Journal of Translational Medicine

REVIEW

Open Access

Facilitating the use of the target product profile in academic research: a systematic review

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Abstract

Background The Target Product Profile (TPP) is a tool used in industry to guide development strategies by addressing user needs and fostering effective communication among stakeholders. However, they are not frequently used in academic research, where they may be equally useful. This systematic review aims to extract the features of accessible TPPs, to identify commonalities and facilitate their integration in academic research methodology.

Methods We searched peer-reviewed papers published in English developing TPPs for different products and health conditions in four biomedical databases. Interrater agreement, computed on random abstract and paper sets (Cohen's Kappa; percentage agreement with zero tolerance) was > 0.91. We interviewed experts from industry contexts to gain insight on the process of TPP development, and extracted general and specific features on TPP use and structure.

Results 138 papers were eligible for data extraction. Of them, 92% ($n = 128$) developed a new TPP, with 41.3% ($n = 57$) focusing on therapeutics. The addressed disease categories were diverse; the largest (47.1%, $n = 65$) was infectious diseases. Only one TPP was identified for several fields, including global priorities like dementia. Our analyses found that 56.5% of papers ($n = 78$) was authored by academics, and 57.8% of TPPs ($n = 80$) featured one threshold level of product performance. The number of TPP features varied widely across and within product types ($n = 3$–44). Common features included purpose/context of use, shelf life for drug stability and validation aspects. Most papers did not describe the methods used to develop the TPP. We identified aspects to be taken into account to build and report TPPs, as a starting point for more focused initiatives guiding use by academics.

Discussion TPPs are used in academic research mostly for infectious diseases and have heterogeneous features. Our extraction of key features and common structures helps to understand the tool and widen its use in academia. This is of particular relevance for areas of notable unmet needs, like dementia. Collaboration between stakeholders is key for innovation. Tools to streamline communication such as TPPs would support the development of products and services in academia as well as industry.

Keywords Target product profile, TPP, Quality by design, Translational research, Translational methods, Methodology

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Introduction

A Target Product Profile (TPP) is a strategic document outlining the desired characteristics of a planned product, procedure or service intended for a particular disease or use case. Its goal is to guide in addressing users' needs, facilitating stakeholders' communication, and making best use of resources to develop a successful product. TPPs encompass context of use features, such as the target disease and populations, and specific desired attributes of the product, procedure or service under development [1–3]. TPPs are widely used in industry as a planning tool to guide product development and ensure that relevant product features be aligned among stakeholders. They are therefore treated confidentially, containing sensitive information about a company's assets, product development plans and strategies (See Table S1 for a concrete example of TPP).

Although not common practice yet, TPPs may be useful in academia as well. Like industry, academics also develop therapeutics and diagnostics. However, academic research is often slower in adopting tools for systematic development, with consequent lower efficiency of translational research [4]. For example, the field of neurodegenerative disorders is validating biomarkers for Alzheimer's disease since 2009 [5, 6], but only in 2017 did it import a systematic validation framework [7], first published in 2001 for oncology research [8] and similar to others used well before for imaging [9] and other biomarkers [10]. Adopting good practice procedures and tools commonly used in industry settings may reduce waste of efforts and costs, and increase the efficiency of academic translational research as well. Noteworthy, the World Health Organization (WHO) recommends the use of TPPs to facilitate the communication with research project funders to align funding strategies with prioritised unmet public healthcare needs. This is now urgent for the dementia field, to strive to meet the innovation goals set by the 2017 Global Action Plan, that, despite many efforts, still remain a distant ambition [11, 12]. Facilitating the incorporation of TPPs among the methods used in this field means therefore bringing a pivotal tool to upgrade translational methods and help boost its innovation efforts. The example of neurodegenerative disorders represents well several fields with a high prevalence of unmet needs.

The effort to help researchers to adopt TPPs was already initiated with a previous systematic review, summarizing the methods currently used to develop them and the sources used for the inclusion for each feature [13]. Focused on diagnostic tests, the authors found TPPs for infectious diseases only, and identified a 3-phase process for their development: (1) identifying the unmet need, (2) initial drafting of the TPP, and (3) building consensus among stakeholders. The outcome of that systematic review provided an insightful first glimpse on TPPs applications outside the pharma industry, as well as the rudiments to adapt the method to academic research. Our review aims to expand on these results and extract key structural features of TPPs across different therapeutic areas and product types, to gain a wider understanding of the tool's structure and development and facilitate its use by academic researchers.

Methods

This work stems from the IMI-2-funded project EPND (European Platform for Neurodegenerative Disorders – epnd.org). IMI (www.imi.europa.eu) is a collaborative initiative between the European Commission and EFPIA (European Federation of Pharmaceutical Industries and Associations), requiring the collaboration between partners from both academia and industry. EPND aims to build a platform making existing data and samples on neurodegenerative disorders FAIR (findable, accessible, interoperable and reusable). During the development of such platform, academic and industry project partners contributed to define a TPP supporting the development of the platform. As researchers, we leveraged this experience and know-how, to generate this review and try to import the tool for academic research.

We reported our methods following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [14]. The PRISMA checklist is provided as supplementary material (see Supplementary material S2). The protocol for this systematic review was not registered in an open access platform. We performed the systematic review as detailed below. Then, based on the extracted data, we highlighted key features and the structure of retrieved TPPs, that we believe are useful to framework the tool.

Information sources

Publication search: We searched relevant publications in the PubMed, Medline, CINHAL, and Scopus biomedical databases in January 2023. Additionally, we hand-searched and screened primary publications in one identified systematic review. For grey literature, a Google search using the terms "target product profile" was used to identify publicly available TPPs (e.g., WHO TPPs, FIND, PATH). These TPPs were used to guide the conceptualization of the systematic review and the development of the search strategy. We also referred to the publicly available WHO TPPs [15] to understand the typical process and the methods commonly used to draft TPPs.

Interviews: We asked availability to experts from the network of the last author, and to 3 regulators (Dutch, German and Norwegian), known for their activity within the European Medicine Agency. Regulators reported no

familiarity with the tool (Netherlands and Germany) or did not reply (Norway). Four experts (AG, MG, MR, JS) from leading medical product development or consultancy companies accepted to be interviewed and provided general information on TPP use in the industry. The interviewed experts were senior professionals with extensive expertise on multiple aspects of research and development in pharma. Here we report their *initials*, affiliation and role at the time of the interview, and any additional expertise particularly relevant for this review: *AG*: UCB, Senior Global Director; external engagement with clinical and governmental communities for early clinical development; additional experience on regulatory intelligence through activities with CIRS (Center for Innovation and Regulatory Science). *MG*: AbbVie, Industry Co-Director. *MR*: IDEA Pharma, CEO. IDEA Pharma is a consultancy company advising on the path-to-market strategy. *JS*: AC Immune, Chief Medical Officer with broad responsibility for all clinical development functions. No confidential material was disclosed during the interviews. The collected qualitative information guided the review process and provided insights into how to process and contextualise the results.

Search strategy

Using iterations of key terms such as "target product profile", TPP, "quality by design" or QbD or QTTP we formulated a comprehensive search strategy applicable to all databases. The search strategy was: ("target product profile" OR TPP OR QTTP OR "quality by design" OR QdB).

Eligibility criteria of included studies for final analysis

We included papers published in English that reported the development or revision of a target product profile (TPP) or described a pre-existing TPP used for the development of products across any health field. There were no restrictions on the publication date. Publications were eligible if they provided a TPP structure in the form of a table, figure or narrative description of the TPP features.

Selection and data collection process

The first author screened all titles and abstracts to identify relevant publications using Rayyan, and then conducted a full-text screening of the included studies. A second reviewer (NL) independently screened 12% of the abstracts ($n=78$) and 15% of the full-texts ($n=52$). We calculated the inter-rater reliability between the two reviewers for both abstract and full-text screening with the Cohen's Kappa and/or percentage agreement with zero tolerance using R Studio [16]. We used Zotero to manage and store references of included studies and created a data extraction tool using Excel.

Data items

The target data items to be extracted included content, product type, disease category and the specific disease, performance thresholds for each TPP feature, authors' affiliation, a full list of TPP features, the number and type of features and categories thereof, and the methods deployed to develop the TPP. We defined the data items as follows:

Content: Describes whether a publication reports the development of a new TPP, revises a pre-defined TPP, or only describes an existing TPP.

Product type: Indicates whether the target product consists of therapeutics, diagnostics, vaccine, medical device, or other (e.g., app, drug delivery system, etc.).

Disease category: Describes whether the disease for which the TPP was reported was an infectious or non-infectious disease, as well as the specific disease.

Thresholds: Reports whether each TPP feature includes one (target), two (minimal, ideal), or three (current practice, minimum acceptable, ideal) levels of possible performance or target quality achievement.

Affiliation of publishing authors: Classifies the affiliation of publishing authors into academic (university, research institute, independent researchers), private (industry, consultancies, or other for-profit organisations), or public-private partnership (PPP) for collaborations between academic and private organisations.

List of TPP features: The names of all features included in each TPP were stratified by product type.

Measure of variability: Consists of the number of TPP features in each TPP.

Categories of TPP features: Includes the number and type of categories by which TPP features were grouped. For example, the category named "Scope" may include TPP features such as target population, intended use, and the level of health care system implementation; similarly, "Operational characteristics" typically includes features such as cost of product, shelf life, power requirements, and training needs.

Framework: Describes which framework was utilised to structure the TPP, e.g., the WHO or the FDA TPP guidance.

Criteria for the choice of TPP features: Reports how an initial pool of TPP features and their target levels were chosen.

Consensus approach: Categorises which kind of consensus procedure was followed to select the final set of TPP features. The approaches were divided into formal (e.g., Delphi process or survey) and informal (e.g., discussion in virtual or in-person meetings).

Experts: Describes which experts were involved (e.g., clinicians, researchers, relevant product manufacturers, etc.).

Patient-public involvement: Reports whether patient populations or the public were involved in the process of developing a TPP.

Results

From the biomedical databases and hand searching, we identified 1314 records. After title and abstract screening, 337 met the eligibility criteria for full-text review, and 138 publications [3, 17–153] were eligible for data extraction (see Fig. 1 and Table S2 for the reasons and references of excluded studies). Raters had 100% agreement for abstract screening and Cohen's Kappa = 0.912 (p-value < 0.001; 96.1% agreement with zero tolerance) for full-text screening.

Reports of TPPs steadily increased following the publications of the FDA [1] and ICH Q8 R2 [154] guidelines (Fig. 2), most contributions being in 2020. Of the 138 papers included in our review, 92% developed a new TPP, 4% revised a predefined TPP, and 4% described an existing TPP, with no overlap among these groups. The ICH Q8 R2 [154] was the most widely used framework (54%), followed by the FIND [155] (26%), the WHO [15] (15.4%) and the FDA guidance [1] (7.7%) (Table 1, upper panel).

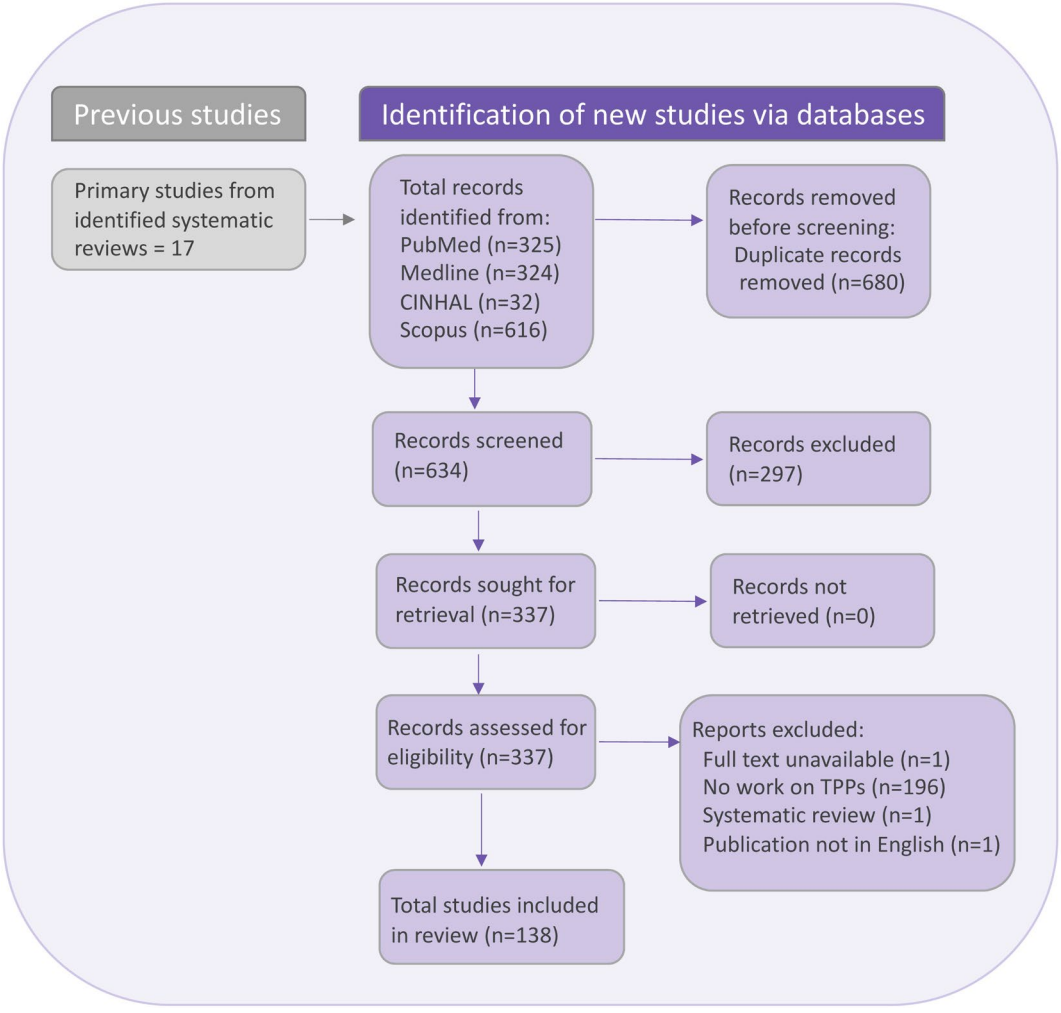

Fig. 1 PRISMA flow chart of abstract and full text screening for including publications on target product profiles (TPP)

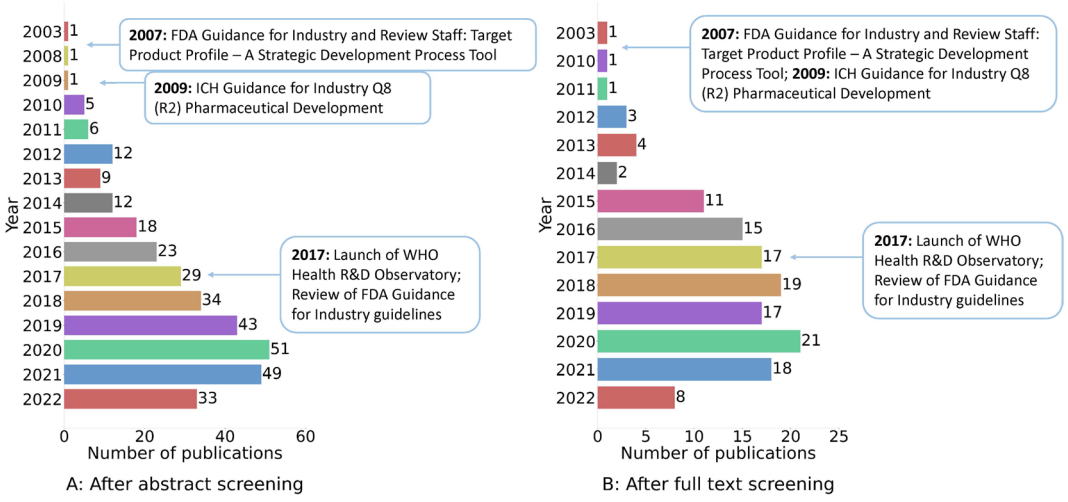

Fig. 2 Distribution of publications on target product profiles (TPP) by year in relation to significant TPP-related events or publications by the WHO and the FDA. Panel **A** demonstrates the distribution of the 337 publications included after title and abstract screening. Panel **B** demonstrates the distribution of the 138 publications included after full text screening. *Abbreviations* TPP: Target product profile, FDA: Food and Drug Administration, WHO: World Health Organisation, R & D: Research and Development

Combinations of frameworks (e.g., WHO and FIND) were also used.

Product types included mostly therapeutics (41.3%) and diagnostics (21%), and a variety of products, like apps, new technology for product development, drug delivery systems, or clinical practice guidelines ("other products": 29.7%; Fig. 3, Table S3). TPPs were used for products targeting infectious (47.1%) and non-infectious (25.4%) diseases, and unspecified disease categories, e.g., skin diseases possibly due to either infectious or non-infectious causes (26.8%; Fig. 3, Table S4). Among non-infectious diseases, one TPP was for a drug for Alzheimer's disease [57], and one for a drug delivery system for an unspecified disease category [118]. The number of included features (range 3–44) was mostly between 3 and 8 (44%), across product types (Fig. 4; Figures S1-3). These included target population, indication, storage conditions and shelf life (Table 2; Table S5). Among TPPs reporting performance thresholds (89.2%), 57.9% set one target threshold, 28.9% set two ("minimum acceptable" and "ideal"), and 2.2% three ("current practice", "minimum acceptable", and "ideal"; Table S3). In the 15% of publications grouping TPP features into categories, "Scope" was the most frequent (90%; Tables S6-S7); others included "Operational", "Performance", and "Test characteristics" (complete list in Table S6). Criteria to define features and target levels were clarified in 17% of papers (Table 1, lower panel). Methods to agree on the TPP features were reported in 22% of the papers: these included formal consensus (e.g., Delphi process; 46%), and combined formal and informal approaches (e.g., virtual/in-person meetings or workshops; 33.3%) (Table S8).

Most of the retrieved TPPs were published by authors from academia (56.5%), 11.6% by authors with non-academic affiliations, and 31.9% within hybrid collaborations. Twenty-seven (20%) of the papers mentioned which experts were involved, and their fields of expertise. These included academic researchers, clinicians, experts from the WHO, and stakeholders related to product development (end users, manufacturing companies, regulators) (Table S9). One group explicitly reported the involvement of civil societies representatives [93], but none reported involving patient populations or the public directly.

Based on the overall extracted data, we identified essential aspects relevant to developing a new TPP, that would be good to report to enable full understanding and replication by other groups (Table 3).

Discussion

We conducted a systematic review to extract the features and structure of published TPPs across various therapeutic areas, to facilitate the incorporation of this tool in academic research. Most papers included in our review developed a new TPP, and mostly focused on developing treatments in the field of infectious diseases. Several medical fields (e.g., poliomyelitis, rheumatic fever, or tropical diseases) had only one TPP reported for any of their products. This happened also for diseases characterized by high unmet need and global prioritization, like the case of Alzheimer's disease [57]. We found that the methods used to develop TPPs, their specific features, and the information provided to understand their structure varied considerably also within product or disease category, most papers providing limited or no explanation of how TPPs were developed.

To our knowledge, only one other systematic review on TPPs exists [13], focusing on diagnostic tests, and

Table 1 Summary of frameworks used in the development of TPPs and an overview of criteria used to select TPP features and their target levels according to appropriate criteria for product types. *Abbreviations* WHO: World Health Organization, TPP: target product profile, ICH: International Council for Harmonization, FDA: Federal Food and Drug Administration, FIND: Foundation for Innovative New Diagnostics, MSF: Médecins sans Frontières, HIV: human immunodeficiency virus

Framework	Number of TPP papers	References
ICH Q8 (R2).	14	[35, 50, 72, 73, 83, 102, 106, 113, 121, 127, 146–148, 152]
FIND TPPs.	7	[58, 62, 87, 100, 106, 119, 127]
WHO TPP.	4	[28, 87, 119, 142]
FDA guidance.	2	[50, 103]
TPP for dual HIV/syphilis tests commissioned in 2013 by UNITAID.	1	[25]
Previously published TPPs.	1	[28]
Published standards and guidelines, input from interviews.	1	[58]
Based on regulatory and practical considerations and limitations.	1	[75]
Own strategic framework, including two complementary TPPs: Target Market Profile (TMP) and Strategic Target Profile (STP).	1	[84]
MSF TPPs.	1	[142]
Own framework for discussion in regulatory and guideline development contexts.	1	[148]
Criteria to select features		
Literature review.	10	[31, 61, 62, 70, 72, 86, 93, 100, 128, 151]
Consensus agreement by a certain agreed percentage.	4	[87, 100, 119, 142]
Existing knowledge.	4	[32, 74, 83, 128]
Diagnostic accuracy parameters based on reference tests.	2	[64, 66]
Systematic review, published predictive models, landscape analysis.	1	[25]
Expert opinion.	1	[58]
Based on the requirements of the interested parties (clinical expectations, patients' and industrial needs, regulatory aspects).	1	[114]

uniquely retrieving contributions for infectious diseases. Like us, Cocco and colleagues found a generally poor description of the methods employed to build TPPs, although they could extract a common 3-phase structure and the distinct dimensions of "activities", "source of input information" and "contributing stakeholders". The authors underlined that further research is needed to improve support for researchers in understanding and adopting the tool. In our review, we extended such examination beyond diagnostic tests, and tried to extract additional dimensions in TPP development that may further help to understand its general structure and logics (Table 3). Such dimensions may not be readily applicable to any field at present. For example, as a starting step, we recommend choosing a reference framework. However, as also noted by Cocco et al. [13], existing frameworks like the FDA guidance apply to drug development. They may not be directly transferable to diagnostics, and formal guidance on developing TPPs for diagnostics is not yet available. We believe that making this gap explicit and inviting researchers to identify a reference framework anyway may elicit consequent constructive steps. In this specific example, researchers developing a new TPP for diagnostics may decide to choose, as a reference framework, the structure of a previous TPP described in greater detail for a biomarker (see for example references 26, 28, 38 and 60 in Cocco's paper); furthermore, outlining such gap explicitly may lead methodologists or other organizations or stakeholders to produce TPP guidance specifically adapted to diagnostics.

By widening the scope of therapeutic areas and products relative to the previous review, we sought to better outline the heterogeneity of TPPs, and extract more features contributing to their structure. To this regard, we underline that the TPPs scope is meant to be heterogeneous in nature, as they serve the development of specific products that need to differentiate themselves in the market. This needed heterogeneity adds to inconsistent reporting across the few documents that can escape confidentiality, which constitutes an additional hurdle to the effort of academic researchers to adopt the tool. On the other hand, a wide representation of different TPPs is needed to extract and communicate their very structure. In their review, Cocco et al. [13] not only focused on the field of diagnostics, and uniquely retrieved TPPs for infectious diseases, but also presented a quite consistent purpose of TPPs, mainly supporting the validation of diagnostic tests within a regulatory perspective. Despite our wider focus, also our study captured a mainly regulatory perspective. Indeed, a task like product validation can easily constitute a shared goal across independent research organizations, and can therefore be retrieved relatively easily in published documents. However, we underline here that TPPs are meant to support any development perspective (e.g., ensuring marketability, competitiveness or refundability within an HTA context). These perspectives, only to a limited degree captured in our review [84], may well be in the interest of academic developments as well. In industry, these other perspectives are usually represented in separate TPPs for the

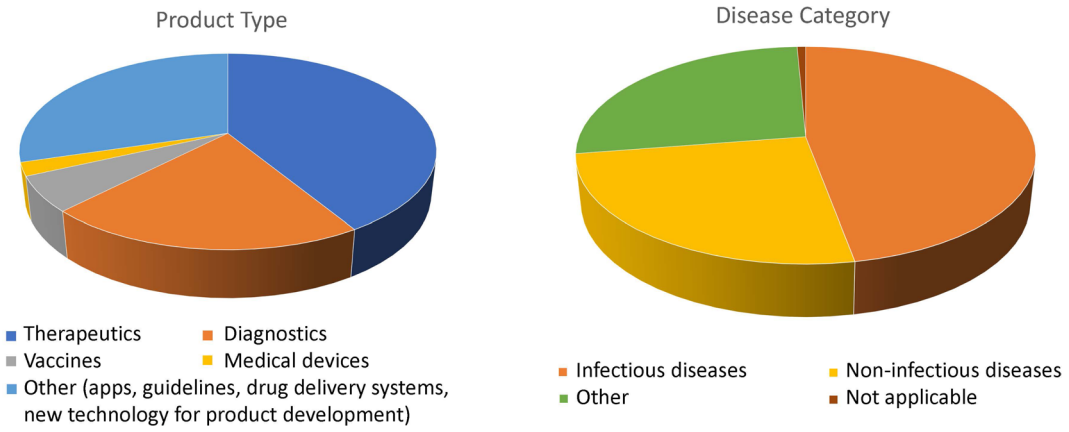

Fig. 3 Proportion of product types (left panel) and disease categories (right panel) represented in the TPPs retrieved by our review

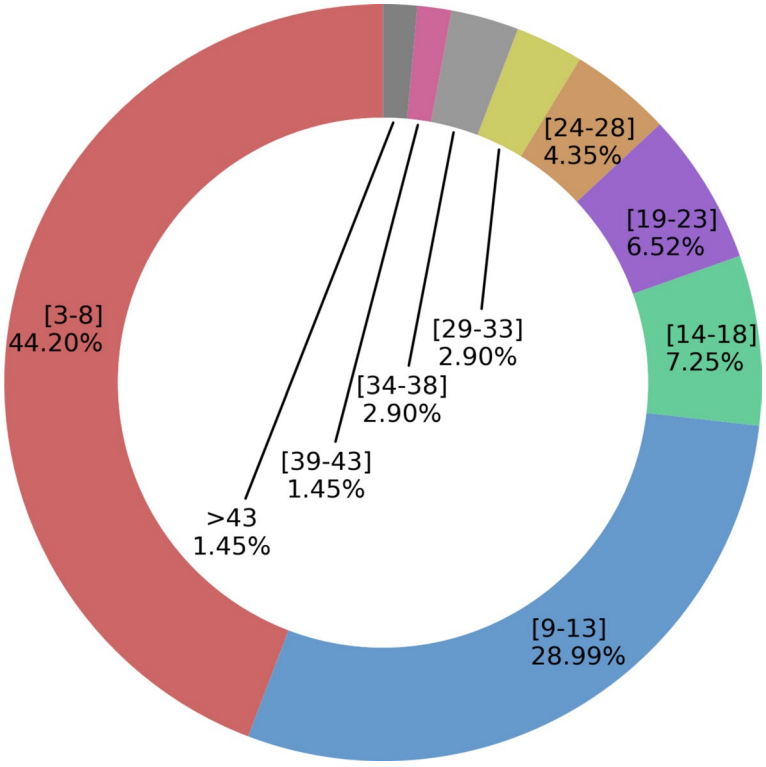

Fig. 4 Proportion of the identified TPPs having low to high number of features (N of features in square brackets) across all product types. The pattern is replicated within specific product categories (see Figures S1-S3), with the exception of TPPs for diagnostics (Figure S1)

same product and each indication identified. We therefore underline that the mainly regulatory perspective emerging from our, as well as from Cocco's, review is not the only nor the main purview of TPPs. Consistently, we do not support the idea that a TPP mainly serves single unitary purposes: indeed, they rather try to serve cross-functional aims, although they may not have one standard, coherent or all-inclusive form. This complexity enables the needed flexibility in operational contexts, but also makes it more difficult to understand the tool, for those who never used it. Finally, within the aim of demonstrating product validity, Cocco et al. highlighted a considerable absence of clinical utility features in TPPs for diagnostic products [13]; consistently, we found that, regardless of product type, the development of TPPs did not directly involve patient populations or the public, whose participation is important to define clinical significance in specific settings and demonstrate impact on clinically relevant outcomes. Different from academia, it is common in industrial practices to include patients or the public directly, and from the early stages of a product development; detailing this aspect in future TPP

Table 2 TPP features most frequently reported in TPPs for different product types. The number of times each TPP feature was reported and the number of TPPs for each product type are indicated in brackets. A comprehensive list of TPP features is provided for each product type in Table S5

Diagnostics (29 TPP)	Drugs (57 TPP)	Vaccines (8 TPP)	Medical devices (3 TPP)	Other products (41 TPP)
Testing Sensitivity and specificity ($n=27$)	Route of administration ($n=32$)	Indication ($n=6$)	Indication ($n=2$)	Route of administration ($n=28$)
Indication ($n=23$)	Stability/shelf life ($n=29$)	Target population ($n=4$)	Cost of test/product/reimbursement ($n=2$)	Stability/shelf life ($n=26$)
Target population ($n=22$)	Dosage form ($n=23$)	Repeatability, stability ($n=4$)	Data output ($n=2$)	Dosage strength ($n=25$)
Target user ($n=22$)	Dosage strength ($n=23$)	Storage conditions and shelf life ($n=3$)	Accuracy ($n=2$)	Dosage form ($n=23$)
Sample type ($n=20$)	Indication ($n=18$)	Dose regimen and amount ($n=3$)	Target user ($n=1$)	Container closure system ($n=13$)

Table 3 Key development steps and structural features (left column) relevant to understand and replicate the construction of TPPs. The right column reports possible specific items for the selected step, feature or category. These features are not exclusive, but rather add to those identified by Cocco et al., [13].

Key structural feature	Possible specific value determinants
1. Defining the purpose and perspective that the TPP will serve	e.g., *Regulatory (meet regulatory requirements, e.g. evidence on validation); HTA (define competitive features in terms of cost-effectiveness); other.*
2. Choosing the appropriate framework to base the TPP on	e.g., *ICH Q8 R2, WHO TPP guidance, FDA TPP guidance, other relevant framework for the specific product to be developed.*
3. Deciding on the approach/criteria to choose TPP features and their target levels	e.g., *Criteria from previous WHO TPPs, criteria from specific regulations/guidance for the product*, etc.
4. Literature review to pool relevant TPP features	e.g., *Systematic literature search.*
5. Formal consensus approach to agree on most critical TPP features	e.g., *Delphi process.*
6. Classifying TPP features into categories	e.g., *Using common categories appropriate for the field/product (e.g., scope, test performance, operational characteristics for diagnostic tests).*
7. Involving relevant stakeholders:	e.g.: *- WHO experts.* *- Researchers in the field.* *- Manufacturers.* *- Regulators.* *- End users: clinicians, technicians, laboratory personnel*, etc. *- Public and/or Patient population.*

guidance may help upgrade academic product development and help it to manage the complex task of demonstrating clinical utility.

Overall, our extensive data extraction aimed to come up with a common structure helping academics to understand and use TPPs. Along with the features previously identified by Cocco et al., the items reported in Table 3 are general enough to be considered for inclusion in most TPPs, and relevant enough to be commendable for potential reporting guidelines on TPP development. Defining guidance as well as reporting recommendations requires independent dedicated efforts. With this work, we provided additional concrete elements for further initiatives supporting TPP integration in academic research. Such efforts are particularly urgent for diseases characterized by numerous unmet needs. Among these, the field of neurodegenerative diseases leading to dementia provides a concrete and current example: the 2017 Global Action Plan set goals to tackle the global priority of dementia [12], but the global status report on the public health response to dementia anticipated that these goals will not be achieved by the 2025 deadline [156]. WHO recommended using TPPs to boost efficiency in the field of infectious disease through a blueprint [157] recently provided also for dementia [11, 158]. Indeed, the use of tools like the TPP, already constituting good industrial practice, is increasingly relevant in any academic contexts, with an increasing interest in developing products also in the pharmacology field, and would support the efficiency of developing any kind of product, including medical procedures or services, by improving communication and interactions with industry and other stakeholders. Despite major dedicated efforts, like those supported by grant frameworks like the European Innovative Health Initiative, requiring that academics be paired with industry partners for large research projects, such interactions are still difficult, and concrete initiatives like ours, focusing on importing specific translational tools, methods and procedures, are essential to enable concrete steps forward. However, this overall picture raises pivotal questions about how to increase the efficiency of translational research. Which are exactly the stakeholders, collectively represented by WHO, supposedly interested in

investing to translate and validate a reference methodology to develop TPPs, and promote their use in academic contexts across disease areas? Which incentives may encourage researchers to use them? Similar questions link our effort to the need to better understand and help improve the ecosystem of current translational research [159], where communication among academia, industry and relevant stakeholders is key to overcome gaps, and deserves greater attention.

Similar to the previous review, also our results show a striking majority of TPPs published for products in infectious diseases, with an exponential increase that, from the publication of the FDA Guidance for Industry guidelines in 2007, peaked during the COVID-19 epidemic. This prevalence of TPPs in the field of infectious diseases can be explained with the urgency to act and control rapidly spreading diseases [160], and can also be attributed to the successful implementation of the WHO blueprint [157]. The fact that we could identify many more publications in this rather than any other field also highlights the main constraint of our study: TPPs are usually confidential documents that cannot be circulated beyond the company producing them. The field of infectious diseases, however, may not be the most attractive area of development for industry: microbial resistance allows only limited time and distribution for a product to be effective, the treatment duration is very limited, antimicrobials' price is generally low, and their need is mostly felt in countries with limited budget. Along with the highly unmet need posed by infectious diseases, a great public and academic involvement pushes the production of dedicated products, which may explain the disproportionate prevalence of public TPPs in this, compared to any other medical fields (Table S4). Some of the features characterizing the field of infectious diseases, like the increasing global unmet need with major distribution in LMICs, also apply to the field of dementia; this may provide additional motivation to greater adoption of TPPs in academic research in this field. On the other hand, developing TPPs in fields with similar features as that of neurodegenerative disorders may present more complex challenges. The etiology of complex diseases is often not definitively understood; genes, as well as their variable interaction with the environment, generate for example different degrees of cerebral reserve, and a number of factors interact with clinical outcomes and treatment effects; the urgency to bring innovation to clinics may lead to overlook validation steps for products or procedures, sometimes mistakenly not expected to originate negative effects, like biomarkers. Analogous considerations and analyses may help support the adoption of TPPs also in other such medical fields, where they are not yet widely used (Table S4). Moreover, the fact that independent laboratories may not be consistently aligned on a common translational methodology could provide additional rationale for producing shared and accessible TPPs, potentially benefitting all those working at a common goal. Indeed, the confidentiality protecting property for industry can well apply to academic research as well, thus it is relevant to identify the specific areas where the use of TPPs can be shared and possibly validated, to enable academics to familiarise with the methodology and then increase their use, either open or confidential. Further research in this direction may include retrieving TPPs developed for assets that subsequently failed, or by companies that are no longer active, and extract further learnings also leveraging reasons for failure.

Our findings indicate that TPP-related publications are mostly published by academics, although this finding is biased by the nature of this study. Different from the previous review [13], we only targeted full papers in scholar communications, using grey literature only to guide our understanding and framing of the data. We did find TPPs published by private organizations or public-private partnerships, however, by definition, we could only access information that was not confidential, an issue in common with the previous review [13]. We attenuated this bias by interviewing and involving some leading experts, all from industry contexts, able to provide a wider and more representative insight into this typically industrial procedure. We did not perform a formal assessment of risk of bias, however not feasible in this type of study, and did not extract data regarding the geographic location of TPP publications, connected with potential variations in unmet needs and priorities across health conditions, and consequently the product, depending on geography. From a methodological point of view, moreover, we guaranteed reliability only by assessing reviewers' consistence on subsets of abstracts and full papers.

Conclusion

This review highlights the heterogenous features of TPPs and their limited representation in academic literature besides the field of infectious diseases, and provides further concrete support for researchers trying to use TPPs in academic research. Our results can also feed future initiatives to adapt guidance for specific fields and to develop TPP reporting guidelines. Besides supporting researchers' understanding and use of the tool in academic contexts, this would improve their ability to interact with regulators, HTA experts, and end users, whose contribution is needed along the whole translational continuum. Much more research is needed however to improve communication between academia and industry, stakeholder alignment, and the efficiency of academic translational research in general. Such efforts should help a wider understanding of the ecosystem and incentives

structuring current translational research, and should be pursued to foster progress on global priorities.

Abbreviations

AD	Alzheimer's disease
FDA	Food and Drug Administration
HTA	Health Technology Assessment
ICH	International Conference on Harmonisation
NDD	Neurodegenerative diseases
PPP	Public-Private Partnership
QbD	Quality by design
TPP	Target product profile
WHO	World Health Organisation

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12967-024-05476-1.

Supplementary Material 1

Supplementary Material 2

Acknowledgements
The authors acknowledge the contribution of Sjak Bott for providing useful information about the method. The part of the work performed under the EPND project has received funding from the Innovative Medicines Initiative 2 (www.imi.europa.eu) Joint Undertaking under grant agreement No 101034344. This Joint Undertaking receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA.

Author contributions
MB and AGa conceived the study. AI contributed to the data collection (screened abstracts and full-texts, extracted the data items, visualised results) and to the first draft of the manuscript. NL performed the random check on the abstract and full-text screening. MB and AI performed the interviews with experts and conceptualised the findings. AGa contributed information about the concept and use of TPPs in industry. AGu, JS, MG, and MR provided general information and know-how about TPPs in industry. EE worked at the revision of the paper after peer review. All authors contributed to the manuscript writing and approved the final submitted version.

Funding
Open Access funding enabled and organized by Projekt DEAL. This work was supported by DZNE (Deutsches Zentrum für Neurodegenerative Erkrankungen) and the EU/EFPIA Innovative Medicines Initiative Joint Undertaking (EPND, grant No 101034344).

Data availability
The datasets generated and analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Not applicable. No ethics approval was required to conduct this review.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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Received: 13 May 2024 / Accepted: 3 July 2024
Published online: 29 July 2024

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