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August 17, 2015

Stephen Ostroff, M.D.
Acting Commissioner
Food and Drug Administration
Department of Health and Human Services
WO 2200
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Silver Spring, MD 20993-0002

Jeffrey E. Shuren, M.D., J.D.
Director
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Food and Drug Administration
10903 New Hampshire Avenue
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Silver Spring, MD 20993

Re: Patient Preference Information — Submission, Review in Premarket Approval Applications, Humanitarian Device Exemption Applications, and *De Novo* Requests, and Inclusion in Device Labeling: Draft Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders; FDA-2015-D-1580

Dear Drs. Ostroff and Shuren,

Public Citizen, a consumer advocacy organization with more than 400,000 members and supporters nationwide, submits these comments on the Food and Drug Administration's (FDA's) proposed draft guidance: *Patient Preference Information — Submission, Review in Premarket Approval Applications, Humanitarian Device Exemption Applications, and* De Novo *Requests, and Inclusion in Device Labeling* (the Draft Guidance), issued on May 18, 2015.[1] Specifically, we write to express our concern that this guidance and other FDA activities related to patient preference information have in effect lowered approval standards for high-risk medical devices, allowing for approval of such devices in cases where data are otherwise insufficient to establish a reasonable assurance that the devices are safe and effective.

[1] Food and Drug Administration. Patient preference information — submission, review in PMAs, HDE applications, and *de novo* requests, and inclusion in device labeling: Draft guidance for industry, Food and Drug Administration staff, and other stakeholders. May 18, 2015. http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM446680.pdf. Accessed August 7, 2015.

In response to these concerns, we request the following actions from the FDA:

1. Termination of the FDA's inappropriate relationship with the Medical Device Innovation Consortium (MDIC), a collaboration dominated by members of the medical device manufacturing industry, and retraction of the Draft Guidance, as well as any other guidance documents developed in coordination with the MDIC.
2. Clarification in any subsequent guidance related to patient preference information that the agency does not intend to rely on such information to lower the standards of regulatory approval for high-risk medical devices.
3. Introduction of measures for greater transparency, including the publication of individualized results generated by regulatory tools developed using patient preference information.

These actions are necessary to prevent patient preference information from being used in ways that are detrimental to public health.

A. Industry Influence in Developing the Guidance and Related Materials

Public Citizen is concerned that recent efforts to incorporate patient preference information into regulatory decision-making have been heavily influenced by members of the medical device manufacturing industry, resulting in an approach to regulatory development that is centered on industry interests, rather than patient and public health interests.

Specifically, in developing the draft guidance, the FDA collaborated with the MDIC,[2] an organization that is predominantly composed of medical device manufacturers and industry trade groups.[3] As part of this collaboration, the MDIC assembled a steering committee (the MDIC Steering Committee) to "establish a credible framework" for incorporating patient preference information into device development and regulatory decisions made by the FDA.[4] This framework was developed to be shared with the FDA for use in guidance documents and regulatory decisions.[5] While the MDIC website represents this effort as focused on developing a "patient centered" approach, the MDIC Steering Committee, like the MDIC itself, is dominated by representatives of the medical device industry. Out of 23 individuals on the MDIC Steering Committee, seven are FDA officials and 11 represent device manufacturers and affiliated industries (including two venture capital groups).[6] By contrast, the steering committee includes only one member from a patient group, and even that group receives substantial funding from medical device and pharmaceutical companies.[7,8] (Three representatives from research

[2] Food and Drug Administration. Draft guidance on patient preference information. May 13, 2015. http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/ucm446778.htm. Accessed August 5, 2015.
[3] Medical Device Innovation Consortium. Members. http://mdic.org/members/. Accessed August 5, 2015.
[4] Medical Device Innovation Consortium. Patient Centered Benefit-Risk Assessment (PCBR). http://mdic.org/pcbr/. Accessed August 5, 2015.
[5] *Ibid.*
[6] Medical Device Innovation Consortium. Medical Device Innovation Consortium (MDIC) Patient Centered Benefit-Risk Project Report: A Framework for Incorporating Information on Patient Preferences Regarding the Benefit and Risk Into Regulatory Assessments of New Medical Technology. 2015. http://mdic.org/wp-content/uploads/2015/05/MDIC_PCBR_Framework_Web.pdf. Accessed August 12, 2015.
[7] *Ibid.*

institutions and a program manager employed by the MDIC make up the balance of the committee).

While the framework developed by the MDIC Steering Committee is not binding on the FDA, the high level of involvement by FDA officials on the committee guarantees that the work of the committee will have a strong influence on the regulatory decision-making process. This influence is confirmed by the fact that the Draft Guidance has adopted many of the concepts put forward by the MDIC Steering Committee — such as "preference sensitivity" and "risk tolerance" — and MDIC documents are explicitly cited in the Draft Guidance and public statement announcing the Draft Guidance.[9,10]

This extensive involvement between members of the medical device industry and the officials who regulate them is inappropriate, particularly when presented as an effort to develop a "patient-centered" approach to product development and regulation. Device manufacturers and affiliated industries have an inherent conflict of interest: In seeking to incorporate patient views into the regulatory process, these companies are necessarily motivated by the desire to increase the sales of medical devices, and thus their own profits. Fostering such an extensive collaboration between members of regulated industry and FDA officials is therefore highly likely to lead to biased recommendations that serve the interests of industry, rather than those of patients and public health.

We urge the FDA to terminate its inappropriate relationship with the MDIC and retract the Draft Guidance on patient preference information, as well as any other guidance documents developed in collaboration with the MDIC.

B. Use of Patient Preference Data to Lower the Standards for Regulatory Approval

We are concerned that use of patient preference information as outlined in the Draft Guidance will effectively lower the standards for regulatory approval, justifying approval in cases where FDA reviewers have identified important safety or effectiveness concerns and which might otherwise result in a rejection of the application under review.

This concern is driven in part by the fact that almost all of the hypothetical examples used by the FDA in the Draft Guidance involve the use of such information to justify approval where evidence of safety and efficacy is inconclusive. Out of all the examples used in the Draft Guidance, only example C indicates that the FDA might deny approval of the device under

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[8] National Organization for Rare Disorders. About the Corporate Council, http://rarediseases.org/for-industry/corporate-council/corporate-council/; and Current members, http://rarediseases.org/for-industry/corporate-council/current-members/. Accessed August 12, 2015.

[9] Food and Drug Administration. Patient preference information — submission, review in PMAs, HDE applications, and *de novo* requests, and inclusion in device labeling: Draft guidance for industry, Food and Drug Administration staff, and other stakeholders. May 18, 2015. http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM446680.pdf. Accessed August 5, 2015.

[10] Food and Drug Administration. Draft guidance on patient preference information. May 13, 2015. http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/ucm446778.htm. Accessed August 5, 2015.

consideration, and this denial is made in spite of patient preference information, not because of it.[11]

Statements in the Draft Guidance also indicate that the FDA may grant approval of a device, despite its low effectiveness or high risk of side effects, based on patient preference information — suggesting that a minority of "risk tolerant" patients would be willing to accept a device with this risk-benefit profile (see example B [lower efficacy] and example D [greater risk of side effects]).[12] In taking this approach, the FDA abdicates its role as market gatekeeper, placing the burden on each individual patient to identify safe and effective devices on a case-by-case basis. This approach makes it possible for individuals who are desperate for treatment to be exploited or harmed by a device that does not offer a meaningful benefit or carries high risks. It also provides for approval in cases where the majority of patients for whom the device is indicated would find its risk-benefit profile unacceptable. Additional warning language in product labeling, and other measures proposed in the draft guidance, will not be sufficient to ensure that all patients are sufficiently well informed to avoid the risks they might find unacceptable. Also, unlike the FDA, individual patients are not in a position to request further clinical testing should existing evidence leave important safety and effectiveness questions unanswered.

Finally, we are troubled by the FDA's January 2015 approval of the Maestro Rechargeable System based in part on patient preference information. The Maestro Rechargeable System is a surgically implanted weight loss device that failed to meet its primary effectiveness endpoint during clinical testing.[13] While the device did produce 8 percent average weight loss, it did not meet the predetermined goal of 10 percent, which was selected to represent a clinically meaningful benefit.[14] The device also received a mixed reception at an advisory committee meeting, with the majority of advisers voting that it had failed to demonstrate effectiveness for the proposed indication.[15] Nevertheless, the FDA approved the device, following consideration of results from the CDRH Patient Preference Weight Loss Devices Study, referenced in the Draft Guidance.[16,17] According to the FDA, that study "showed a group of patients would accept risks

[11] Food and Drug Administration. Patient preference information — submission, review in PMAs, HDE applications, and *de novo* requests, and inclusion in device labeling: Draft guidance for industry, Food and Drug Administration staff, and other stakeholders. May 18, 2015. http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM446680.pdf. Accessed August 5, 2015.
[12] *Ibid*.
[13] Food and Drug Administration. FDA approves first-of-kind device to treat obesity. January 14, 2015. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm430223.htm. Accessed August 5, 2015.
[14] Food and Drug Administration. Transcript: Meeting of the Center for Devices and Radiological Health Medical Devices Advisory Committee, Gastroenterology and Urology Devices Panel. June 17, 2014. http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/Gastroenterology-UrologyDevicesPanel/UCM413091.pdf. Accessed August 5, 2015.
[15] *Ibid*.
[16] Food and Drug Administration. FDA approves first-of-kind device to treat obesity. January 14, 2015. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm430223.htm. Accessed August 5, 2015.
[17] Food and Drug Administration. Patient preference information — submission, review in PMAs, HDE applications, and *de novo* requests, and inclusion in device labeling: Draft guidance for industry, Food and Drug Administration staff, and other stakeholders. May 18, 2015. http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM446680.pdf. Accessed August 5, 2015.

associated with [the Maestro] surgically implanted device for the amounts of weight loss expected to be provided by the device."[18] In effect, patient preference information was substituted for evidence of efficacy where the device had failed to achieve a clinically meaningful benefit.

To avoid further troubling use of patient preference information, we urge the FDA to make clear in any subsequent guidance that the agency does not intend to rely on patient preference information to lower the standards of regulatory approval for high-risk medical devices.

Specifically, we ask that the agency include the following in any subsequent guidance on patient preference information:

- Examples describing how patient preference information might be relied upon by the agency in denying approvals for high-risk medical devices.
- Clarification that approvals will not be made based on the preferences of a minority of "risk tolerant" patients, but rather on the basis of the entire population of patients for whom the device is indicated.
- Statements cautioning against use of patient preference information to justify approval where a device has failed to meet its primary safety or effectiveness endpoints during clinical testing.

C. Lack of transparency regarding the use of patient preference information

Public Citizen is concerned that recent use of patient preference information by the FDA has not been adequately transparent. As noted above, the FDA utilized data from the recent CDRH Patient Preference Weight Loss Devices Study in granting approval of the Maestro Rechargeable System. Yet in announcing this decision, the agency cited only the methodology of that study, not its general or specific results.[19] Moreover, general results from the study, published elsewhere, provide little insight into how data from the study may have been used to justify approval of the Maestro Rechargeable System, as these results suggested that patients expressed a low willingness to make trade-offs for the average percent weight loss achieved by the Maestro device (which was less than 10 percent).[20]

We are also aware that the agency has used data from the CDRH Patient Preference Weight Loss Devices Study to develop a specialized MaxR-MinB calculator, which agency officials have referred to as "the tool."[21] This tool is apparently intended to be used to aid in regulatory decisions related to obesity devices.[22] Yet the tool is not accessible to the public, and it is not clear how this instrument has been incorporated into regulatory decision-making to date.

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[18] Food and Drug Administration. FDA approves first-of-kind device to treat obesity. January 14, 2015. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm430223.htm. Accessed August 5, 2015.
[19] Instead, the FDA posted a background paper describing the general purpose of the survey study and the study methodology. Food and Drug Administration. FDA approves first-of-kind device to treat obesity. January 14, 2015. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm430223.htm. Accessed August 5, 2015.
[20] Ho MP, Gonzalez JM, Lerner HP, et al. Incorporating patient-preference evidence into regulatory decision making. *Surg Endosc.* Jan. 1, 2015. [Epub ahead of print] doi:10.1007/s00464-014-4044-2.
[21] *Ibid*.
[22] *Ibid.*

We urge the FDA to include steps for greater transparency in any subsequent version of the guidance, including a pledge to publish individualized results generated by regulatory tools developed using patient preference information, such as the tool developed based on data from the CDRH Patient Preference Weight Loss Devices Study.

D. Conclusion

Based on the foregoing, we request the following actions from the FDA:

1. Termination of the FDA's inappropriate relationship with the MDIC, a collaboration dominated by members of the medical device manufacturing industry, and retraction of the Draft Guidance, as well as any other guidance documents developed in coordination with the MDIC.
2. Clarification in any subsequent guidance related to patient preference information that the agency does not intend to rely on such information to lower the standards of regulatory approval for high-risk medical devices.
3. Introduction of measures for greater transparency, including the publication of individualized results generated by regulatory tools developed using patient preference information.

These actions are necessary to protect the public health.

We thank you for the opportunity to comment on this important matter.

Sincerely,

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