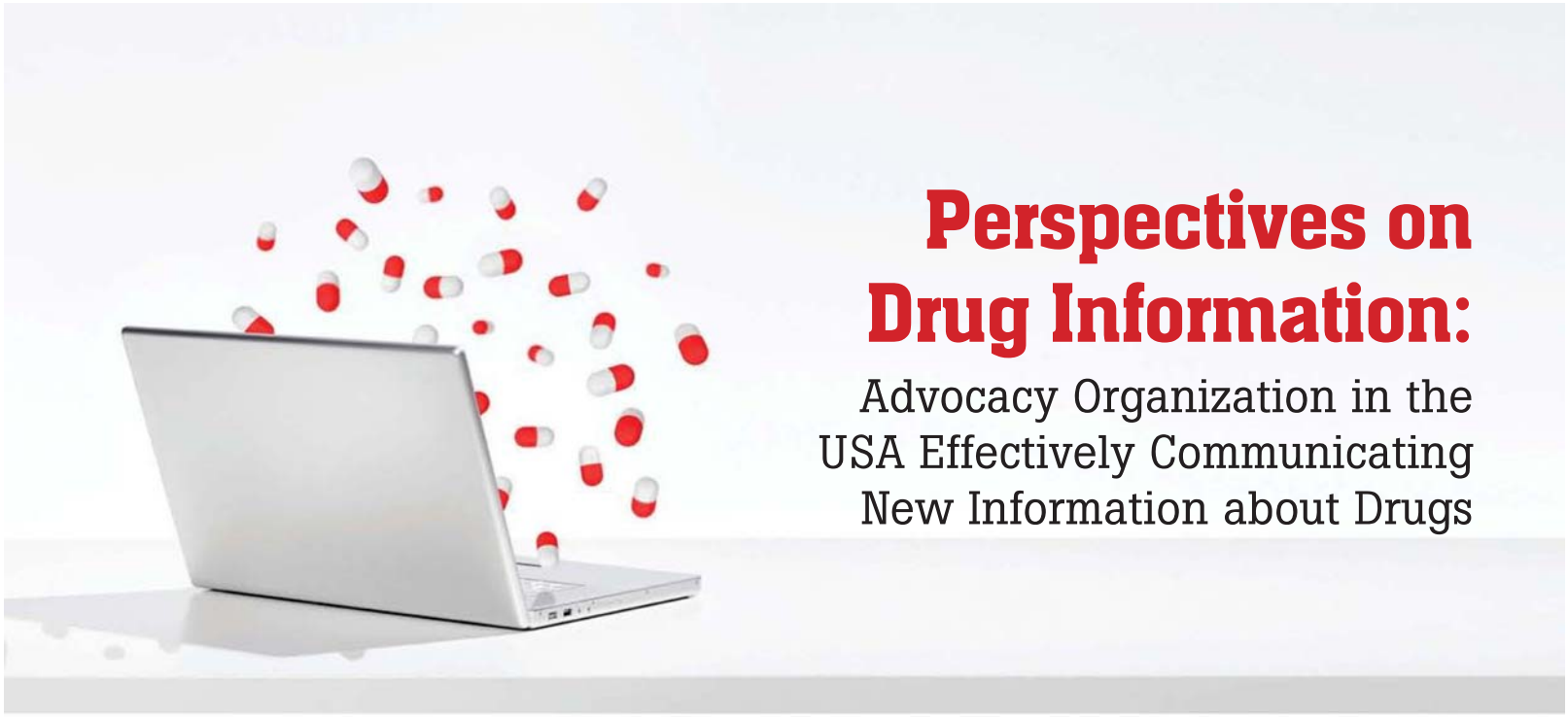

Perspectives on Drug Information:

Advocacy Organization in the USA Effectively Communicating New Information about Drugs

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The US Food and Drug Administration (FDA) is responsible for advancing and protecting the public health. A great deal of attention given to the agency is focused on the premarket review, approval, and ostmarketing monitoring of prescription drugs. However, the FDA is also faced with the challenge of effectively communicating information about its regulated products to a very diverse population in a timely manner. There are many end users of the information the FDA provides about medical products, including medical professionals, patients, family members, researchers, and developers, but ultimately this information exists to address the needs of patients who receive and use the treatments.

Undoubtedly, patients desire clear information about the safety and efficacy of their drugs. Having information about medical products readily available helps to answer questions about the potential benefits and risks of treatments for patients and care providers. However, in the case of many cancer treatments, for example, the drug may only work for a relatively small percentage of patients, and the reason for this is not always biologically known.

The biologic complexity of many diseases, like most forms of cancer, makes it difficult to determine what will work for whom, and therefore muddles benefit-risk decisions. In addition to the diversity of these diseases, the stage at which an intervention may be available, ranging from a preventative setting to end-of-life care, demonstrates that a standard "one size" approach to weighing benefits and risks would be inappropriate. Therefore, there needs to be flexibility in the policies that the FDA sets and the tools that are used to convey information to patients and health care providers. Communicating information about new medical products is a process that involves developing the data, translating it into meaningful information, and applying it in the clinical setting.

Ongoing Data Collection on Medical Products

Effective communication about new treatments begins with generating scientifically valid information itself. Despite the rigorous studies required, it is impossible to know everything about a new drug at the point of FDA approval. This can be attributed to a number of factors, including the relatively homogeneous population that is typically included in clinical trials. For example, to minimize the number of variables in a study, some patients may not qualify for a trial for reasons such as the presence of co-morbid conditions. It is possible that the presence of a secondary disease or disorder, which is common particularly in elderly cancer patients, may alter the benefit-risk profile of a drug. Or perhaps there is a side effect of a drug that is rare enough or results only after longer-term use, that it cannot be readily detected in the population size and duration of a clinical trial. These challenges with developing data pertaining to a new drug are not highlighted to suggest that larger and longer trials should be commonplace or that current clinical research processes are invalid, but that there is a need to collect data beyond the scope of the original approvals process, as well as in patient populations that may not have been included in the registration trials.

Converting Data into Meaningful Information

While collecting additional data over time is critical, translating that data into usable information is a growing challenge. As a result of new

programs and policies, the US health care system is on the verge of a data revolution. In the coming years, over forty million additional Americans will have access to meaningful health care, which will likely result in a large increase in the use of prescription drugs and other medical services. Additionally, many policy makers are examining how recent large investments in the widespread adoption of electronic medical records could lead to a tool for longitudinal research. A number of efforts, including the FDA's Sentinel Network or the Observational Medical Outcomes Partnership managed by the Foundation for the National Institutes of Health (NIH), have helped to develop methods to leverage and connect existing electronic data sources as an additional tool for safety monitoring. Building upon these models will be an important step in harnessing the large volume and new sources of data to ensure that it can be efficiently and effectively communicated to aid medical decisions.

Facilitating Clinical Application

The actual use of emerging information can be measured through changes in medical practice, which can be remarkably slow. In fact, it has been reported that there is a 17-year lag between new science and its adoption into clinical practice.[1] Furthermore, managing patient behavior and providing the right information to do so in a limited amount of time has become increasingly difficult for health care providers. It is estimated that on average, physicians spend less than 20 minutes with a patient during an office visit.[2] This duration has decreased over time, and presents a challenge to the delivery and therefore utility of emerging information about the benefits and risks of a medication which will ultimately impact patient behavior.

Communication Strategies to Minimize Risk

A recent policy approach to improve communication of new information and minimize risks is the establishment of Risk Evaluation and Mitigation Strategies (REMS). REMS were established as a part of the FDA Amendments Act of 2007 to help ensure that the benefits of a drug outweigh the risk.[3] At the core of the REMS program are communication strategies to help convey information about a drug that may include elements such as a medication guide, patient package insert, or a tailored communication plan such as a letter to health care providers. In the event that a drug has serious known risks that could cause it to be unavailable unless measures are developed to significantly minimize the risk, additional elements beyond a communication plan can be established. These "Elements to Assure Safe Use" could include special certification for health care providers, required specific settings for a drug to be dispensed, or establishing a registry for patients to enroll to facilitate monitoring of the drug.

To date, the majority of REMS programs have been limited to a medication guide to communicate the potential risks associated with the use of the drug.[4] Whether it is a medication guide or a more comprehensive strategy, it is important to develop metrics to evaluate the impact of a REMS program and optimize their use over time. The FDA draft guidance to industry states that the specific goals of a REMS should be stated up front.[5] This will allow the overall impact of the REMS to be examined, but other facts such as time for review and burden on practice should also be evaluated.

A number of factors could impact the effectiveness of a REMS, such as health literacy. For example, a review of approved medication guides determined that they are currently written at an 11-12 grade level,[6] despite federal recommendations that they should be developed to a 6-8 grade level. Additionally, geographic variation for the implementation of a REMS program should be examined. Eighty-five percent of cancer patients are treated at community-based hospitals,[7] which can create challenges to dissemination of information when compared to a large academic center.

Another area for consideration is the influence REMS places on off-label prescribing, which is frequently accepted in oncology. Off-label use refers to the prescribing of medication for an indication that is not specifically included in the drug label. According to the Government Accountability Office, one third of all drugs administered to cancer patients were off-label, and more than half of cancer patients received at least one drug for an off-label indication.[8] As REMS programs continue to be developed, there are questions about how they may impact off-label use and communication.

Conclusion

Communicating information about medical products is a fundamental role of the FDA. Evaluating the effects of communication plans, whether or not as part of a REMS, is important to optimize resources and strategies. This includes gaining the perspective of various stakeholders, including patients. The FDA has taken several steps to gain input directly from patients such as the "Patient Representative Program" to include patients in the advisory committee process and the "Drug Development Patient Consultant Program," which allows input

into other steps in the regulatory process.

As FDA and sponsors work to implement new policies for communicating drug information, such as REMS, stakeholder input will continue to be important and should be sought. A common template as a starting point for the development of REMS would help establish processes to gain valuable input. In addition, methods to engage advocacy organizations and professional societies should be examined. Disseminating new information can be challenging, but optimizing methods of communication will continue to enhance overall medical decision making. ■

References

1. Shine, K. I. (2001) Health care quality and how to achieve it. Robert H. Ebert Memorial Lecture, Milbank Memorial Fund, 1–13.
2. McCarthy and Leatherman, Performance Snapshots, 2006. www.cmwf.org/snapshots Accessed 5/27/10
3. FDA Amendments Act, Sept. 27, 2007, P.L. 110-85, as provided by § 909(a) of such Act, which appears as 21 USC § 331.
4. U.S. Food and Drug Administration http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm111350.htm Accessed 8/12/10
5. Guidance for Industry: Format and Content of Proposed Risk Evaluation and Mitigation Strategies (REMS), REMS assessment, and proposed REMS modifications. September 2009. http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM184128.pdf Accessed 8/12/10
6. Wolf MS, Davis TC, Shrank WH, et al. A critical review of FDA-approved Medication Guides. *Patient Educ Couns.* 2006;62:316-322
7. NCI Community Cancer Centers Program http://ncccp.cancer.gov/Media/FactSheet.htm Accessed 8/12/10
8. Government Accountability Office, *Off-Label Drugs: Reimbursement Policies Constrain Physicians in Their Choice of Cancer Therapies* http://archive.gao.gov/d18t9/144933.pdf Accessed 8/12/10

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