BIOBUSINESS BRIEFS

REGULATORY WATCH

FDA PDUFA goals missed

As part of the Prescription Drug User Fee Act (PDUFA) — now in its fourth incarnation in the Food and Drug Administration Amendments Act (FDAAA) 2007 — the US FDA has a goal to review and act on 90% of all submissions in a given time frame. The general review goal for a drug application is 10 months for a standard application and 6 months for priority review.

Historically, the FDA has been able to exceed this PDUFA performance goal. Complete data from the FDA's fiscal year (FY) 2006 submissions were made available in its FY 2007 Performance Report to the President and Congress (see Further information). The FDA acted within its goal on 153 out of 158 (97%) original applications, 59 out of 60 (98%) resubmitted applications and 180 out of 188 (95%) efficacy supplements. Only 14 applications were not reviewed within the stated goal.

However, as acknowledged in the debate leading up to the FDAAA, the FDA is considered to be understaffed — a situation exacerbated by increased concerns over drug safety. Although a major recruitment programme to add 1,300 positions is ongoing, such challenges led John Jenkins, Director of the Office of New Drugs at the FDA, to issue a memo in January 2008 allowing staff to miss PDUFA goals in order "to bring their unit's workload into better balance with their existing resources."

Based on data compiled from BioMedTracker, as of 5 December 2008 we identified 21 instances dating back to late 2007 in which the FDA may have missed its PDUFA goal (Supplementary information S1 (table); selected examples are shown in TABLE 1). There may also be additional instances of delays that are not reflected in this number owing to a lack of public disclosure. The most common therapeutic areas experiencing delays are cardiovascular medicine and neurology. In addition, drugs that require risk-management programmes (such as romiplostim (Nplate; Amgen)), advisory committees (such as telavancin; Theravance) or complex label negotiations (such as sapropterin (Kuvan; BioMarin)), were also more likely to experience delays. There is currently no clear trend as to the length of time by which FDA decisions have been extended, with delays ranging from weeks to over 7 months.

It is interesting to consider whether the missing of PDUFA performance goals by the FDA is positive or negative for the industry overall. On the negative side, delays can exacerbate cash constraints for smaller companies, and are often perceived by the market as leaving a drug in limbo without a clear explanation as to the FDA's thought-process, and therefore enhance the sense of risk. However, on the positive side, a missed PDUFA goal that allows the agency enough time to properly complete its review may be preferable to its meeting the PDUFA goal by issuing a Complete Response letter, which might lead to protracted procedural delays and expenses.

At present, sufficient data to assess whether increased delays might be positively affecting approval rates are not available, as nine of the delays identified have decisions still pending. Nevertheless, at the time of going to press, the total number of new molecular entities and biologics license applications approved by the FDA in 2008 stood at 20, with over a dozen decisions still expected by the end of the year. This is already an improvement on the corresponding tally of 18 approved in 2007.

Table 1 | **Selected PDUFA dates missed in 2008***

Drug	Company	Indication	PDUFA date missed	Date acted on	Current status
Prasugrel	Eli Lilly	Acute coronary syndrome	26 Sep 2008	Pending	Pending
Milnacipran	Cypress Bioscience	Fibromyalgia	18 Oct 2008	Pending	Pending
Romiplostim	Amgen	ITP	23 Jul 2008	22 Aug 2008	Approved
ABT-335	Abbott Labs	Dyslipidaemia	Oct 2008	Pending	Pending
Vernakalant	Cardiome	Dysrhythmia	19 Jan 2008	8 Aug 2008	Approvable

*As of 5 December 2008. ITP, immune thrombocytopaenic purpura; PDUFA, Prescription Drug User Fee Act.

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FURTHER INFORMATION

Performance report to the President and the Congress for the Prescription Drug User Fee Act: http://www.fda.gov/ope/pdufa/report2007/PDUFAFY2007Perf.html

SUPPLEMENTARY INFORMATION

See online article: S1 (table)

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