

**Engelberg Center for Health Care Reform
Sentinel Workshop—January 11, 2009
Margaret A. Hamburg, Commissioner of Food and Drugs**

Thank you so much, Mark for that very gracious introduction. On a personal note, I'd like to start by saying how much I appreciate Mark McClellan for his friendship and wise counsel.

Although most FDA Commissioners deal with the challenge of always needing more... more resources, staff, funding and legal authorities, to name a few, we usually have a surplus of advice and opinions from every quarter, on every imaginable topic. But Mark's guidance is particularly valuable to me because he is one of the few people who have been where I am now and knows first-hand the realities and challenges of leading, what I believe to be, the most important public health agency in America. I think we are all very fortunate that he has chosen to continue to devote his career to the goal of enhancing the FDA's ability to achieve its public health mission.

And, of course, that is the reason we are gathered here today...to engage, in a deep and meaningful way, in work that will produce the methodologies, technologies, safeguards, guidelines which, as a whole, will illuminate the way forward into a new era of medical product safety.

I use the term "new" in a qualified, but deliberate, way.

Of course, the FDA's focus on medical product safety is not new; the agency was founded more than a century ago for the express purpose of assuring the safety of America's food and drugs. While the FDA's legal authority to accomplish that mission has expanded and evolved significantly over the past several decades, enactment of the FDA Amendments Act (FDAAA) in 2007 gave the agency significant new authorities to protect the public from undue harm relating to drugs and medical products.

Along with new authorities, FDAAA requires the agency to broaden its view of medical product safety to the horizon of the post-market environment. While the promise of such an approach had recognized for a while, I can tell you that few things have the power to focus the attention of a regulatory agency like Congressional mandates that specify ambitious goals with date-certain deadlines.

And, of course, Sentinel represents an important element of this new approach....an initiative to create a national electronic safety surveillance system that will enhance FDA's ability to conduct monitoring of the safety and emerging risks of FDA approved medical products. Section 905 of the statute sets the goal that FDA will have access to data from 25 million patients, for the purpose of post-market safety surveillance, by July 1, 2010... less than seven months from today. There is a lot of vital work to be done.

And while I firmly believe that public health protection is a critically important role of government, I also know that there are some things that government agencies can not and should not do alone. The FDA has a vast and far-reaching mission, and our work represents a core responsibility of government. But I also strongly believe that it is important for government leaders, like myself, to have the wisdom to recognize where, and when, it makes sense for us to develop partnerships with important experts outside government.

And when it comes to convening a broad and diverse group of stakeholders to help establish the framework for a new safety surveillance system that will have a huge impact on society far into the future, it is essential for the agency to find partners who have the right kind of expertise. And I must say that the Engelberg Center is uniquely qualified in facilitating the kinds of meaningful exchanges that must take place in order to make progress in an endeavor as ambitious and important as Sentinel.

In the lexicon of the policy world it is easy for certain words to degenerate into meaningless buzzwords through overuse, but in the Sentinel Initiative we have an endeavor that enables us to reclaim the deepest meaning of some those well-worn terms.

By its very nature, Sentinel must be transparent, because when we are dealing with information contained in millions of patient records, we must be completely open, honest and public about what we are doing and why....and about what is done to safeguard the privacy of patients and assure that their medical records are secure.

By its very nature, Sentinel exemplifies the public-private partnership on a large scale. It is a collaboration made possible through the active engagement of public and private sector health care providers, companies, insurers, scientists and, of course, thought leaders and stakeholders like all of you, who represent a broad spectrum of interests and perspectives throughout society. Through this collaboration, the framework that will advance the science of drug safety and enhance the protection of public health will be created.

By its very nature, Sentinel illustrates the incredible power of leveraging science and technology in order to achieve important public health goals.

This is more than a significant change; it is a fundamental transformation. In a historical sense, it is an inevitable evolution of science, technology and policy that will enable the FDA to use the full range of tools it now has under statute to protect patients from undue harm.

While the capability to mine millions of patient records for evidence of an emerging risk will empower the FDA to accomplish its mission in new and powerful ways, it is a goal that many of you realized early on is essential to a fuller and more accurate understanding of the relative risks and benefits of medical products.

We have long known that, even the best pre-market clinical trials can track the impact of a drug on only a relatively small, and carefully selected, sample of patients, for a limited period of time. The data we glean from these studies stop far short of giving us a full picture what really happens when hundreds of thousands of patients actually use the drug—and in the case of therapies for chronic conditions—for the rest of their lives.

Clinical trial data can not anticipate, or account for, the variability of each individual patient, encompassing multiple factors such as genetics, personal health habits, environmental influences, pre-existing conditions, and drug interactions.

Today, more than ever before, those variables are critical factors in determining whether a particular drug is suitable for a particular patient. To an increasing degree we are mobilizing the potential of pharmacogenomics, or personalized medicine, to enable the agency to achieve a finer attenuation of the risk-benefit balance by helping us understand which patient sub-populations may face an increased risk from a particular medical product and which patients are most likely to realize a therapeutic benefit.

We also recognize the expanding role of medical products in health care today, often in our most vulnerable patients. It is striking that next year, the leading edge of the huge demographic bulge known as the baby boomers will turn 65. By 2030, nearly 71 million Americans, roughly 20% of the population, will be older than 65 and more than half of them will take medication every day to manage age-related chronic conditions such as type 2 diabetes, high blood pressure and arthritis.

In this, the beginning of a *new* era for drug safety, protecting public health means that the FDA's responsibility doesn't end when we grant a product pre-market approval; that is merely the first check point in assuring safety. A fuller and more accurate picture emerges when a drug enters the real world of the mass market. And the FDA's responsibility to actively monitor and act on safety risks which emerge in the general population, is one that extends for the entire time those products remain on the market.

This life-cycle approach—as codified in the statute—is a critical advance in public health protection.

At the heart of the FDA’s ability to meet these responsibilities are members of the agency’s safety review staff, many of whom are here today. These safety review teams are comprised of a wide range of experts in disciplines like pharmaceutical science, clinical medicine, toxicology, chemistry, epidemiology and public health; together, they practice the safety-focused science of pharmacovigilance.

Sentinel will give them a powerful tool in conducting near real time surveillance in the post-market environment. Ultimately, with a fully functioning Sentinel System that has the ability to query millions of patient records at a time, they will be able to detect patterns of emerging risk more effectively, and at an earlier point in the lifecycle of the product. After detecting a risk signal they will be able to further evaluate whether that early pattern can be strengthened and validated to provide an accurate picture of the measures required to mitigate the risk.

If a heightened risk is identified and confirmed, the agency may then require a range of measures to alert healthcare providers and consumers about the new safety information. These measures may include product labeling changes and requiring the manufacturer to develop a Risk Evaluation and Mitigation Strategy, or REMS, for that particular drug. In many cases, the FDA will require that a medication guide, fully explaining the new safety information, is provided to every patient who has the prescription filled. Depending on the nature and severity of the risk, the agency may also do targeted outreach to health care professionals and pharmacists.

In cases where a significant risk to certain patients is clearly identified, the FDA will take appropriate action to protect the public. This may include placing restrictions on who may prescribe the drug and also, under what circumstances an at-risk patient may take the drug. For example, if we know that a drug is likely to cause birth defects, we may require that a woman of childbearing age produce the results of a negative pregnancy test

before she can get a monthly prescription refill. This is just one illustration that the FDA will do what's necessary to prevent harm to at-risk patients, and in doing so, the agency ensures that the drug can continue to be available to all other patients who derive benefit from the drug.

The statute also gives the FDA the authority to require a company to conduct safety studies and clinical trials if a potential safety risk emerges in the post-market environment. As of today, the agency has asked companies for 180 post-market safety studies. The results of these studies will give the agency a clearer picture of elevated risk, and help us determine the appropriate course of action for risk mitigation.

Underpinning the FDA's heightened attention to post-market safety vigilance and action is the recognition of a fundamental truth: the scales of the risk-benefit balance are never frozen in a particular point in time; they are constantly shifting. With robust post-market safety surveillance, and the tools we now have under the law, the FDA can endeavor to continually adjust those scales so that therapeutic benefits always outweigh the potential risk to patients.

These new methods of protecting patients and consumers will become possible because all of you have chosen to devote years to the study and mastery of particular disciplines and areas of expertise which meet at the nexus of Sentinel. The work you do, and have done for years the fields of consumer advocacy, privacy rights protection, health care, medical product development and science is not new to you as individuals.

What *is* new is the fact that we have come together—and that we have arrived at this particular point in time where the technology has matured, expectations have been raised, authorities have been codified and, hopefully, all roads lead to the intersection of enhanced safety monitoring and better options and outcomes for all patients.

There is a powerful alchemy that results from the act of convening all of you in one place at the same time... of focusing your expertise, experiences and points of view on the issues at hand.

In this effort you are grappling with fascinating and important questions, such as,

- How can we protect patient privacy and ensure the security of data, while enabling access to data with enough detail to produce research that is scientifically robust and clinically useful?
- How do we design a common data model so that data sets can be compared and analyzed in a meaningful way? And,
- How do we reach consensus on the types of methodologies and protocols that should be employed in the quest to prove and disprove causal relationships between a product and an outcome?

The process will involve a great deal of time and effort, open minds, a posture of objective inquiry and along the way, there will be encouraging results, dead-ends, exhilaration and frustration. When it comes to discovering new ways of accomplishing important things, we know that, we sometimes learn more from the false starts and dead ends than the easy, early successes.

I am confident that a decade from now, the important questions you are grappling with today will be well addressed, appropriate methodologies firmly established, and the processes embedded in the way the FDA establishes safeguards for patients.

I am confident that a decade from now, the American people will be safer because of the work you are engaged in today.

And as FDA Commissioner, I believe that perhaps the most important thing I can do is to support and encourage you in that work and wrap up my remarks so you can get back to it. With deep gratitude, I thank you for your service to public health and our nation.