual's participation is not necessary to afford the advisory committee essential expertise, the individual may not participate in the meeting.

Alternatively, if staff concludes that the individual's participation is necessary to afford the advisory committee essential expertise, staff should proceed to Step 10a, if the individual is an SGE, or Step 10b, if the individual is a regular Government employee.

K. Step 10a – If the Individual is a Special Government Employee, Does the Need for the Individual's Services Outweigh the Potential for a Conflict of Interest Created by the Financial Interest Involved?

Under 18 U.S.C. 208(b)(3), a provision that applies to advisory committee members who are SGEs, the standard for evaluating whether a waiver may be granted is whether the need for the individual's services outweighs the potential for a conflict of interest created by the financial interest involved.

In determining whether the need for the individual's services outweighs the potential for a conflict of interest, we may consider a number of factors, including the type of interest that is creating the disqualification, the relationship of the person whose financial interest is involved to the member, the uniqueness of the individual's qualifications, the difficulty of locating a similarly qualified individual without a disqualifying financial interest, the dollar value of the disqualifying financial interest, and the extent to which the disqualifying financial interest could be affected by the actions of the advisory committee. (see 5 CFR 2640.302(b)).

Because staff has already determined in Step 9 that the individual's participation is necessary to afford the advisory committee essential expertise, in most cases, the individual will already have met the balancing test required under 18 U.S.C. 208(b)(3).

FDA expects that an SGE who has reached this stage in the algorithm (i.e., met the "essential expertise" test outlined in Step 9) would, in most cases, also qualify for a waiver under 18 U.S.C. 208(b)(3). However, the

agency will ensure that waivers will be issued to only those individuals who qualify for a waiver under all applicable statutory provisions and will fully analyze the matter under 18 U.S.C. 208(b)(3).

If staff concludes that the need for the individual's services does not outweigh the potential for a conflict of interest, the individual does not qualify for a waiver and may not participate in the meeting.

Alternatively, if staff concludes that the need for the individual's services outweighs the potential for a conflict of interest, staff should proceed to Step 11.

L. Step 10b – If the Individual is a Regular Government Employee, Is the Financial Interest Not So Substantial as to be Deemed Likely to Affect the Integrity of the Services Provided by that Individual?

Under 18 U.S.C. 208(b)(1), a provision that applies to advisory committee members who are regular Government employees, the standard for evaluating whether a waiver may be granted is whether the member's financial interest is not so substantial as to be deemed likely to affect the integrity of the services provided by that individual.

In determining whether the member's financial interest is not so substantial as to be deemed likely to affect the integrity of the services provided by that individual, we may consider a number of factors, including the type of financial interest that is creating the disqualification, the relationship of the person whose financial interest is involved to the member, the dollar value of the disqualifying financial interest, the nature and importance of the employee's role in the matter, the sensitivity of the matter, and the need for the employee's services in the particular matter (see 5 CFR 2640.301(b)).

If staff determines that this standard is not met – that the member's financial interest is so substantial as to be deemed likely to affect the integrity of the services provided by that individual, the individual does not qualify for a waiver and he may not participate in the advisory committee meeting.

Alternatively, if staff concludes that the member's financial interest is not so substantial as to be deemed likely to affect the integrity of the services provided by that individual, staff should proceed to Step 11.

M. Step 11 – Waiver May Be Recommended If Consistent With Waiver Cap.

In reaching Step 11, staff has concluded that a waiver would meet the statutory standards and FDA's more stringent policy considerations. Under Step 11, staff should evaluate whether recommending a waiver for the individual would be consistent with the target rate established for the current fiscal year for issuing waivers under section 712(c)(2)(C) of the Act. Provided that the applicable waiver cap would not be exceeded, staff may recommend that a waiver for the individual be granted. FDA has discretion to issue limited waivers under 18 U.S.C. 208 and under section 712(c)(2)(C) of the Act; e.g., by limiting participation to non-voting. If staff decides to recommend that a waiver be granted, they should determine which type of waiver(s) (including any recommended limitations) is appropriate to recommend to FDA officials who will review and decide whether to approve the waiver.[13]

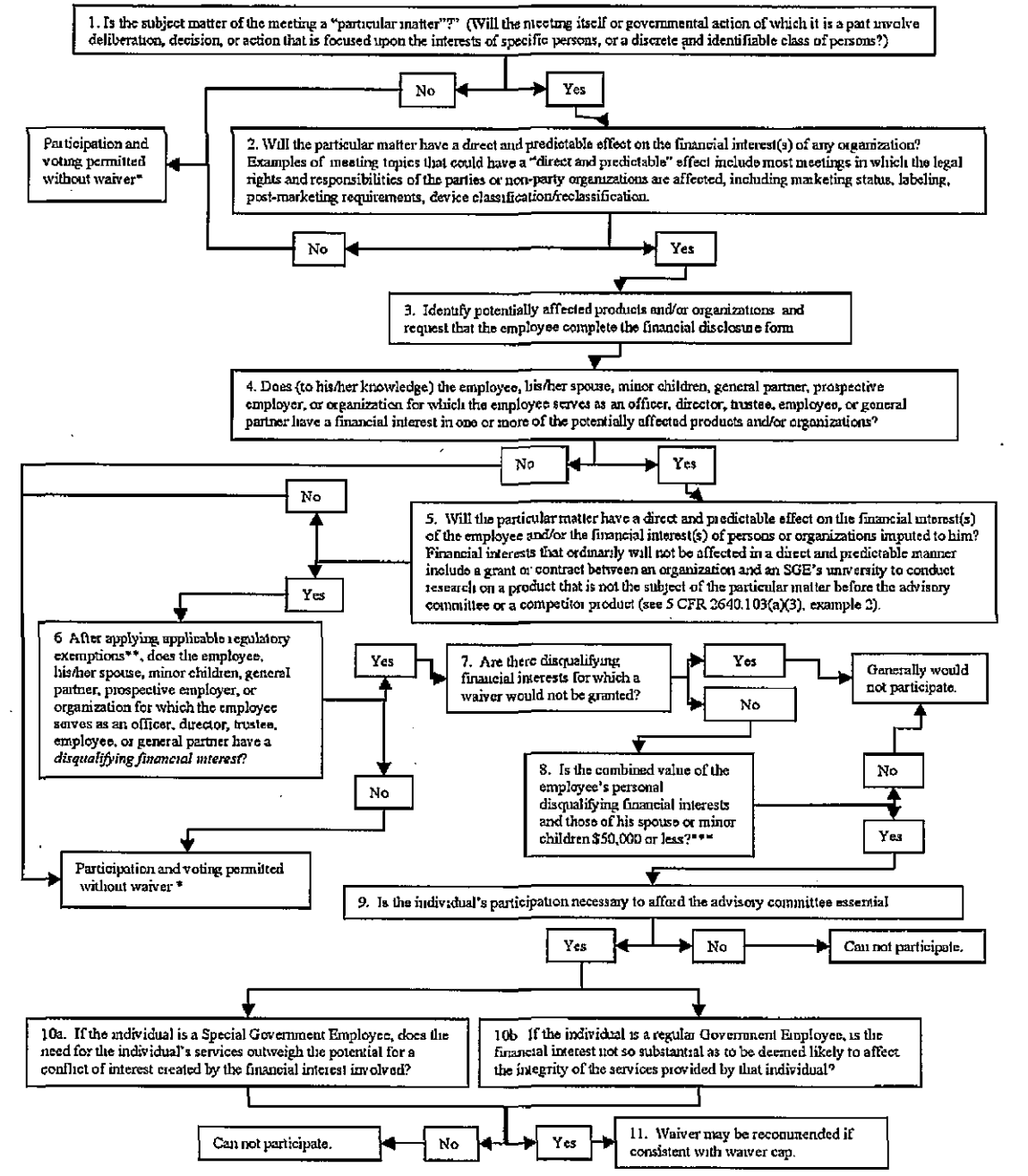
If the individual, his spouse, or minor child has personal disqualifying financial interests, a waiver under section 712 of the Act should be prepared. In such cases, 18 U.S.C. 208 also applies and a 208 waiver should be prepared. If the individual is a regular Government employee, a 208(b)(1) waiver should be recommended. If the individual is an SGE, a 208(b)(3) waiver should be recommended.

---

[13] As a practical matter, staff may prepare a single waiver for an individual that includes the necessary information for all applicable statutory authorities.

If the individual, his spouse, and minor children do not have personal disqualifying interests, but the financial interests of other persons or organizations (other than those of his spouse and minor children) have been imputed to him, section 712(c)(2)(A) of the Act does not apply, and staff should not prepare a 712 waiver. However, 18 U.S.C. 208 does apply in such cases, and a 208 waiver should be prepared. If the individual is a regular Government employee, a 208(b)(1) waiver should be recommended. If the individual is an SGE, a 208(b)(3) waiver should be recommended.

Appendix 1



*In some cases, an employee will have a financial interest or relationship that, while not a disqualifying financial interest, may cause a reasonable person with knowledge of the relevant facts to question his impartiality in the matter. *See* 5 CFR 2635.502. Such matters should be evaluated under that regulatory standard and, if appropriate, an impartiality determination should be requested.

**The applicable regulatory exemptions are found in 5 CFR 2640.201-206.

***In rare cases, OGE may pursue whether a conflict of interest waiver is appropriate where the combined value of the employee's personal disqualifying financial interests and those of his