NEWS IN BRIEF

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European regulators launch 'breakthrough' equivalent programme

The European Medicines Agency (EMA) launched the Priority Medicines (PRIME) scheme in March to speed up the development of promising medicines. PRIME is similar, but not identical, to the FDA's breakthrough therapy programme, which the US regulators launched in 2012.

PRIME is aimed at medicines that could offer a major therapeutic advantage over existing treatments, or that will benefit patients with no treatment options, given early-stage clinical data. Large pharmaceutical companies are eligible after completing proof-of-concept trials, whereas smaller companies and academic groups can apply as soon as they have compelling non-clinical data and tolerability data from initial clinical trials. Because small companies and academic groups generally have less experience with the regulatory framework, they could benefit in particular from earlier scientific and regulatory advice, the agency noted.

Successful applicants will gain access to earlier interactions with the EMA's representatives, scientific advice from regulators and speedier assessment timelines. The big wins will come from being able to plan better clinical trial programmes, said Tomas Salmonson, Chair of the agency's Committee for Medicinal Products for Human Use (CHMP). "For some [drugs] there may be very limited benefits. For others, I'm convinced there will be a significant gain."

A recent analysis of the FDA's breakthrough programme found that breakthrough-designated cancer drugs spent on average 5.2 years in clinical trials, compared with an average of 7.4 years for non-designated drugs (*Nat. Rev. Drug Discov.* **15**, 152; 2016). Because the breakthrough programme is still young, and because some of the designated drugs were already well into their clinical trials when they received breakthrough designation, it is unclear how much of this gain is attributable to the additional support that sponsors received from the FDA.

Salmonson added that the PRIME scheme is just one part of the regulatory jigsaw puzzle. PRIME candidates can also benefit from other regulatory tools, such as the agency's conditional marketing pathway, a temporary approval that can be granted in the absence of comprehensive clinical data, and its parallel scientific advice process, which provides drug development guidance from health technology assessment (HTA) groups (*Nat. Rev. Drug Discov.* **13**, 8; 2014).

The EMA expects approximately 100 submissions for PRIME eligibility per year, but Salmonson cautioned that "a large number of the applications will be turned down." When the FDA launched its breakthrough programme it anticipated granting only a few designations per year. It has already granted the designation to over 100 products.

The EMA will publish monthly statistics on the uptake of the programme.

Asher Mullard

Amarin agreement opens off-label promotion door

The FDA has agreed to allow Amarin to promote its omega-3 drug icosapent ethyl for 'off-label' uses, potentially opening a door for other drug developers to promote drugs for uses for which they are not explicitly approved.

The agreement settles a lawsuit launched by Amarin to promote its drug — which is approved to reduce triglycerides in patients with severe hypertriglyceridemia — for off-label use with statins in patients with persistently high triglycerides. The FDA had denied approval of this supplemental indication, following the advice of its independent advisory committee. In August 2015, a judge ruled that the biotech "may engage in truthful and non-misleading speech" to promote the off-label use of its drug, under the company's right to free speech. At the time, some experts expected the FDA to appeal the decision.

The FDA has said that the settlement applies only to the Amarin case. But it is the latest in a series of legal cases that have put the agency's approach to off-label promotion under pressure. Some estimates hold that as many as 40% of overall prescribing decisions are for off-label uses.

A recent white paper — from authors in academia, at law firms and at organizations such as Friends of Cancer Research and The American Society of Clinical Oncology — says that litigation is not the best way to establish a new regulatory framework for off-label information. It proposes some possible solutions.

One option would be for the agency to "clarify how [information that does not meet current labelling standards] could be incorporated in efficacy claims and potentially in extensions of FDA-regulated labelling," they write. Perhaps lower levels of evidence could be allowed under certain circumstances or for particular audiences, they suggest. "A more extensive policy shift would involve introducing additional, clearly delineated tiers of evidence into the product labelling: primary efficacy claims and information for an approved indication would be given the most weight and highest placement, but additional evidence with appropriate qualifications could be added to the labelling as a greater body of evidence is generated on the product's use in different contexts."

Alternatively, they cautiously suggest that a third party could be charged with accrediting off-label information. Under this system, "approval could be given within a rank, score or grade system that confers greater weight to better evidence, and could be given contingent upon continued evidence generation and resubmission to the clearing body. For example, an off-label communication may be approved and given an initial grade or rating that sunsets within a specified number of years barring updated submission of relevant evidence," they write. The authors did not universally support this 'third party' solution.

Joshua Sharfstein, a former deputy FDA commissioner and an associate dean at the Johns Hopkins Bloomberg School of Public Health, told StatNews that this white paper is asking the wrong question. "I fear this is all about asking how we can allow companies to promote as much as possible," he said. "Instead, we should be asking: how can we create the correct incentives so that good research is done and we get the best information to distribute?"

Asher Mullard