It's good to talk

A new report suggests that greater interaction between the US FDA and drug sponsors during drug development leads to drugs being approved sooner. But more resources could be needed to achieve this routinely, raising the thorny question of where the funding would come from.

With the fall in new drug approvals last year still attracting frequent comment, approaches that could help smooth the way of innovative therapies to market are in the spotlight again. For example, as discussed in the news story on p177 of this issue, two recent initiatives from the FDA should make it easier to get drugs into early-stage human trials, potentially accelerating the validation of a particular therapeutic strategy. A recent report now highlights how the FDA could help speed the progress of drugs from early-stage clinical development to approval[1].

The study was conducted as part of an independent assessment of the effects of the 2002 amendments to the Prescription Drug User Fee Act (PDUFA) legislation, which authorizes the FDA to collect fees from sponsors submitting New Drug Applications (NDAs) and Biologic License Applications (BLAs) to fund additional resources such as staff, thereby facilitating more rapid application review. In particular, the report focuses on differences between NDAs and BLAs that were approved in the first 'cycle' of FDA review and those applications that went through multiple review cycles before being approved. Of the 77 submissions analysed — 63 NDAs and 14 BLAs made between fiscal year 2002 and fiscal year 2004 — 36 received first-cycle approval, 18 were approved in multiple cycles and 22 were still pending.

Several factors seem to influence whether a product goes through multiple review cycles or is approved first time. Unsurprisingly, priority and 'fast-track' products have higher first-cycle approval rates, reflecting not only the urgency for new therapies with such designations, but also, the report suggests, increased attention from the FDA and sponsors for these products. Greater sponsor attention is presumably also an important contributor to another of the trends identified: 65% of in-licensed products were approved in the first cycle, compared with 42% of products originated in-house. Experience with the FDA was a further sponsor-related factor that stood out clearly, with the first-cycle approval rate for sponsors that had already had drugs approved previously being 51%, compared with 30% for sponsors with no prior approved drugs, highlighting the benefits of familiarity with the FDA regulations and processes.

But perhaps the most important factor identified in the report is the positive impact of meetings between sponsors and the FDA at the end of Phase II trials, which can highlight deficiencies and concerns in areas such as the design and execution of the pivotal Phase III trials. For the 46 products for which meetings were held at the end of Phase II, 52% received first-cycle approval, compared with 29% for products that did not have such meetings. And interestingly, meetings at the pre-NDA/BLA stage, although important, did not seem to have as much of a beneficial effect, perhaps reflecting a typically greater focus on administrative considerations in these late-stage meetings.

Officials at the FDA, including the Acting Commissioner, Andrew von Eschenbach, agree that early-stage meetings are particularly valuable, but note that such meetings are labour intensive and would require further resources if they were to become more standard. And looking at the same issue from the industry perspective, a recent survey indicates that senior R&D personnel not only show considerable interest in the possibility of better communication with the FDA during the clinical phases of drug development, but also support the idea of establishing a user-fee programme to facilitate such communication[2]. As PDUFA comes up to its next reauthorization in 2007, the debate on how best to set and distribute user fees is already underway, and of course improving drug safety is high on the agenda. The voices of those who are already critical of the 'cosiness' of drug sponsors and the agency that polices them, and the potential conflicts of interest associated with industry funding of the FDA, will also be prominent. But given the benefits indicated so far and the interest of both regulators and sponsors in communicating more during drug development, finding ways to facilitate appropriate discussions between them should also be a priority.

1. Independent evaluation of the Food and Drug Adminstration's first cycle review performance – retrospective analysis final report. <http://www.fda.gov/OHRMS/DOCKETS/98fr/oc05257-rpt0001.pdf> (2006).
2. Berndt, E. R. *et al*. Opportunities for improving the drug development process: results from a survey of industry and the FDA. <http://www.nber.org/papers/W11425> (2005).