FDA lays out regulatory science strategy

The FDA plans to revolutionise the science used in developing and evaluating regulated products. Its success will determine the future of medical innovation.

The US Food and Drug Administration has released a detailed plan explaining how it intends to more effectively translate cutting-edge scientific and technological developments into the delivery of new therapies to the market. *The Strategic Plan for Regulatory Science* published on 17 August 2011 describes steps the agency will take to modernise the science used in developing and evaluating the products it regulates.[1]

The main goal is to speed up medical innovation by overcoming shortfalls in seven 'science priority areas' that are impeding pipeline output. (The document includes an eighth priority area on food safety, which this article does not discuss.)

Among other things, the plan seeks to address the agency's urgent need to understand emerging fields such as nanotechnology, gene therapy, cell therapy, tissue engineering and information technology. It builds on two broader documents released over the past year: *Advancing Regulatory Science for Public Health* (October 2010) and *FDA Strategic Priorities: 2011-2015* (April 2011). The FDA's senior advisor for science innovation and policy, Vicki Seyfert-Margolis, described the plan as a call to action not only for the agency, but also for the scientific community, the medical product development sector of industry and the people involved in monitoring the safety of medical products.[2] "I think it's something we all can't afford to not do," she said.

Indeed, the FDA acknowledges that to achieve its objectives, it will need to work with domestic and international partners in government and academia, as well as stakeholders from the private sector. The action points it describes in the seven priority areas below all involve collaboration with these external resources to some extent.

Modernising toxicology: Serious and sometimes rare and unexpected adverse events occur in clinical trials or post-approval, suggesting that critical gaps exist in the FDA's understanding of the relationship between patient response and preclinical toxicology findings. To address this, the agency plans to invest in three particular areas of regulatory science: evaluating and developing models and assays that better predict patient response; identifying and evaluating more reliable biomarkers for monitoring toxicities, side effects and abnormalities; and using computational tools to integrate and draw conclusions from a wide range of preclinical safety data types and sources.

Stimulating innovation in clinical evaluations and personalised medicine: Despite progress in genomics, translating new scientific findings into safe and effective use of medical products and optimising the use of existing products for all populations remains a major challenge. Clinical development programmes are lengthy and expensive with uncertain outcomes. The FDA intends to develop the new tools and approaches it needs to "catalyse" the development of personalised medicine. It will also modernise and advance the science and conduct of clinical trials. This will involve: developing and refining clinical trial designs, endpoints and analysis methods; leveraging existing and future clinical trial data; identifying and qualifying biomarkers and study endpoints; increasing the accuracy and consistency, and reducing inter-platform variability of analytical methods to measure biomarkers; and developing a virtual physiologic patient.

Supporting new approaches to product manufacturing: In conjunction with its ongoing activities to improve quality by design (i.e. understanding the manufacturing process and identifying the key steps for obtaining and assuring a pre-defined final product quality), the agency aims to improve product manufacturing and quality by enabling development and evaluation of novel and improved manufacturing methods. It also intends to develop new analytical methods and take action to reduce the risk of microbial contamination of products.

Ensuring FDA readiness to evaluate new technologies: The agency must be equipped with the tools and methods needed to assess reliably the safety and efficacy of products derived from ground-breaking discoveries in areas including complex chemistry and biosynthesis, electronics, nanotechnology, gene therapy, cell therapy, tissue engineering, optogenetics, high-intensity focused ultrasound and information technology. To that end, the FDA will develop its expertise and infrastructure so that it can evaluate these technologies. Its activities will focus on: stimulating the development of innovative medical products while concurrently developing novel assessment tools and methodologies; developing assessment tools for novel therapies; assuring safe and effective medical innovation; and enhancing readiness for new applications of information technology.

Harnessing diverse data through information sciences: The FDA is in the early stages of constructing the information technology infrastructure it needs to integrate data from a variety of sources including product submissions, adverse event reports, de-identified patient data from healthcare providers, and results from surveys and basic scientific research. By integrating and analysing these data, the FDA says it will be able to provide industry with new information that it can apply to future product development – potentially saving billions of dollars.

However, to achieve this, the agency requires extensive improvements to its existing IT environment, as well as new analytic approaches and tools. The plan explains how the agency will improve its information sciences capability to enhance IT infrastructure development and data mining. It will also develop and apply simulation models for product life cycles, risk assessment and other regulatory science uses. Additional action points include analysing large-scale clinical and preclinical data sets, and incorporating knowledge from FDA regulatory files into a database integrating a broad array

of data types to facilitate development of predictive toxicology models and model validation.

Facilitating development of medical countermeasures (MCMs): The FDA has identified a need to advance regulatory science to be better prepared for potential public health emergencies involving chemical, biological, radiological or nuclear threat agents or naturally occurring infectious disease outbreaks. It intends to do this by establishing more flexible and nimble manufacturing processes and creating data, tools and methods to speed development and evaluation of MCM product safety, efficacy and quality. Some of the specific areas that need to be addressed are: developing, characterising and qualifying animal models for MCM development; modernising tools to evaluate MCM product safety, efficacy and quality; developing and qualifying biomarkers of diseases or conditions; and enhancing emergency communication.

Strengthening social and behavioural science: The aim here is to help consumers and professionals make informed decisions about FDA-regulated products. To enhance the utility of information provided to the public, the agency says it needs a science-based approach for developing an effective communications strategy. Among other things, FDA scientists will continue to work on improving their understanding of how various factors related to the individual (e.g. age, sex, race/ethnicity and literacy) and the information provided on or with products (e.g. wording and placement) impact decision makers' responses to product, label and agency-provided information.

Little impact on review processes

Dr Seyfert-Margolis pointed out that the plan would not change the agency's review processes "except to the extent that this knowledge and this base of science... will really help facilitate a better understanding during the review process and of course make for a more effective review process."

She added: "We're going to continue going about our business and [do] it in a very high-quality fashion but I think this is really about how do we get to that next level, how do we get to those next generation medical products that incorporate things like investments in the human genome project and investments in new technologies... like nanotechnology or in more complex... biologic products."

The FDA says it will use the strategic plan to ensure that its regulatory science programmes focus on the identified priorities in combination with centre-specific approaches. The Center for Drug Evaluation and Research, for example, published a draft report in July 2011 entitled *Identifying CDER's Science and Research Needs*, which discusses current priorities in regulatory science related to the drug centre's mission.[3]

To make sure regulatory science stays up to date, the FDA will periodically use its Science Board and other outside scientific expertise to identify and prioritise research efforts. These resources will also provide input on the relevance, quality and productivity of the agency's regulatory science programmes.

The plan notes that while the FDA is a science-based agency that will continue to directly support regulatory science research, "it is not primarily a funding agency". The agency describes some of the potential avenues for fostering a strong regulatory science culture and promoting the regulatory science research agenda set out in the plan.

These include staff scientific training and professional development, partnerships with government agencies such as the National Institutes of Health, direct funding mechanisms and public-private partnerships (PPPs).

The plan says that PPPs will be a key component of the implementation strategy for FDA regulatory science, as they provide a means to leverage funds from academic institutions, the FDA, other government agencies and industry to support the regulatory science priority areas defined in the plan. The agency's own limited funds will generally be targeted for initial pilots or start-up funds that will be used to exploit resources from other sources, such as other government agencies, industry through consortium models or philanthropy.

Enough to quell criticism?

The FDA's efforts to improve regulatory science have been ongoing for several years, particularly since a subcommittee of its Science Board said in 2007 that the agency "suffers from serious scientific deficiencies and is not positioned to meet current or emerging regulatory responsibilities".[4] The subcommittee concluded that the impact of the deficiency was profound "precisely because science is at the heart of everything FDA does. The Agency will flounder and ultimately fail without a strong scientific foundation."

Three years later, the Government Accountability Office published a critical report on FDA strategic planning and management.[5] According to the report, only 36% of the FDA managers it surveyed believed the agency was making great progress in keeping pace with scientific advances. Furthermore, it found that the agency's IT capabilities were still inadequate.

It is widely recognised that by 2011 the FDA had still not caught up with the science; the FDA's plan appears to contain concrete steps to tackle this problem. According to FDA Commissioner Margaret Hamburg, "there is a troubling gap between advances in science and patient care. We need to build a bridge across this gap… and that bridge, in my view, is regulatory science."

References:

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