PROMOTING DRUG SAFETY IN THE US

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From aspirin to cancer treatments, CDER ensures the safety and efficacy of all drugs available in the US. Director Dr Janet Woodcock highlights the broad range of activities the Center is undertaking to ensure all prescription and over-the-counter drugs, both brand name and generic, work correctly and that healthcare professionals and patients are fully aware of the benefits and risks.

**What is the role of the Center for Drug Evaluation and Research (CDER) within the US Food and Drug Administration (FDA)? Can you offer a brief history of the Center?**

We regulate all medical drugs in the US – be they generic, new or over-the-counter medications. Anything with a drug claim that could be marketed in the US is regulated by us. The early 20th Century saw a series of tragedies associated with medications and the US Congress consequently enacted more restrictive legislation. Before then it was a virtual ‘Wild West’ and people were dying. In 1938, the US Government issued a law that required all drugs to pass a safety test before they came to market. Following this, in 1962, there were laws put in place to show that drugs were also effective. Ever since then, the safety and efficacy of drugs must be proven before they can be released onto the US market.

**Can you explain how your involvement with FDA initially began?**

I started working for FDA in 1986 at the Center for Biologics Evaluation and Research (CBER). I had previously been conducting research on monoclonal antibodies, which were approaching therapeutics stage at the time. After establishing myself at CBER, working there for about eight years, I then took over as CDER Director from 1994–2005. Following this, I worked in the Commissioner’s office as Deputy Commissioner and Chief Medical Officer, before returning to CDER in 2007.

**How does CDER promote, protect and enhance the health of the American people through its core mission and activities?**

CDER not only ensures that the drugs that are out there work, and are reasonably safe for use, but also regulates their quality. In addition, we make sure that issues such as counterfeit drugs and contamination are taken care of, and make efforts to address and prevent drug shortages. Our generic programme, which is huge, helps to ensure the affordability of medicine in the US.

**What are the key priority areas for CDER at present?**

Right now we have a long list of priorities. Number one is compounding regulation as we had a huge tragedy a number of years ago. FDA does not totally regulate compounding, it’s primarily regulated by the states, but we have a duty to make sure the states do not overstep their bounds – we are extremely influential in new legislation here.

Our second priority is the Generic Drug User Fee Amendments (GDUFA). GDUFA, which was enacted alongside the Food and Drug Safety Innovation Act several years ago, requires us to begin meeting our goals on the review of new generic drugs. A large number of applications are submitted every year; unfortunately, we are approximately 3,000 applications behind at present because the industry has exploded, but our staff numbers have not grown. With the GDUFA we are obtaining adequate staffing and are now able to deal with the backlog.

Another key priority is our new breakthrough drugs programme that was established in 2000. The programme is a designation for drugs that are potential game changers for patients with serious
and life-threatening diseases, and last year the Agency approved 10 breakthrough drugs.

Drug safety continues to be a priority – we have recently set up a new sentinel system (a safety surveillance system for the US), using electronic health information. The system contains information on 148 million people, allowing us to check for safety signals contained within it. This complements our spontaneous reporting, where people send in any side effects and adverse events they have experienced for us to evaluate – we receive almost a million reports like this a year.

Can you provide further insight into the Sentinel Initiative? Since its launch in 2008, what progress has been achieved?

The Initiative is a way to learn from the use of drugs and biomarkers in healthcare without interfering with personal privacy. CDER established the Initiative through a distributed network of healthcare data holders – electronic health record systems, administrative and insurance claims databases, and registries – who transform healthcare system data into a common model. Then, through our coordinating centre, we run the code behind a firewall and evaluate the results. It is very important that no personal information moves in this system. The data can be used in a large variety of ways to watch for any unusual signals in newly approved drugs; to obtain rapid answers to any questions on a drug’s side effects if there is a signal; and, more formally, to answer broader drug safety questions and/or provide more information. The system can now do this much faster and much cheaper than was ever possible before. Sentinel is the future – as electronic health records become more common and more standardised, we will be able to find out what is happening in the real world faster than ever before.

Could you elaborate on the GDUFA regulatory science programme? In your view, what are the significant benefits of this programme?

Our generic drug programme at CDER is a great benefit to the public, and this has been proven countless times by the huge amounts of money it has saved. Generic drugs make up around 85% of the drugs dispensed right now in the US. The generic drug industry grew up under this programme from a small industry to the powerhouse that it is now, so GDUFA has saved patients a lot of money.

However, there is a strict regulator programme in place to ensure that generic drugs are just as good as innovator drugs. With the huge growth of the industry, we felt behind because our programme was too small. But GDUFA gives us enough staff to review all generic drug applications. It also contains a very important provision in which we agreed to have parity between inspections that occur outside and inside the US. Many generic drug manufacturers make their drugs offshore, so this ensures the inspections have equal intensity. Further to this, CDER is now ramping up its safety and inspectional surveillance overseas.

Has the recent Ebola outbreak impacted upon the Center’s activities and focus for the near future?

We are doctors here, so we have always understood that there are many diseases out there that could become pandemic. CDER has worked with many government authorities and scientists, as well as groups like the Biomedical Advanced Research and Development Authority (BARDA), for example, to develop a whole range of countermeasures and treatments for these types of fatal diseases, which often occur in outbreaks. We are very flexible when issues like this happen. For instance, CDER published an editorial in the New England Journal of Medicine about how adaptive trials could be carried out to address the Ebola epidemic by rapidly evaluating new treatments. Our sister centre, CBER, regulates the vaccines and they are also very active and aggressive in public health matters.

FDA established the Drug Safety Oversight Board (DSB) in 2005. Can you explain the relationship between DSB and CDER? How significant is the input of the broad range of DSB’s representatives to the central aims of the Board?

DSB was created in 2005 and mandated in 2007 by the FDA Amendments Act. The Board advises us on a wide range of drug safety matters and has many federal employees due to the provisions of the Federal Advisory Committee. DSB is therefore a mix of people from government and healthcare systems, and this gives us a real-world perspective on our safety actions. The Board provides valuable input into potential side effects and other drug safety issues, and informs CDER of the impact of certain safety measures on these healthcare systems. They are extremely helpful to CDER.

To what extent is CDER helping to overcome the challenges of personalised medicine?

CDER has been in the lead on this for a very long time, since the early 2000s. We have produced editorials, scientific papers and guidelines,
30 in 2011
39 in 2012
27 in 2013
41 in 2014

NOVEL NEW DRUGS

Novel new drugs offer new and innovative therapies for patients, serving previously unmet medical needs or providing significant improvements that advance patient care and public health. In 2014, CDER approved 41 novel new drugs, exceeding the previous averaged 25 novel new drug approvals per year from 2005-13.

BY WHAT MEANS DOES CDER COMMUNICATE DRUG SAFETY INFORMATION TO THE PUBLIC?

Our Drug Safety Communications provide patients, consumers and healthcare providers with information and advice on newly observed potential risks of FDA-approved drugs. There are top line messages for patients, as well as data and expansive information for doctors and scientists, who require in-depth medical information. Our philosophy is one of transparency – we may send out a communication after the public has informed us, even before we know whether an event is relevant. In certain terms, they want to know when we know. We also have a Twitter feed, podcasts, iTunes, radio and many other ways to try and get the message out through different channels.

WHAT ARE YOUR AMBITIONS FOR CDER OVER THE NEXT FIVE TO 10 YEARS? ARE THERE ANY RECENT SUCCESSES YOU WOULD PARTICULARLY LIKE TO HIGHLIGHT?

I would like to keep up with the science – continue to evolve our regulatory paradigm to meet new scientific developments so that we do not fall behind. CDER must, within two to three years, become fully automated in our review processes, submissions, etc. Furthermore, I would like CDER to continue to be a leader in clinical trials both in the US and worldwide – we want to keep on streamlining clinical trials to make them more effective.

In addition, the Center has just established a large office dedicated to pharmaceutical quality that will regulate the manufacturing and quality of pharmaceuticals across the globe. Over the coming years, this office is intended to shepherd the industry as they transition to modern manufacturing techniques, which they are beginning to do.

Are there any particular trends in new drug approvals? In your opinion, what are the main drivers behind this observed growth?

One trend is increased drug approvals for treating rare diseases, and that’s driven directly by personalised medicine because as you subset diseases, the representation becomes smaller and smaller. So these targeted therapies are often orphaned. We are also seeing more first-in-class drugs – drugs which, for example, use a new and unique mechanism of action for treating a medical condition. These drugs are becoming more innovative and will most likely continue because people need choice – many people experience side effects after using a particular drug so switch to an alternative. In the 1990s, there may have been around 14 alternative drugs to a class, but now we are seeing much less, and instead we have drugs that are highly effective. An example of this is FDA’s 10 breakthrough drugs – the drugs that we believe hold tremendous promise to be game changers for a disease.

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