Common goals

As concerns over the adverse effects of the diabetes drug rosiglitazone (Avandia; GlaxoSmithKline) keep the spotlight focused on safety issues in the ongoing debate on drug regulation and the role of regulators such as the FDA and EMEA, it is important that the value of continuing to improve the regulatory processes leading to drug approval is not forgotten.

On 21 May this year, the publication of a meta-analysis of trials of rosiglitazone suggesting that the diabetes drug increased the risk of heart attacks[1] set off a wave of reaction reminiscent of that to the withdrawal of the painkiller rofecoxib (Vioxx; Merck) in 2004. News stories in many countries highlighted the reported 43% increase in relative risk, GSK's share price fell 10% and once again the ability of US drug safety systems — and in particular the FDA — to protect the public health was called into question (see page 505 of this issue).

This latest high-profile drug safety issue comes at a critical juncture in the evolution of the US regulatory environment. The Prescription Drug User Fee Act (PDUFA), through which companies submitting applications to the FDA for new drugs to be licensed contribute user fees to help provide resources such as staff for drug reviews, is up for its third reauthorization this year. And as the latest version of PDUFA needs to be passed into law this summer if the jobs of FDA staff are not to be at risk, there is acute pressure on the legislators.

Unsurprisingly, improvements to the systems for monitoring drug safety have been a key priority for PDUFA IV. In the version passed by the Senate, the FDA's powers to take action to ensure the safety of marketed drugs have been increased considerably, and user fees are to be directed specifically towards drug safety assessment for the first time[2].

Indeed, in 1992 when the first version of PDUFA was authorized, the major concern was that slow regulatory reviews were putting the US at a disadvantage compared with elsewhere. The user fees contributed by companies submitting drug applications enabled the FDA to hire additional review staff to facilitate more rapid review, and, in exchange, the FDA was legally obliged to review and act on submissions (but not necessarily grant or refuse approval) within a certain time frame.

Studies on the impact of the PDUFA legislation have found that it has been successful in achieving the goal of reducing drug approval times[3], and it seems that this has been achieved without compromising drug safety[3]. And a recent survey of 66 life-sciences companies on their working relationship with the FDA over the past decade, conducted by PricewaterhouseCoopers and the industry association BIOCOM, indicates that most consider that both the FDA and their working relationship with the agency have improved significantly in this time[4].

However, the survey also highlights resourcing concerns about the FDA — with FDA staffing shortages and turnover identified as the biggest ongoing issue for life-science firms, and faster turnaround times as the area where improvement is needed the most. Some companies also indicated that the FDA changed its position during the review of product submissions. Such changes can be damaging and might, in part, reflect growing risk-averseness among regulators, an issue that is discussed in a Perspective on page 532.

In this respect, it is worth remembering that a lack of efficacious therapies can also be highly detrimental. For example, an article in *Fortune* last year noted that the absence of an effective vaccine for rotavirus — owing to now seemingly unjustified concerns over a potential rare side effect of the first vaccine to be approved — might have led to the unnecessary deaths of an estimated 3.6 million children[5]. Alternatively, looking at the issue the other way, there is a considerable health benefit to bringing efficacious therapies to the market in a more timely manner. For instance, another study on PDUFA found that the more rapid access of drugs on the market enabled by PDUFA saved the equivalent of 180,000–310,000 life-years[6]. Although much-needed strategies to enhance drug safety are justifiably in the spotlight, the benefits of timely drug approval should be kept in mind as the debate on drug regulation in the US and elsewhere continues, and a common goal of drug developers and regulatory agencies — enhancing public health through the introduction of safe and effective therapies — emphasized.

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