BIOBUSINESS BRIEFS

REGULATORY WATCH

The target product profile as a tool for regulatory communication: advantageous but underused

A key objective in interactions between the pharmaceutical industry and regulatory authorities is to achieve clarity on the goals and expectations for the drug development process. In the United States, the target product profile (TPP) is a tool to facilitate communication between the pharmaceutical industry and the FDA, as well as between stakeholders in and outside of the industry. There are two main aims for TPPs used by the industry in regulatory communications. One aim is to obtain feedback on labelling claims, laying the groundwork for the clinical development plan and ultimately, the drug labelling. We term this a labelling-type TPP (LTPP). The other aim is to gain feedback on the formulation attributes of the product, which we term a quality TPP (QTPP).

To characterize how TPPs facilitate regulatory communication and planning, we used the PharmaPendium database (Elsevier; last accessed 29 June 2016) to identify publicly available documentation on drugs approved by the FDA in summary basis of approval documents (SBOAs) in which the use of a TPP was mentioned. Variables were systematically abstracted that describe the small-molecule drug or biologic product, the associated new drug application (NDA) or biologics licence application (BLA) and the product development history.

Our analyses reveal that TPPs are infrequently used, potentially costing applicants the opportunity for more meaningful regulatory interactions that could result in better organized and more successful development programmes. Of the 2,138 approved NDAs and BLAs from 1999 to 2015, only 91 SBOAs mentioned an LTPP or QTPP in this same period. The first mention of each TPP by year is illustrated in FIG. 1a. TPP use seems to increase following related regulatory initiatives, such as the launch of the 2007 FDA Guidance on TPPs, the 2009 release of ICHQ8(R2), which describes quality-by-design or QTPP concepts, and the introduction of the FDA's breakthrough therapy designation in 2012.

We also evaluated the time from investigational new drug (IND) application submission to the first mention of the TPP in review documentation, which shows that TPPs are most frequently introduced into the regulatory dialogue at a late stage of the process, usually at the time of the pre-NDA or BLA meeting or following NDA or BLA submission (FIG. 1b). Although TPPs may have been submitted earlier, they were notably absent from discussion in meetings before submission and meetings at the end of phases I and II. So, valuable FDA input that could be provided on the design of phase II and III studies in the context of the proposed labelling claims is not received in most cases.

A potential reason for the paucity of TPPs submitted for discussion is that questions regarding individual studies are submitted as questions for meetings between sponsors and the FDA. Our inspection of meeting minutes in SBOAs corroborates this for a large proportion of development programmes. However, this approach may miss the benefits of thinking through and documenting the pathway to develop a drug's value in a TPP.

In summary, our study indicates that there is a large amount of untapped benefit that could be gained from earlier and more frequent use of TPPs by sponsors. This is surprising as TPPs are frequently used within the pharmaceutical industry, albeit for slightly different objectives. We hope that this article will raise awareness of the potential value of TPPs.

Adria Tyndall is at Catalent Pharma Solutions, 2210 Lakeshore Drive, Woodstock, Illinois 60098, USA.

Wenny Du is at Bayer, 100 Bayer Boulevard, Whippany, New Jersey 07981, USA.

Christopher D. Breder is at Johns Hopkins University, Advanced Academic Programs in Regulatory Science (JHUAAP), 9601 Medical Center Drive, Rockville, Maryland 20850, USA. He is also a medical officer at the US Food and Drug Administration.

A.T. and W.D. are Master's degree candidates at the JHUAAP and contributed equally to this project.

Correspondence to C.D.B.
cbreder1@jhu.edu

doi:10.1038/nrd.2016.264
Published online 17 Feb 2017

The authors declare no competing interests.

Disclaimer
The opinions and conclusions in this article are those of the authors and not necessarily those of Catalent Pharma Solutions, Bayer HealthCare Pharmaceuticals or the FDA.

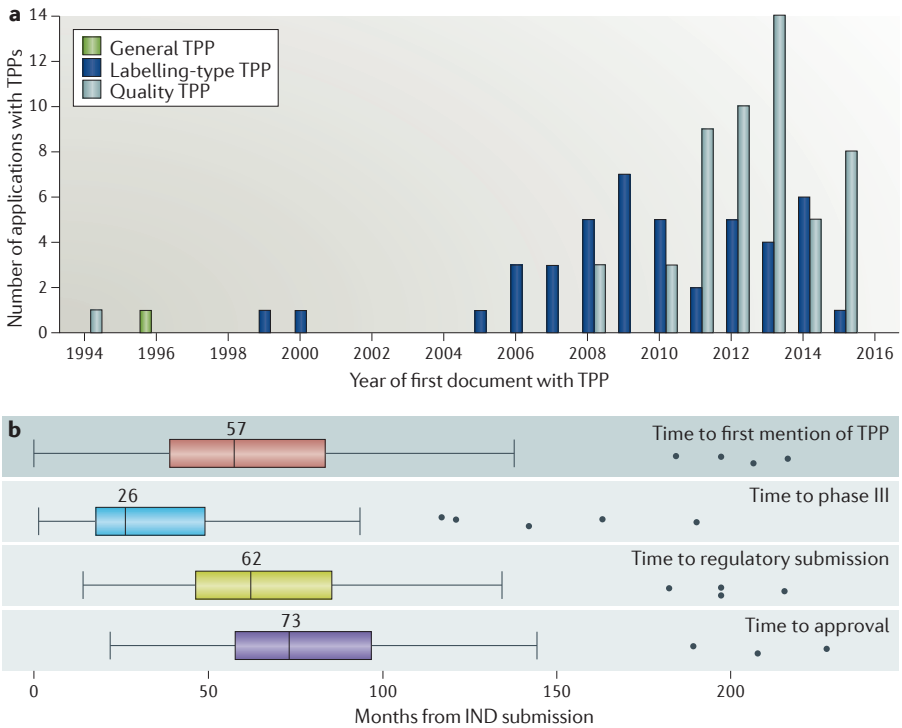

Figure 1 | **Use and impact of target product profiles. a** | Numbers of target product profiles (TPPs) per year found in regulatory documentation from the summary basis of approvals documents of drugs and biologics approved by the US FDA. **b** | Plots of median time following submission of an investigational new drug (IND) application until the first appearance of a TPP in regulatory documentation, compared with time to the first phase III study , time to submission of a new drug application (NDA) or biologics licence application (BLA), and time to approval. Boxes indicate the 25th to 75th quantile, whiskers indicate ±1.5 x the interquartile range and dots are outliers.