

SMG 9001.1

FDA STAFF MANUAL GUIDES, VOLUME IV – AGENCY PROGRAM DIRECTIVES

GENERAL OR MULTIDISCIPLINE

SCIENTIFIC INTEGRITY

SCIENTIFIC INTEGRITY AT FDA

Effective Date: 02/03/2012

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1. PURPOSE

The purpose of this Staff Manual Guide (SMG) is to provide an overview of FDA principles, policies, and practices that relate to the preservation and promotion of scientific integrity.

2. POLICY

Access to reliable scientific and technological information is central to FDA's mission and the agency's regulation of human and veterinary drugs, biological products, medical devices, cosmetics, tobacco, and food. FDA must rely on the best available science to make difficult decisions with respect to those products. In making those decisions, an unbiased presentation and full evaluation and analysis of the data, including its uncertainties, is absolutely critical. Establishing and maintaining integrity of the scientific process and of scientific data is crucial to the agency's ability to arrive at sound decisions and to maintain public trust. While there may be differing views with respect to what one can conclude from the data, and while there are often multiple

options that can be considered in a policy approach or regulatory decision that is made based on the science, the underlying research data and findings should be obtained and reported with integrity and should never be altered for any reason.

It is important to highlight the importance of scientific integrity early in the document, including an acknowledgement of communicating uncertainty. It would be even better if this section called out transparency as a way to ensure that data are not altered or suppressed.

The policy could do better by explicitly stating that all scientific information will be subject to this policy, including information that is submitted to the agency from interested parties.

FDA has a long, and continuing, history of working to ensure integrity in its scientific and regulatory processes and, as a result, has put in place related policies, procedures and initiatives. The following key principles undergird FDA's approach to preserving and promoting scientific integrity:¹

- | Key Principles of Scientific Integrity at FDA | |
|--|--|
| | ➤ Maintaining a firm commitment to science-based, data-driven decision-making; |
| | ➤ Shielding the agency's science and its scientific staff from political influence; |
| | ➤ Facilitating the free flow of scientific and technical information; |
| | ➤ Protecting the integrity of scientific data and ensuring its accurate presentation, including the underlying assumptions and uncertainties; |
| | ➤ Requiring a fair and transparent approach to resolving internal scientific disputes, including hearing and carefully considering differing views; |
| | ➤ Supporting whistleblower protections; |
| | ➤ Selecting and promoting scientists based on their knowledge, expertise and integrity; |
| | ➤ Utilizing peer review of data and research used in decision-making, where feasible, appropriate and consistent with the law; |
| | ➤ Maintaining openness and selecting qualified advisory committee members based on expertise, with transparency about conflicts of interest; |
| | ➤ Allowing FDA staff to communicate their personal scientific or policy views to the public, even when those views differ from official Agency opinions; and |

It's important to put these principles forward. But while these commitments are strong, the policy should better detail a path for how they will be upheld.

These commitments are sufficiently thorough.

This should include not only considering but also documenting differing scientific opinions and making that information publicly available.

This is an important commitment, but this could be strengthened by better stating the explicit rights of whistleblowers in this policy.

While transparency is important, the goal should be conflict-free committees.

¹ This document addresses scientific decision-making and not, directly, scientific research conducted by, or in collaboration with, the agency. As a result, the key principles stated here and the content of the remainder of this document do not focus on additional statutes, regulations, policies, and procedures that apply to the conduct of scientific research at the agency or by organizations acting on behalf of FDA pursuant to a grant, such as regulations pertaining to human and animal subject protection and scientific research integrity.

Key Principles of Scientific Integrity at FDA

- Promoting the professional development of our scientists by encouraging publication in and editorial service to peer reviewed journals, presentations at professional meetings, and full participation in appropriate professional or scholarly societies and related activities that may benefit the public health.

While scientists should have the right to participate on the boards of scientific societies, their involvement could create fiduciary conflicts of interest. FDA employees should be required to disclose their affiliations.

The policies and procedures at FDA that preserve and protect scientific integrity (as discussed and set forth below) include the following examples, which are representative of the agency's overall approach to the issue and incorporate several of the foregoing key principles:

- "Scientific Dispute Resolution at FDA" (Staff Manual Guide ("SMG") 9010.1) requires the agency's organizational units to establish processes for resolving scientific disputes. These processes must include, among other things: key messages that employees are encouraged to voice scientific disagreements and that they are protected from retaliation and repercussions for raising such disagreements within their organization; a requirement that the head of the organization render a written decision if the dispute cannot be resolved at a lower level; and appropriate timeframes. The agency-wide SMG also provides a mechanism for employees to elevate scientific disputes to the Office of the Commissioner. An Agency Dispute Process Review Board, chaired by the agency's Chief Scientist, is then responsible for conducting full and fair evaluations of the disputes to evaluate whether the appropriate processes were followed, whether the decisions made were based on consideration of all relevant evidence and views bearing on the scientific question at issue, and whether the initiating employee was provided an opportunity to express his or her concerns at all appropriate levels.

Existing law--the FDA Amendments Act of 2007--requires that dissenting opinions be publicly documented in an "Action Package" that is put forward within 30 days of a new product approval. This policy should reference that requirement.

- "Review of FDA-Related Articles and Speeches" (SMG 2126.3). FDA encourages employees to share scientific or technical information that may benefit the public health by giving speeches and publishing articles in professional journals or other publications. The SMG is important for both FDA and public health in that it provides for a clear set of processes for agency employees to follow when they are contemplating an article or presentation that relates to their work, or the work of others, at FDA. Perhaps just as importantly, the policy makes it clear that scientists within the agency are free to publish or present their findings even when they are not in agreement with the agency on the findings, conclusions, or policy implications in the article or speech, provided they identify the findings, conclusions, or policy implications as their own and follow all statutes and regulations applicable to such activities.

This policy is fairly strong, granting FDA employees the ability to publish their own scientific analysis. It would be helpful if some of this language were included in this policy rather than just linking to it externally.

3. BACKGROUND

On March 9, 2009, the President issued a Memorandum articulating a set of principles critical to the preservation and promotion of scientific integrity. On December 17, 2010, Dr. John Holdren, Assistant to the President for Science and Technology, issued a memorandum further describing key principles for executive departments and agencies to address through the development of policies and procedures as a means of ensuring scientific integrity in their decision-making. This document identifies key principles of scientific integrity upheld by FDA and provides an overview of existing FDA-wide policies and procedures that address these principles.

4. APPLICATION

FDA has nine (9) major organizational components with distinct responsibilities: the Office of the Commissioner, Office of Regulatory Affairs, Center for Food Safety and Applied Nutrition, Center for Drug Evaluation and Research, Center for Biologics Evaluation and Research, Center for Devices and Radiological Health, Center for Veterinary Medicine, Center for Tobacco Products, and National Center for Toxicological Research. This document collectively refers to those organizations as Centers.

Centers will implement and follow the general principles and procedures set forth in this policy and the policies and procedures to which it refers. Centers may supplement and expand upon the policy and procedures to meet their specific needs through issuance of written standard operating procedures (SOPs), so long as those SOPs support and do not conflict with the general principles set forth in this SMG and the policies and procedures to which it refers.

5. PRINCIPLES, RESPONSIBILITIES, PROCEDURES, AND RESOURCES

A. Foundations of Scientific Integrity

1. Ensuring a culture of scientific integrity;

A culture of scientific integrity is one that ensures that scientific decisions are the product of honest investigation, open discussion, refined understanding, and a firm commitment to evidence, and at the same time are shielded from inappropriate political influence.

FDA's Office of Scientific Integrity (OSI) seeks to promote a culture of scientific integrity across the agency. Created in 2009, OSI reports to the Chief Scientist and works with the Office of the Commissioner and the agency's other Centers to: 1) ensure that the agency's policies and procedures with respect to scientific integrity are up to date and

The policy should state specifically to whom this policy applies, and should include all employees, including supervisors and political appointees, as well as contractors.

While this represents a good start, some companies present selective scientific information to the FDA, including data that supports approval of their products and withholding data that does not. The FDA should ensure that scientific information from interested parties outside the agency is complete and of the utmost scientific integrity.

This is excellent. It is important to state that political influences should not interfere with agency science.

The FDA should also include a web portal where all related policies can be easily found.

applied across the agency; and 2) review and work to resolve both informal and formal scientific disputes.

In addition to supporting Departmental regulations and policies for scientific integrity, FDA's regulations and policies promote openness and robust and vigorous debate on the scientific principles that underlie its decisions. FDA's regulations:

- Require the agency to document any significant scientific decision – and the basis for that decision – in an administrative file that must include all “relevant evaluations, reviews, memoranda, letters, opinions of consultants, minutes of meetings, and other pertinent written documentation” and must reflect “significant controversies or differences of opinion and their resolution” (21 CFR 10.70).
- Enable individual employees or interested parties outside the agency to request internal agency review of scientific decisions and their bases (21 CFR 10.75).
- Permit interested parties to petition the agency to revise its approach to particular scientific issues (21 CFR 10.30), petition the agency to issue, amend, or revoke a regulation, or take or refrain from taking any administrative action (21 CFR 10.25), and to comment on the regulations and guidance documents that bear directly on scientific issues before the agency (21 CFR 10.40, 10.115(f)).

The FDA should commit to making these documents available to the public in a timely manner.

In addition, as described in more detail above, FDA's SMG entitled “Scientific Dispute Resolution at FDA” ([SMG 9010.1](#)), sets forth mandatory elements to be included in all scientific dispute resolution processes at the Centers and establishes an agency-wide appeals process for internal scientific disputes.

In addition, FDA's [SMG on scientific disputes](#) states that, “[i]t is the responsibility of all those involved [in the dispute process] to ensure that all initiators of disputes are protected from any retaliation by their supervisors, peers, leadership and others, related to initiating or engaging in this process.” All FDA employees are required to complete training on their rights and protections under the Notification and Federal Employee Antidiscrimination and Retaliation (No FEAR) Act of 2002 within 90 days of their entrance on duty and every two years thereafter.

This is excellent. Training is important to make these policies part of the agency's culture.

2. Strengthening the actual and perceived credibility of scientific reviews and decision-making;

The following FDA policies and programs seek to strengthen the scientific quality, integrity and credibility of scientific reviews and decision-making at the agency:

- FDA Scientist Review Committees – a system of committees designed to review the scientific credentials and qualifications of prospective and current scientific employees and to ensure that selection of scientists is based on their scientific and technical knowledge, credentials, and integrity.
- Scientific Peer Review – consistent with the “Final Information Quality Bulletin for Peer Review” issued by the Office of Management and Budget in 2005, FDA publishes on its website [an agenda of peer review plans and completed peer review reports](#) for scientific information that is likely to have a clear and substantial impact on important policies or private sector decisions.
- Federal Standards of Conduct– all FDA employees are required to comply with all applicable rules and regulations regarding financial conflicts of interest (see 5 CFR 2635, 5501, and 5502). FDA makes training modules on conflicts of interest available on the agency Intranet and requires all confidential and public filers to take annual training. FDA’s [Ethics and Integrity Staff](#) provide advice and assistance to employees on legal and ethical requirements related to financial disclosure, prohibited financial interests, outside activities, co-sponsorship agreements, post-employment practices, and other issues related to conflicts of interest.

3. Facilitating the free flow of scientific and technological information and establishing principles for conveying this information to the public;

FDA collects, and often creates, a vast amount of scientific and technological information regarding the products it regulates. Facilitating the free flow of information underlying the agency’s decision-making, to the extent permitted by law, allows the public, Congress, media, and industry to better understand FDA’s decisions.

- FDA routinely posts large amounts of information concerning its regulated products and its regulatory decisions on its Internet site, and provides important information to diverse audiences through a variety of means, from listservs to social media. FDA scientists are encouraged to present at scientific meetings and/or publish their

It is important for scientists to receive explicit encouragement to publish research, and for FDA to use a diversity of methods to distribute information.

research findings in the peer reviewed literature and routinely do so.

- **Transparency Initiative** – In 2009, FDA launched an agency-wide Transparency Initiative that seeks to identify new ways in which FDA can make its activities and decision-making more transparent to the public as well as to the regulated industry.
- **Public Hearings and Advisory Committees** – FDA seeks expert and public input on a broad scope of complex issues related to the products it regulates, consistent with the Federal Advisory Committee Act, the agency’s implementing regulations (21 CFR part 14) and numerous guidances. FDA’s 50 advisory committees and panels provide independent expert advice on scientific, technical and policy matters related to FDA-related products. Public hearings before an advisory committee are convened whenever the agency concludes that it is in the public interest for an advisory committee to hold a public meeting and to review and make recommendations on any matter before the agency. FDA holds approximately 75 meetings per year that, collectively, include the participation of over 1000 outside experts.
- **Freedom of Information Act Requests** – FDA makes many of its records containing scientific and technical information available to the public through its regulations in 21 CFR part 20, which implement the Freedom of Information Act. As stated in 21 CFR 20.20, FDA makes “the fullest possible disclosure of records to the public, consistent with the rights of individuals to privacy, the property rights of persons in trade secrets and confidential commercial or financial information, and the need for the agency to promote frank internal policy deliberations and to pursue its regulatory activities without disruption.”
- **Risk Communication** – In 2009, FDA released its Strategic Plan for Risk Communication. The report describes FDA's strategy for improving how the agency communicates about the products it regulates in the context of a dynamic environment where rapidly evolving technologies enable patients and consumers to become increasingly involved in managing their health and well-being. The Strategic Plan defines three key areas—science, capacity, and policy—in which strategic actions can help improve how the agency communicates about the risks and benefits of the products it regulates.

[The policy is missing critical components. We have highlighted additional tenets that should be included.]

While the FDA has developed a Transparency Initiative, for the most part, implementation has been uneven.

In addition to fully implementing its Transparency Initiative, the FDA should follow the lead of the White House and release visitor logs in a timely manner so that the public may better understand who is influencing science-based policy decisions. The visitor log policy should apply to political appointees, Senior Executive Service and GS-14 and GS-15 level employees.

This section is incomplete. The policy is only effective if it is embraced by its employees. The FDA should commit to comprehensive training employees in scientific integrity.

In addition, the policy does not indicate who will enforce the policy, and fails to lay out a procedure for addressing instances of scientific misconduct in a way that is publicly accountable.

The FDA should be required to publicly report both the aggregate number of misconduct allegations and the specifics regarding those cases where misconduct is confirmed.

In addition, as mentioned, it is important that the policy pertain to scientific information from interested parties outside the agency that is submitted to the agency for review.

B. Public Communications

Media relations at FDA are primarily coordinated by the Office of Public Affairs (OPA), which is part of the Office of External Affairs (OEA) in the Office of the Commissioner. In September 2011, the Department of Health and Human Service (HHS) issued guidelines, which apply to FDA, that outline HHS's policies regarding media relations. FDA is currently developing its own written media relations policy, consistent with HHS's guidelines and the agency's current practices, that describes FDA's commitment to responding quickly, thoroughly, and openly to news organizations while observing legal requirements to protect and prevent disclosure of certain information. The written policy will include a code of conduct for FDA press officers and a detailed description of the policies and procedures for releasing information to the media. To reflect current practices, there will be an explicit provision prohibiting press officers from asking or directing federal scientists to alter scientific findings.

The FDA should grant scientists the right of last review for documents which rely heavily on their research. FDA employees should also have the right to speak publicly about any issues as long as they explain they are presenting their individual opinions, not the official views of the FDA. In addition, it is unclear of how Department of Health and Human Services policies relates to or contradicts this. Finally, the policy should give scientists the right to speak freely to the media regardless of whether they receive permission from an agency public affairs officer.

This is vague. What does certain information mean? What are the standards for determining the confidentiality of this information?

C. Use of Federal Advisory Committees

FDA's advisory committee program is governed by a number of federal laws, including recent amendments to the Federal Food, Drug, and Cosmetic Act (FDCA) with respect to conflicts of interest (i.e., section 712 of the FDCA). FDA's regulations at 21 CFR part 14 set forth standards and procedures for convening advisory committees, reviewing potential conflicts of interest, and otherwise ensuring that advisory meetings are conducted in accordance with the law. FDA has a dedicated staff within its Office of the Commissioner—the Advisory Committee Oversight and Management Staff (ACOMS)—that oversees the agency's advisory committee program and works collaboratively with the agency's product-based Centers to implement the governing laws and regulations.

Also, while altering of scientific findings is a problem, the policy sidesteps the main problem: press officers acting as filters by preventing reporters from speaking to scientists whose analysis the press officers do not like. Press officers should also be prohibited from serving as gatekeepers.

FDA is to be commended for compliance with the FDAAA and reducing the number of conflicted experts in committees. It should continue this work until committees are conflict free.

1. Recruitment process

FDA conducts its recruitment process for new members of its federal advisory committees in an open and transparent manner.

- Under 21 CFR 14.82 and 14.84, the agency seeks nominations for scientific members—as well as consumer, industry and patient representatives—from professional societies, industry, consumer and patient advocacy groups, the individual himself, or other interested persons.
- To assist all potential advisory committee members and the committees in need of members, a dedicated staff member in ACOMS serves as the liaison and point of contact for information

regarding the agency's advisory committee recruitment activities, vacancies, and nominations.

2. Availability of professional biographical information

- FDA posts a roster of all advisory committee members expected to attend a specific meeting at the same time briefing materials for that meeting are posted. See Guidance for Industry: Advisory Committee Meetings – Preparation and Public Availability of Information Given to Advisory Committee Members.
- FDA provides information on each committee on the applicable committee web page, including: Advisory Committee meeting announcements; meeting materials (briefing material, agenda, meeting roster and waivers for conflicts of interest if applicable); committee charter; membership roster with links to CVs; and a list of current membership vacancies.

3. Selection of members

- In accordance with agency regulations, members of policy advisory committees are selected based on diverse interests, education, training and experience; specific technical expertise is not a requirement. 21 CFR 14.80(a)
- Members of technical advisory committees are selected based on expertise in the subject matter with which the committee is concerned and have diverse professional education, training and experience so that the committee can handle the scientific issues that may arise. 21 CFR 14.80(b)
- Consistent with the requirements of the Federal Advisory Committee Act (FACA) and corresponding regulations at 41 CFR § 102-3.60(b)(3), the charter for each advisory committee contains a "Membership Balance Plan" that describes the process used to ensure the committee is balanced in terms of the points of view represented by the members. The regulations require that, "in the selection of members for the advisory committee, the agency will consider a cross-section of those directly affected, interested, and qualified, as appropriate to the nature and functions of the advisory committee" and that those committees requiring technical expertise include persons with demonstrated qualifications and relevant experience.

4. Public availability of waivers

- To increase the transparency, consistency, and clarity of the advisory committee process, consistent with the requirements of section 712(c) of the FDCA, FDA recently developed a draft guidance that provides procedures regarding disclosure of financial interest information applicable to all special government employees (SGEs) and regular government employees who are eligible to receive a conflict of interest waiver to participate in FDA advisory committee meetings: Guidance for the Public, FDA Advisory Committee Members, and FDA Staff: Public Availability of Advisory Committee Members' Financial Interest Information and Waivers.

This disclosure is important.

- For waivers that are granted, the disclosure statement signed by the advisory committee member is posted on FDA's website, along with the agency's waiver. FDA posts these documents on the FDA website at least 15 days prior to the relevant advisory committee meeting, except for disqualifying financial interests that do not become known to FDA until shortly before the meeting. For disqualifying financial interests that FDA becomes aware of less than 30 days prior to the meeting and for which a waiver is issued, FDA posts the documents as soon as practicable and no later than the day of the meeting. These time frames are consistent with the requirements of section 712(c)(3) of the FDCA.

The FDA should commit to conflict-free committees. Conflicted experts should be able to share their knowledge with committee members but should be prohibited from chairing the committees or voting for or against product approval.

5. Reports and Findings of AC.

As stated in FDA's Guidance on Voting Procedures for Advisory Committee Meetings, FDA's advisory committees provide valuable independent expert advice on a range of complex scientific, technical and policy issues. As the agency makes its final decision, FDA considers the recommendations made by advisory committees, including the committee deliberations and voting. The reports and recommendations of the advisory committees are not changed or modified; however, FDA division staff review the transcripts of the meetings for accuracy. Advisory committees provide recommendations to FDA while FDA is responsible for the final agency decisions.

D. PROFESSIONAL DEVELOPMENT OF GOVERNMENT SCIENTISTS AND ENGINEERS

In 2011, FDA's Office of the Chief Scientist created a new Office of Scientific and Professional Development (OSPD) that promotes and facilitates scientific excellence and the professional development of scientists throughout the agency. The program complements activities throughout the organization and is directed at all scientific areas (e.g.,

This section could be clarified so employees understand that this applies when FDA employees are engaged in official and non-official capacities.

population/statistical, review, laboratory and manufacturing sciences) and includes continuing education and interactions with universities and others. FDA policies also encourage both the publication of research findings in professional journals and the presentation of research findings at professional meetings. FDA further permits its scientists and engineers to become editorial board members, to participate in professional societies, and to receive honors and awards, consistent with applicable ethical rules.

- In February 2011, FDA issued an agency- wide SMG on the publication or presentation of FDA-related articles or speeches by agency employees. As reflected in the SMG and described in more detail above, FDA encourages employees to share scientific or technological information that may benefit the public health by giving speeches and publishing articles in professional journals or other publications.
- The OSPD maintains a page on the agency's Intranet called "Science FIRST," which serves as a resource for scientific personnel. Science FIRST lists, among other things, training opportunities, procedures for promotions, and nomination processes for internal awards.
- Consistent with the ethical rules and regulations established by the Office of Government Ethics and the HHS for outside activities, FDA permits its scientific personnel to serve as editors and to receive outside honors and awards that do not provide prohibited compensation.²
- FDA permits its employees to serve as officers and directors of professional and scholarly societies when done as an approved outside activity and with appropriate recusals from affected matters. Consistent with regulations and guidelines from HHS and the Office of Government Ethics regarding 18 USC 208, FDA also permits its employees: (1) to serve, in their official capacity, as federal liaisons to such organizations and (2) if a waiver is obtained after consultation with HHS's Office of General Counsel, to serve, in their official capacity, as officers or directors of such organizations.³

[The policy is missing critical components. We have highlighted additional sections that should be included.]

6. EFFECTIVE DATE

The effective date of this guide is February 3, 2012.

² Indeed, FDA itself issues awards for excellence in scientific research on an annual basis.

³ Note, however, that in May 2011 the Office of Government Ethics proposed to eliminate the need for a waiver.

To create meaningful change at the agency, the policy will need to be improved to address implementation, such as how misconduct is reported and oversight of how the FDA addresses allegations of misconduct.

7. Document History – SMG 9001.1, Scientific Integrity at FDA

STATUS (I, R, C)	DATE APPROVED	LOCATION OF CHANGE HISTORY	CONTACT	APPROVING OFFICIAL
Initial	02/03/2012	N/a	OC/OSI	Jesse Goodman, Chief Scientist

NOTE: The policies, procedures, and practices documented above are the key tools for protecting and promoting scientific integrity at FDA. They are critical to the agency's ability to make the best possible decisions, to support a culture of science based decision-making for public health, and to maintain both internally and externally an environment of open discussion and trust.

(c)

Comment [.1]: