U.S. Food and Drug Administration and American Dental Association: Ensuring Oral Care Product Safety for the Public

Frederick A. Curro, DMD, PhD

Director, PEARL Network
Clinical Professor and Director of Regulatory Affairs
Bluestone Center for Clinical Research
New York University College of Dentistry
New York, NY, USA

Kenneth H. Burrell, DDS, MS

President, Burrell Consulting, Inc., Lisle, IL, USA
Former Senior Director, Council on Scientific Affairs
American Dental Association
Chicago, IL, USA

Introduction

In every developed and developing country where healthcare products are sold, there is a regulatory agency in place to oversee product safety and the emergence of new products. An effective medicines regulatory authority (MRA) is a crucial part of a reliable health and supply system.[1] The MRA in the United States is the Food and Drug Administration (FDA).

Founded more than 150 years ago, the American Dental Association (ADA) is the nation's largest dental association, advocating on behalf of its more than 150,000 members. The ADA, an independent body, is the leading source of oral health-related product information for dentists and their patients, and devotes their time and resources to determining if an over-the-counter dental product is safe and effective using current testing and evaluation techniques.

This article looks at the important work being done by both the FDA and the ADA to ensure the initial and on-going safety and efficacy of dental products, allowing oral care professionals to recommend these products with the utmost confidence.

The U.S. Food and Drug Administration

The FDA oversees both prescription and nonprescription (over-the-counter [OTC]) drug products. Overseen by the U.S. Department of Health and Human Services, the FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation. The FDA is also responsible for advancing the public health by facilitating innovations that make these products more effective, safer, and more affordable. Additionally, the FDA assists the public in getting the accurate, science-based information they need to properly use medicines and foods to improve their health.[2]

Historical Perspective

It is generally accepted that the United States is the world's leader in regulatory science and product safety, dating back to 1820 when eleven doctors set up the U.S. Pharmacopeia and recorded the first list of standard drugs.[3] The FDA presently, through recent initiatives, continues its advancement of regulatory science.[4,5] Briefly, the original Food and Drug Act was passed by Congress on June 30, 1906, and signed by President Theodore Roosevelt. The Act outlawed states from buying and selling food, drinks, and drugs that had been mislabeled and tainted. In 1938, Congress passed the Federal Food, Drug, and Cosmetic (FDC) Act, which required new drugs to demonstrate safety before permission to sell could be granted.

In 1941, the FDA drastically changed the industry's manufacturing and quality controls, which led to the development of good manufacturing practices (GMP). In 1951, Congress passed the Durham-Humphrey Amendment, which required any drug that is habit forming or potentially harmful to be dispensed under the supervision of a health practitioner as a prescription drug. Further, it required such drugs to carry the statement, "Caution: Federal law prohibits dispensing without a prescription." All other drugs were available without a prescription.

In 1962, in response to a potential thalidomide tragedy in the United States, Congress passed the Kefauver-Harris Drug Amendments that, for the first time, compelled drug makers to prove a product's efficacy and safety before the FDA would approve it for sale. The amendments further required drug advertising to disclose accurate information about side effects and effectiveness of treatments. In 1972, the OTC drug review began enhancing the safety, effectiveness, and appropriate labeling of drugs sold without a prescription. In 1993, the FDA launched MedWatch, a system designed to collect safety reports from health professionals on problems associated with drugs and other medical products. In 2005, refining its mission of safety, the Drug Safety Board was formed consisting of FDA staff and representatives from the National Institutes of Health and the Veterans Administration. Its role was to advise the director of the FDA Center for Drug Evaluation and Research on drug safety issues and work with the agency to share vital product information to health professionals and patients.

FDA Organization and Product Approval

The drug development process and continued monitoring of product safety is the purview of the FDA's Center for Drug Evaluation and Research (CDER).[6] The CDER's mission is to promote and protect the public health by ensuring that all prescription and OTC drugs are safe and effective. The CDER evaluates all new drugs before they are sold, serves as a consumer watchdog for the more than 10,000 drugs currently on the market, and oversees ongoing drug safety post approval. The CDER is one of seven centers within the FDA ultimately reporting to the Office of the Commissioner. Other centers are involved in overseeing devices, biologics, tobacco, veterinary medicine, food safety, and toxicological research.

Briefly, the drug development process consists of four phases, all of which include safety, the common thread throughout the drug development process. Phase I consists of pharmacology and pharmacokinetic studies, outlining the evidence for safety and early evidence of activity. These studies are done to determine the initial dosing for the next series of studies. Phase II evaluates the drug in patients with the target disease to determine efficacy and the doses to be used in follow-up trials. In Phase III, the drug is evaluated in larger patient populations with the target disease to further establish and confirm safety and efficacy. Phase IV is for post-marketing surveillance to continue the safety program of the marketed drug beyond the controlled clinical trials data established in the earlier phases of development.

FDA Post-Market Surveillance

FDA post-market surveillance programs constantly monitor the safety of marketed drugs. The Adverse Event Reporting System of the FDA relies upon signals to detect rare adverse drug events. The FDA requires drug manufacturers to perform post-marketing surveillance of prescription drugs, and similar regulations exist for nonprescription products. The FDA also operates a voluntary reporting system named MedWatch, available to both health professionals and consumers.[7] The FDA provides consumers, patients, caregivers, and providers with access to understandable, science-based material related to drugs and their safety for use in making informed healthcare decisions. The goal of the FDA is to protect the public health by ensuring that marketed drugs are safe and effective.

Drug vs. Cosmetic

The FDA defines all of its components that it oversees as either food, drug, device, or cosmetic. The definitions are limited to those terms that are relevant to this review. The term "drug" is defined, in part, by its intended use as: (1) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; (2) articles intended to affect the structure or any function of the body of man or other animals; (3) articles recognized in the official United States Pharmacopoeia, official Homoeopathic Pharmacopoeia of the United States, or official National Formulary, or any supplement to any of them.[8]

The Federal Food, Drug, and Cosmetic Act defines "cosmetic" by its intended use as: (1) articles intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body or any part thereof for cleansing, beautifying, promoting attractiveness, or altering the appearance; and (2) articles intended for use as a component of any such articles, except that such terms shall not include soap. Among the products included in this definition are skin moisturizers, perfumes, lipsticks, fingernail polishes, cleansing shampoos, etc. Soap is a special category that is regulated by the Consumer Product Safety Commission.[9] Intended use can be established in a number of ways by the claims stated on the product labeling, in advertising, consumer perception, and by the ingredients themselves.

OTC Drug Monograph vs. New Drug Application

OTC Drug Monograph

OTC drug products play an increasingly vital role in the U.S. healthcare system. The profession of dentistry resides mainly in the OTC sector, where toothpastes have the largest market share and are most competitive in that space. OTC drugs are defined as drugs that are safe and effective for use by the general public without seeking treatment by a health professional. There are over 300,000 marketed OTC drug products in the United States for which the FDA reviews the active ingredients and the labeling of over 80 therapeutic classes, such as analgesics or antacids. For each category, an OTC drug monograph is developed and published in the *Federal Register.*

OTC drug monographs can be viewed as "recipe books," covering acceptable ingredients, dosage forms, dose or concentration, required labeling, and, in some cases, packaging and/or testing requirements.[10] Once a final monograph is implemented, companies can produce and market an OTC product without the need for FDA pre-approval. These monographs define the safety, effectiveness, and labeling of all marketed OTC active ingredients. New products that conform to a final monograph may be marketed without further FDA review. For example, most toothpastes are designed with core ingredients that are listed in a monograph as safe and effective by the FDA.

New Drug Application (NDA)

An NDA is the means through which companies formally propose that the FDA approve a new active ingredient or drug for sale and marketing in the United States. The FDA only approves an NDA after determining, for example, that the data is adequate to show the drug's safety and effectiveness for its proposed use, and that its benefits of use outweigh the potential risks. The NDA system is also used for new ingredients and for new indications entering the OTC marketplace for the first time.

When an additional active component is added to a product for a specific label claim, clinical studies are required to be performed to substantiate the claim. Those drugs or actives that do not conform must be reviewed by the New Drug Application (NDA) process. Currently, the only toothpaste on the market with a proprietary NDA for a product containing fluoride and an active antimicrobial agent is Colgate Total toothpaste, which uses core ingredients with an additional active (triclosan) in a novel delivery system to increase the substantivity of the active ingredient.[11]

An Investigational New Drug (IND) application is submit-

ted to the FDA if a drug not previously authorized for use in the United States is intended to be used for the purposes of clinical investigation or, in certain cases, for clinical treatment when no approved therapies are available. Triclosan is an example of a drug that was widely used around the world but not in the United States, and underwent the rigorous NDA process to further establish its safety and efficacy for its intended use.

The contrasting differences between OTC Monograph and NDA approval processes are shown in Table I.

Table I
Differences Between NDAs and Monographs

NDA	Monograph
• Pre-approval required	• Pre-approval NOT required
• Clinical studies and fees may be required	• Clinical studies and fees may not be required
• Review process is proprietary	• Notice and comment process is public
• Approved labeling unique to the drug	• Labeling is same for all like drugs
• Possible marketing exclusivity	• No marketing exclusivity
• Approved NDA is a license to market	• Final monograph is open to anyone

Product Safety Remains the FDA's Primary Concern

Drug safety is the primary objective of the FDA. It is the common denominator for a drug in its life cycle, from development to the marketplace and thereafter. The process of drug safety includes all stakeholders: prescriber, patient, and caretaker.

In 2008, the FDA shifted authority on drug safety regulatory issues from the Office of New Drugs (OND) to a shared responsibility between the OND and the Office of Surveillance (OSE). Under the new agreement, the drug review and drug safety offices share equal responsibility on "significant safety issues" for pending and approved products, such as post-marketing studies and clinical trials, and safety labeling changes.[12] Safety pharmacology is now a specialty of pharmacology, focused on the identification and characterization of pharmacological activities that influence the clinical safety of a drug or drug class.

Safety considerations for OTC drugs differ distinctly from those of prescription drugs. With worldwide drug safety monitoring programs now in place, a multitude of resources are available to monitor the safety of OTC drug products, allowing authorities to identify any adverse side effects very early on.

A proprietary NDA raises the level of safety for an OTC drug product in that it requires the company to file annual reports, and, moreover, formalizes the safety database prior to approval. The volume of information on the continuous tracking of an NDA-approved OTC drug product can reassure the profession of dentistry and the public of its continued safe use.

The ADA Seal: What It Adds to an Oral Hygiene Product Recommendation

For more than 80 years, the ADA has conducted dental product evaluations through its Seal of Acceptance program.[13] The program was established to help dentists, hygienists, and consumers select products that were evaluated by the ADA's Council on Dental Therapeutics initially, and after 1995, the Council on Scientific Affairs. The program originally evaluated both professional and consumer products, but the professional product component was eliminated on December 31, 2004. The Association subsequently launched a Professional Product Review newsletter, which is now online at ADA.org.

The Council on Scientific Affairs

The Council on Scientific Affairs is a standing committee of the American Dental Association's House of Delegates, its highest governing body. The House appoints the Council members that are nominated by the Board of Trustees. The 16 members are chosen at-large; that is, they do not represent the Association's 16 nationwide districts. Instead, more than one candidate for each Council position can be nominated by any number of Trustees. A 17th member is the current recipient of the Gold Medal Award for Excellence in Research.

To assist the Council, an experienced staffer, either specifically assigned to the Council or any staff member from the Division of Science or any other division in the organization, is at the Council's disposal. Further, since the Council members and staff cannot be expected to be experts in all fields pertaining to the evaluation of all products submitted, more than 80 consultants — leading scientists in their respective areas of expertise — assist and advise throughout the course of product evaluation.[14]

The bylaws also require the Council to perform other duties that aid in its ability to evaluate products.[14] For example, the Council is required to "evaluate and issue statements to the profession regarding the efficacy of concepts, procedures, and techniques for use in the treatment of patients." Knowledge gathered from this activity may require the Council to reconsider the status of existing products in the Seal program. Although products have rarely been dropped due to their obsolescence or lack of relevance, it has occurred. For example, when the old Council on Dental Therapeutics determined back in the 1970s that the use of quaternary ammonium compounds was no longer adequate for disinfection, the category was eliminated.

The Council must also "determine the safety and effectiveness of and disseminate information on materials, instruments, and equipment that are offered to the public…" as well as "dental therapeutic agents, their adjuncts, and dental cosmetic agents that are offered to the public and profession." This requires the Council to monitor both categories of products not included in the Seal program and products of companies that choose not to participate in it. The Professional Product Review program helps fulfill this responsibility.[14]

The Council must also "guide, assist, and collaborate with the ADA's Center for Evidence-Based Dentistry." Any findings from the Center that are in conflict with the indications for use of some Seal-bearing products may have ramifications.[14]

What the Seal Program Means

The Seal program requires that a manufacturer or distributor demonstrate the safety and effectiveness of OTC products sub-

mitted for evaluation to the Council on Scientific Affairs. The Council also reviews the labeling, package inserts, and other promotional material to make sure that all product claims are consistent with the safety and effectiveness data submitted. The FDA requires the same thing of companies, but the Seal program offers a level of day-to-day scrutiny that the FDA cannot provide.

To the consumer, this means that a nonprofit, nationally recognized organization closely monitors the dental products within its program in a proactive manner. Consequently, consumers can be assured that the Seal-bearing products on store shelves have maintained quality and the product claims are accurate (Figure 1).

Figure 1. *The ADA Seal.*

For dentists and hygienists, the program means that they can recommend Seal-bearing products to patients, confident in knowing their colleagues on the Council on Scientific Affairs have done their due diligence.

Products Considered for the Seal Program

The number of categories included in the Seal program has varied through the years, but the trend has been to limit evaluations to consumer products. Currently, the Council invites manufacturers to submit for evaluation products "that have been cleared by the U.S. Food and Drug Administration for market directly to consumers, regardless of whether the company elects to market the products over-the-counter or exclusively through oral healthcare professionals."[15] The Council on Scientific Affairs evaluates consumer dental products such as therapeutic agents, drugs, chemicals, materials, instruments, and equipment that are employed in the treatment or prevention of dental disease. In addition, cosmetic agents may also be eligible for the Seal. When evaluating these products, the Council utilizes published technical standards, including official ADA Guidelines and ANSI (American National Standards Institute)/ADA and ISO (International Organization for Standardization) specifications. Products for which ADA Guidelines or technical standards do not exist may also be evaluated if sufficient acceptable data demonstrating safety and efficacy are submitted. ADA Guidelines and technical standards may be modified at any time. The ADA will notify companies of any changes applicable to their products.[15]

Product Submission and Acceptance

The Council on Dental Therapeutics initially relied upon the General Criteria for Acceptance[16] (Figure 2), which originally was called the General Provisions for Acceptance. These provisions were similar to the requirements that currently exist. Some of these acceptance criteria merit explanation.

General Criteria for Acceptance
The name of the product being submitted
The composition, nature, and function of the product
Evidence of safety and efficacy
Government regulations
Use of biodegradable and recyclable materials
Labeling, package inserts, advertising, and other promotional material
Reference to Council Acceptance
Changes to the ADA Seal of Acceptance Program
Withdrawal of Acceptance
Confidentiality of Submission Material

Figure 2. *General criteria for ADA Seal acceptance.*

Both the generic and trade names must be submitted to the Council. These names must be in compliance with the Food, Drug, and Cosmetic Act; that is, the established or generic name must be consistent with the officially recognized names for a given category of product. Any deviation would be considered an attempt by the applicant to mislead the public and dental professionals into thinking that the product is something it is not. For example, a toothpaste trade name that suggests the product cures periodontal diseases without sufficient evidence would be unacceptable.

The Council requires the applicant to provide composition, nature, and function of the product being evaluated. For example, the Council wants to know if all the ingredients in a therapeutic agent meet a recognized standard of quality. Ingredients that meet the United States Pharmacopeia standards or their equivalent would meet that level of quality. Further, the Council determines if the manufacturer of the product maintains a quality assurance program that follows Good Manufacturing Practices.

ADA Guidelines and Data Submissions

Finally, the applicant must comply with relevant ADA Guidelines and/or specifications recognized by the Council. Currently, the Council on Scientific Affairs maintains 19 Guidelines that are listed on ADA.org (Figure 3).[17] These Guidelines cite the various research methods that can be utilized to demonstrate safety and effectiveness. When applicable, relevant ANSI/ADA specifications must also be employed.

The Guidelines can be downloaded without a formal request to the ADA. However, companies should feel free to discuss their plans to submit an application with the Council staff. The staff can then advise applicants how these Guidelines can be used either individually or in combination. For example, two Guidelines offer the company general advice on clinical study design in "Clinical Trial Protocols" and how it can demonstrate superiority, equivalency, and "at least as good as" properties for products in "Determination of Efficacy in Product Evaluation." The remaining 17 Guidelines pertain to specific categories of products.

One of the most interesting examples of a company's product submission to demonstrate safety and effectiveness can be

ADA Acceptance Program Product Guidelines[17]
Adjunctive Dental Therapies for the Reduction of Plaque and Gingivitis
Bottled Water with Fluoride
Chemotherapeutic Agents to Slow, Arrest, or Reverse Periodontitis
Chemotherapeutic Products for Control of Gingivitis
Cleansers for Removable Prostheses
Clinical Trial Protocols
Dental Floss or Other Interdental Cleaners
Dentist-Dispensed Home-Use Tooth Bleaching Products
Denture Adherents
Determination of Efficacy in Product Evaluation
Fluoride-Containing Dentifrices (Toothpastes)
Home-Use Tooth Stain Removal Products
Oral Irrigating Devices
Over-the-Counter Home-Use Tooth Bleaching Products
Products for the Cessation of Smoking and Use of Smokeless Tobacco
Products for the Treatment of Dentinal Hypersensitivity
Products Used in the Management of Oral Malodor
Sugar-Free Chewing Gums to Help Reduce-Prevent Cavities
Toothbrushes

Figure 3. *Acceptance Program product guidelines.*

found in the Colgate-Palmolive Company's application for the Acceptance of Colgate Total toothpaste in the 1990s. The application was, at the time, the most complex and comprehensive evaluation the Council and the company had undertaken. It took several years to complete using several ADA Guidelines because the company was making multiple claims of effectiveness; *i.e.*, supragingival plaque and gingivitis, caries, and supragingival calculus. The company later demonstrated effectiveness against oral malodor and tooth whitening by removing extrinsic stains.[18] Although the Colgate Total toothpaste evaluation was long and complicated, the process was otherwise uneventful due, in large measure, to the company's willingness to communicate frequently and openly with the Council and its staff. The Council has always encouraged open dialogue with companies.

Along with the safety and efficacy data submitted by the manufacturer or distributor, the ADA may also elect to conduct its own testing. This is especially the case when a product submitted for evaluation must use ANSI/ADA specifications. Such products will be tested by the ADA to determine if they meet those standards.

The Council also requires that the successful applicants provide safety and efficacy data generated following the marketing of the product (post-marketing surveillance). In these cases, a limited number of subjects are used to demonstrate safety and effectiveness in clinical trials. The marketing and sustained use of these products sometimes reveals side effects that compromise their safety and effectiveness.

Further, the applicant "must disclose any past, present, or anticipated financial arrangements between the investigators and the company, its affiliates or subsidiaries, including, but not limited to, consulting agreements, speakers' fees, grants or contracts to conduct research, or membership on the company's advisory committees, including remuneration policies, or in the product that is the subject of the investigation."[17] If the Council determines that the financial interests raise a question about the integrity of the data, it may take any action it deems necessary to ensure the reliability of the data, including but not limited to further data analysis, additional independent studies, or rejection of the data.

Finally, the product must be shown by the company to comply with all federal laws and regulations before use of the Seal can be announced or displayed.

Use of Biodegradable and Recyclable Materials

In keeping with ADA policy, companies are encouraged to use materials that are biodegradable and/or recyclable.

Labeling, Package Inserts, Advertising, and Other Promotional Materials

All labeling, package inserts, advertising, and other promotional materials must be consistent with the safety and efficacy data submitted in support of the Seal application. The Council evaluates these materials to determine if they make misleading claims and if they comply with the ADA's advertising standards and certification mark usage guidelines. The materials must also conform to the Association's rules for use of the Seal and its accompanying Seal statement that appears in a box on the accepted product's packaging. The statement lets the public and the dental professional know exactly why the product received the Seal. The message in the statement is designed to be easily understood by the average consumer.

Reference to Council Acceptance

The ADA does not want its Seal to be used as part of a marketing campaign. However, the ADA may grant permission to allow a company to promote the significance of the Seal to the public and profession.

Changes to the Seal of Acceptance Program

As with any long-standing program of this type, modifications can and will be made. These changes come about, for example, when product evaluation guidelines and ANSI/ADA specification are revised, testing criteria are changed to reflect scientific advances, and modifications to advertising and licensing agreements are made. In some cases, a change could result in the permanent withdrawal of the product or product category from the Seal program.

Withdrawal of Acceptance

The most common reason for withdrawal of the Seal is due to the changes described above. Rarely, however, when a company violates the license agreement, it may justify the reason for withdrawal.

Confidentiality of Submission Material

The ADA staff involved in the Seal program, the members of the Council, and its consultants must sign the ADA's Code of Conduct. Therefore, it is not necessary for companies to require individual nondisclosure agreements since the Code of Conduct includes confidentiality requirements.

Fees

For more than 20 years, the ADA has required application and maintenance fees to help cover the costs of the Seal program. Currently, the one-time application fee is $14,500, in addition to an annual maintenance fee of $3,500.[19]

Conclusion

This review demonstrates that the approval and post-marketing tracking of an NDA-approved OTC drug product, combined with the ADA Seal, represents to the public and dental professionals that both a federal regulatory and an independent, dispassionate body have determined that an over-the-counter dental product is safe and effective based on current testing and evaluation methodologies. Further, it means that the product claims are accurately reflected in the product's labeling, package inserts, and promotional material. Products that carry both designations should be recommended with confidence in their continued safe use.

Acknowledgment: The authors thank the Colgate-Palmolive Company for graciously providing the funding for the development of this article.

For correspondence with the authors of this paper, contact Dr. Frederick Curro – fac3@nyu.edu or Dr. Kenneth Burrell – burrellkh@yahoo.com.

References

1. Gray A. Access to Medicines and Drug Regulation in Developing Countries: A Resource Guide for Department for International Development (DFID). DFID Health Systems Resource Centre, London, 2004.
2. http://www.fda.gov/AboutFDA/WhatWeDo/default.htm, 2009.
3. CDRH 2014 Strategic Priorities www.fda.gov/.../centersoffice/officeofmedicalproductsandtobacco/cdrh/cdrhvisionandmission/ucm384132.htm. Accessed May 2, 2014.
4. Advancing Regulatory Science for Public Health. Accessible at: http://www.fda.gov/downloads/Scienceresearch/SpecialTopics/RegulatoryScience/UCM228444.pdf.
5. FDA Strategic Priorities. Accessible at: http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/ucm227527.htm.
6. www.fda.gov/.../aboutfda/centersoffice/officeofmedicalproductsandtobacco/cder/faqsaboutcder/default.htm, 2008.
7. http://www.fda.gov/SafetyMedWatch/default.htm.
8. www.fda.gov/regulatoryinformation/legislation/federalfooddrugandcosmeticactfdcact/fdcactchapterstandiishorttitleanddefinitionssec21usc321.htm.
9. www.fda.gov/cosmetics/guidanceregulation/lawsregulations/ucm074201.htm 2009.
10. www.fda.gov/drugs/developmentapprovalprocess/howdrugsaredevelopedandapproved/ucm317137.htm, 2012.
11. Curro FA. The clinical importance of drug evaluation. *J Appl Res Clin Dent* 2005;2:10-7.
12. The Future of Drug Safety: Promoting and Protecting the Health of the Public. http://www.nap.edu, 2006.
13. Clifford W. Whall, Jr. A Case Study: How to Develop a Seal of Approval Program. *Forum*, November 2006, p. 75.
14. American Dental Association Constitution and Bylaws. Revised January 1, 2014. ADA.org. Accessed April 21, 2014.
15. Guidelines for Earning the Seal. American Dental Association. ADA.org. Accessed April 19, 2014.
16. General Criteria for Acceptance, Revised November, 2011 American Dental Association, ADA.org.
17. Guidelines for Product Acceptance, ADA.org. Accessed April 21, 2014.
18. Anthony R. Volpe, DDS, MS, VP Clinical Research and Scientific Affairs (Retired), Colgate-Palmolive Company. Personal communication, April 21, 2014.
19. M. Mazher Said, PhD, Assistant Director, Acceptance Program, Council on Scientific Affairs. Personal communication, April 21, 2014.