

REPORT OF THE BOARD OF TRUSTEES

B of T Report 19-A-19

Subject: FDA Conflict of Interest
(Resolution 216-A-18)

Presented by: Jack Resneck, Jr., MD, Chair

Referred to: Reference Committee B
(Charles Rothberg, MD, Chair)

At the 2018 Annual Meeting of the House of Delegates (HOD), Resolution 216-A-18, “[Food and Drug Administration] FDA Conflict of Interest,” was referred for report back at the 2019 Annual Meeting. Resolution 216-A-18, sponsored by the Medical Student Section, asked that:

Our American Medical Association (AMA) advocate (1) that the Food and Drug Administration [(FDA)] place a greater emphasis on a candidate’s conflict of interest when selecting members for advisory committees (New HOD Policy); and (2) for a reduction in conflict of interest waivers granted to Advisory Committee candidates.

There was mixed testimony on Resolution 216 during the reference committee. Testimony was offered that disclosure and transparency into conflicts of interest (COI) are important, but on the other hand challenges may exist to find qualified individuals without COIs. Others offered that the FDA should utilize generally accepted COI policies and should limit waivers of such policies for advisory committees.

FDA AND THE ROLE OF ADVISORY COMMITTEES

The FDA utilizes advisory committees to obtain independent expert advice and recommendations on scientific, technical, and policy matters related to FDA-regulated products. There are 50 advisory committees and panels.¹ The recommendations of advisory committees do not bind the FDA. Although the advisory committees include permanent non-voting members who are FDA employees (typically responsible for administering the meetings), the majority are external experts who are considered special government employees (SGEs) while performing their advisory committee duties. The advisory committees cover a range of products.²

The FDA’s advisory committees are governed by several federal laws and regulations that: (1) establish standards for convening advisory committees; (2) specify criteria for what constitutes a COI; and (3) outline the requirements for disclosing, assessing, and managing COIs. In addition, the FDA has issued guidance documents interpreting government-wide regulations pertaining to the appearance of COIs as well as guidance related to the public availability of advisor COI disclosures and associated FDA waivers. For the most part, the federal laws, regulations, and guidance are generally the same whether a committee advisor is a permanent federal employee or SGE with some exceptions as outlined below. For over a decade, the FDA and Congress have implemented reforms to the FDA’s process for assessing COIs, managing COIs including waivers, and public disclosure.³ Members of the FDA’s advisory committees are subject to Federal COI laws (18 USC section 208) as well as government-wide standards of ethical conduct regulations

(5 CFR section 2635.502). Even where a member has no financial interests that would require the member to refrain from participating in an advisory committee meeting (“recuse”) under Federal COI laws, the member may be disqualified from participation under the government-wide Federal regulation at 5 CFR section 2635.502 if the member has interests or relationships that may create the appearance that the member lacks impartiality on the issue before the advisory committee.

As specified in federal law, the FDA has a process for determining whether to grant a waiver for an advisory committee member with an actual financial COI. The FDA also has guidance outlining how the Agency evaluates whether an advisory committee member has potentially disqualifying interests or relationships that fall into the second category of interests: appearance of a COI. (In this latter case, the regulations provide that an authorization to participate would be issued as opposed to issuance of a waiver.) In both cases, the decision to permit voting, permit participation, or recusal will be made by the FDA.

PROHIBITION AGAINST FINANCIAL COI

Unless granted a waiver, a federal employee may not “personally and substantially participate” in an official capacity in any particular matter which, to the employee’s knowledge, the employee or a related person or organization (whose interests are imputed to the employee under 18 U.S.C. section 208) has a “financial interest” if the particular matter will have a “direct and predictable effect” on that interest (5 CFR section 2640.103(a)). In this analysis, federal employees includes FDA advisory committee members who are considered SGEs. A financial interest is defined as the potential for gain or loss as a result of governmental action on the particular matter which includes stock options, a salary, job offer, indebtedness, and similar interests (5 CFR section 2640.103(b)). Under this law, the financial interests of other, related persons and organizations (as defined in law and statute)⁴ are imputed to the employee and may disqualify an employee to the same extent as the employee’s own interests. Under the law, a COI arises when the employee participates in an official matter and there is a direct and predictable link between the matters in which the federal employee participates and the employee’s financial interests. The link cannot be contingent and dependent on other events.

Process for Reviewing Financial COIs and Granting Waivers

The FDA reviews financial COI disclosures made by potential advisory committee members and the member’s expertise with respect to the specific product or policy to be evaluated at a particular meeting. Each adviser is required to certify to the truth and completeness of any information provided.⁵ The Agency can issue a waiver to permit participation despite a current conflict or one that ended during the 12 months preceding a meeting consistent with applicable law. The FDA is required by law to apply different standards to SGEs (who constitute the majority of advisory committee members) and permanent government employees in order to determine if an applicable standard for granting a waiver pursuant to 18 USC section 208 is met.

If the individual is a SGE, the FDA’s “determination must be based on a certification that the need for the [SGE’s] ... services outweighs the potential for a conflict of interest created by the financial interest involved,” (5 CFR section 2640.302). The FDA considers 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 SGE, the uniqueness of the SGE’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.⁶ If the individual is a permanent government employee, the FDA determines 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 making this determination, the FDA considers 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, and the need for the employee's services in the particular matter.⁷ FDA guidance provides that a common factor to be considered for both categories of advisory committee members is the "need" for the individual's services. In deciding whether there is a need, the FDA will consider: (1) the uniqueness of the member's qualifications; (2) the difficulty locating similarly qualified individuals without a disqualifying financial interest; (3) the value and utility of the member's expertise to the matter being addressed by the committee; and, (4) the nature and extent of the disqualifying financial interest.

In addition, the FDA must apply one more standard to members serving on drug or biologic advisory committees that provide scientific advice and recommendations regarding a clinical investigation or marketing approval. For these members, the standard for a waiver to permit voting is whether a waiver is "necessary" to afford the committee "essential expertise."⁸ Where a financial COI exists, the FDA determines whether the member may: (1) participate as a non-voting member, or (2) not participate in the advisory committee.⁹ Individuals with financial COIs are not permitted to vote as a matter of FDA policy. A waiver may not be granted when the member's own scientific work is involved.¹⁰

The Food and Drug Administration Amendments Act of 2007 included a provision capping the number of COI waivers the FDA could grant in any given year. Subsequently, this cap was rescinded in the Food and Drug Administration Safety and Innovation Act of 2012.¹¹ A recent analysis of FDA COI waivers found that in fiscal year (FY) 2012, the waiver rate did not exceed one percent and this was less than in earlier years.¹² Additionally, the FDA reports COI waiver rates of less than one percent for FYs 2013, 2014, 2015, and 2016 on its online [FDA-TRACK Advisory Committees Dashboard](#).¹³

Public Disclosure

The FDA publicly discloses¹⁴ on the Agency's website the type, nature, and magnitude of the financial interests of each advisory committee member who has received a waiver under 18 U.S.C. section 208. The FDA also provides the reasons for granting each waiver prior to the advisory committee meeting,¹⁵ including, as appropriate, the public health interest in having the expertise of the member with respect to the particular matter.¹⁶

APPEARANCE OF A CONFLICT OF INTEREST – PERSONAL AND BUSINESS RELATIONSHIPS

Federal law also contains provisions to help ensure that an employee takes appropriate steps to avoid an appearance of loss of impartiality in the performance of his or her official duties. Under 5 CFR section 2635.502 where an agency employee (including FDA advisory committee members), "knows that a particular matter involving specific parties is likely to have a direct and predictable effect on the financial interest of a member" of the employee's household, or knows that a person with whom the employee has a "covered relationship is or represents a party to such matter," and "where the employee determines that the circumstances would cause a reasonable person with knowledge of the relevant facts" to question the employee's impartiality in the matter, the employee should not participate in the matter unless the employee has informed the agency designee of the appearance problem and received authorization from the agency designee. An employee has a "covered relationship" with:

- a person other than a prospective employer with whom the employee has or seeks a business, contractual or other financial relationship that involves other than a routine consumer transaction;
- a person who is a member of the employee's household, or who is a relative with whom the employee has a close personal relationship;
- a person for whom the employee's spouse, parent or dependent child is, to the employee's knowledge, serving or seeking to serve as an officer, director, trustee, general partner, agent, attorney, consultant, contractor or employee; any person for whom the employee has, within the last year, served as officer, director, trustee, general partner, agent, attorney, consultant, contractor or employee; or
- an organization, other than a political party,¹⁷ in which the employee is an "active participant."¹⁸

Granting a Section 502 Authorization

If the FDA concludes that an appearance issue exists, a determination is made whether the Agency's interest in the member's participation outweighs the concern that a reasonable person may question the integrity of the Agency's programs and operations. If so, the FDA may grant an authorization (i.e., a waiver) before the meeting to allow the member to participate. The FDA may limit authorization or deny authorization. The Agency takes into consideration a number of factors including, but not limited to: (1) the nature of the relationship involved; (2) the effect that resolution of the matter would have upon the financial interests of the person involved in the relationship; (3) the nature and importance of the member's role in the matter, including the extent to which the member is called upon to exercise discretion in the matter; (4) the sensitivity of the matter; (5) the difficulty of reassigning the matter to another expert; and (6) adjustments that may be made in the member's duties that would reduce or eliminate the likelihood that a reasonable person would question her impartiality.

RESEARCH ON COI AND FDA ADVISORY COMMITTEE RECOMMENDATIONS

Despite long-standing federal laws governing COIs and waivers applicable to FDA advisory committee members, there have remained persistent concerns in the general public that waivers of COIs negatively impact the trustworthiness and independence of advisory committee recommendations. However, the research and investigations into this matter have produced mixed results. In a 2014 study of FDA advisory committee member COIs, a researcher found that, where an advisory committee member had an exclusive financial relationship with the manufacturer (referred to as a sponsor) of the product under review, the member appeared to be biased in support of the product sponsor.¹⁹ No similar bias was found where members had financial ties to both a sponsor and its competitors.²⁰ The study author noted that "[t]hese findings point to important heterogeneities in financial ties and suggest that policymakers will need to be nuanced in their management of financial relationships of FDA advisory committee members."²¹ In another study, the researchers found little significant evidence that advisory committee members vote in their financial interests.²² The authors also found that the perverse exclusion of "financially-conflicted members resulted in a sharp drop in average member expertise, and an unintended increase in approval voting." The study authors concluded that "[e]liminating conflicts could sharply reduce the level of expertise of the decision makers and lead to unexpected voting tendencies."²³ More recently, an investigation of FDA advisory committee members COIs has called into question: (1) the completeness of COI disclosures submitted by members; (2) whether the FDA does enough to verify the completeness and accuracy of such disclosures; and (3) whether past or current COI assessments are inadequate as pay-later COIs may play a more significant role in influencing a member's deliberations and vote. Specifically, a 2018 investigation found that, at the time of or in

the year leading up to the advisory committee meetings under scrutiny, many of the members received payments or other financial support from the sponsoring drug firm or key competitors for consulting, travel, lectures, or research.²⁴ The investigators concluded that the FDA did not publicly disclose those ties even though this information was disclosed in scholarly journals.²⁵ In the same investigation, a review was undertaken of compensation records from drug sponsors to advisory committee members who advised the FDA on whether to approve psychopharmacologic, arthritis, and cardiac or renal drugs between 2008 and 2014.²⁶ The investigators concluded that there were “widespread after-the-fact payments or research support to panel members.”²⁷ As correctly noted by the investigators: “[t]he agency’s safeguards against potential conflicts of interest are not designed to prevent such future financial ties.”

AMA POLICY

The AMA has policy addressing COIs applicable to FDA advisory committees (Policy H-100.992, “FDA”) as well as ethics policy concerning COIs in the areas of research (Ethics Opinion 7.1.4/AMA Principles of Medical Ethics: II, IV,V, “Conflicts of Interest in Research”) and clinical practice guidelines (Policy H-410.953, “Ethical Considerations in the Development of Clinical Practice Guidelines”).

DISCUSSION

The resolved clauses in Resolution 216 would have the AMA adopt policy that specifies that the FDA should place a greater emphasis on advisory committee member COIs and seek a further reduction in the number of COI waivers granted by the FDA. While there is widespread consensus that COI policies are appropriate and necessary along with a measured approach to granting COI waivers for FDA advisory committee members, there is also concern that an overzealous approach to waivers will undermine the actual or perceived quality of advisory committee recommendations. The FDA has reduced the number of waivers granted, but there are conflicting reports with regard to the magnitude of the challenge the Agency faces filling advisory committee vacancies. For example, one article reported that in FY 2017, “218 advisory committee positions of the 600-plus on the FDA’s 49 advisory committees had not been filled.”²⁸ Yet, data disclosed by FDA indicates that in FY 2017 there were 64 vacancies out of 564²⁹ and in FY 2018 there were 57 total vacancies out of 547 members.³⁰ A 10 percent vacancy is substantially lower than a nearly 50 percent vacancy. Nonetheless, the COI waiver rate has remained consistently below one percent. Lowering this percentage further is reasonably likely to increase vacancies which are hovering at 10 percent.

Existing AMA ethics policy provides a clear set of parameters concerning COIs and waivers regarding clinical practice guidelines development and clinical research that should be utilized to expand upon AMA policy concerning FDA advisory committee member COIs and waivers. Our current AMA policy related to advisory committee members provides that a FDA decision to approve a new drug, to withdraw a drug’s approval, or to change the indications for use of a drug must be based on sound scientific and medical evidence derived from controlled trials and/or postmarket incident reports as provided by statute and evidence of such should be evaluated by the FDA, in consultation with its advisory committees (Policy H-100.992, “FDA”). The policy also provides that the FDA should not let COIs overrule scientific evidence in making policy decisions. Building on the above policy, our AMA has ethics policy noting how minimizing and mitigating COIs in clinical research is imperative to justify and maintain trust in the medical research community (7.1.4, “Conflicts of Interest in Research”). This is equally true for FDA advisory committee member recommendations. This same policy provides that physicians who engage in research should disclose material ties to companies whose products they are investigating or other ties that create real or perceived COIs. Similarly, AMA ethics policy concerning clinical practice

guidelines provides that patients, the public, physicians, and other stakeholders must have confidence that published guidelines are the ethically and scientifically credible product of development processes that are rigorous, independent, transparent, and accountable (Policy H-410.953, “Ethical Considerations in the Development of Clinical Practice Guidelines”). Notably, while Policy H-410.953 specifies that published guidelines/updates are to be developed independent of direct financial support from entities that have an interest in the recommendations, it does specify consideration for COIs (actual and perceived) for individuals associated in the development of the guidelines. The policy states: “ideally, all individuals associated with guideline development will be free of conflicts of interest during the development process and will remain so for a defined period following the publication of the guideline.” In order to ensure credibility, our AMA policy provides that:

formal procedures would be adopted to minimize the potential for financial or other interests to influence the process at all key steps (selection of topic, review of evidence, panel deliberations, development and approval of specific recommendations, and dissemination of final product). These should include: a) required disclosure of all potential conflicts of interest by panel members, consultants, staff, and other participants; b) clearly defined criteria for identifying and assessing the seriousness of conflicts of interest; and c) clearly defined strategies for eliminating or mitigating the influence of identified conflicts of interest (such as prohibiting individuals from participating in deliberations, drafting, or voting on recommendations on which they have conflicts) in those limited circumstances when participation by an individual with a conflicting interest cannot be avoided.

Finally, the policy provides for a clear statement of methodology, COI policy and procedures, and disclosures of panel members’ COIs. Extending the foregoing policies to FDA advisory committee member COIs and waivers will underscore the importance of existing FDA laws, regulations, and policies. However, the policy does not address concerns that advisory committee members may not be fully disclosing conflicts and independent targeted auditing for sufficiency may be warranted. In addition, existing policy does not address the impact of pay-later COIs (e.g., where a FDA advisory committee member develops a financial COI only after his or her initial appointment on the advisory committee has expired). Since there is limited research on the topic, this is important area for the FDA and researchers to more fully evaluate and craft appropriate policy.

RECOMMENDATION

In light of these considerations, your Board of Trustees recommends that the following be adopted in lieu of Resolution 216-A-18 and the remainder of this report be filed:

1. That our AMA reaffirm Policy H-100.992, “FDA,” which supports that FDA conflicts of interest should not overrule scientific evidence in making policy decisions and the FDA should include clinical experts on advisory committees. (Reaffirm HOD Policy)
2. That our AMA adopt the following new policy:

It is the position of the American Medical Association that decisions of the Food and Drug Administration (FDA) must be trustworthy. Patients, the public, physicians, other health care professionals and health administrators, and policymakers must have confidence that FDA decisions and the recommendations of FDA advisory committees are ethically and scientifically credible and derived through a process that is rigorous, independent, transparent, and accountable. Rigorous policies and procedures should be in place to minimize the potential for financial or other interests to influence the process at all key steps. These should include,

1 but not necessarily be limited to: a) required disclosure of all relevant actual or potential
2 conflicts of interest, both financial and personal; b) a mechanism to independently audit
3 disclosures when warranted; c) clearly defined criteria for identifying and assessing the
4 magnitude and materiality of conflicts of interest; and d) clearly defined processes for
5 preventing or terminating the participation of a conflicted member, and mitigating the
6 influence of identified conflicts of interest (such as prohibiting individuals from participating in
7 deliberations, drafting, or voting on recommendations on which they have conflicts) in those
8 limited circumstances when an individual's participation cannot be terminated due to the
9 individual's unique or rare skillset or background that is deemed highly valuable to the process.
10 Further, clear statements of COI policy and procedures, and disclosures of FDA advisory
11 committee members' conflicts of interest relating to specific recommendations, should be
12 published or otherwise made public. Finally, it is recognized that, to the extent feasible in
13 accordance with the principles stated above, participation on advisory committees should be
14 facilitated through appropriate balancing of the relative scarcity or uniqueness of an
15 individual's expertise and ability to contribute to the process, on the one hand, as compared to
16 the feasibility and effectiveness of mitigation measures including those noted above. (New
17 HOD Policy)

18
19 3. That our AMA adopt the following new policy:

20
21 It is the position of the American Medical Association that the FDA should undertake an
22 evaluation of pay-later conflicts of interest (e.g., where a FDA advisory committee member
23 develops a financial conflict of interest only after his or her initial appointment on the advisory
24 committee has expired) to assess whether these undermine the independence of advisory
25 committee member recommendations and whether policies should be adopted to address this
26 issue. (New HOD Policy)

Fiscal Note: Less than \$500

REFERENCES

¹ FDA Advisory Committees, Accessed on February 25, 2019

² Id. Products include blood, vaccines and other biologics; human drugs; food; medical devices; patient engagement; pediatric; radiation-emitting products; risk communication; science board; toxicological research; veterinary; and tobacco.

³ See, for example, the FDA Amendments Act (FDAA) of 2007 which mandated that by 2012 no more than thirteen percent of committee advisors per year could receive COI waivers. The FDA reduced the maximum size of financial interests eligible for waivers from a combined financial interest of up to \$100,000, to a maximum of \$50,000. See also Draft Guidance for the Public, FDA Advisory Committee Members, and FDA Staff on Procedures for Determining COI and Eligibility for Participation in FDA Advisory Committees (March 2007); Public Availability of Advisory Committee Members' Financial Interest Information and Waivers-Final Guidance (2014); and, Procedures for Evaluating Appearance Issues and Granting Authorizations for Participation in FDA Advisory Committees (2016).

⁴ Related persons and organizations include: the employee's spouse, minor child, or general partner; an organization or entity for which the employee serves as officer, director, trustee, general partner, or employee; and a person with whom the employee is negotiating for, or has an arrangement concerning, prospective employment.

⁵ In preparation for advisory committee meetings involving particular matters, SGEs invited to participate in the meetings are required to report to FDA any financial interests related to the subject matter of the advisory committee meeting. 5 CFR § 2634.904(a)(2). Permanent government employees also report financial interests on a yearly basis and/or just prior to the advisory committee meeting they are planning to attend. 5 CFR §§ 2634.202 and 2634.904(a)(1). The FDA reviews not only the financial interests of a potential advisory committee participant and the individual's immediate family, but also the financial interests, of which the individual has knowledge, of the participant's business partners, organizations for which the individual serves as officer, director, trustee, general partner, or employee, and any prospective employer of the member (if there are ongoing employment negotiations or an agreement regarding future employment). See 18 U.S.C. § 208(a).

⁶ 5 CFR 2640.302(b)

⁷ 5 CFR 2640.301(b)

⁸ Food, Drug, and Cosmetic Act section 505 (n)(4) "Each member of a panel shall publicly disclose all conflicts of interest that member may have with the work to be undertaken by the panel. No member of a panel may vote on any matter where the member or the immediate family of such member could gain financially from the advice given to the Secretary. The Secretary may grant a waiver of any conflict of interest requirement upon public disclosure of such conflict of interest if such waiver is necessary to afford the panel essential expertise, except that the Secretary may not grant a waiver for a member of a panel when the member's own scientific work is involved."

⁹ Draft Guidance for the Public, FDA Advisory Committee Members, and FDA Staff on Procedures for Determining COI and Eligibility for Participation in FDA Advisory Committees March 2007

¹⁰ Id.

¹¹ Wood SF, Mador JK. *Science and regulation. Uncapping conflict of interest?* Science (2013)

¹² Lurie P. *Suggestions for Improving Conflict of Interest Processes in the US Food and Drug Administration Advisory Committees—Past Imperfect*. JAMA Intern Med. 2018;178(7):997–998. doi:10.1001/jamainternmed.2018.1324

¹³ Report to Congress Food and Drug Administration Safety and Innovation Act, Section 712 (e) of the Federal Food, Drug, and Cosmetic Act, Fiscal Year 2016 Annual Report on FDA Advisory Committee Vacancies and Public Disclosures Accessed on February 27, 2019

¹⁴ The FDA does not publicly disclose financial interest information if it is exempt from disclosure under the Freedom of Information Act or otherwise protected from disclosure by statute or regulation, except if necessary to describe the type, nature, and magnitude of the financial conflict being waived.

¹⁵ This information must be published within specified time frames before advisory committee meetings. Food, Drug, and Cosmetic Act section 712(c).

¹⁶ FDA Guidance on Publication of Financial COI waivers.

https://www.fda.gov/RegulatoryInformation/Guidances/ucm391034.htm#_ftn11

¹⁷ Political party as described in 26 U.S.C. 527(e)

¹⁸ Participation is active if, for example, it involves service as an official of the organization or in a capacity similar to that of a committee or subcommittee chairperson or spokesperson, or participation in directing the activities of the organization. In other cases, significant time devoted to promoting specific programs of the organization, including coordination of fundraising efforts, is an indication of active participation. Payment of dues or the donation or solicitation of financial support does not, in itself, constitute active participation.

¹⁹ Pham-Kanter G., Revisiting Financial Conflicts of Interest in FDA Advisory Committees, Milbank Quarterly, September 2014 Volume 92, Issue 3 (pages 446–470), DOI: 10.1111/1468-0009.12073

²⁰ Id.

²¹ Id.

²² Cooper J., Golec J. Conflicts of Interest on Expert Committees: The Case of FDA Drug Advisory Committees, University of Connecticut School of Business Research Paper No. 17-02, April 2018 Accessed February 24, 2019

²³ Id.

²⁴ Piller C., You J. Hidden conflicts? Pharma payments to FDA advisers after drug approvals spark ethical concerns, Science Magazine, July 5, 2018 Accessed February 24, 2019

²⁵ Id.

²⁶ Id.

²⁷ Piller C., You J. Hidden conflicts? Pharma payments to FDA advisers after drug approvals spark ethical concerns, Science Magazine, July 5, 2018 Accessed February 24, 2019

²⁸ Sullivan, T., FDA Conflicts of Interest Rules Means Fewer Experts on Advisory Panels, Policy and Medicine Blog, May 5, 2018 Accessed on February 24, 2019.

²⁹ FDA website – online Percent of FDA advisory committee member positions vacant at the end of the month Accessed February 27, 2019

³⁰ FDA website – online Percent of FDA advisory committee member positions vacant at the end of the month Accessed February 27, 2019

APPENDIX: RELEVANT AMA POLICY

Policy H-100.992, “FDA”

(1) Our AMA reaffirms its support for the principles that: (a) an FDA decision to approve a new drug, to withdraw a drug’s approval, or to change the indications for use of a drug must be based on sound scientific and medical evidence derived from controlled trials and/or postmarket incident reports as provided by statute; (b) this evidence should be evaluated by the FDA, in consultation with its Advisory Committees and expert extramural advisory bodies; and (c) any risk/benefit analysis or relative safety or efficacy judgments should not be grounds for limiting access to or indications for use of a drug unless the weight of the evidence from clinical trials and postmarket reports shows that the drug is unsafe and/or ineffective for its labeled indications.

(2) The AMA believes that social and economic concerns and disputes per se should not be permitted to play a significant part in the FDA’s decision-making process in the course of FDA devising either general or product specific drug regulation.

(3) It is the position of our AMA that the Food and Drug Administration should not permit political considerations or conflicts of interest to overrule scientific evidence in making policy decisions; and our AMA urges the current administration and all future administrations to consider our best and brightest scientists for positions on advisory committees and councils regardless of their political affiliation and voting history.

7.1.4 Conflicts of Interest in Research

Increasing numbers of physicians, both within and outside academic health centers, are becoming involved in partnerships with industry to conduct biomedical and health research. As they do so, physicians must be mindful of the conflicts such engagement poses to the integrity of the research and the welfare of human participants. In addition to financial conflicts of interest created by

incentives to conduct trials and recruit subjects, physicians must be sensitive to the differing roles of clinician and investigator, which may require them to balance dual commitments to participants and science. This conflict of commitment is particularly acute when a physician-investigator has treated or continues to treat a patient who is eligible to enroll as a participant in a clinical trial the physician is conducting.

Minimizing and mitigating conflicts of interest in clinical research is imperative if the medical community is to justify and maintain trust in the medical research community.

Physicians who engage in research should:

- (a) Decline financial compensation that awards in excess of the physician's research efforts and does not reflect fair market value. Physicians should not accept payment solely for referring patients to research studies.
- (b) Ensure that the research protocol includes provision for funding participants' medical care in the event of complications associated with the research. A physician should not double-bill a third-party payer for additional expenses related to conducting the trial if he or she has already received funds from a sponsor for those expenses.
- (c) As part of the informed consent process, disclose to prospective participants the nature and source of funding and financial incentives offered to the investigators. This disclosure should be included in any written consent materials.
- (d) Avoid engaging in any research where there is an understanding that limitations can be placed on the presentation or publication of results by the research sponsor.
- (e) Refrain from knowingly participating in a financial relationship with a commercial entity with whom they have a research relationship until the research relationship ends and the research results have been published or otherwise disseminated to the public.
- (f) Disclose material ties to companies whose products they are investigating or other ties that create real or perceived conflicts of interest to:
 - (i) institutions where the research will be carried out;
 - (ii) organizations that are funding the research;
 - (iii) any journal or publication where the research results are being submitted.
- (g) Physicians who have leadership roles in institutions that conduct biomedical and health research as well as the entities that fund research with human participants should promote the development of guidelines on conflicts of interest that clarify physician-investigators responsibilities.

AMA Principles of Medical Ethics: II,IV,V; The Opinions in this chapter are offered as ethics guidance for physicians and are not intended to establish standards of clinical practice or rules of law. Issued: 2016

Policy H-410.953, "Ethical Considerations in the Development of Clinical Practice Guidelines"

Clinical practice guidelines are statements that include recommendations intended to optimize patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options. Clinical practice guidelines help inform physician judgment and decision making by physicians and patients. Clinical practice guidelines also have significant potential to meaningfully inform efforts to provide care of consistently high quality for all patients and to help shape development of sound public policy in health care. To achieve those ends, clinical practice guidelines must be trustworthy. Patients, the public, physicians, other health care professionals and health administrators, and policymakers must have confidence that published guidelines are the ethically and scientifically credible product of development processes that are rigorous, independent, transparent, and accountable.

To that end, the development or updating of clinical practice guidelines should meet the following expectations:

1. Guidelines/updates are developed independent of direct financial support from entities that have an interest in the recommendations to be developed.
2. Formal, scientifically rigorous methods and explicit standards are adopted for the review and weighting of evidence, the integration of expert judgment, and the strength of clinical recommendations.
3. Guideline panels have access to appropriate expertise among members or consultants, including not only relevantly qualified clinical experts but also appropriately qualified methodologists, representatives of key stakeholders, and, ideally, one or more individuals skilled in facilitating groups.
4. Ideally, all individuals associated with guideline development will be free of conflicts of interest during the development process and will remain so for a defined period following the publication of the guideline.
5. Formal procedures are adopted to minimize the potential for financial or other interests to influence the process at all key steps (selection of topic, review of evidence, panel deliberations, development and approval of specific recommendations, and dissemination of final product). These should include: a) required disclosure of all potential conflicts of interest by panel members, consultants, staff, and other participants; b) clearly defined criteria for identifying and assessing the seriousness of conflicts of interest; and c) clearly defined strategies for eliminating or mitigating the influence of identified conflicts of interest (such as prohibiting individuals from participating in deliberations, drafting, or voting on recommendations on which they have conflicts) in those limited circumstances when participation by an individual with a conflicting interest cannot be avoided.
6. Guidelines are subject to rigorous, independent peer review.
7. Clear statements of methodology, COI policy and procedures, and disclosures of panel members' conflicts of interest relating to specific recommendations are published with any guideline or otherwise made public.
8. Guidelines are in the first instance disseminated independent of support from or participation by individuals or entities that have a direct interest in the recommendations.