BIOBUSINESS BRIEFS

REGULATORY WATCH

Efficiency indicators for new drugs approved by the FDA from 2003 to 2013

Drug research and development (R&D) costs have increased substantially in recent decades, while the number of new drugs has remained fairly constant, leading to concerns about the sustainability of drug R&D and questions about the factors that could be responsible. To help understand such factors, this analysis investigates efficiency in the development of new drugs (new molecular entities and new biologic entities) approved by the US Food and Drug Administration (FDA) from 2003 to 2013 (see Supplementary information S1 (box) for details).

The data set consisted of 257 new drugs that were approved by the FDA from 2003 to 2013. About 21% of these drugs were biologics, 9.3% were approved for more than one indication and 7% were for rare genetic diseases and received orphan designation (see Supplementary information S2 (figure)). Approximately 57% of the drugs were assigned to at least one special-designation programme: the most frequent programme was priority review (45%), followed by orphan designation (31%), fast track (27%) and accelerated approval (12%). Frequently (38%), new drugs were assigned to more than one programme, and cancer drugs were almost always assigned to at least one programme (56 out of 58, 97%), compared with 46% of non-cancer drugs (see Supplementary information S3 (figure)).

We analysed four parameters that we regarded to be efficiency indicators: the proportion of drugs approved at the first review cycle, the number of pivotal trials per drug, the average number of patients per pivotal trial and the time from submission to approval. Each indicator was analysed separately (using appropriate Bayesian regression models) to assess whether there was any change from 2003 to 2013, while accounting for potential prognostic factors, such as assignment to a special designation programme, approval for multiple indications and whether the drug was a biologic or for a rare genetic disease.

Two efficiency indicators showed improvement over the period (FIG. 1 and Supplementary information S4 (figure)). We estimated an increase in the proportion of drugs approved at the first review cycle (estimated odds ratio (OR) for 10 years' difference of 3.9 — that is, the odds that a drug was approved at first review cycle increased almost fourfold from 2003 to 2013 — with a 95% credible interval (CI) of 1.6–10.0-fold) and a decrease in the number of pivotal trials per drug (OR = 0.38; 95% CI = 0.19–0.80 — that is, the odds that a drug had more pivotal trials decreased by 62% over the period). By contrast, we estimated an approximate doubling in the average number of patients per pivotal trial (ratio of the average number of patients per pivotal trial in 2013 compared with 2003 = 1.98; 95% CI = 1.43–2.72). Finally, we found no change in the time from submission to approval.

Assignment to a special-designation programme was always associated with efficiency improvements: it increased the probability that a drug was approved at the first review cycle (OR = 4.7; 95% CI = 2.3–9.3) and it decreased the probability that drugs had a higher number of pivotal trials (OR = 0.15; 95% CI = 0.09–0.26). Furthermore, drugs with orphan designation had 70% fewer patients in the pivotal trials (estimated ratio of the average number of patients per pivotal trial for orphan compared with non-orphan drugs = 0.30; 95% CI = 0.23–0.39) and the time from submission to approval was 35% shorter for drugs assigned to priority review (estimated ratio of the time for priority review compared to standard review = 0.65; 95% CI = 0.58–0.73).

In conclusion, drugs targeting serious diseases and assigned to special-designation programmes had higher chances of early approval, and also fewer pivotal trials, involving fewer patients. Special-designation programmes were used extensively in the development of cancer drugs and there are still opportunities to increase their use for drugs in other areas. The increase in the proportion of drugs approved at the first review cycle and the decrease in the number of pivotal trials provide evidence of increased efficiency in the development of new drugs in these respects in the period studied. However, the lack of improvement in drug approval timelines and the large increases in pivotal trial size indicate new strategies are needed if efficiency gains related to these indicators are to be achieved.

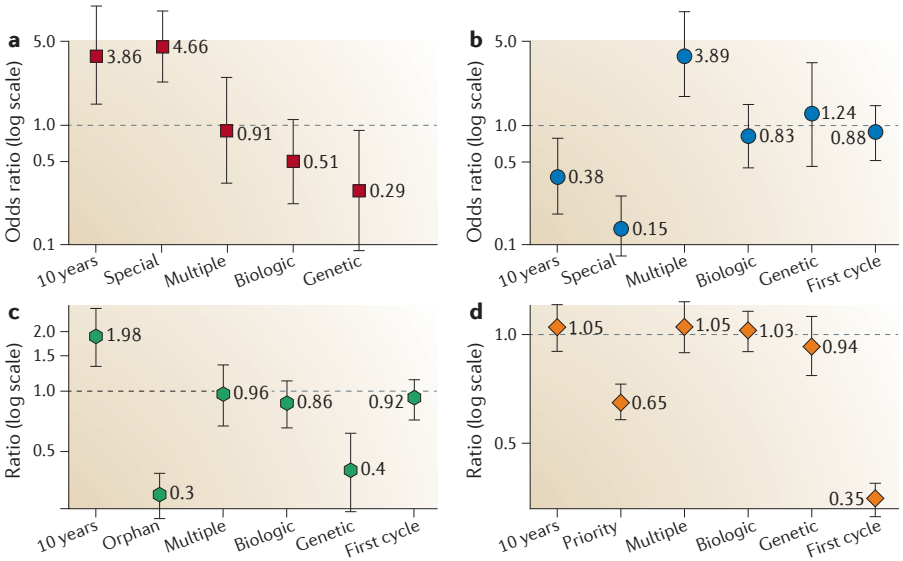

Figure 1 | **Analysis of potential efficiency indicators for approval of new drugs by the US Food and Drug Administration between 2003 and 2013.** **a** | Proportion of drugs approved at the first review cycle. **b** | Number of pivotal trials per drug. **c** | Average number of patients per pivotal trial. **d** | Time from submission to approval. In each panel, the estimated odds ratios (**a**, **b**) or ratios (**c**, **d**) are shown for each of the potential explanatory variables considered on the x-axis. Error bars represent 95% credible intervals. For details, see Supplementary information S1 (box).

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The authors declare competing interests: see Web version for details.

SUPPLEMENTARY INFORMATION

See online article: S1 (box) | S2 (figure) | S3 (figure) | S4 (figure)

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