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October 19, 2011

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Docket No. FDA–2011-D-0530: Draft Guidance for Industry and Food and Drug Administration Staff on Mobile Medical Applications

Dear Sir/Madam:

The Biotechnology Industry Organization (BIO) thanks the Food and Drug Administration ("FDA" or "the Agency") for the opportunity to submit comments on "Draft Guidance for Industry and Food and Drug Administration Staff on Mobile Medical Applications" ("Draft Guidance"). While BIO welcomes additional clarity from the Agency regarding the regulatory framework for evaluation of mobile medical applications, BIO does not agree with the suggestion that basic dose and disease-risk and stage modeling calculators should be regulated as medical devices. These basic types of electronic mobile applications are based on straightforward calculations of information reflected in a drug or biologic's label, medical textbooks, or in available published literature and on disease risk and stage modeling, and can be easily verified by other non-electronic techniques. Consistent with current FDA policy, we suggest that the Sponsor continue to be fully responsible for the quality and accuracy of these basic calculators without becoming a "device manufacturer" with the associated regulatory requirements.

BIO represents more than 1,100 biotechnology companies, academic institutions, state biotechnology centers and related organizations across the United States and in more than 30 other nations. BIO members are involved in the research and development of innovative healthcare, agricultural, industrial and environmental biotechnology products, thereby expanding the boundaries of science to benefit humanity by providing better healthcare, enhanced agriculture, and a cleaner and safer environment.

GENERAL COMMENTS:

The Draft Guidance sets forth FDA's intention to apply its regulatory authorities to select software applications including "mobile medical apps that allow the user to input patient-specific information and – *using formulae or a processing algorithm* – output a *patient-specific* result, diagnosis, or treatment recommendation that is used in clinical practice or to assist in making clinical decisions" including "apps that perform calculations intended to be used by clinicians for automating tasks such as eGFR with CKD-Epi, Cockcroft-Gault, and MDRD; A-a gradient, etc."[1] FDA specifically notes that drug dose calculators have been previously classified by the Agency (21 C.F.R. 868.1890) and encourages manufacturers of apps that perform this function to contact the Agency to discuss regulatory requirements.[2]

Many biopharmaceutical companies have FDA-approved product labeling that requires use of a drug or biologic based, in part, on calculations or algorithms that provide an index, score, scale, or other similar result. FDA-approved product labeling may state the need for dose-adjustment, either for safety or efficacy, based on body surface area, a patient's weight or age, or other patient-specific parameters. For example, the Gail Model for breast cancer prevention has been used as a tool to help physicians determine whether to prescribe a particular oncology drug for women with a "high risk" of developing breast cancer.[3] Further, numerous drug labels recommend dose adjustment based on a calculation of renal function or glomerular filtration rate (GFR) which is included in a variety of medical textbooks.

To provide convenient access to information about the safe and effective use of drugs and biologics, manufacturers sometimes provide prescribers with mobile calculating tools accessible online for download or through the product information website, by a phone number, or in other formats. In general, these calculators perform relatively trivial calculations, providing the same information set forth in FDA-approved product labeling or a standard medical textbook. It has been FDA's prior position that such straightforward calculators are not subject to active regulation, as they easily can be verified using other techniques and are primarily used for physician convenience, not for the purpose of making a treatment decision.

The draft guidance implies that all such aids, if automated, would render the biopharmaceutical company supplying such calculators a device manufacturer and all regulatory requirements applicable to device manufacturers would apply, including but not limited to registration of device establishments, submission of 510(k) applications if not exempt, and annual reporting.

BIO believes this is an unintended and unnecessary consequence of the draft guidance as currently written. In FDA's 1989 draft policy on the regulation of computer products as medical

[1] P. 19-20, Appendix A provides several additional examples including: (1) applications that act as calculators or utilize algorithms to produce an index, score, scale, or other similar calculations (e.g., Glasgow Coma Scale, pain index, Apgar score, NIH stroke scale, etc.); and (2) applications that act as a dosing calculators for a treatment regimen intended for a specific patient population (pediatrics).

[2] P. 15, Appendix B

[3] The Breast Cancer Risk Assessment Tool (The Gail model) was designed by researchers at the National Cancer Institute and the National Surgical Adjuvant Breast And Bowel Project as a tool for health care providers.

devices,[4] FDA set forth a general policy statement that certain types of software would not be regulated as devices. Of note, this included software intended:

- only for use as traditional 'library' functions such as storage, retrieval, and
- dissemination of medical information - functions traditionally carried out through textbooks and journals;
- only for use as general accounting or communications functions; or
- for educational purposes rather than to diagnose or treat patients.

Moreover, the policy also carved out software products "that are intended to involve competent human intervention before any impact on human health occurs, (e.g., where clinical judgment and experience can be used to check and interpret a system's output)." Specifically, it was noted that these types of products would be "exempt from Registration, Listing, Premarket Notification, and compliance with the MDR and GMP regulations."

BIO recognizes that the 1989 draft policy was not finalized and was withdrawn in 2005. Nevertheless, we believe that "competent human intervention" or use by a learned intermediary continues to be a legitimate consideration when determining whether a simple calculator should be considered a medical device regulated under the current classification system. While we recognize that one factor may not be determinative, we encourage FDA to identify factors that may limit or exempt dose calculators that provide information that is reflected in the product labeling or in a medical textbook. Other considerations, such as the transparency of the underlying calculations to the user and the ability of the user to independently verify the result, may also be appropriate factors to limit or exempt the application of FDA's device regulations to such dose calculators.

Where FDA-approved product labeling recommends certain calculations for the safe and effective use of a product, or a straightforward calculation is described in a medical textbook, and a biopharmaceutical company provides automated calculators that help healthcare professionals to understand the product labeling, we recommend that the biopharmaceutical company be fully responsible for the quality and accuracy of the software programs without incurring the label of "device manufacturer" and its associated regulatory requirements.

Specifically, BIO would like FDA to clarify that its long-standing approach to simple dose calculators has not changed, and that the mere adaptation of these calculators to a mobile or web-based platform will not render them "mobile medical apps" subject to FDA regulation. Regardless of the platform, these simple calculators do not represent a product that should be the subject of FDA regulation as a medical device.

[4] FDA Draft Policy for the Regulation of Computer Products (November 13, 1989, Withdrawn).

CONCLUSION:

BIO appreciates this opportunity to comment on the "Draft Guidance for Industry and Food and Drug Administration Staff on Mobile Medical Applications." We would be pleased to provide further input or clarification of our comments, as needed.

Sincerely,

/S/

Andrew J. Emmett
Managing Director, Science and Regulatory Affairs
Biotechnology Industry Organization