NEWS IN BRIEF

Should the FDA disclose complete response letters?

Companies rarely adequately disclose the rationale for drug rejections, shows a US Food and Drug Administration (FDA) analysis of complete response letters. Press releases not only often omit key details about rejections — such as the need for more clinical trials or increased mortality in the treatment arm of a trial — but also sometimes state a rationale for rejection that bears no similarity to that included in regulatory complete response letters.

In the study, a team of FDA researchers compared 61 complete response letters that were issued between 2008 and 2013 to the press releases that these rejections triggered (*BMJ* **350**, h2758; 2015). The press release statements matched only 93 of 687 (14%) of the statements actually made in complete response letters. Out of 32 complete response letters that called for new clinical trials, only 19 (59%) of the associated press releases reported this recommendation. Out of 7 complete response letters noting higher mortality rates in treated patients, only 1 (14%) press release disclosed this problem.

The analysis also found that in 11 cases (18%), companies did not issue a press release about the complete response letter. A further 13 (21%) press releases did not include any statements that matched the statements included in the complete response letter. And 22 (26%) press releases noted rationale that could not be matched to that of the complete response letter.

In 2010, the FDA had proposed disclosing complete response letters to the public, but drew criticism because of the potential to violate trade secrets and confidential information. "Our analysis found that the FDA's reasons for not approving marketing applications for new molecular entities are not being fully conveyed to the public," the authors now write. "The potential benefits of publicly disclosing the agency's detailed rationale for refusing approval include better informing the development of new drugs, facilitating a richer public health discourse, and counteracting misconceptions regarding FDA's reasons for denial of applications."

The analysis also found that applications under priority review were less likely to receive complete response letters than those under standard review. Drug applications that were referred to advisory committees were marginally more likely to receive complete response letters than were applications that didn't go to committee (unless the advisory committee voted favourably on the drug).

Asher Mullard

Robust biotech sector increases R&D spend

The biotech sector increased its research and development (R&D) spending to US$35.4 billion in 2014, up 14% from $29.4 million in 2013, shows the latest Ernst & Young Biotechnology Industry Report. This increase brings biotech R&D spending back above spending levels in 2008, before the recession (see FIG. 1). Biotech R&D spending was up by 22% in the United States, and by 14% in Europe.

"On almost every measure we track — revenues, profitability, capital raised and more — the industry reached new heights in 2014," the authors of the report write. Across the United States, Europe, Australia and Canada, biotech companies cumulatively grew their revenue by 24% in 2014. Although 12% of this growth was solely attributable to Gilead's hepatitis C success, the remaining 12% growth still beats the 10% delivered in 2013.

"[2014] was a year for the record books," they add. "Against a backdrop of booming stock markets and expansionary monetary policies, these product successes helped propel the biotech industry's market capitalization above the US$1 trillion threshold, a new high."

A separate analysis by the lobby group PhRMA shows that pharmaceutical R&D spending was down slightly in 2014, to just over $51 billion.

Asher Mullard

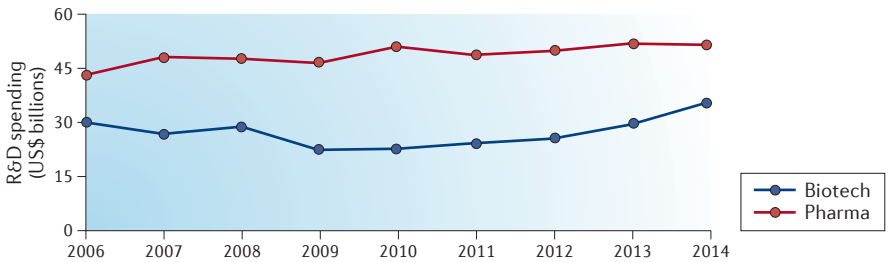

Figure 1 | **R&D spending from 2006 to 2014.** Biotech R&D spending data are from the Ernst & Young Biotechnology Reports 2008–2015. Where annual reports provided inconsistent R&D spending data, data from the latest report were used. Pharmaceutical R&D spending data are from the PhRMA 2015 Profile. Some companies are included in both cohorts.

FDA approves two IBS drugs

In May, the US Food and Drug Administration (FDA) approved two drugs for irritable bowel syndrome (IBS) with diarrhoea.

One approval went to eluxadoline, which was developed by Actavis (which last month rebranded itself as Allergan). Eluxadoline is a mixed opioid receptor agonist that acts on the nervous system to reduce bowel contractions. The most common side-effects of the drug included constipation, nausea and abdominal pain. Annual global sales of the drug could reach US$450 million by 2020, shows Cortellis consensus sales forecasts.

A second approval went to Valeant's rifaximin. Rifaximin is an antibiotic derived from rifampin that is thought to act by changing the bacterial make-up of the gastrointestinal tract. Common side-effects include nausea and an increase in alanine aminotransferase levels. The drug is also already approved for travellers' diarrhoea caused by *Escherichia coli*, and for recurrences of hepatic encephalopathy. Drug sales were around $400 million in 2014, but are set to rise to $1.75 billion by 2019, suggests Cortellis consensus sales forecasts.

At least two other drugs are in Phase III development for IBS. The Menarini Group's ibodutant blocks the NK_2 tachykinin receptor, modulating intestinal motility and reducing the hyper-responsiveness that occurs following intestinal inflammation. Synergy Pharmaceuticals' plecanatide is an analogue of a natural gastrointestinal hormone that activates the guanylate cyclase 2C receptor, promoting fluid and ion transport in the gastrointestinal tract.

Asher Mullard