AMERICAN COLLEGE OF GASTROENTEROLOGY

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April 6, 2015

Steven Ostroff, MD
Acting Commissioner
U.S. Food and Drug Administration
5630 Fischer Lane
Rockville, MD 20852

Re: FDA Docket No. FDA-2012-N-1029. Agency Collection Activities; Proposed Collection Comment Request; General licensing Provisions; Section 351(k) Biosimilar Applications.

Dear Dr. Ostroff

The American College of Gastroenterology (ACG) appreciates the opportunity to provide comment in response to the FDA's solicitation on improving the quality of information in the 351(k) application process. With respect to the following collection of information, FDA invited comments on the following topics:

> (1) Whether the proposed collection of information is necessary for the proper performance of FDA's functions, including whether the information will have practical utility; (2) the accuracy of FDA's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) ways to minimize the burden of the collection of information on respondents, including through the use of automated collection techniques, when appropriate, and other forms of information technology.

The ACG is a physician organization representing gastroenterologists and other gastrointestinal specialists. Founded in 1932, our organization includes over 13,000 providers of gastroenterology specialty care. We focus on the clinical issues confronting the gastrointestinal specialist in treatment of patients. The primary activities of ACG have been, and continue to be, promoting evidence-based medicine and optimizing quality of patient care.

The College offers the following comments to enhance the practical utility, quality, and clarity of the information collected by the FDA.

ACG's Guiding Principle: the Physician-Patient Relationship

The ACG continues to stress the importance of protecting the physician-patient relationship. The provider, after reviewing the scientific data and in consultation with the patient, is in the best position to determine the most appropriate course of treatment for each unique patient. This guiding principle presumes the data are available to help ACG members make these important clinical decisions for each patient.

However, the ACG understands we must strike a balance between all data helpful for providers to make informed clinical decisions and the data required to comply with the Agency's statutory mandate of a streamlined 351(k) review process to increase access to safe, efficacious, and cost-effective biosimilar products.

We appreciate that biologics have revolutionized treatment of many life-threatening and debilitating diseases and that biosimilars may revolutionize the access to these treatments. There are still many questions ACG members have on the topic of biosimilars and how their use will affect patients. As an educational organization, it is our mission to help our membership better understand these issues and answer these questions. For example, the ACG's Committee on FDA Related Matters often writes articles for the *American Journal of Gastroenterology* on FDA-related topics important to clinical gastroenterology. This includes a recently published manuscript describing the biosimilar review process (Am J Gastroenterol 2014; 109:1856–1859).

ACG welcomes the opportunity to work with the FDA in ways to improve the quality and utility of data as part of the 351(k) application process as it applies to helping gastroenterologists answer important clinical and everyday questions. For example --and until there is a greater comfort level and knowledge-base on biologics-- one way to improve quality and practical utility of information is having the application include for FDA review and approval some common "real world scenario" questions both patients and providers will likely have when weighing the options of using, prescribing, and/or substituting biologic products in the course of treatment. For example, therapeutic drug monitoring is very important in clinical practice in determining patient-response or loss of response, as data suggest the ability to monitor drug levels is associated with maintaining remission, durability of response, and likelihood of relapse. Also, the ability to check antibodies to drugs is very important in determining a cause for loss of efficacy. As we move to a new form of drug development, we look forward to the Agency's ideas on helping clinicians stratify patient-response and answer these important clinical questions during the approval process or as part of the drug's labeling requirements.

We understand that there will be an extensive post-marketing surveillance program for drugs entering this new area of development. Regular provider alerts/updates describing the duration and types of data included in these post-market studies may help to safeguard patients and answer important questions in clinical practice. For example, clinicians will want to know whether a patient will respond to a biologic drug if the biosimilar version fails or causes adverse reactions since the drugs are not equivalent; or whether both drugs should be avoided since both have the same active ingredients and deemed to be equally safe and effective. We must implement approval and post-market policies that allow providers to make these informative decisions when treating patients. This includes the practice of prescribing medications and the data required for informed decision-making.

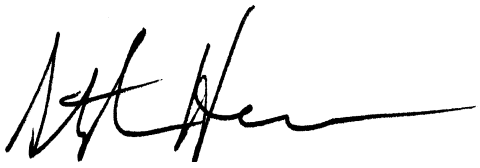
While not an issue specific to the 351(k) application process, guidance on third party substitutions of biosimilars without the knowledge of the physician is very important. The FDA could consider these issues as part of the drug's labeling instructions. These issues are also subject to state laws and regulation. However, the implications of switching similar biologic drugs without the provider's knowledge may increase the subsequent risks of the patient developing antibodies without the provider's knowledge, thus requiring the drug treatment to be restarted after a period of time.

ACG and FDA's Partnership

The ACG and the FDA have worked together on various joint-workshops to assist the Agency in developing proper endpoints when reviewing drugs and products in gastroenterology such as inflammatory bowel disease (IBD), celiac disease, Eosinophilic esophagitis (EoE), and products used in bowel preparation. These workshops have been held as part of the College's annual scientific meetings and are always very well attended, demonstrating the demand for guidance and information from those clinicians on the front line treating patients. These sessions also help explain to these front-line providers the intricacies of the FDA's regulatory authority and review process. ACG welcomes the opportunity to use these public workshops and clinician forums to help the FDA improve the quality and utility of information collected as part of the 351(k) review process or during any post-market review.

The ACG welcomes the opportunity to discuss further and to continue working closely with the FDA. Please contact Brad Conway, Vice President, Public Policy, Coverage & Reimbursement, at 301.263.9000 or bconway@gi.org.

Sincerely,



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