PATENTS

Intellectual property policies in early-phase research in public-private partnerships

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Supplementary Information

RESULTS

Mapping of early-phase PPPs

Research phase – Eight (40%) out of 20 precompetitive PPPs conducted projects with a POC character, thereof 6 (30%) PPPs continued with projects up to the PD phase, and 3 (15%) of them conducted projects from the precompetitive phase up till the PA phase (**Supplementary Fig. 1-2**).

Project focus – The 20 PPPs under study focus their research projects either on PRNDs (4 or 20%) (4 International), diseases of affluence (11 (2 International, 4 US, 1 EU, 4 National) or both, i.e., a mixed focus (5) (1 Internat, 2 US, 1 EU, 1 EU Nat) (**Table 1**). In the 5 PPPs with a mixed focus, only a minority of the total amount of projects are focused on PRNDs. PPPs focused on PRNDs conduct projects in the different phases of the drug development cycle, in contrast with PPPs focused on diseases of affluence that are mainly operating in the early research phase (**Supplementary Fig. 1**).

Project deliverables – The short-term outputs and the long-term outcomes envisioned in the mission and objectives of the 20 precompetitive PPPs were mapped. The PPPs focused in this study will not actually deliver drugs or therapies ready to market, as they are precompetitive; some PPPs mention such deliverables in the long term. Nine (45%) out of 20 PPPs envisioned drug development tools, such as technology platforms and databases, 3 (15%) target diagnostic tests, drugs or therapies in the long term, and 8 (40%) envisioned a mix of these outputs and outcomes (**Table 1**).

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PPP Funding - Nine out of the 20 (45%) selected PPPs operating in the precompetitive phase are funded by non-profit organizations, such as governments, intergovernmental institutions or non-profit organizations (whether or not funded with private or public money) (**Table 1**). Eleven out of those 20 (55%) PPPs are funded by a mixed group of funders, being a combination of non-profit organizations and private industry funders. None of the PPPs focusing on PRNDs are funded solely by private industry, and only 3 out of 11 PPPs co-funded by the private industry focus (a minority of) their projects on PRNDs (**Supplementary Fig. 3**).

Transparency of IP information

Twenty of the 30 (67%) precompetitive PPPs contacted offered information regarding IP via an IP policy or guidance document. Actually, only 14 (47%) of such PPPs made this information publicly available. For 6 (20%) of the 30 PPPs, the information was received through personal contact. Of the latter, 3 (10%) PPPs requested confidentiality regarding the documents obtained. With respect to the last 10 (33%) PPPs, no IP policy could be retrieved (2 (7%) PPPs stopped their activities and 8 (27%) PPPs did not respond to emails). Nineteen of the 20 (95%) PPPs provided information regarding the of IP elements under investigation (ownership of background IP, ownership of foreground IP, access rights to background IP, access rights to foreground IP and IP management) in the documentation offered. One of the 20 (5%) PPPs only provide minimal information regarding publication guidelines or the use of clinical data (**Table 2**).

Clarity of IP information

Remarkably, the majority of the PPPs do not provide clear definitions on the concepts used in their IP policy. Only 7 (35%) IP policies provide a clear definition for background IP, and 6 (30%) do so for foreground IP. Further, IP policies do not always provide clear definitions for access (rights) and use and do not make a distinction between the right to use background IP or foreground IP and the concept of 'freedom-to-operate'.

Ownership of IP

Background IP - Thirteen of 20 (65%) PPPs (6 non-profit funded (2 International, 2 US, 1 EU, 1 National) and 7 mixed funded PPPs (1 International, 1 US, 1 EU, 4 National)) provide information on ownership of background IP. Twelve of 20 (60%) PPPs claimed that ownership of background IP remains with the original owner (**Table 2**).

Foreground IP – Not every IP policy clearly specifies the possibility to file for patents on research results. Via information regarding foreground IP (**Table 2**), and especially regarding the access rights to foreground IP, this information can be deducted. Half of the selected PPPs

(50%, 3 US, 2 EU, 5 National) allow for IP protection via patenting of research results. Six (30%, 5 International, 1 US) PPPs state that patenting is possible, but that research results are preferable put within the public domain. Three (15%, 2 International, 1 US) PPPs state that research results in the project scope are not to be patented , or limit the potential to file for patents on specific research results, and in 1 PPP IP policy (5%, US), the possibilities with regards to patent protection of foreground IP are not specified.

Compared to information related to ownership of background IP, more information is provided about the ownership of results generated during the course of the project, commonly referred to as foreground IP (**Table 2**). Eighteen (90%) PPPs provide information about foreground IP ownership, namely 8 out of 9 non-profit funded PPPs (5 International, 1 US, 1 EU, 1 National) and 10 out of 11 mixed funded PPPs (2 International, 3 US, 1 EU, 4 National) (**Table 2**). There are differences to be noticed between non-profit funded and mixed funded PPPs (**Table 2**). For 3 (15%) PPPs, collaborative research resulting from the project is owned by the PPP itself. It concerns 2 out of 8 non-profit funded PPPs (1 International, 1 US) and 1 out of the 9 mixed funded PPPs (1 National) that provided foreground IP information. Four (20%) non-profit funded PPPs (2 International, 1 EU, 1 National) allow the idea generator to be owner of the IP to the invention. In case of mixed funded PPPs, 6 out of 9 (1 International, 2 US, 1 EU, 2 EU National) allow the idea generator to own the foreground IP. One (5%, International) mixed funded PPP does not allow the institution to own research results. Eight (40%) PPPs (1 US, 2 EU, 5 National) allow joint ownership of the foreground IP, 3 (15%) of them are funded by non-profit institutes, 5 (25%) are mixed funded. One (5%) PPP (1 National) is joint owner for all research results of the PPP. A non-profit funded National PPP allowing joint ownership, explicitly states that *'joint ownership is only possible in exceptional circumstances, ownership by the industrial partner is favored'*. Joint ownership is thus more common within mixed funded PPPs.

Access Rights to IP

In the majority of the cases, IP policies refer to 'access rights' where it would be more correct to refer to 'use rights' or 'user rights'. The possibility to use IP linked to the project depends on the moment of generation of IP (background IP/foreground IP), the party using the IPRs (the PPP, project participants and/or affiliates, third parties), and the purpose of the research activity (research use/commercial use). Many of the PPPs make a distinction in access to (and thus 'use of') IPRs i) for completion of the project, ii) for research use outside the project scope, iii) to practice foreground IP outside the project scope and iv) for direct exploitation. Further, the way these rights are granted can vary: the majority of the PPPs state that these

rights will be granted by means of a contractual agreement, signed between the licensor and the licensee, but there are also PPPs that grant those use rights by means of a (virtual) license, which might be agreed upon by the licensor (the respective PPP) and the licensee (members of the PPP community, or the research community in general) via ticking a box on the website (**Table 3**).

Access rights to background IP - Ten of the 20 (50%) investigated PPP policies provide information on access rights to background IP. Five of the 9 non-profit funded PPPs provide information regarding access rights to background IP. In case of mixed funded PPPs, information is provided by 5 out of 11 PPPs (**Table 2**). The terms and conditions serving as a base for access rights to background IP range from 'royalty-free access rights' to 'royalty-free access OR access on fair and reasonable conditions'.

Seven PPPs (35%) provide a framework for partners' access rights to background IP *for completion of the project*. Five (25%) PPPs provide access to background IP for free (1 International, 1 EU, 3 National), 2 out of 7 (1 EU, 1 National) provide flexibility by stating that the access is for free, unless otherwise agreed. Three out of 5 (2 International, 1 US) provide royalty-free access rights *for research use*, 1 out of those 3 geographically limits the access rights for research directed to the needs of the least developed countries (LDC). Two out of 5 (2 EU) provide this access on a royalty-free or on fair and reasonable conditions base. The *practice of foreground IP* by means of background IP is on free or fair and reasonable conditions in 3 (15%) PPPs (2 EU, 1 National). *Direct exploitation of beneficiary's IP* is to be negotiated in 1 (5%) PPP (EU) and explicitly not obliged in 2 (10%) PPPs (2 National). A free license is provided in 1 (5%) PPP (International) for use of the IP in the LDC. An International non-profit funded PPP, states that '*One may retain the rights over the patents except to the extent to be used in the open source drug discovery process and for selling any product or process arising out of the use of your invention in that process',* suggesting that you may bring in background IP in the projects, but when this background IP is used by other partners for Open Source drug discovery, that you provide the licensing rights to the requesting party.

Access rights to foreground IP – Thirteen of the 20 (65%) investigated PPP policies provide information on access rights to foreground IP, whereof 6 out of 9 non-profit funded PPPs and 7 out of 11 mixed funded PPPs (**Table 2**). The terms and conditions on which access rights to foreground IP are granted range from 'royalty-free access rights' to 'royalty-free access OR access on fair and reasonable conditions' with some specifications. Often, there is a further specification that the license is worldwide, non-exclusive and non-sub-licensable.

Seven of those 13 PPPs provide a framework for partners' access rights to foreground IP *for completion of the project*. Six (2 International, 2 EU, 2 National) out of 7 PPPs explicitly provide access to foreground IP on a royalty-free base, 1 PPP thereof specifies that the partners have such access rights, but that the coordinating PPP has no access rights to the foreground IP. One (5%) (National) states that the access to non-tangible foreground know-how is for free, meaning that the know-how built in the consortium can be freely used by the partners. Five (2 International, 3 National) out of 10 (5 non-profit funded and 5 mixed funded) PPPs provide (conditional) royalty-free access rights *for research use*; access rights in 1 (International) PPP out of those 5 are geographically limited to the LDC, 1 (5%) (National) PPP specifies that free access for research use is guaranteed to academia and another PPP (5%) (National) specifies that royalty-free access is provided to 'the Licensee Group' to which project partners can commit. Two (2 EU) PPPs out of 10 provide this access on a royalty-free or on fair and reasonable conditions base. One (US) PPP out of 10 provides this access on fair and reasonable conditions. One (National) PPP out of 10 states that the access to non-tangible foreground know-how for research use is for free, 1 (National) PPP out of 10 states that foreground IP can be freely used by partners up to clinical phase IIA. The *practice of foreground IP* is for free in 1 (5%) (International) PPP in the LDC, and on fair and reasonable or on royalty-free conditions in another PPP (5%) (EU). One (5%) (US) PPP does not provide financial conditions, and only states that the license should be non-exclusive and that it should not be sublicensed, except to affiliates and Third Party contractors. Two (National) out of 5 PPPs state that the access to non-tangible foreground know-how is for free. *Direct exploitation of beneficiary's IP* is to be negotiated in 5 (25%) (1 EU, 4 National) PPPs, whereby 1 (5%) grants free access to (non-)tangible foreground IP to partners. One (5%) (National) PPP obliges the academic partner to grant rights to the enterprises to exploit the results in predefined fields. One (5%) (US) PPP states that free exploitation of the foreground IP is possible for diagnostic testing methods and for consortium technology. A free license is requested by 2 (10%) (International) PPPs for use of the foreground IP in the LDC.

IP Management

***IP expertise* –** Eight out of 20 (40%) PPPs specifically appoint an IP responsible or IP committee to manage specific co-ordination tasks related to the creation, maintenance and prosecution of IP within the consortium. Five (25%) of them are non-profit funded PPPs (3 International, 2 US), 3 (15%) are mixed funded (National). In case of the international PPPs, decisions regarding IP are taken by the IP expert or a body of experts representing the PPP.

For the US PPPs, a Coordinating Committee (representative of each partner and a PPP representative), resp. the sponsoring foundation reviews decisions on IP prosecution and licensing. In case of the 3 (15%) European national PPPs, a dedicated person is appointed as Project IP Manager and coordinates tasks related to the creation, maintenance and prosecution of IP. This person is an employee of one of the partners or, in 1 (5%) PPP, it can be a third party (**Table 1**).

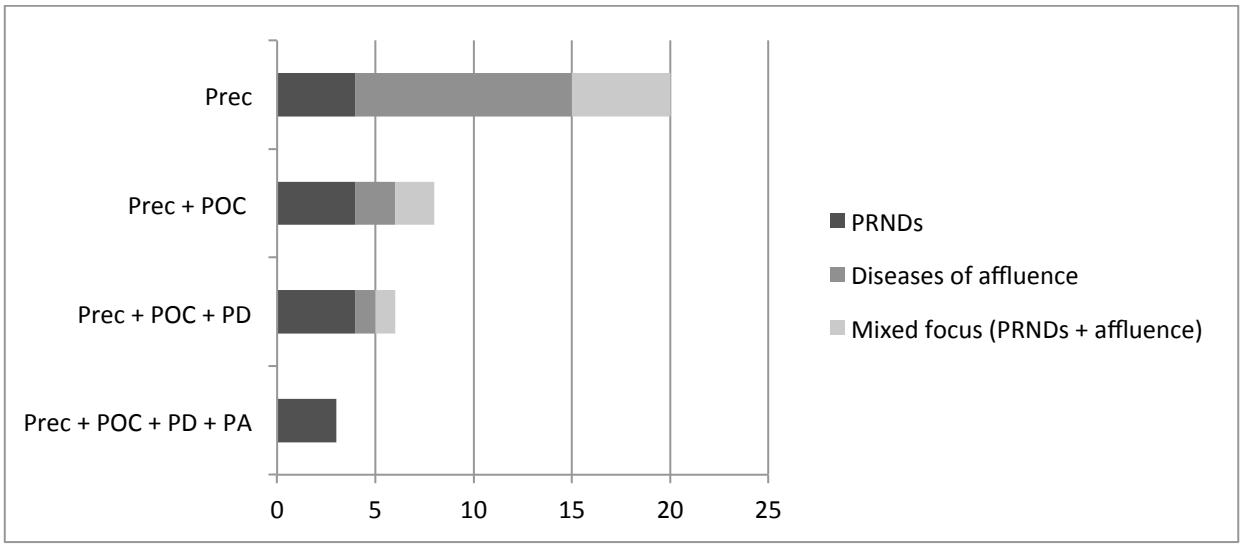
Customization/room for negotiation - Three out of 20 (15%) PPPs (1 International, 2 National) explicitly state their IP policy to be binding. To become a partner in the PPP, you agree upon the IP policy by signing the terms and conditions in the agreement. In these 3 cases, the IP policy does not provide room for negotiations (e.g., whether access rights to background IP for use of foreground IP are on free or fair and reasonable conditions). Two of these 3 PPPs are mixed funded; the third is a non-profit (Open Source) PPP.

Two (10%) other mixed funded PPPs (National) state that only minor amendments to the clauses proposed can be considered. Three (15%) non-profit funded PPPs (International) explicitly state that each project is negotiated on a case-by-case base, whereby the minimal standard is accessibility of the foreground IP for use and commercialization in the LDC. In 2 (10%) PPPs, private industry is a partner only in specific predefined phases of the drug development. In those 2 PPPs, a stage-gate approach to negotiating IP is applied: new contracts are negotiated based on milestones reached in the product development phase. For each new phase, new rules and clauses are agreed between those 2 PPPs and their respective partners. The minimal standard of the negotiations is a royalty-free, exclusive license for geographically defined endemic areas or the LDC. It is the goal of both PPPs to enforce public dissemination of the research results to the widest possible extent, but they consider acquiring or otherwise enforcing IPRs when needed to ensure market access of the drug in the envisioned countries. In 3 (15%) PPPs (2 EU, 1 National), the IP policy provides the possibility to negotiate within a given framework, 2 of them are non-profit funded, 1 is a mixed funded PPP. Only in 4 out of 20 (20%) PPP policies, support from an expert is advised in case of unsuccessful negotiations or disputes, those 4 PPPs respectively allowed or i) no room for negotiation (1 National) or ii) little room for negotiation (1 National), or iii) stated that the proposed IP rules need to be agreed upon case by case (2 International). Several PPPs, explicitly or less explicit, provide the role of an honest broker in the different consortia (**Table 1**).

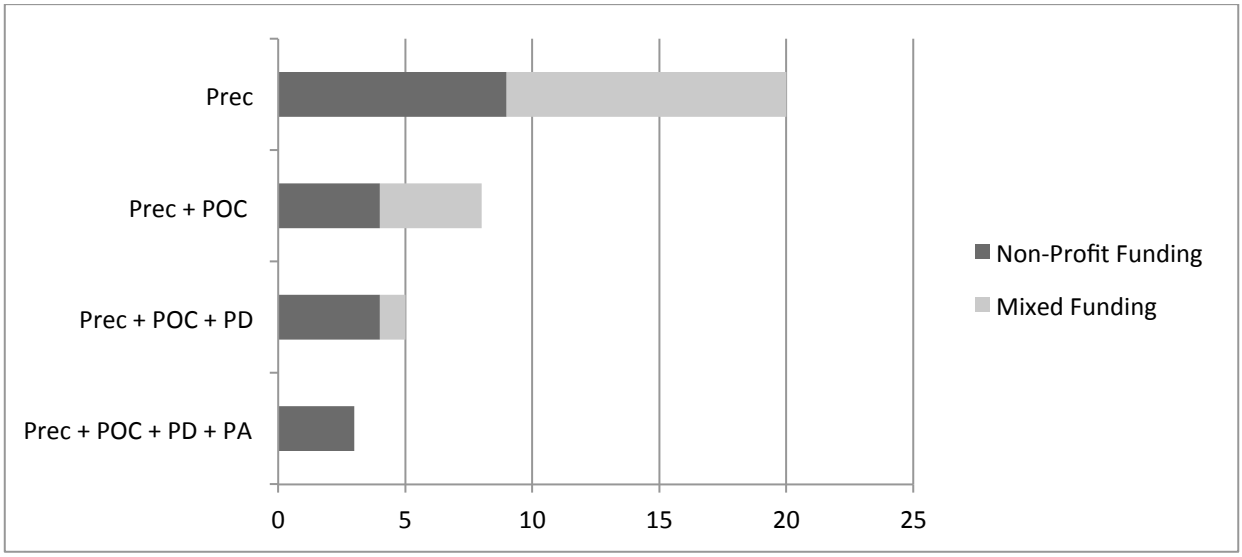
Variation of IP frameworks

The current study provides a snapshot of the IP framework applied by PPPs operating in the earliest phase of the drug development cycle (**Table 1**). We found that there is quite some variation in the type of IP framework or knowledge-sharing strategy adopted to structure the ownership, the use and the transfer of knowledge. The study allows distinguishing 3 different types of knowledge sharing strategies or IP frameworks: 1) a partnership-focused strategy, 2) an open collaboration strategy and 3) a hybrid strategy (**Table 3**). Nine of the 20 (45%) PPPs (2 US, 2 EU, 5 National), 6 (30%) mixed funded and 3 (15%) non-profit funded PPPs, apply a partnership-focused strategy, wherein patenting is a possibility for safeguarding exclusive rights and the access to background IP and foreground IP is preferably preserved to the project partners. Seven (35%) PPPs (4 International, 3 US) apply an open collaboration strategy, wherein patenting is only possible in specific cases and research results are shared with the public under specific licensing conditions. Four (20%) PPPs (3 International, 1 US) explicitly state that a mix of strategies is possible and adopt a hybrid model; they allow patenting of research results, but request to preferably put the research results in the public domain (**Tables 1** and **3**).

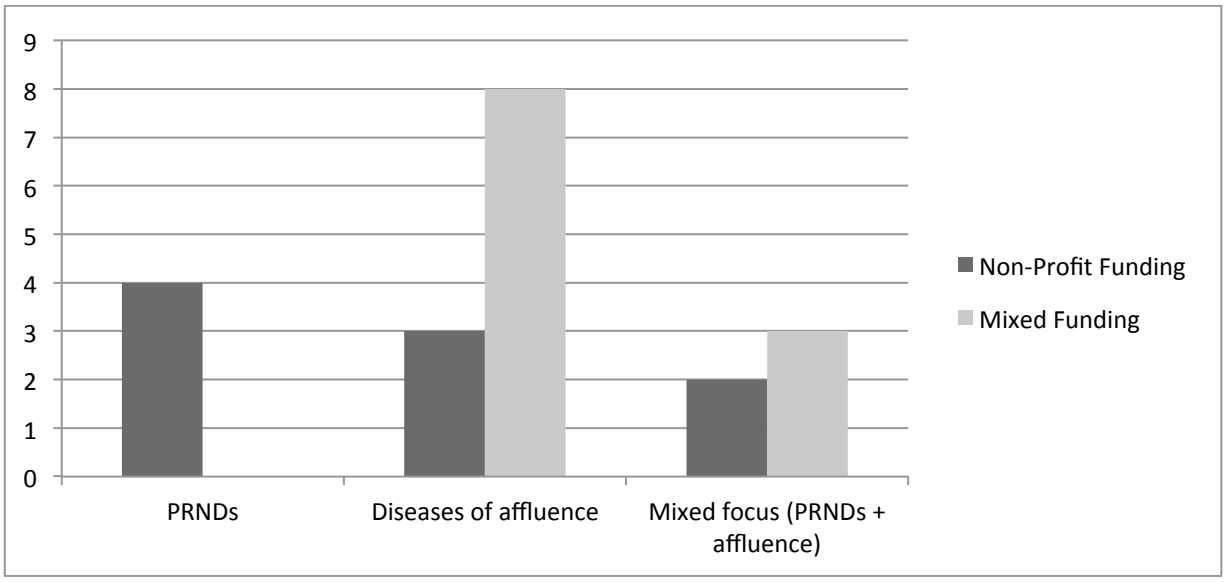
Certain PPPs combine these strategies for different projects situated within one and the same PPP (i.e., a combination of different knowledge-sharing strategies, depending on the specific project and the needs of the partners therein). Further, it sometimes occurs that particular projects apply a mix of strategies depending on the type of knowledge developed (e.g., the dominant IP framework within IMI is a partnership-focused strategy, however, the U-BIOPRED consortium, a 1st Call project, applies an open collaboration strategy for the majority of its research results, and a partnership-focused strategy for research tools that are being developed). In this study, we classified the PPPs based on the dominant PPP IP framework: i.e., the IP framework described in the IP policy and applied in the majority of the projects.



Supplementary Figure 1 Relationship between focus of research projects of PPPs starting activities as of the early research phase and phases they target in the product development lifecycle



Supplementary Figure 2 Relationship between funding of the PPPs starting activities as of the early research phase and phases they target in the product development lifecycle



Supplementary Figure 3 Relationship between funding source of PPPs having activities in the early research phase and the focus of research projects