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Analysis Report: Understanding the Role of Partnerships in Medical Product Development

Report

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Hui-Hsing Wong, MD, JD

Office of the Assistant Secretary for Planning and Evaluation
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Prepared by

Doris Rouse, PhD
Bonnie Jones, MSPH
Katelin Moran, MPH
Diana Severynse-Stevens, PhD
RTI International
3040 Cornwallis Road
Research Triangle Park, NC 27709

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DISCLAIMER

This report was prepared by RTI International under contract to ASPE. The findings and conclusions of this report are those of the authors and do not necessarily represent the views of ASPE, FDA, or HHS.

Acronyms

ANDI	African Network for Drugs and Diagnostics Innovation
ASEAN-NDI	Association of Southeastern Asian Nations – Network for Drugs, Diagnostics and Vaccine Initiatives
ASPE	Department of Health and Human Services’ Office of the Assistant Secretary for Planning and Evaluation
CARE	Carbapenem Resistance
CNS	Central Nervous System
COMBACTE	Combatting Bacterial Resistance in Europe
C-PATH	Critical Path Institute
CRO	Contract Research Organization
CSRC	Cardiac Safety Research Consortium
DRIVE-AB	Driving Re-Investment in R&D and Responsible Antibiotic Use
DNDI	Drugs for Neglected Diseases initiative (DNDi)
EDCTP	European and Developing Countries Clinical Trials Partnership
ENABLE	European Gram Negative AntiBacterial Engine
ETP	Enabling Technology Partnership
FDA	Food and Drug Administration
FNIH	Foundation for NIH
GHIT	Global Health Innovative Technology
HAT	Human African Trypanosomiasis
HIV	Human Immunodeficiency Virus
I-SPY	Investigation of Serial Studies to Predict Your Therapeutic Response with Imaging and Molecular Analysis
IMI	Innovative Medicines Initiative
IP	Intellectual Property
MAGNET	Molecules Against Gram Negative Infections

MD	Medical Doctor
MIATA	Minimal Information About T cell Assays (MIATA)
MMV	Medicines for Malaria Venture
MOU	Memorandum of Understanding
ND4BB	New Drugs for Bad Bugs
NECT	Nifurtimox-Eflornithine Combination Therapy
OTA	Other Transaction Authority
PDP	Product Development Partnership
PhD	Doctor of Philosophy
PPP	Public Private Partnership
PreDiCT TB	Model-based Preclinical Development of Anti-Tuberculosis Drug Combinations
R&D	Research and Development
RTI	RTI International
TB	Tuberculosis
TI Pharma	Top Institute Pharma
WHO	World Health Organization
WIPO	World Intellectual Property Organization

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EXECUTIVE SUMMARY

Partnerships involving collaborations between the pharmaceutical industry, government agencies, academics, foundations, and independent nonprofit organizations hold promise for addressing unmet needs in medical product research and development. Effective partnerships can enhance access to innovation, reduce risk, and manage costs and may provide a means for steering research and development investment to address societal objectives. The numerous public-private partnerships (PPPs) that have emerged over the past 20 years reflect different models of operation and different approaches to aspects such as the partnership objective, participants and their roles, intellectual property (IP) policies, funding sources, and governance.

In response to the growing interest in PPPs as a method for advancing drug development, the Department of Health and Human Services' Office of the Assistant Secretary for Planning and Evaluation (ASPE) commissioned an analysis of the factors that contribute to the success of PPPs. This analysis, conducted by RTI International, examined partnership structures, approaches, and outcomes to identify the key components needed for partnerships to thrive. The study also examines the evolution of partnership characteristics in response to the changing product development environment over the last 20 years.

E.1 Framework for Analysis

The PPPs included in this analysis were restricted to PPPs focused on drug development, defined in this study as small molecule and therapeutic biological products. Each partnership included was categorized according to its therapeutic area(s) of focus: oncology, central nervous system, cardiovascular disease, infectious disease, rare and genetic diseases addressing therapeutic areas outside of the previous four categories and general drug development. These six therapeutic areas captured the majority of PPPs of interest and the diverse methods of structuring, funding, and implementing a partnership. We later refined these topic areas to three primary topic areas of interest (i.e., oncology, cardiovascular disease, and infectious disease).

Partnerships between industry, academia, and governments have been formed to develop new therapeutics more efficiently and effectively. The partnership objectives are a major determinant of their approach to composition, governance, funding requirements, IP policies, and measures of success. To begin the analysis, RTI divided the PPPs into two major categories based on their objectives:

- **Product Development Partnerships (PDPs):** The objective of these partnerships is to develop a new medical product for prevention, diagnosis, or treatment.
- **Enabling Technology Partnerships (ETPs):** These partnerships are often labeled as "precompetitive," as they do not seek to develop a proprietary medical product.

Rather, their objective is to develop tools, methods, or knowledge to support medical product development.

We developed Analytical Frameworks for these two categories of partnerships to assess key structural elements that facilitate the successful completion of their objectives. Successful partnerships are defined as those that have achieved their objectives for formation and operation, advancing effectively toward the overall goal of their partnership to develop a specific medical product or to develop tools, methods or knowledge to support medical product development. These frameworks are an adaptation of a standardized and widely accepted public health intervention framework for measuring performance by displaying relationships between input resources, activities, outputs, and system-level outcomes (Handler, Issel, & Turnock, 2011; CDC, 2014).

The analytical frameworks enable a structured analysis of partnerships for medical product development, illustrating the relationship between the inputs and activities of the partnership and the targeted outputs, outcomes, and impact for public health. In addition, they show the increasing influence of external threats and facilitating factors as these external factors become more distal to the foundational constructs and direct activities of the partnership. By analyzing these constructs and the relationships between them, one can examine the elements of successful partnerships and areas to support growing partnerships to achieve greater success.

E.2 Application of the Framework

We analyzed data from 84 partnerships. Key findings regarding success factors across partnerships are presented here.

Broad Goals and Small Successes: It is important to have both broad goals and small, measurable steps (short-term successes or milestones) at the inception of the partnership. Broad goals define the long term outcome for which the partnership was formed. Incremental, early successes can provide the partnership with internal and external credibility and allow the partners to feel more deeply engaged and to envision ways to accomplish larger, longer-term goals together.

Diverse Stakeholder Inclusion: Industry, government, donors, regulatory bodies, and non-profits/other stakeholder groups all have a particular role in the formation of the partnership. In setting the priorities for the partnership, it is important to engage industry as an essential participant from the beginning.

Early Agreements: Setting up initial agreements appears to be crucial for partnership success and minimizing challenges in the future of the partnership. Agreements may address IP, publishing policy, or data sharing.

Partnership Flexibility: Although it is important to work in a collaborative process to establish initial partnership agreements, it is also important to have flexibility built into partnerships to revisit milestones and agreements regularly.

Harnessing Synergies: Build mutual benefits for multiple partner goals through the following:

- share best practices among participants;
- establish best practices and re-using key elements of IP agreements and other agreements after successful implementation;
- add partners incrementally instead of building new partnerships;
- develop and/or use a central agency or umbrella organization with administrative, regulatory, and legal agreement expertise to support multiple partnerships rather than each partnership developing internal capability;
- hold frequent team meetings to foster open communication needed to identify possible efficiencies as well as problem areas that could be best addressed by all partners.

Mutual Goals: One should not assume that all partnership members share a common perception of partnership goals and success. A clear vision of the goals of the partnership must be developed in an open, direct dialogue among the partners across sectors.

A critical activity suggested for clarifying goals of a partnership is the development of a target product profile that includes factors across the value chain from therapeutic efficacy and safety to manufacturing, cost, and supply chain considerations.

Passing It Forward: Partnerships share best practices. Effective methods to facilitate sharing have included:

- develop toolkits that outline early partnership agreements;
- directly mentor a new partnership;
- members of a mature partnership become members of newer partnerships' governing boards.

Funding Considerations: To prevent dependence on one funder, partnerships seek diverse and sustainable funding. Some partnerships strategize to not have more than 25% of their support from one funder. Others have a goal of a long-term funding commitment within their partnership. The most successful partnerships examined in this study could continue their work at their current level of effort for at least 9 months to 2 years without securing additional funding.

Partner Engagement and Commitment: Among the most successful partnerships we noted a deeper level of partner commitment and buy-in. Partners contributed in a variety of ways. For example, successful partnerships:

- were more likely to acknowledge and to be sustained by both in-kind and financial resources (examples of in-kind resources included donated lab space or materials);
- have members representing diverse sectors (industry, academic, non-profit, and government), who often co-authored publications and co-presented at press releases or conferences.

E.3 Key Factors for Success Unique to PDPs and ETPs

E.3.1 Key Success Factors for PDPs

Full Pipeline: With an objective of developing a medical product, a PDP has a much greater likelihood of success with a full pipeline of drug candidates, as is the practice in the pharmaceutical industry. The high failure rate in drug development demands a development pipeline of multiple candidates from differing classes with different mechanisms of action.

Staff with Pharma Experience: A partnership's success in drug development and regulatory approval benefits from inclusion on the staff of individuals with pharmaceutical industry experience.

Engagement of Partner Senior Management: The extended timeline for drug development increases the probability of staff turnover within a PDP's partner organizations in either the public or private sector. With the departure of the partner's key staff member(s), the commitment and strong support of the partner organization can be lost. To build sustainable support of partner organizations, successful PDPs have engaged Senior Management in the partner organizations to facilitate continuity of commitment to their role in the PDP.

E.3.2 Key Success Factors for ETPs

Strong Industry Role in Defining Objectives: The most successful ETPs engage industry partners in defining those precompetitive needs that would improve the product development process. Input by public sector agencies and academia, combined with a strong industry role in defining objectives, is important to the medical product industry's participation in the partnerships and utilization of the outcomes for product development in all sectors.

Shared Infrastructure Elements: Many of the most successful ETPs benefit from operating within an umbrella organization that provides established management, regulatory, and financial systems to minimize overhead costs and start-up delays. Examples include the partnerships within the Foundation for NIH (FNIH) and the Innovative Medicines Initiative (IMI).

E.4 Evolving Partnership Models

Over the past 20 years of PPP formation, partnership models have evolved beyond PDPs and ETPs to improve their efficiency and effectiveness in response to changes in the technical, regulatory, and business environments.

Umbrella Organization: One example of evolving models is the emergence of a central management entity or “umbrella” organization model used increasingly by PPPs, especially ETPs. The objective of an umbrella organization is to support the efforts of multiple partnerships, providing an infrastructure and an efficient approach for sharing resources and knowledge in the establishment and operation of new partnerships. Examples of umbrella models include FNIH, the Critical Path Institute (C-PATH), and IMI.

The umbrella organization can offer a proven infrastructure for funding coordination, IP and legal services, and general business management advice that may relieve individual PPPs from investment in these services, thus allowing them to maintain a focus on their mission. Successful umbrella organizations can also establish best practices and adapt or re-use key elements of IP agreements and other agreements after successful implementation.

Hybrid Umbrella Organization: The continuing evolution of partnership models to address emerging needs is seen in the new “hybrid umbrella” model. While umbrella organizations have focused primarily on enabling technology development, a recent hybrid umbrella organization model has emerged in which both PDPs and ETPs are included within one umbrella partnership. The 2012 formation of the IMI hybrid umbrella partnership, New Drugs for Bad Bugs (ND4BB), was the first hybrid umbrella organization. This organization took a novel, integrated approach to launch four sub-partnerships that included both product development and enabling technology activities.

An ongoing understanding of the key factors for partnership success can inform the continued evolution of partnerships and enhance their contributions to the development of new medical products.

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1. BACKGROUND

Partnerships involving public sector organizations, academia, and pharmaceutical companies hold promise for addressing unmet needs in medical product research and development. Effective partnerships can enhance access to innovation, reduce risk, and manage costs and may provide a means for steering R&D investment to address societal objectives. In some therapeutic areas, the trend of industry reducing investment and engagement has stimulated U.S. and European agency initiatives such as the Critical Path Institute (C-PATH), Foundation for NIH (FNIH), and the Innovative Medicines Initiative (IMI).

Collaborations between the pharmaceutical industry, government agencies, academics, and independent non-profit organizations have demonstrated the potential of joint efforts to discover and advance new drugs and vaccines in areas of need. Successful partnerships have confirmed the feasibility and value of bringing together the resources, expertise, and facilities of government, academic, philanthropic, and private industry participants. The numerous public-private partnerships (PPPs) that have emerged over the past 20 years reflect different models of operation and different approaches to aspects such as the partnership objective, participants and their roles, intellectual property (IP) policies, funding sources, and governance.

In response to the growing interest in PPPs as a method for advancing drug development, the Department of Health and Human Services' Office of the Assistant Secretary for Planning and Evaluation (ASPE) commissioned an analysis of the factors that contribute to the success of PPPs. This analysis, conducted by RTI International, examined partnership structures, approaches, and outcomes to identify the key components needed for partnerships to thrive.

Prior studies have examined public-private partnerships (Table 1.1). Pozen & Kline (2011) used metrics such as diverse funding, development pipeline, and scientific knowledge as key elements of successful partnerships. FSG Social Impact Advisors (2007) also evaluated PPPs using metrics such as agreements on IP and commercialization strategies. Finally, FasterCures (2013) used similar partnership characterization parameters including mission, IP policy, governance, oversight bodies, and secure funding. The work of Buse and Harmer (2007) also reflects these key elements, with an emphasis on the need for ongoing oversight and performance assessment across performance areas.

Table 1.1. Studies Characterizing Medical Product Development Partnerships

Study Title	Authors	Partnership Parameters
Defining Success for Translational Research Organizations	R. Pozen and H. Kline (2011)	Funding, talent, creation of research pipeline, validation through publication and oversight, dissemination, external uptake, and collaboration
Toward a New Approach to Product Development Partnership Performance Measurement	FSG Social Impact Advisors (2007)	R&D to commercialization, organizational strength, enabling environment health Impact
Consortia-pedia	FasterCures (2013)	Mission and governance, financing, human capital, IP, data-sharing, patient participation, measurement of value and impact
Seven Habits of Highly Effective Global Public-Private Health Partnerships: Practice and Potential	Buse and Harmer (2007)	International alignment, stakeholder representation, effective approach, operating procedures, oversight, financial resources, partner role negotiation

RTI expands on these partnership characterization studies by analyzing key elements for the success of a partnership across a range of measures including overall structure and objectives as well as inputs, activities, short-term outcomes, mid-term outcomes, and long-term outcomes. These elements and their impact on success of the partnership are examined in this report.

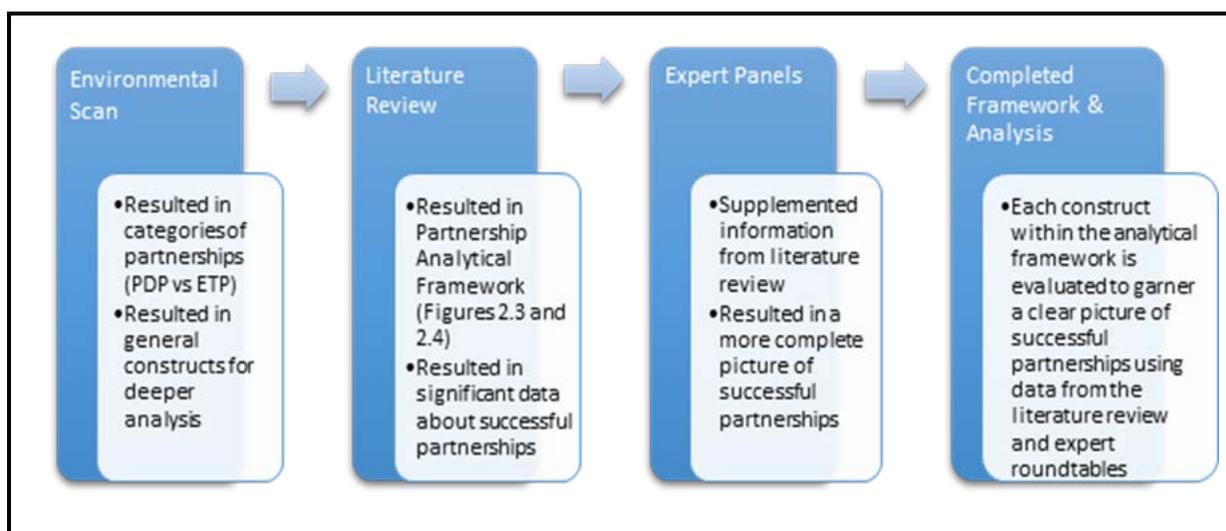
This report will explain our analytical process through the following steps:

- Develop an analytical framework, informed by an environmental scan and literature review. These findings were supplemented with information gathered from expert roundtables (Section 2).
- Apply the assembled information to an analytical framework. This effort includes (1) analyzing data for all partnerships relative to the analytical framework, (2) examining the interrelationship of and dependence between the constructs in the analytical framework, and (3) examining how the relationships of the constructs in the framework might lead to successful partnerships (Section 3).
- Synthesize the partnership characteristics that correlate with successful partnerships and describe common characteristics of partnerships and types of partnerships that have experienced success (Section 4).
- Discuss characteristics of success noted in the partnerships’ planning, formation, and ongoing operations time periods (Section 5).
- Summarize the value and evolution of partnerships (Section 6).

2. METHODS: DEVELOPING A FRAMEWORK FOR ANALYSIS

RTI used an iterative, mixed methods approach to analyze trends in successful PPPs. We began by conducting an environmental scan to identify PPPs for medical product development and to determine how to categorize these PPPs and what information from them to evaluate. We then conducted a literature review to refine this information into an analytical framework and analyzed each partnership based on the framework. Next, we convened expert roundtable participants to supplement information that was unavailable through literature and other sources. The aggregate information resulted in a finalized analytical framework that was used to evaluate partnerships by their relative success in achieving their stated goals. Figure 2.1 outlines this process.

Figure 2.1. Process for Developing an Analytical Framework for Public-Private Partnerships



The PPPs included in this analysis were restricted to PPPs focused on drug development, defined in this study as small molecule and therapeutic biological products. We removed partnerships focused on vaccines, diagnostic kits, and biomedical research. Each partnership included was categorized according to its therapeutic area(s) of focus. Initially, we considered six therapeutic areas, including oncology, central nervous system, cardiovascular disease, infectious disease, rare and genetic diseases addressing therapeutic areas outside of the previous four categories, and general drug development. These six therapeutic areas captured the majority of PPPs of interest, and the diverse methods of structuring, funding, and implementing a partnership. We later refined these topics areas to three primary topic areas of interest (i.e., oncology, cardiovascular disease, and infectious disease). We chose these three because they included the most partnerships from the initial environmental scan

and retained the representation of diverse partnership structures and methods for implementation.

We examined partnerships individually even if they are included in a central management entity (i.e., umbrella organization) that manages several partnerships. For example, the IMI, C-PATH, and FNIH all host many partnerships with varied goals. Partnerships within these umbrella organizations often have differences in objectives, funding, and governance. We examined these differences as well as common factors and policies across those partnerships in the analysis.

2.1 Categories of Partnership

Partnerships between industry, academia, and governments have been formed to develop new therapeutics more efficiently and effectively. The partnership objectives are a major determinant of their approach to composition, governance, funding requirements, IP policies, and measures of success. To begin the analysis, RTI divided the PPPs into two major categories based on their objectives:

- Product Development Partnerships (PDPs):** The objective of these partnerships is to develop a new medical product for prevention, diagnosis, or treatment. We defined three major categories of partnerships within PDPs: Independent Entity, Partnering Platform—Public Sector, and Partnering Platform—Private Sector (Table 2.1)
- Enabling Technology Partnerships (ETPs):** These partnerships are often labeled as “precompetitive,” as they do not seek to develop a proprietary medical product. Rather, their objective is to develop tools, methods, or knowledge to support medical product development. We defined four major categories of partnerships within ETPs: Independent Entity, Partnering Platform—Public Sector, Partnering Platform—Private Sector, and Knowledge Sharing (Table 2.2).

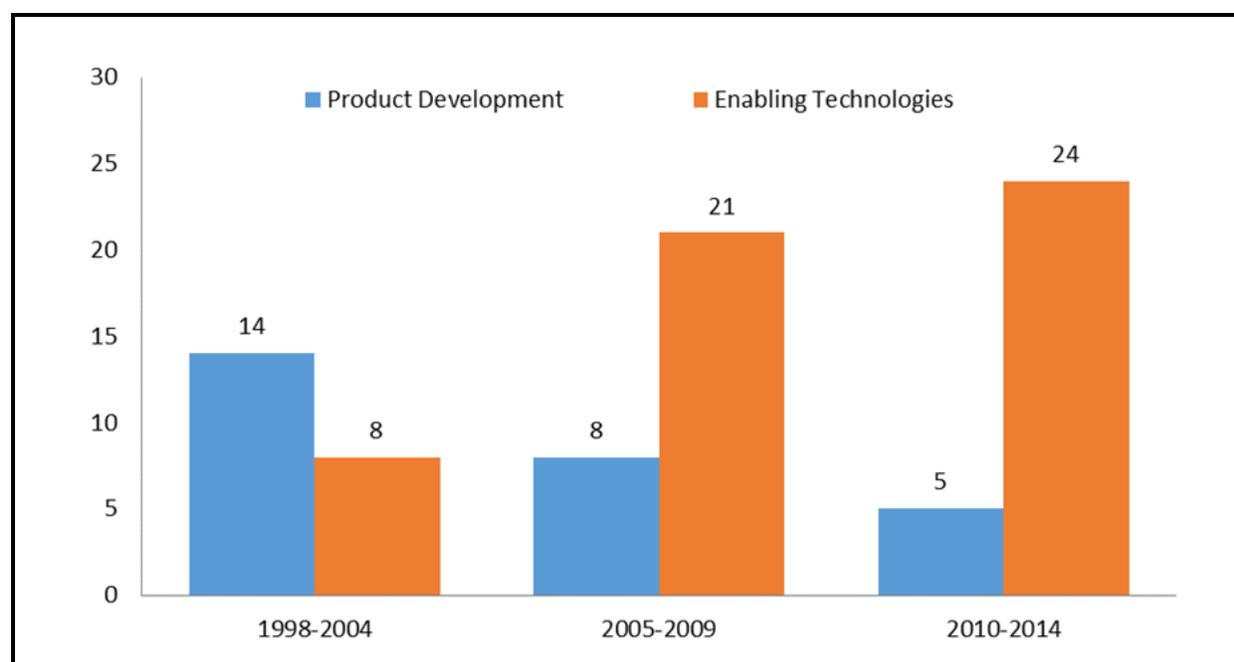
Table 2.1. Product Development Partnerships

Categories	Description	Examples
Independent Entity	Selects compounds, funds and provides centralized direction of drug development studies	Global Alliance for TB Drug Development, Medicines for Malaria Venture, Cancer Research Institute Clinical Accelerator
Partnering Platform—Public Sector	Convener and funding organization that brings together industry and academia, providing funds for drug development studies directed by grantee	Multiple Myeloma Research Consortium, Progeria Research Foundation, Consortium for Parasitic Drug Development
Partnering Platform—Private Sector	Pharma company funding and collaborations with academics for drug discovery and development jointly directed by grantee and pharma	Centers for Therapeutic Innovation (Pfizer)

Table 2.2. Enabling Technologies Partnerships

Structure	Description	Examples
Independent Entity	Establishes and manages public-private partnership to define and fund development of an enabling tool, method, or knowledge for drug development	Critical Path Institute, Cardiac Safety Research Consortium
Partnering Platform—Public Sector	Convener and funding organization from public sector that brings together industry and academia, providing funds for enabling tool, method, or knowledge for drug development	Biomarkers Consortium, IMI, ASEAN-NDI
Partnering Platform—Private Sector	Convener and funding organization from private sector that brings academia together with industry, providing funds for enabling tool, method, or knowledge for drug development	Tres Cantos Open Lab Foundation, Lilly Drug Discovery Initiative
Knowledge Sharing	Coordinating entity and executive committee to define and fund an enabling tool or knowledge for drug development	WIPO Re:Search, Project DataSphere, The European Rare Diseases Therapeutic Initiative

In our analysis, we found a changing environment over time in the types of partnerships being formed, with a predominance of PDPs in the 1998–2004 time period, followed by an increasing number of ETPs thereafter, as shown in Figure 2.2. This trend reflects the growth of PPPs from focusing primarily on developing treatments to precompetitive tools.

Figure 2.2. Time Trends and Number/Types of Partnerships Formed

2.2 General Constructs

The categories of measures (i.e., general constructs) analyzed are: partnership characteristics, composition, business practices, and governance. These four general categories ultimately will inform the analytical framework and the subsequent topics for analysis.

- **Partnership Characteristics** were gathered to learn about topics such as the partnership's size, age, mission, objectives, etc.
- **Composition** refers to who is a part of the PPP (e.g., industry, academic, government, foundation, or other third party).
- **Business Practices** refers to the organizational policies of the PPP.
- **Governance** refers to the composition and type of governing bodies of the PPP.

2.3 Analytical Framework

The information gathered in both the environmental scan and subsequent in-depth literature review informed the development of the analytical framework for the evaluation of PPPs. The Public-Private Partnership Analytical Framework is an adaptation of a standardized and widely accepted public health intervention framework for measuring performance by displaying relationships between input resources, activities, outputs, and system-level outcomes (Handler, Issel, & Turnock, 2011; CDC, 2014). Our analytical framework format is guided by an analytical framework developed by the government of Alberta to assess their health system (Alberta Government, 2013). This framework uses a hierarchical structure to diagram input, activity, output, and outcome constructs, which are supported by foundational constructs. Thus, the analytical framework evaluates both process and outcome measures. Analysis of the key constructs of inputs, outputs, and outcomes of partnerships were guided by the Analytical Framework presented in the PDP and ETP analytical frameworks described in *Analytical Frameworks* below (Figures 2.3 and 2.4). While similar, two frameworks were developed to denote some of the differences between PDPs and ETPs. Within each general construct, we organized information by inputs, activities, outputs, and outcomes of each partnership (Table 2.3). Constructs are depicted in the small boxes of Figure 2.3 and 2.4. The framework organizes these constructs in hierarchical form displaying the relational paths from inputs toward outcomes.

Figure 2.3. Product Development Analysis Framework

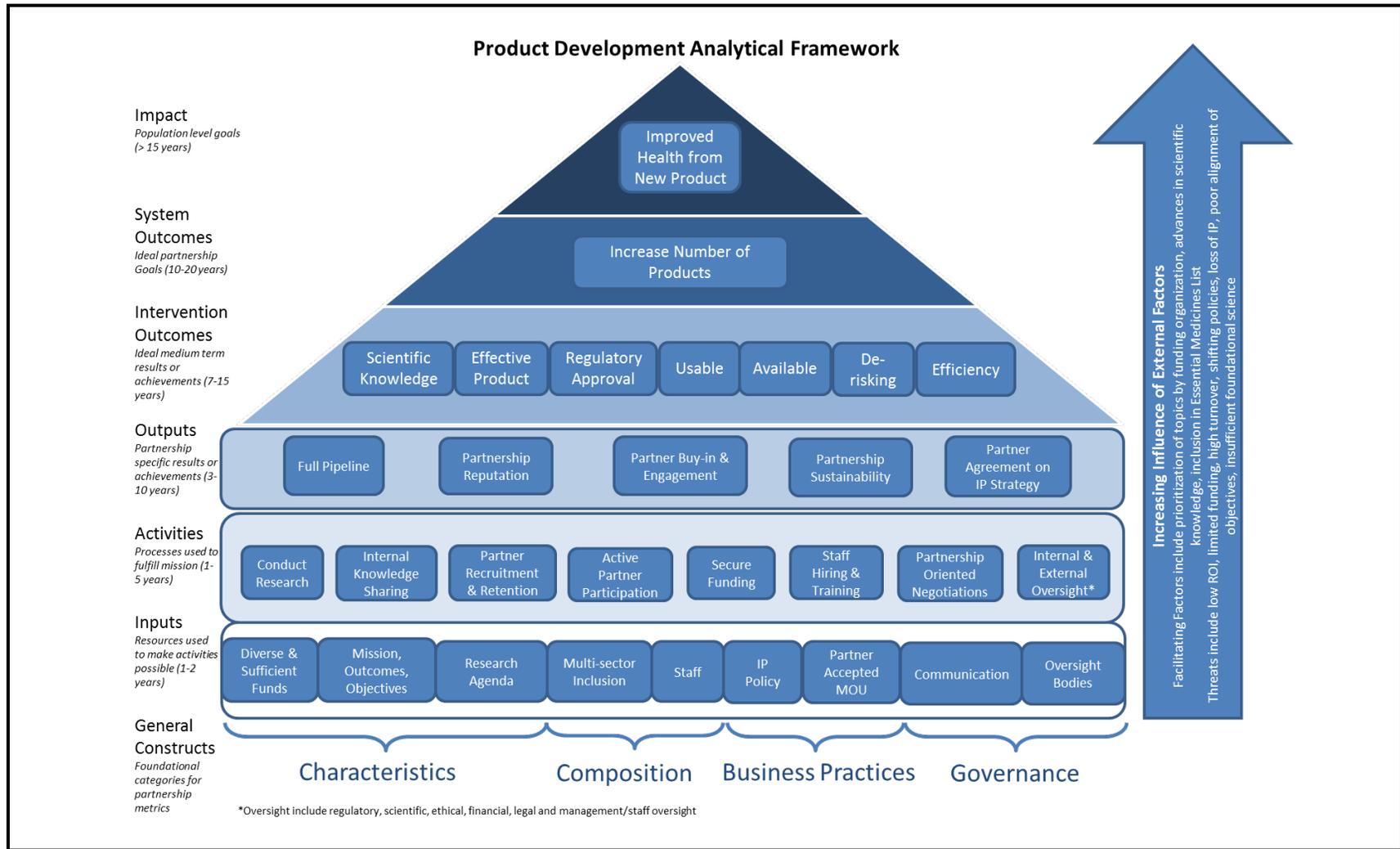


Figure 2.4. Enabling Technologies Analysis Framework

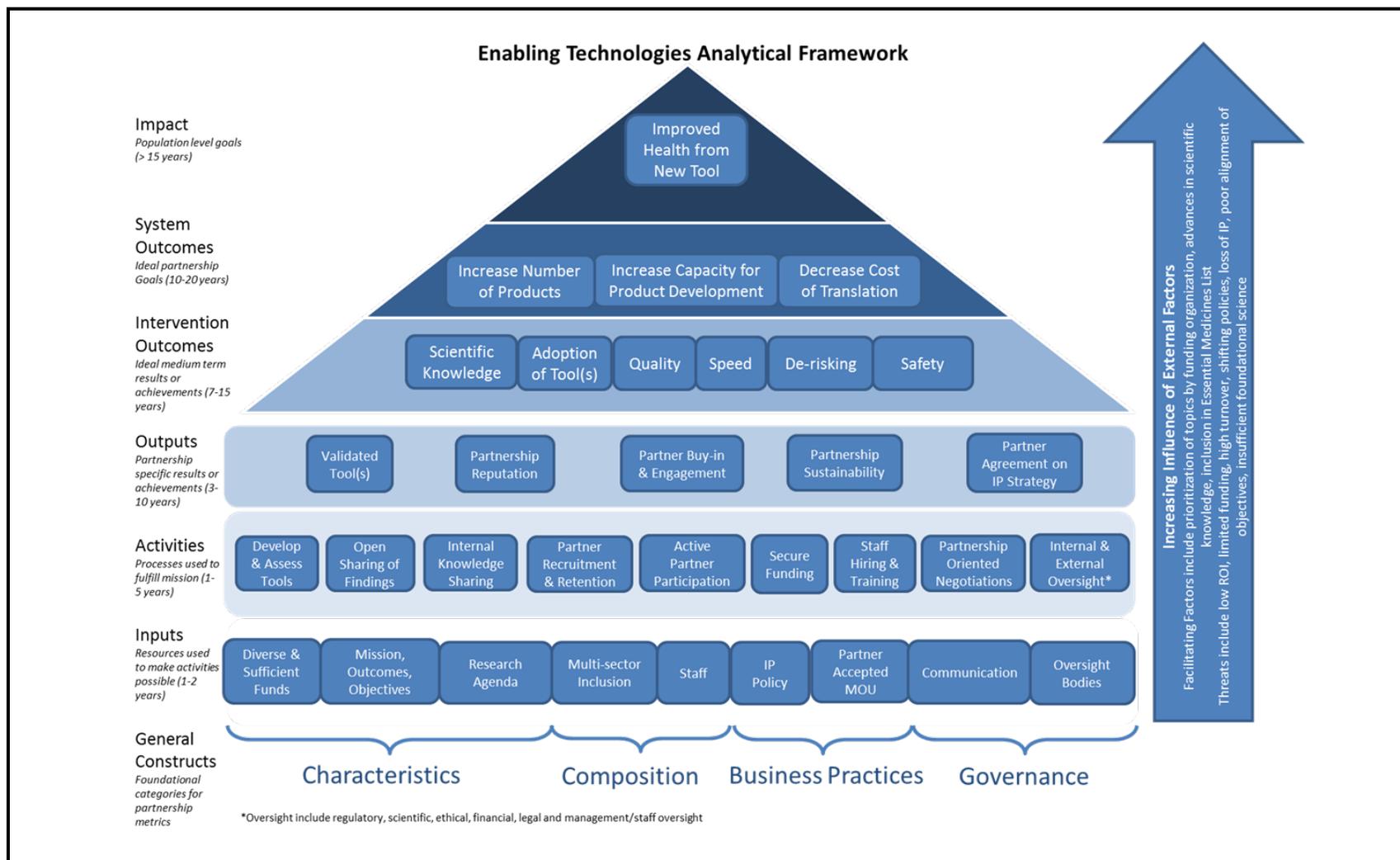


Table 2.3. Definitions of Organizing Constructs

Concept	Definition
General Constructs	The categories of performance measures are partnership characteristics, composition, business practices, and governance. These four pillars form the foundational constructs and base of the framework that defines subsequent input categories.
Inputs	Inputs are resources used to produce results. For example, funding and staff are needed to conduct research. Without sufficient and appropriate inputs, the partnership's activities would not be possible.
Activities	Activities are the actions the partnership conducts to fulfill its mission. Without conducting these activities, the partnership would be unable to achieve the outcomes stated in their missions and objectives.
Outputs	Outputs are the partnership's direct results, achievements, products, or services delivered by the partnership. The partnership's outputs are necessary to meet the partnership outcomes.
Intervention Outcomes	Intervention Outcomes are the medium-term results from the partnership. These outcomes can take 7 or more years to achieve, but reflect the partnership's goals. An example of an intervention outcome can be the adoption of a new tool or the development of an effective product.
System Outcomes	System Outcomes are the medium- to long-term results from the partnership's efforts. These outcomes often take more than 10 years to achieve and, in the case of ETPs, reflect changes to the systems that influence drug translation and development. In PDPs, the outcomes increase the effective treatment options for the targeted therapeutic area.
Impact	The impact is the long-term results of achieving specific outcomes. The characteristics of the outcome have a substantial influence on impact. For example, a breakthrough new therapeutic with a new mechanism of action will likely have greater impact than an incremental improvement on an existing class of drugs. Impacts are generally population-level goals, which may take many years to achieve. The failure of any one factor within inputs, activities, outputs, and outcomes does not guarantee the failure of achieving this impact; however, it may significantly reduce the likelihood of success. In addition, the success of all preceding factors does not guarantee a successful impact, as the influence of external factors can limit the success of a project.

2.4 Data Capture from Literature Review

We developed the analytical framework so that characteristics common among successful PPPs could be analyzed. In order to analyze this information, we developed a standard definition as well as measures. Our definitions and measures built upon the work of Pozen, FSG Social Impact Advisors, FasterCures, and Buse and Harmer (Table 1.1), and were supplemented by consulting with experts to refine the measures we developed and used to analyze each construct.

Inputs

Inputs describe the various resources dedicated to a program, in this instance, to develop and sustain a PPP. From the literature review we determined the key inputs that contribute to the foundational stability of a PPP (shown in Table 2.4 for both PDPs and ETPs). Table 2.4 states the construct (i.e., input), defines the input, and defines the quantitative or categorical measure used to evaluate the input. Inputs are usually assumed to be a component of the type of logic model used for our framework and rarely analyzed.

Table 2.4. Inputs for Public-Private Partnership Analytical Framework

Construct (Inputs)	Definition	Key Measures
Diverse and Sufficient Funding	Diverse and sufficient funding indicates that a partnership has adequate funds and varied funding sources to accomplish its goals and objectives.	<ul style="list-style-type: none"> ▪ # of sources of funding for partnership ▪ % of funding from biggest funder for partnership ▪ # of sources of funding for umbrella organization ▪ % of funding from biggest funder for umbrella organization ▪ Funds sufficient to complete partnership objectives (provide ratio) ▪ Funding contingencies or restrictions
Mission, Outcomes, Objectives	Mission, outcomes, and objectives refer to a partnership having a stated mission as well as a set of outcomes and objectives that the partnership is striving to obtain.	<ul style="list-style-type: none"> ▪ Clearly stated mission ▪ Clearly stated outcomes ▪ Clearly stated objectives ▪ Measureable objectives and/or impact ▪ From whom is the information generated and to whom is partnership's assistance focused?
Research Agenda	Partnerships often have a defined research agenda that includes specific topics. Some partnerships focus on their established research agenda, while others modify from their original agenda based on experience in the partnership's activities and external factors.	<ul style="list-style-type: none"> ▪ Clearly stated research agenda ▪ Profile of target product (product development) ▪ Profile of target tool (enabling technology)
Multi-sector Inclusion	The nature of a partnership necessitates that more than one sector be included in the partnership. Multi-sector inclusion focuses on which sectors are included, how many partners from each sector are included, and the role and the level of involvement by each sector in the partnership.	<ul style="list-style-type: none"> ▪ Sector responsible for initiating partnership ▪ # of sectors represented ▪ Total number of partners

(continued)

Table 2.4. Inputs for Public-Private Partnership Analytical Framework (continued)

Construct (Inputs)	Definition	Key Measures
Staff	Staff refers to the need to have sufficient and appropriate staff to execute the research agenda and partnership activities.	<ul style="list-style-type: none"> ▪ Staff clearly stated (names) ▪ Staff organized by responsibilities (work titles) ▪ How many working groups are in partnership? ▪ Staff with relevant experience and training
Intellectual Property (IP) Policy	IP policy refers to the existence of an IP policy or policies for the partnership developed in consultation with all participating sectors.	<ul style="list-style-type: none"> ▪ Clearly stated IP policy ▪ IP policy developed with stakeholders and partners
Partner Accepted Memorandum of Understanding (MOU)	Partner accepted MOU refers to the partnership having a chartering document that accounts for the needs of each partner and establishes a partnership membership. The MOU will include the roles and responsibilities of partners and the IP policy. Partners would include private sector organizations, patient representative organizations, government agencies, and non-profits.	<ul style="list-style-type: none"> ▪ Clearly stated MOU or other Partnership Agreement Form ▪ MOU/agreement developed with stakeholder and partners
Communication	Communication refers to established communication channels, schedule and process for partnership updates, and productive communication styles to carry out activities of the partnership.	<ul style="list-style-type: none"> ▪ Expectations for partner participation ▪ Regular press releases and publications regarding partnership ▪ Presentations to stakeholders
Oversight Bodies	The oversight body input refers to the presence of governing or oversight bodies for the partnership. These bodies may include a board of directors, a scientific advisory committee, an executive committee, an external auditing organization, and other guiding entities for the partnership. Ongoing assessments by oversight bodies have the benefit of communicating progress to staff and stakeholders, providing feedback to funders, and identifying areas for improvement.	<ul style="list-style-type: none"> ▪ Any oversight body(ies) ▪ Scientific advisory group ▪ Executive board

Source: Lavinghouze et al., 2013

Activities

The aforementioned inputs prepare a partnership to conduct activities aimed at fulfilling the partnership’s mission. These partnership activities are common to PPPs and describe their program’s processes for achieving its goals and mission. Both PDPs and ETPs have many activities that are common to both types of partnerships; however, some unique activities exist for PDPs and ETPs as well. Table 2.5 lists the activities for PDPs and ETPs.

Table 2.5. Activities for Public-Private Partnership Analytical Framework*

Construct (Activities)	Definition	Measure
Conduct Research (Product Development)	Conducting research can include preclinical, Phase 1, 2, and 3 clinical trials.	<ul style="list-style-type: none"> ▪ Development plan—activities, dependencies, timelines and budget for each development project; interim milestones identified and process for objective review to assess progress ▪ Go/no-go decision points identified, process for objective assessment defined ▪ Process for identifying, selecting, and monitoring qualified CROs ▪ Plan (feedback plan) for meetings/reviews by project team, partners, and scientific advisory committee ▪ Regulatory discussions and plan for approval pathway
Develop and Assess Tools (Enabling Technology)	ETPs often create and evaluate tools to aid product translation.	<ul style="list-style-type: none"> ▪ Project plan prepared for developing the tool ▪ Go/no-go decisions incorporated in project plan ▪ Partner responsibilities and approach defined in plan
Open Sharing of Findings in Partnership (Enabling Technologies)	<p>Information and discoveries made by the partnership are shared with all partners to facilitate the building of enabling tools for product translation.</p> <p>Of note: This activity was not included in the PDP activities because some partners within PDPs retain some proprietary information or IP.</p>	<ul style="list-style-type: none"> ▪ Project portal for all partners ▪ Who has access to the information/products/tools developed by PPP? ▪ Is this different from the intended audience stated ▪ Periodic partner updates
Internal Knowledge Sharing	Knowledge sharing refers to a range of activities including academic publications, distribution of reports, or conferences hosted by the partnership.	<ul style="list-style-type: none"> ▪ Is there support for publications, presentations, or articles? ▪ Scheduled presentations for stakeholders (internal and/or external) ▪ Communication of progress on website

(continued)

Table 2.5. Activities for Public-Private Partnership Analytical Framework (continued)

Construct (Activities)	Definition	Measure
Partner Recruitment and Retention	The ability to attract and retain partners in a partnership or add additional partners when necessary must be a deliberate and ongoing effort.	<ul style="list-style-type: none"> ▪ # of new partners each year ▪ % of partners remaining from beginning to end
Active Partner Participation	In addition to maintaining or growing the number of partners, partnerships must make a deliberate effort to keep partners engaged and working toward common goals.	<ul style="list-style-type: none"> ▪ Partner contributions (financial or in-kind) ▪ Frequency of partnership meeting ▪ Partner Participation in stakeholder meetings
Secure Funding	Partnerships should plan, staff, and implement efforts to secure, sustain, and grow financial resources for the partnership.	<ul style="list-style-type: none"> ▪ Business plan outlining financial objectives ▪ "Partnership has grown over time (current revenue funding/inception revenue funding)" ▪ "Partnership has grown over time (current income funding/gross income from 5 years ago)" ▪ Clearly stated person(s) responsible for finances and fundraising ▪ # of total donors since start ▪ # of new donors per year
Staff Hiring and Training	Appropriate expertise must be available to hire and train new staff to ensure they are capable of executing their roles to their highest potential.	<ul style="list-style-type: none"> ▪ Job descriptions developed and distributed ▪ Plan for recruiting staff ▪ Time between position opening and hiring ▪ Use of recruiting companies ▪ What is the function of working group?
Partnership Oriented Negotiations	Partnership oriented negotiations refers to the active engagement in discussing and responding to the needs of all partners.	<ul style="list-style-type: none"> ▪ IP agreement developed with partners ▪ IP agreement on specific projects developed with partners ▪ Partners represented in decision making process

(continued)

Table 2.5. Activities for Public-Private Partnership Analytical Framework (continued)

Construct (Activities)	Definition	Measure
Internal and External Oversight	Oversight includes regulatory, scientific, ethical, financial, legal, and management or staff guidance and management.	<ul style="list-style-type: none"> ▪ # of oversight bodies ▪ Type of oversight bodies ▪ Oversight bodies produce actionable directions ▪ Scientific oversight (if applicable)—2 or more times per year ▪ Financial oversight—establish schedule and process for internal review ▪ Financial oversight—retain external audit ▪ Financial oversight—report financial status to board 2x per year ▪ Oversight—public reporting of financials available ▪ Overall management oversight—board convenes 2x per year and reviews operations and management

* When an activity only applies to PDPs and/or ETPs, that distinction is noted within the 'construct' column. Measures were quantified (or defined as categorical variables for) the subjective definitions.

Outputs

Outputs can be used to analyze the immediate results of certain partnership activities; it generally takes 3-10 years for a partnership to see results or achievements. Several outputs are common to both PDPs and ETPs, and others are unique to each type of partnership. Table 2.6 lists the outputs' definitions and measures that were developed by RTI and that are common to both types of partnerships.

Table 2.6. Outputs for Public-Private Partnership Analytical Framework*

Construct (Outputs)	Definition	Measure
Full Pipeline (Product Development)	A full pipeline refers to having multiple compounds in various stages of product development and thus having multiple drug candidates in preclinical, Phase 1, 2, and/or 3 clinical trial.	<ul style="list-style-type: none"> ▪ Current number of lead compounds entered each phase of development pipeline by year ▪ Number of compounds advancing to next phase ▪ Number of compounds that do not advance to next phase ▪ Speed of transition from pre-clinical to Phase 1,2,3, and New Drug Application ▪ Number of clinical trials initiated ▪ Number of drugs pass through finish line ▪ Number of clinical trials completed
Validated Tools (Enabling Technology)	The production of a useful and valid tool to facilitate product development.	<ul style="list-style-type: none"> ▪ PPP completed at least one of intended tools ▪ Evaluation of tools by external experts ▪ Similar results achieved with tool by external expert ▪ Regulatory approval of tool, where required
Partnership Reputation	Partnership reputation refers to external commentary on the effectiveness of the partnership. Other important measures include new partnerships seeking advice, mentorship, or guidance from the partnership and modeling their structure and operation on elements of that partnership.	<ul style="list-style-type: none"> ▪ # partnership publications—total ▪ # partnership publications—yearly average ▪ # of citations by others—total ▪ # of citations by others—yearly average ▪ Partnership used as model for others
Partner Buy-in and Engagement	Partner buy-in and engagement refers to maintaining partners who are committed to the mission, objectives, and processes of the partnership.	<ul style="list-style-type: none"> ▪ Partner financial and in-kind contribution ▪ Project objectives set with industry input and concurrence ▪ Partner participation in stakeholder meetings ▪ Partner participation in key funding, regulatory, and technical meetings ▪ Partners co-authors on publications

(continued)

Table 2.6. Outputs for Public-Private Partnership Analytical Framework (continued)

Construct (Outputs)	Definition	Measure
Partnership Sustainability	This output refers to a partnership successfully working toward its mission. Progress to achieving the mission may be due, in part, to activities such as funding acquisition, partner recruitment, and retention, active partner participation, and appropriate oversight.	<ul style="list-style-type: none"> ▪ Funding commitments sufficient to achieve objectives ▪ Partner commitment to continuing collaboration ▪ Leadership long-term tenure ▪ Processes in place to make changes to objectives, goals, staffing ▪ "Partnership has grown over time (current revenue funding/inception revenue funding)" ▪ "Partnership has grown over time (current income funding/gross income from 5 years ago)"
Partner Agreement on IP Strategy	Partner agreement on IP strategy refers to having an IP agreement that is acceptable to all partners, establishing definitive and equitable terms for mutual benefit of the partnerships and its individual partners. For PDPs, agreements should also include the approach and responsibilities for manufacturing and distribution.	<ul style="list-style-type: none"> ▪ All partners sign IP documents ▪ Each sector expresses equitability in contributions and benefits established in IP agreement

* When an output only applies to PDPs and/or ETPs, that distinction is noted within the 'construct' column. Measures were quantified (or defined as categorical variables for) the subjective definitions.

Intervention Outcome

Successful outputs from the partnership can result in successful intervention outcomes. Intervention outcomes usually occur within 7–15 years of the partnership's inception. Both PDPs and ETPs have some shared intervention outcomes, and others are noted as being unique to either PDPs or ETPs. The constructs that were defined and measured for the intervention outcomes are provided in Table 2.7. In contrast to the inputs, activities, and outputs, the outcome measures do have value statements associated with the measure. Since we are analyzing partnerships to better understand successes, the intervention outcomes (and subsequent system outcomes and impact) do have directionality or value statements associated with the measures such as 'higher likelihood,' 'reduced cost,' or 'deeper understanding.'

Table 2.7. Intervention Outcome for Public-Private Partnership Analytical Framework*

Construct (Intervention Outcome)	Definition	Measure
Scientific Knowledge	Increasing knowledge about drug development, including increased knowledge of a therapeutic area, drug targets, mechanisms of action, and classes of compounds is an important outcome of PPPs.	<ul style="list-style-type: none"> ▪ A deeper understanding of disease course and interventions ▪ Others refine tool profiles due to PPP findings ▪ Lead compounds show higher likelihood of success
Effective Product (Product Development)	A product that can effectively treat a medical condition.	<ul style="list-style-type: none"> ▪ Meets target Product Profile for efficacy
Regulatory Approval (Product Development)	A product that has been approved by a government regulating agency.	<ul style="list-style-type: none"> ▪ Improved sensitivity and specificity as compared to existing products (Quality) ▪ Product meets safety parameters specified in Target Product Profile (Safety)
Usable (Product Development)	A product that is safe, easy to use, and in a formulation appropriate for the intended population. For example, a pediatric formulation would be necessary if the product is intended for use in children.	<ul style="list-style-type: none"> ▪ Meets target Product Profile for method and frequency
Available (Product Development)	A new therapeutic that has received regulatory approval for marketing and is manufactured and marketed.	<ul style="list-style-type: none"> ▪ Received regulatory approval in multiple countries ▪ Manufactured and distributed ▪ Affordable price ▪ Added to Essential Medicines List for WHO and individual countries ▪ % of high risk population receiving therapeutic
De-risking	De-risking refers to making drug translation more attainable for industry partners. For PDPs, this may mean screening many drug candidates to find the candidates most likely to make it to market and sharing the cost for advancing promising candidates. Alternatively, for ETPs this may mean identifying effective tools as predictors of success for potential drug candidates, thus enabling more rapid, less expensive identification and development of successful drugs.	<ul style="list-style-type: none"> ▪ Reduced development cost ▪ Financial burden of development shared among several partners ▪ Areas of shared expertise, knowledge, and data improve development process

(continued)

Table 2.7. Intervention Outcome for Public-Private Partnership Analytical Framework (continued)

Construct (Intervention Outcome)	Definition	Measure
Efficiency (Product Development)	A new therapeutic that optimizes product use.	<ul style="list-style-type: none"> ▪ Reduces dosing duration to achieve therapeutic outcome
Adoption of Tools (Enabling Technologies)	Adoption of tools means the use of the products developed from an Enabling Partnership. The adoption of these tools indicates a recognized need that the Enabling Partnership fulfilled for medical product development in industry and other partnerships.	<ul style="list-style-type: none"> ▪ Companies incorporate use of tool or knowledge ▪ Academic and government researchers incorporate use of tool ▪ Clinicians (if applicable) incorporate use of tool in clinical practice
Quality	Quality is producing a product with a high degree of excellence.	<ul style="list-style-type: none"> ▪ Improved sensitivity and specificity as compared to existing tools or products
Speed (Enabling Technologies)	Speed refers to a partnership’s ability to accomplish their mission and objectives as fast as or faster than any of the contributing partners could have accomplished the mission and objectives independent from the partnership.	<ul style="list-style-type: none"> ▪ Time to completion of tool development ▪ Time to validation of tool ▪ Time to regulatory approval (if time) ▪ Time to adoption of tool
Safety	Safety refers to either a product with rigorously evaluated safety standards that will not be harmful to patients, or knowledge that reduces risk for potential drug candidates. For example, a biomarker may provide an early indication that a drug candidate may cause liver damage, and not pursuing this drug candidate would reduce risk to potential patients.	<ul style="list-style-type: none"> ▪ Improves safety of the drug development process ▪ Product meets safety parameters specified in Target Product Profile (Safety)

* When an outcome only applies to PDPs and/or ETPs, that distinction is noted within the ‘construct’ column. Measures were quantified (or defined as categorical variables for) the subjective definitions.

System Outcome

System outcomes are difficult to measure, but are directly linked to the outputs and intervention outcomes of a partnership. System outcomes usually occur within 10-20 years of the partnership’s inception. While PDPs and ETPs share a goal of decreasing the cost of translations, PDPs and ETPs also have their own unique system outcomes, as described in Table 2.8. Similar to intervention outcomes, we associated value statements or directionality associated with many of these measures to indicate success.

Table 2.8. System Outcome for Public-Private Partnership Analytical Framework*

Construct (System Outcome)	Definition	Measure
Increased Number of Products (Product Development & Enabling Technologies)	Increased number of products refers to increasing the number of drugs that are successfully developed as well as increasing the number of promising leads and drug candidates. Increased therapeutic products refer to the development of more drugs that can successfully prevent or treat a disease.	<ul style="list-style-type: none"> ▪ # of products and tools created by partnership ▪ # of product development activities facilitated by the tool ▪ Increased number of therapeutics available to prevent or treat targeted disease.
Increased Capacity for Product Development (Enabling Technologies)	Increased capacity for product development refers to enabling the process of developing a drug.	<ul style="list-style-type: none"> ▪ Tool makes product development more certain ▪ Tool makes product development timeline shorter ▪ Tool makes regulatory approval more rapid
Decreased Cost of Translation	Decreased cost of translation refers to reducing financial burdens associated with drug development. For example, if an organization can more rapidly identify the most promising leads, then resources can be applied to more focused drug development rather than more diffuse funding of multiple leads.	<ul style="list-style-type: none"> ▪ Total cost of development of tool/Average cost of development of tool ▪ Cost of developing new therapeutics reduced by successful tool ▪ Reducing amount of money spent on failed compounds

* When an outcome only applies to PDPs and/or ETPs, that distinction is noted within the 'construct' column. Measures were quantified (or defined as categorical variables for) the subjective definitions.

Impact

Impact is the improvement of health outcomes for the intended population. In the case of ETPs, the impact is improved health resulting from a new tool that provides new pathways for more efficient development of drugs with improved efficacy, safety, cost and/or compliance that improve the health of the population.

The ultimate impact of a PDP is improved health from a new product. Impact is realized when the partnership develops and moves to market drugs with improved efficacy, safety, cost and/or compliance that improve the health of the population. For example, a decrease in global mortality attributed to the infectious disease targeted by the partnership as a result of a therapeutic(s) developed by the partnership would constitute a population-level impact. Improvement of health outcomes is the ultimate goal of partnerships. Relative impact will depend on whether the new therapeutic represents an incremental improvement on existing drugs or a breakthrough new therapeutic with a new mechanism of action resulting in substantial improvements in safety, efficacy, cost, or compliance.

Increasing Influence of External Factors: Facilitating Factors and Threats

The organizing constructs, described above in Section 2.2, were used to develop the measures for analyzing the activities and success of a public-private partnership. In addition, there were concepts outside of the scope of this analysis that could influence the success of partnerships, but are external factors that cannot be planned for in the partnership development process. Although a partnership may be engaging in “successful” inputs and activities, external factors known as threats may inhibit an otherwise successful partnership. Furthermore, a partnership may be supported by external factors known as facilitating factors, which improve the success of a partnership even when a partnership did not successfully execute all inputs, activities, and outputs.

These factors are indicated in the large upward arrow (in the analytical framework), indicating that movement from the foundational input level towards the outcome level lessens the control of the partnership over the influence of external factors that may impede or facilitate the success of the partnership. Impeding factors are labeled as threats. In the case of “threats,” a PDP may have secure funding, good partnership recruitment and retention, and an active research program; however, a shift in policy in the partnership’s host country may halt the partnership’s progress. Conversely, in the instance of “facilitating factors,” a partnership’s product may be endorsed by the World Health Organization or other influential body, and that endorsement may alter intervention outcomes such as the availability of a product.

2.5 Expert Roundtables

To gain additional insights into the critical factors for partnership formation and success, we convened three expert roundtables with a total of 27 participants representing 17 partnerships. Expert participants also included representatives from government, academia, pharma, and non-profit organizations. In addition to the experts, attendance at the roundtables was augmented with select representatives from ASPE, FDA, and RTI International.

RTI, in collaboration with ASPE, developed a list of prompts to analyze the gaps identified in the literature review process. The topics of the expert roundtables were guided by four broad categories:

1. Compare and contrast the partnership operational structure
2. Define key factors that contributed to a partnership’s success
3. Explore challenges for partnerships and methods to resolve these challenges
4. Discuss implications of market and health care trends on medical PDPs.

2.6 Final Analytical Framework and Complete Analysis

By aggregating information gleaned from each step in our analytical process, we were able to create a composite picture not only of trends, but also of themes that appear to correlate with the success of many partnerships. We describe the results from this process in Section 3 below.

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3. APPLICATION OF THE FRAMEWORK

We present findings in two sections:

1. The bottom portion of the analytical framework, addressing process findings.
2. The top portion of the framework, addressing outcome findings.

We derived these findings by analyzing data from 99 partnerships in the environmental scan and 84 partnerships in the literature review, and obtaining input in the expert roundtables which included 27 experts from 17 partnerships, academia, industry, and government agencies. After presenting these findings, we present factors for success seen in different partnership categories and considerations for future partnership development.

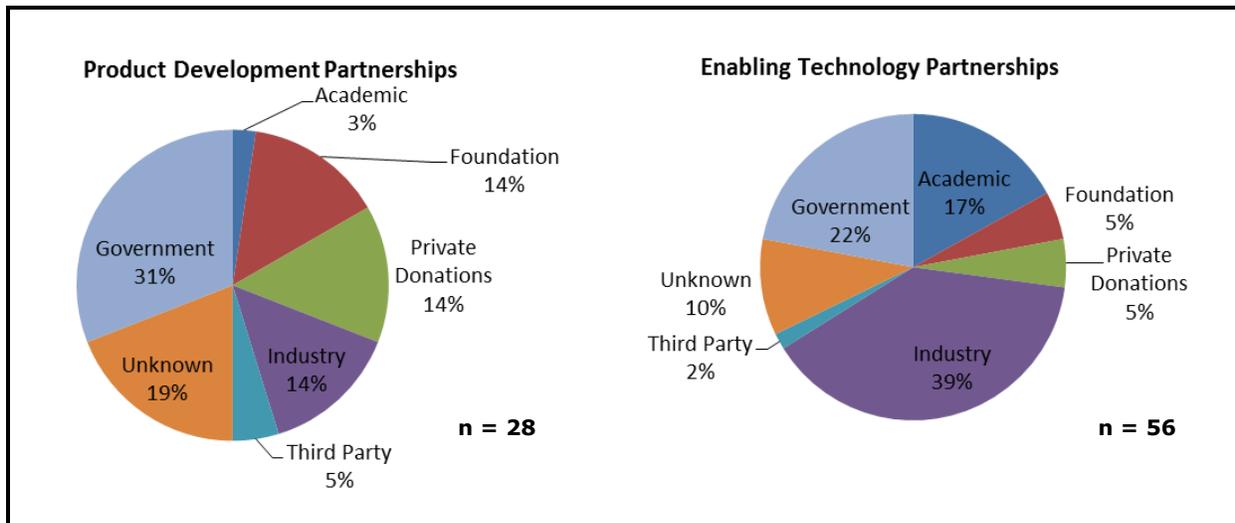
3.1 Summary of Process Findings

For this analysis, inputs, activities, and outputs are considered to be process measures. These process measures describe and document a PPP's activities and are generally used to assess whether those activities are conducted as planned and whether they reach their intended audience and goals (CDC, 1999).

3.1.1 Diverse and Sufficient Funds

Over 90% of partnerships reported on their funding sources, reflecting significant efforts to maintain financial transparency among most partnerships. Figure 3.1 explores the relationship between partnership objective (product development or enabling technology) and current sectors providing funding. Percentages indicate sector representation, not amount of funding by sector. Annual funding for PPPs comes from a variety of sources that include industry, foundations, academic institutions, government, third party, and private donors. As noted in Figure 3.1, the sources of funding vary widely between PDPs and ETPs. PDPs receive support from multiple government funding sources with additional supporters including foundations, industry, and private donations. Among the 56 enabling technology PPPs, the majority of funding sources come from industry, government, and academic contributions.

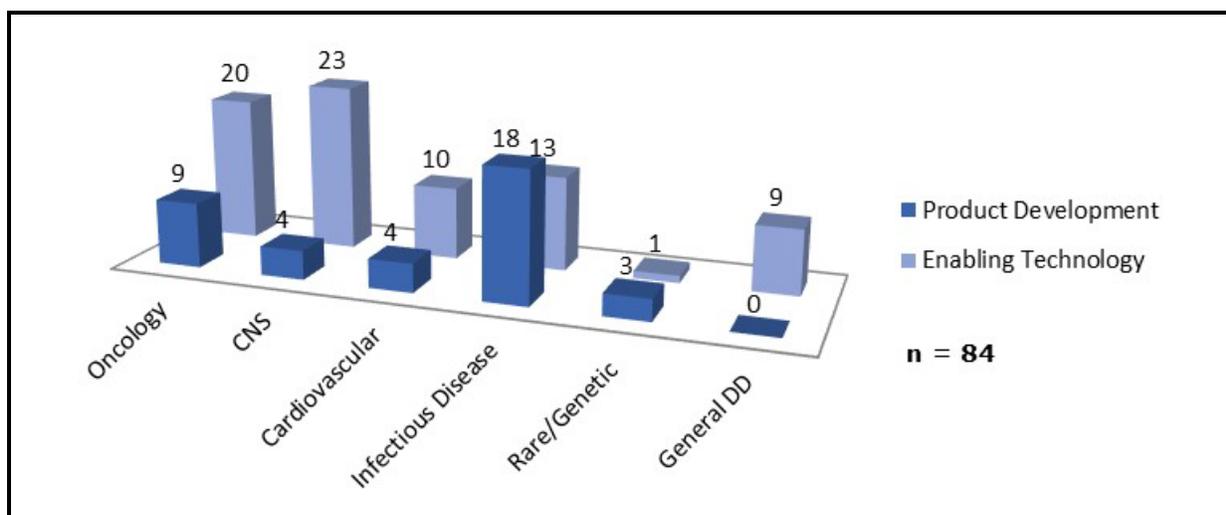
Figure 3.1. Funding Sources in PDPs and ETPs



3.1.2 Mission, Outcomes, and Objectives

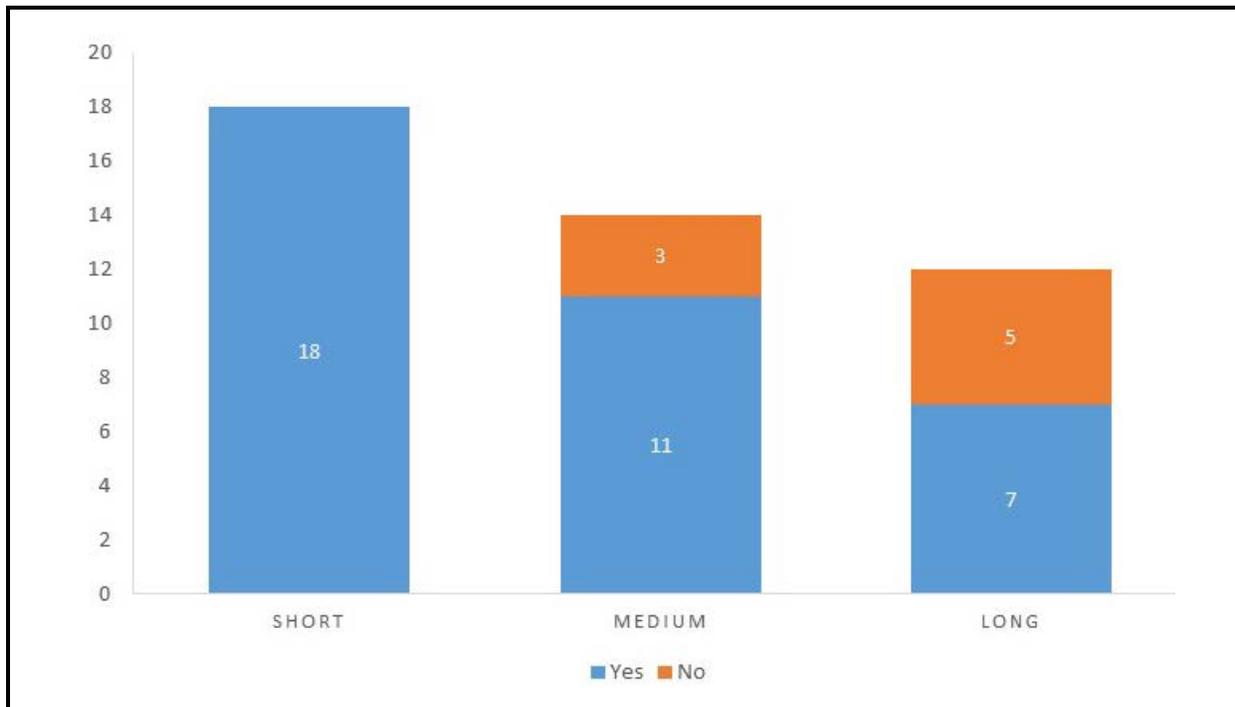
With the exception of one historical partnership that is now defunct, and thus has limited data available, all partnerships stated their missions, as well as their intended outcomes or objectives.

Figure 3.2 explores the relationship between partnership objective (product development or enabling technology) and therapeutic area (oncology, CNS, cardiovascular, infectious disease, rare/genetic disease, and general drug development). Partnerships may focus on more than one therapeutic area; thus the sum may appear to be greater than the 84 included in the literature review. As noted in Figure 3.2, infectious disease partnerships and rare and genetic disease partnerships are composed of more PDPs than ETPs. However, oncology, central nervous system (CNS), cardiovascular, and general drug development partnerships tended to be ETPs.

Figure 3.2. Partnership Objectives and Therapeutic Area

We were able to analyze the stated objectives of 28 partnerships to evaluate if they had achieved their stated objectives. Figure 3.3 examines trends in partnerships with stated objectives, their time frame, and achievement of these objectives. Both PDPs and ETPs can have short, mid, or long-term objectives. Short-term objectives are accomplishments such as publishing a journal article or organizing a forum or conference. Mid-term objectives are accomplishments such as developing a tool, recommendations, data sharing platform, or animal model, and an example of a long-term objective is developing a medical product. Of the 18 partnerships that had stated short-term (less than 2 years) objectives, all 18 had achieved those objectives (Figure 3.3). Of the 14 partnerships that had medium-term (2-5 year) objectives, 11 had achieved those objectives. Finally, of the 12 partnerships that stated long-term (greater than 5 years) objectives, 7 had achieved their goals. Partnerships may have more than one objective; thus the sum may appear to be greater than 28.

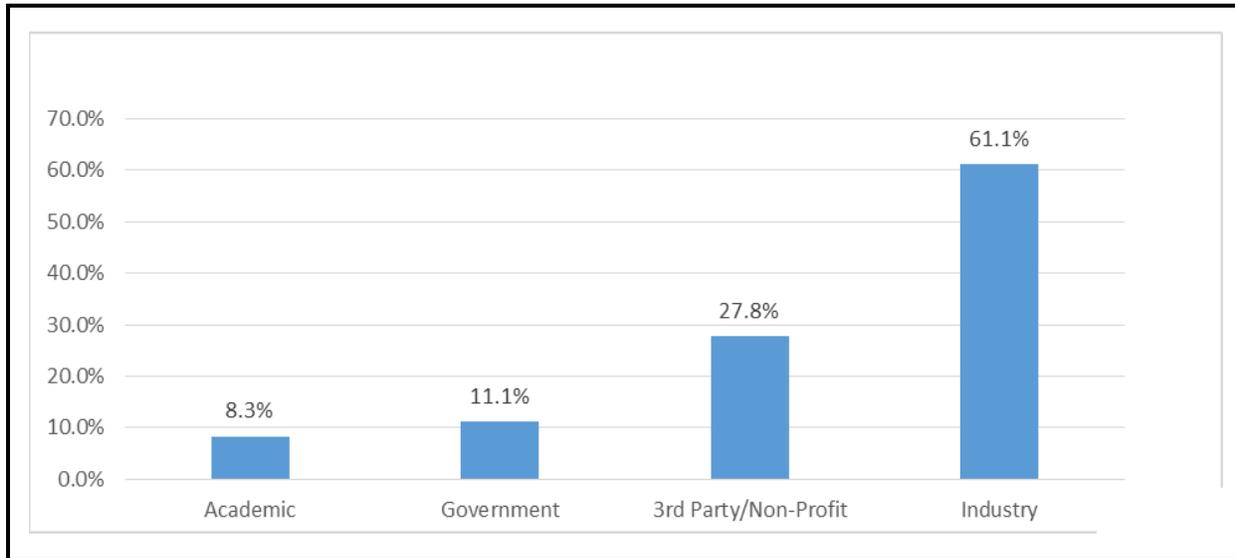
Figure 3.3 PPP Achievement of Objectives



3.1.3 Research Agenda

100% of PDPs clearly stated their research agendas in their program materials. For ETPs, 50 of 56 (89.3%) stated their research agenda. In most of these cases the absence of a stated agenda was due to the relatively young age of the ETP, and information available on these partnerships was limited to press releases or relatively new websites.

Another finding of interest concerns “who sets the research agenda.” While only 42% of partnerships published information about who is the driver of their partnership’s research agenda, the most common driver of the research agenda was the industry-based partner. Many partnerships’ agenda was set by more than one type of partner (e.g., academic, industry, government, or third party/non-profit). Figure 3.4 depicts these findings. Of note, these findings do not total 100% because the agenda of some partnerships was set by more than one type of partner. Of note, ETPs were far more likely to have their agenda defined by industry than PDPs.

Figure 3.4. Type of Partners Involved in Setting Research Agenda

3.1.4 Multi-sector Inclusion

The common sectors represented in the PPPs include academics, foundations, government, industry, and third parties. We defined third parties as non-profit organizations, non-government organizations, research institutions, hospitals, and other miscellaneous entities. Only three partnerships did not disclose the current members of their partnership. Figure 3.5 highlights the number of partners by sector across all of the partnerships in each of the two overarching categories of partnerships (product development and enabling technology). In PDPs as well as ETPs, the academic and industry sectors have the largest representation. In PDPs, third parties play a more active role alongside academic and industry partners.

Figure 3.5. PPP Members by Sector

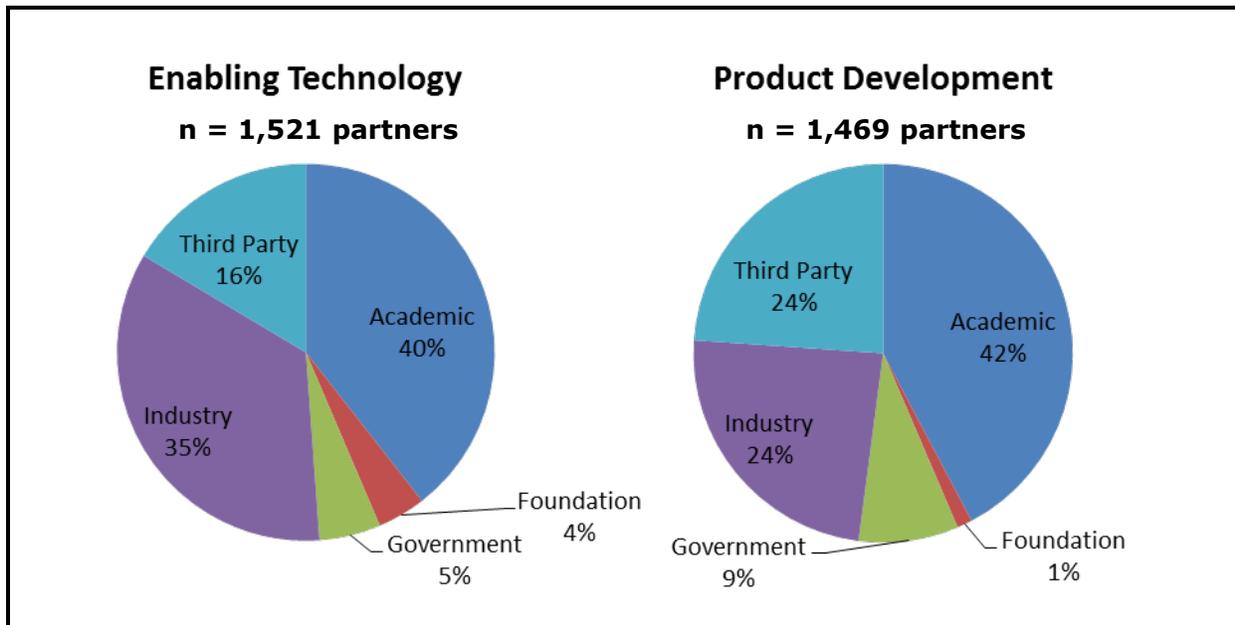
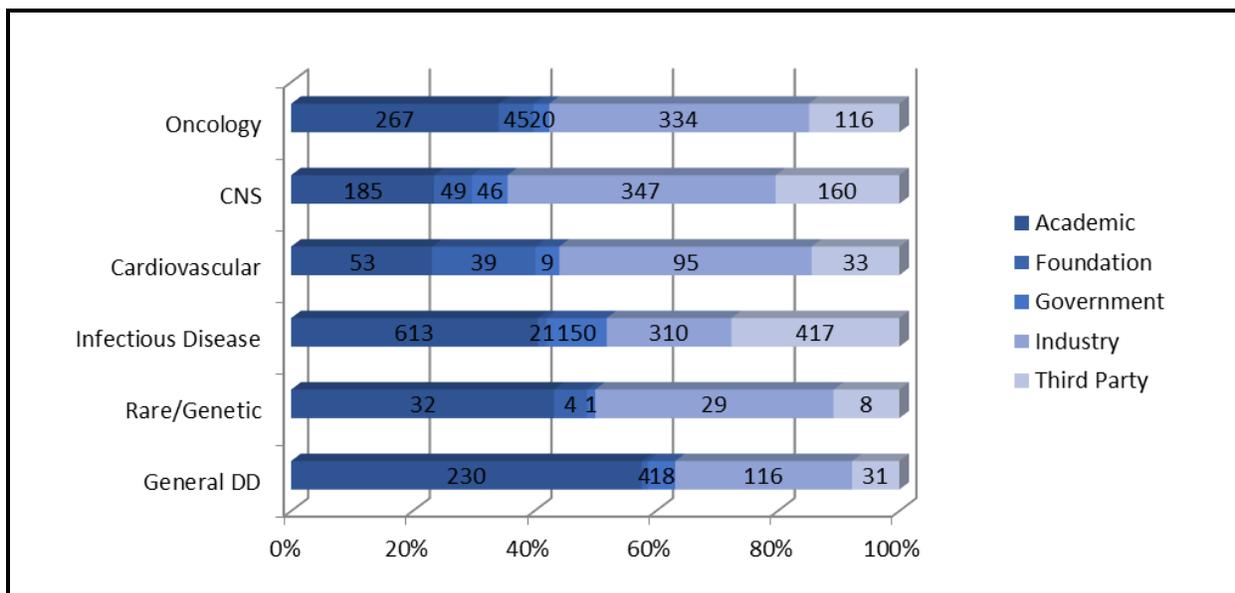


Figure 3.6 shows the partnership membership by sectors among all therapeutic areas. Within partnerships focused on oncology, CNS, cardiovascular disease, and rare/genetic disease, we see that industry is most highly represented. Among partnerships focused on infectious disease and general drug development, academics seem to play the most active role in partnerships. Government partners have a more limited involvement, except in infectious disease in which they comprise approximately 10% of partnership membership.

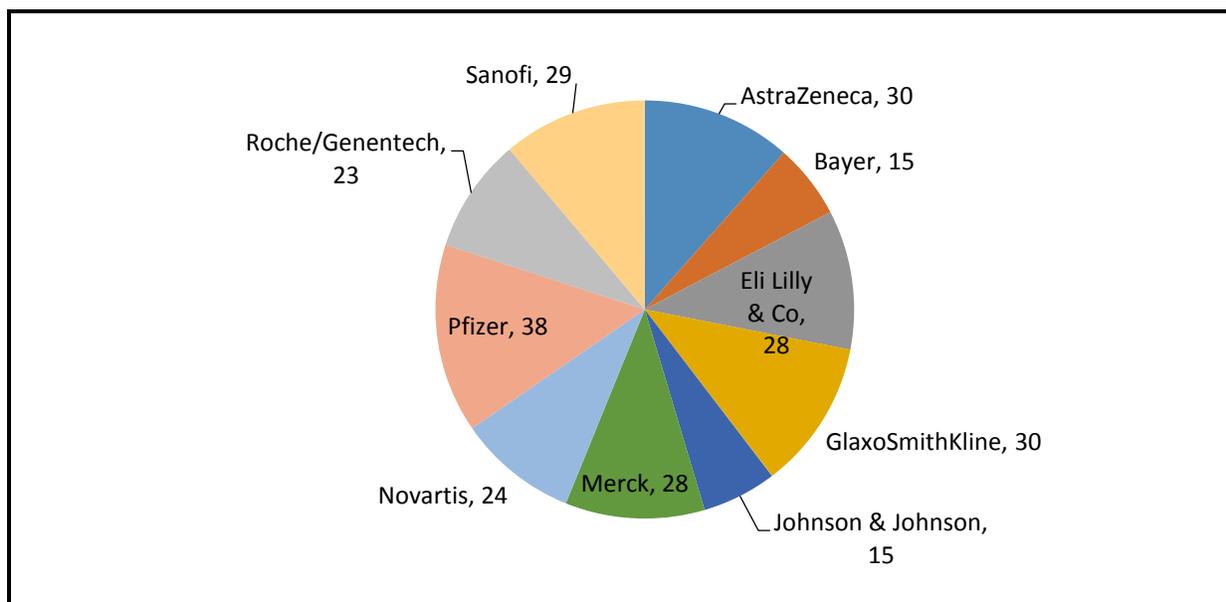
Figure 3.6. PPP Member Distribution by Therapeutic Area



Our analysis included a total of 881 reported industry partners. Many of these industry partners were in multiple partnerships. For example, AstraZeneca, GlaxoSmithKline, and Pfizer were in 30 or more partnerships.

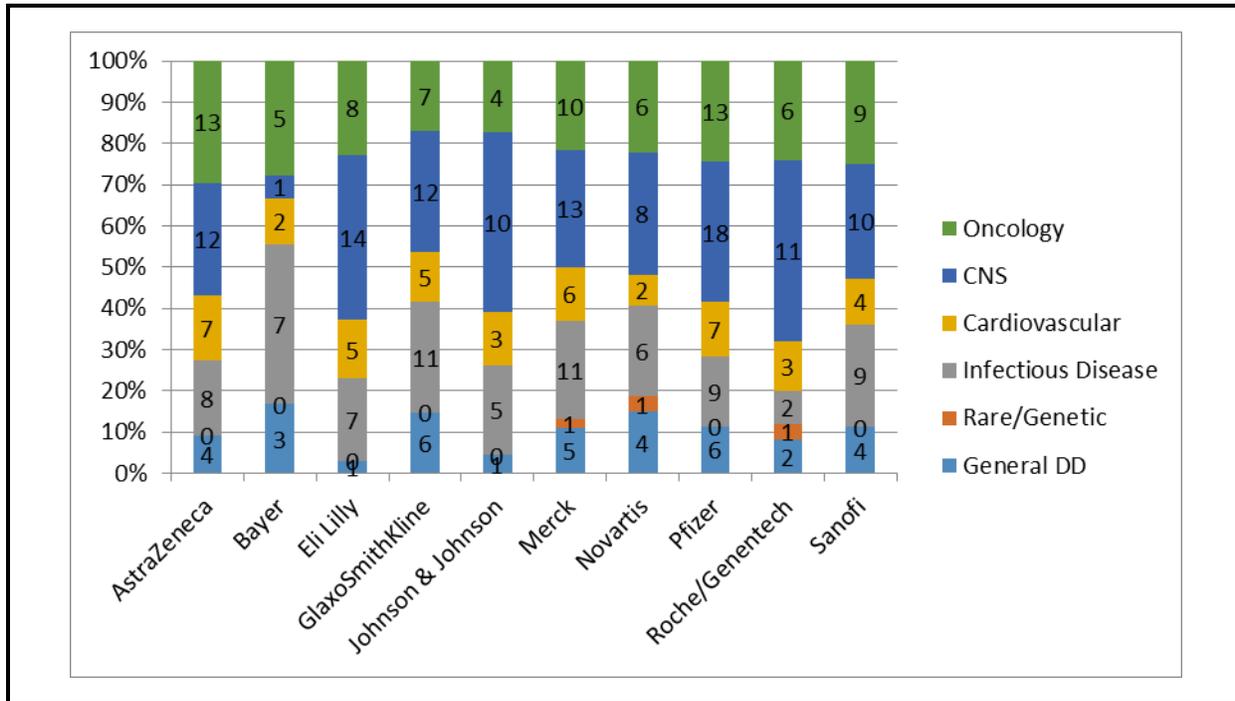
Figure 3.7 displays the ten most cited industry partners across all partnerships. The number by each industry name represents the total number of partnerships with whom they are involved. Each partnership may have multiple industry partners.

Figure 3.7. PPP Top Ten Industry Members



As of 2014, the top ten most cited industry partners were mostly involved in partnerships focused on oncology, CNS, and infectious disease. Figure 3.8 shows the involvement of the top ten industry partners across the six therapeutic areas (oncology, CNS, cardiovascular, infectious disease, rare/genetic disease, and general drug development). AstraZeneca was the most prominent industry partner focused on oncology. Eli Lilly was the most involved in partnerships focused on CNS. Bayer was the most cited industry partner in infectious disease partnerships. Roche/Genentech, Novartis, and Merck were the only industry partners among the top ten who were involved in partnerships focused on rare/genetic diseases. Finally, Novartis, Bayer, and GlaxoSmithKline were the industry partners who had the most involvement in partnerships focused on general drug development.

Figure 3.8. Top Ten Industry Partners across Therapeutic Areas



3.1.5 Staff

The majority of partnerships did not report the professional background of their founders and core team members. Of those that did report this information, MD and PhD were most often cited as the degree represented. During the virtual roundtables, experts spoke to the importance of having full time staff, especially with pharmaceutical industry experience, devoted to the partnerships.

3.1.6 Intellectual Property (IP) Policy

IP is a highly cited consideration of PPPs. We explored the IP of PPPs across categories of metrics that include: if IP has been generated, the form of IP agreements, the entity that retains IP, and other IP considerations.

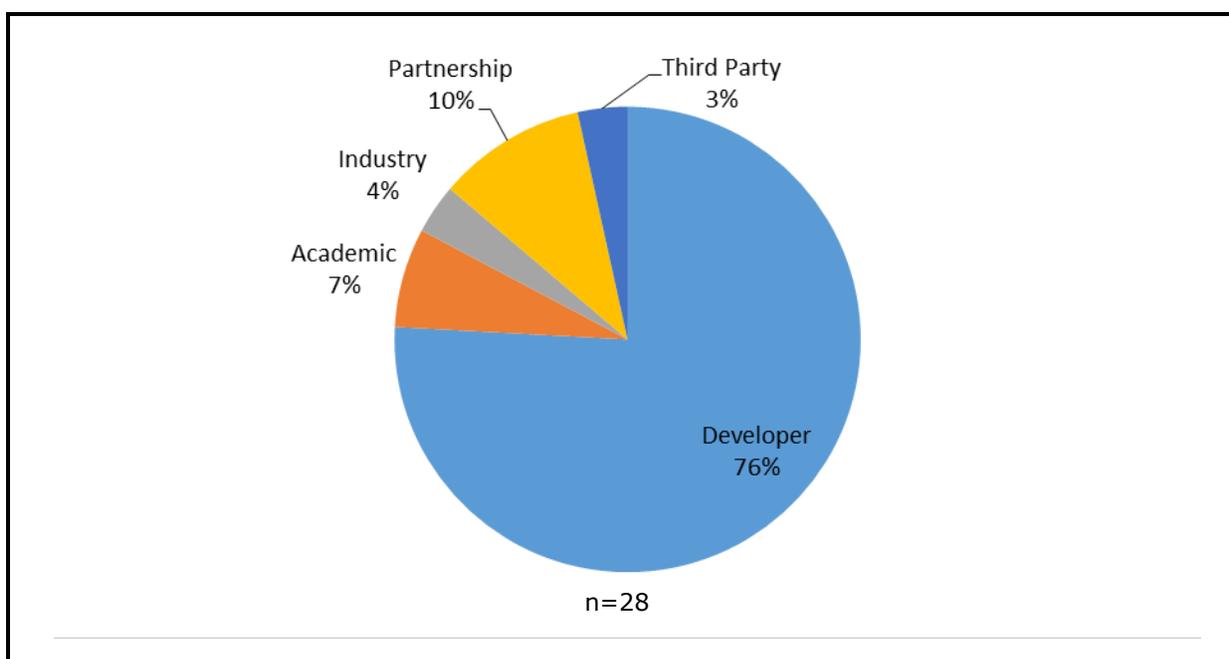
Only one-fourth of all PPPs referenced having generated IP. A little less than half (42%) of all PPPs referenced having some form of IP agreement, and the majority stated they had formal documents with IP agreement. Eighteen PPPs reported that their IP agreements have remained static throughout the partnership, while two PPPs stated that they renegotiated their IP agreements at least once during the partnership history.

In IP agreements, almost one-third of PPPs stated that there should be some form of reduced price for products developed and sold. Only five (~20%) of these partnerships

explicitly stated that the reduced price should be for partners only. Two PPPs stated that the reduced price should be for low income countries.

A total of 28 out of 84 PPPs provided information on their IP policy. Embedded within the 28 PPP IP agreements, we found that there were explicit instructions on who retained ownership of IP. Of note, the 15 PPPs in this group that were formed by IMI reported a similar IP structure, stating that in general the IP rights remain with the developer. Figure 3.9 highlights which sector retains rights to IP. Most partnerships state that IP follows the developer (who may be an academic, industry, or third party); however, some partnerships explicitly state that IP will always be retained by one sector, such as industry.

Figure 3.9. Retainer of IP in PPPs



3.1.7 Partner Accepted Memorandum of Understanding (MOU)

Slightly over half of partnerships made references to their Memorandum of Understanding (MOU), and among those, 14 partnerships described their MOU on their website or highlighted the collaborative process used to develop their MOU. Expert roundtable participants discussed the importance of the MOU, but also the struggle to keep the same early stakeholders involved throughout the MOU development process. Other experts highlighted the benefits of working with industry, government, academic or third party partners who have previously worked together, because they can start developing a new MOU from a pre-existing MOU.

3.1.8 Communication

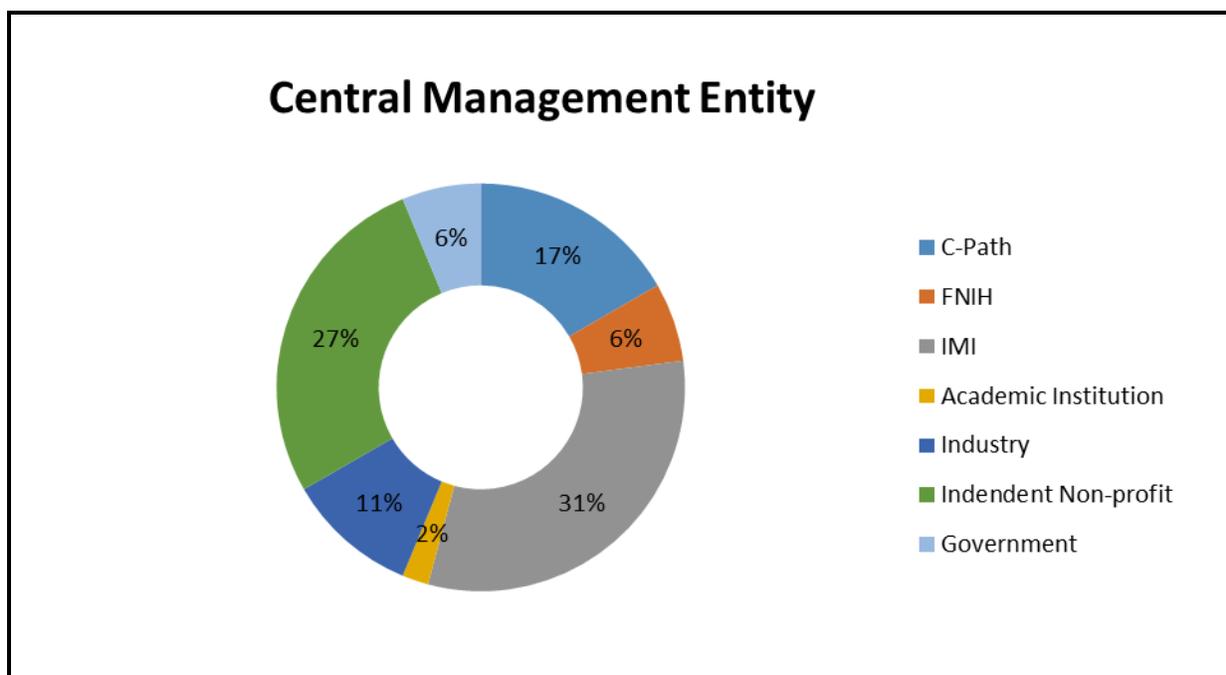
Few partnerships described their communication processes through their websites or literature sources. However, expert roundtable participants emphasized the importance of regular communication with partners. The experts also highlighted that having full time staff available to coordinate and streamline communications was critical to success, especially during the early partnership years and during key development times.

3.1.9 Oversight Bodies

Governance is crucial in understanding how a partnership coordinates and manages itself. We explored factors within governance including who are the responsible parties, whether there is an oversight body and if so who, type and number of governing bodies, and communication methods among governing bodies. As with constructs that relate to the composition of a PPP, not all PPPs have accessible information about their governing structure.

We found that many PPPs are formed as substructures of a greater organizational entity. Figure 3.10 examines trends of central management entities in PPPs. A total of 52 out of 84 PPPs are substructures of a central entity. Out of 84 partnerships, we found that 52 partnerships were housed under another entity such as C-Path, IMI, FNIH and other independent non-profits. For example, FNIH is the management entity for multiple biomarker consortia projects. We found that industry tends to not house PPPs, although they serve as critical members of these PPPs.

Over two-thirds of all PPPs report having a formal governing board(s) to provide leadership and direction. These boards include boards of directors, executive boards, advisory boards, steering committees, ethics committees, and IP committees that are often made up of a representative sample of their partners. The most cited governing bodies are advisory boards (50% of all PPPs) and boards of directors (46% of all PPPs).

Figure 3.10. Central Management Entity of PPPs

3.1.10 Conduct Research for Product Development (PDPs)

In order to develop products effectively, PPPs often engage in planning activities to appropriately position the partnership to carry out their intended work. Among PDPs, over 75% of PPPs stated that they had created a development plan with activities, timelines, and budgets to carry out the work of the partnership. Further, approximately one-third of all PDPs developed specific milestones and process objectives to assess their progress. Approximately 20% of these partnerships already engaged in conversations with regulatory bodies to ensure they have a plan for the appropriate approval pathway. Another 20% of partnerships have a feedback plan established for project reviews. The experts confirmed that setting milestones early is important for guiding the direction of the partnership and communicating expectations to partners. Further, they suggested that developing an incremental set of milestones with early successes helps establish internal and external credibility of the partnership.

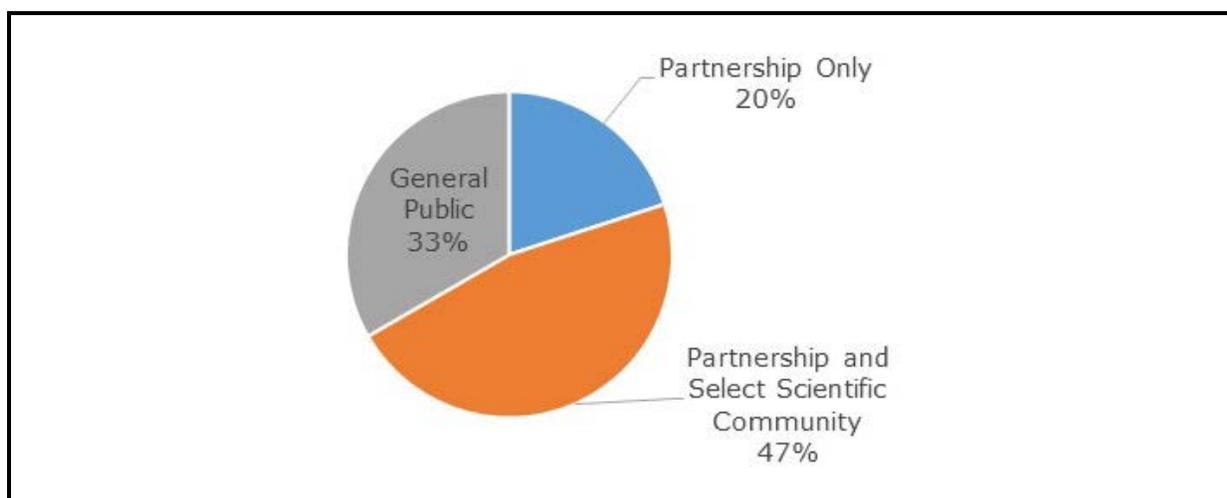
3.1.11 Develop and Assess Tools (ETPs)

To effectively develop tools, ETPs may engage in planning activities to appropriately position the partnership to carry out their intended work. Approximately half of these partnerships report developing a comprehensive development plan to create their intended tool. Of these PPPs, approximately one-third clearly stated the role of each partner in creating the intended technology.

3.1.12 Open Sharing of Findings (ETPs)

Many partnerships seek to develop internal mechanisms to facilitate the sharing of data, especially ETPs as they are precompetitive in nature. Approximately half of partnerships report having an internal portal for them to communicate and share data. PPPs vary in the intended audience for the information and tools generated by their partnership. Approximately 60% of PPPs identified the intended audience of their partnership (see Figure 3.11). Only 20% of partnerships intend to keep their findings internally, while the rest intend to share their data with either some specific scientific community or the general public.

Figure 3.11 Audience for Partnership Data



3.1.13 Internal Knowledge Sharing

We assessed the mechanism by which PPPs share the knowledge they have generated through their work. Over 75% of partnerships support publishing their findings in presentations and/or publications. Over 65% of partnerships have scheduled stakeholder meetings, often annually, to disseminate their findings. Further, over 75% of partnerships actively update their websites indicating progress they are making toward their goal(s).

3.1.14 Partner Recruitment and Retention

Approximately half of PPPs report that their founding partnership members are still active members of their partnership, highlighting the importance of ensuring all strategic partners are involved with the formation of a partnership. The experts in the virtual roundtables stated a strategy to retain partners was to ensure that they had upper management buy-in from each partnering organization. They found that if they had upper management support from each partnering organization from the onset, then the organization would continue to prioritize their involvement in the partnership over time. Further, many experts stated that

engaging pharmaceutical industry partners in the formation of their partnership was critical to success, as they are important sources of funding and can be key partners in the clinical trial phases of product development.

3.1.15 Active Partner Participation

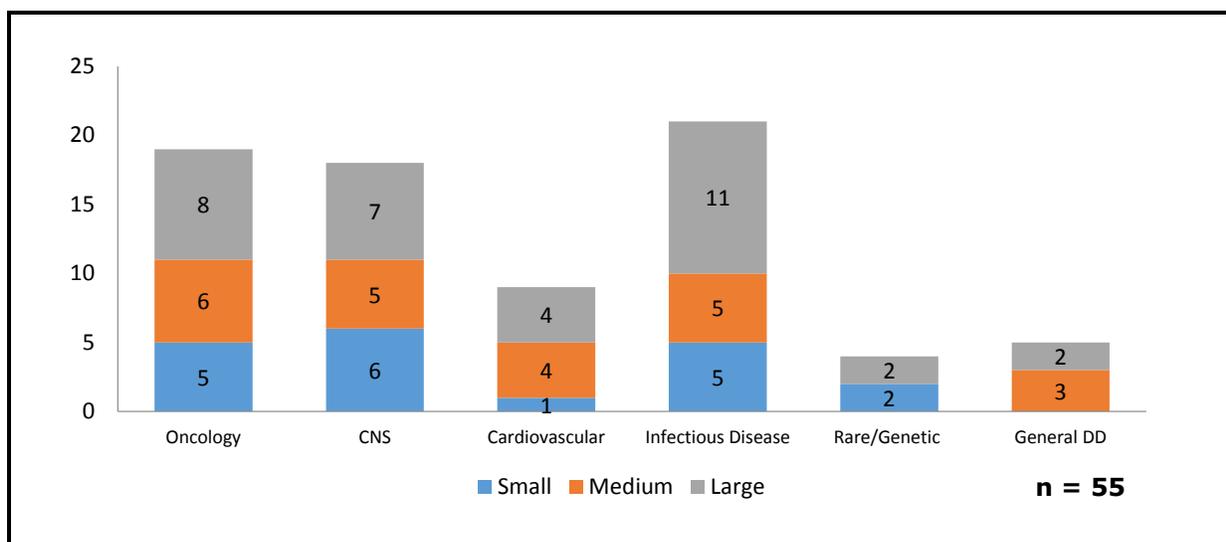
PPPs implement various strategies to ensure their partners stay engaged in their partnerships mission over time. Over 60% of partnerships state that their partners support the PPP through financial and/or in-kind contributions. This strategy is used by many PDPs and ETPs to keep partners actively involved in the work of the partnership. Further, about half of PPPs report that their partners participate in stakeholder meetings. Finally, experts in the virtual roundtables found that frequent (monthly or quarterly meetings most often cited) partnership meetings scheduled in advance were crucial for consistent communication and maintaining timelines.

3.1.16 Secure Funding

In terms of financing, we categorized the partnerships as small (less than \$5 million per year), medium (between \$5 and \$10 million per year), and large (greater than \$10 million per year). There is a relatively even split among the PPPs, with 17 categorized as small, 19 as medium, and 18 as large (30 partnerships did not report current financial arrangements). Figure 3.12 shows the distribution of annual budget ranges by therapeutic area. Interestingly, among the ETPs who successfully developed tools, their budgets ranged from “small” to “large;” however, no PDPs have successfully developed a product without a “large” budget, unless their goal was repurposing existing drugs.

Of the partnerships that reported having grown financially since their inception, the majority (75%) have secured at least three consistent donors to fund their work. Experts from the virtual roundtable stated that securing funding was an activity in their partnership that required consistent attention and was one of the greatest challenges identified.

Figure 3.12. Distribution of Annual Funding Levels across Therapeutic Areas



3.1.17 Staff Hiring and Training

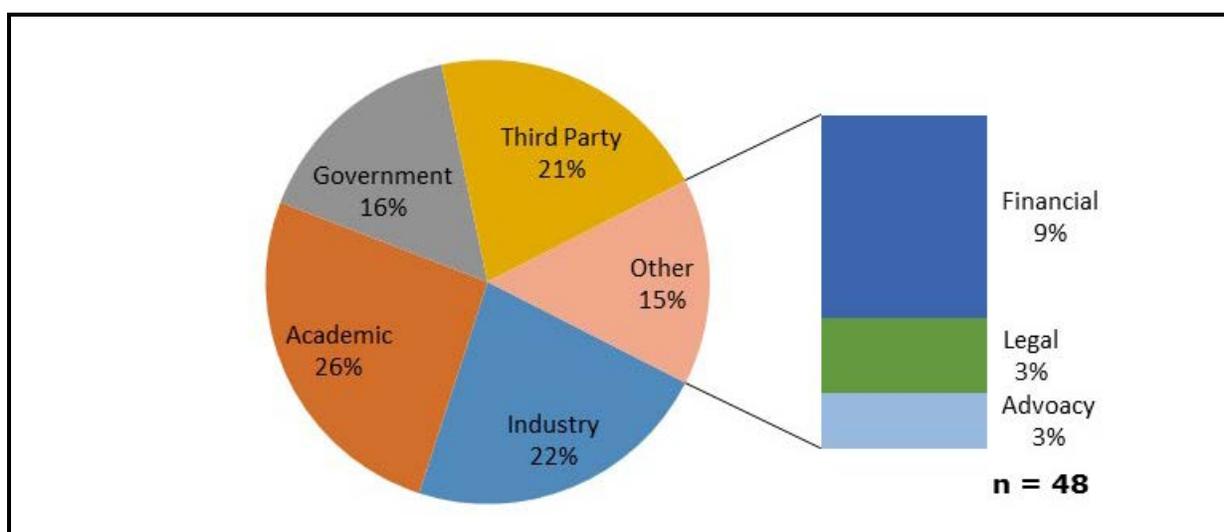
The majority of partnerships did not report their process for recruiting, hiring, and training staff members. Some partnerships include in their goals ideal staff whom they would like to hire in the future. During the virtual roundtables, experts spoke to the importance of having some full time staff devoted to the partnerships, especially staff with pharmaceutical industry experience. IMI has each partnership led by one pharmaceutical industry partner and one academic and/or third party partner. This cross-sector staffing allows for shared responsibility and organizational buy-in from the partners.

3.1.18 Internal and External Oversight

We examined the type of oversight exercised by governing boards in PDPs and ETPs. Approximately half of all PPPs reported the sectors represented in their governing bodies. These sectors included industry, academic, government, foundation, third party, financial, legal, and advocates. Academics, industry, and third parties are the sectors most often represented in governing bodies, as illustrated in Figure 3.13.

Figure 3.13 examines trends of sectors that are represented in PPP governing bodies. A total of 48 out of 84 PPPs report the composition of their governing body. Data represent overarching sectors represented, not the count from each sector.

Both PDPs and ETPs had an average of three governing bodies. These governing bodies were most often comprised of an executive board, a scientific advisory board, and a steering committee. Few partnerships disclosed the agenda items and the meeting schedule of these governing boards, thus it was difficult to analyze the effectiveness of the activities of these bodies.

Figure 3.13. Composition of Governing Bodies

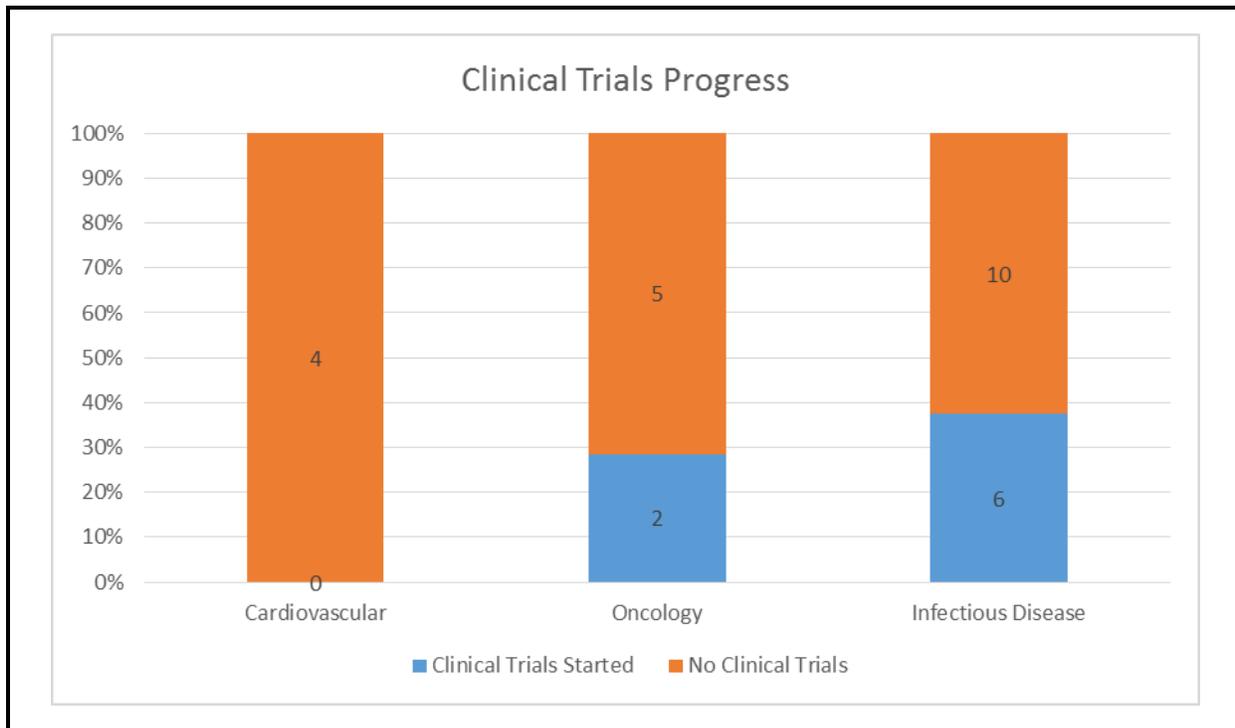
3.1.19 Partnership-Oriented Negotiations

The role partners play in the development of partnership policies and decision-making varies across PPPs. Approximately one-third of PPPs report having most, if not all, partners represented in their decision-making process. Almost 20% of partnerships in our analysis stated explicitly that they consulted with all partners while developing their IP policy. Experts stated that setting up initial IP, data-sharing, MOUs, and other forms of agreement at the inception of the partnership with all partners is important for minimizing challenges in the future. In addition, some experts suggested revisiting these policies at specified time periods to ensure that the policies are still relevant and agreeable to all partners.

3.1.20 Full Pipeline (PDPs)

Of the 23 PDPs across cardiovascular, oncology, and infectious disease therapeutic areas, approximately one-third have started clinical trials (see Figure 3.14). Half of those that have started clinical trials have successfully moved at least one drug to market. With the exception of one partnership, all PPPs that have begun clinical trials have existed for at least 8 years and have primarily focused on neglected infectious diseases such as malaria, tuberculosis, and HIV. Partnerships that were founded less than 8 years ago tend to still be in the partnership formation, drug discovery, and pre-clinical phases.

Figure 3.14. Clinical Trial Progress for PDPs



3.1.21 Validated Tool(s) (ETPs)

Approximately one-third of ETPs have completed at least one of their intended tools. On average, the partnerships that have completed tools have existed for less than 8 years. More than 75% of the tools developed were for oncology and cardiovascular disease partnerships, highlighting the trend of cardiovascular and oncology partnerships focused primarily on ETPs.

3.1.22 Partnership Reputation

We tracked the publication record of each PPP in this analysis. The average partnership has published at least 20 peer-reviewed journal articles and has been cited at least 200 times by others. Nearly half of partnerships have had third parties publish on their promised and/or proven partnership model.

3.1.23 Partner Buy-in and Engagement

To assess partnership buy-in and engagement, we assessed shared roles of partners in presentations and publications, industry representation on governing boards, and partners’ financial and in-kind investment in the partnership. Approximately half of partnerships have publications with authorship shared among multiple partners. Experts in the virtual roundtables noted that establishing clear expectations and guidelines for publications was

vital for partnership cohesion. Among PDPs and ETPs, approximately half report having pharmaceutical industry representation on their governing boards, most with at least 25% of their board comprised of pharmaceutical industry representation. Over 60% of partnerships state that their partners support the PPP through financial and/or in-kind contributions.

3.1.24 Partnership Sustainability

To examine a partnership's ability to sustain their work, we looked at a partnership across several metrics to include sufficient funding to achieve current objectives, financial growth over time, leadership tenure, and commitment of partners to continual collaboration. Of the 16 partnerships with public financial records available over time, 75% had enough funds to cover their annual expenses. Of note, those with this sufficient funding had an average of eight funding sources supporting their partnership. An additional 16 partnerships reported that they had on average 65% of their original leadership staff still employed. Approximately half of partners had public documents highlighting the roles their partners had committed to play over time to fulfill the partnership goals.

3.1.25 Partnership Agreement on IP Strategy

We investigated the extent to which all partners express equitability and agreement with the partnership IP policy; however, few partnerships disclosed who was involved with developing their IP policy. The virtual roundtable experts agreed that mutual agreement on IP strategy was critical for a partnership's success.

3.2 Summary of Outcome Findings

For this analysis, we considered outcome measures to be intervention outcomes, system outcomes, and impacts; see in Figure 3.15. These outcomes measures describe the extent to which a PPP is achieving its goals and outcomes. Achievement of these outcomes generally reflects whether the partnership activities are being successfully implemented (CDC, 1999). The outcome measures are outlined in the top portion of the analytical framework, which denotes measures shared by both PDPs and ETPs as blue, measures for PDPs only in green, and measures for ETPs only in orange.

Figure 3.15. Outcome Measures for Analyzing Public Private Partnerships



Blue boxes indicate measures that are shared by PDPs and ETPs, orange boxes are unique to ETPs, and green boxes are unique to PDPs.

3.2.1 Intervention Outcomes

Ultimately, the outcome most important to partnerships is to increase the number of tools that support developing new therapeutics, or to develop new therapeutics that improve human health. These outcomes include:

- Effective Product:** Of the PDPs analyzed, six partnerships have successfully marketed a new therapeutic drug. For a new therapeutic to be marketed to the public, its efficacy must at minimum demonstrate its non-inferiority to the current standards of care. Some partnerships, such as Cures Within Reach, specifically focus on repurposing therapeutics that have otherwise been proven safe and efficacious for other medical conditions. In this case, their goal is to find therapeutics that are efficacious for additional medical conditions. By repurposing these drugs, Cures Within Reach is offering a creative solution to aid those with rare diseases that might otherwise not be fully researched.
- Adoption of Tool(s):** The World Intellectual Property Organization (WIPO) is a widely used resource for other public-private partnerships (WIPO, 2014). WIPO provides support and templates for IP agreements for dozens of partnerships. By providing access to previously accepted IP agreements, WIPO helps partnerships fast track the process of building their IP agreements.
- Regulatory Approval:** The evidence of new therapeutics again notes that several therapeutic drugs have been approved by regulatory agencies. However, very few partnerships highlighted their regulatory process or successes. Interestingly, every partnership that publicly discussed its regulatory processes was focused on therapeutics to treat infectious diseases.

- **Usable:** Very few partnerships disclosed their efforts to make a therapeutic more usable. Of those that did, information was usually found by comparing their target product profile with their new therapeutic(s).
- **Available:** Of the oncology, cardiovascular, and infectious disease partnerships, four partnerships have successfully taken a therapeutic to market. Three of these were infectious diseases partnerships, and one partnership was focused on repurposing drugs. Even though only four partnerships have produced new therapeutics, a total of 21 new therapeutics are now on the market due to these four partnerships.
- **De-risking:** By combining resources, PPPs work to de-risk product development by sharing the risk burden across many partners. In the IMI model, finances are usually combined from both industry and government sources, and academic institutions donate in-kind services to the partnership (IMI, 2010).
- **Scientific Knowledge:** Whether by creating biologic specimen banks, creating an innovative model to test the safety of new therapeutics, or developing a new therapeutic, PPPs are collectively and individually deepening our understanding of the drug development process. Hundreds of journal articles, conferences and press releases attest to the wealth of knowledge brought before the scientific community through PPPs.
- **Efficiency:** One example of improved efficiency is seen in the work of the Global Alliance for TB Drug Development (TB Alliance). One of their drug compounds, pretomanid, formally known as PA-824, is entering a Phase 3 trial to evaluate if pretomanid (in combination with moxifloxacin and pyrazinamide) can reduce the treatment duration of active TB and improve treatment outcomes for multi-drug resistant tuberculosis (Dawson & Diacon, 2013). Their model for reducing treatment duration and/or treating drug resistant strains could become increasingly important as more anti-infectives become less effective against drug resistant strains.
- **Quality:** The Top Institute (TI pharma) has developed several tools that improve the quality of diagnostics. For example, MammaPrint is a breast tumor typing tool that helps to predict remission (or metastasis) in the first 5 years after treatment, thus informing chemotherapy decisions (Mook, 2011). This tool could significantly improve decisions on which chemotherapy is most appropriate for patients.
- **Speed:** By expanding funding, access to facilities and expertise, PPPs can accelerate the development of a therapeutic or precompetitive tool. For example, The FNIH Biomarkers Consortium completed the Adiponectin project, which developed a tool that used adiponectin to predict HbA1c response in patients with type 2 diabetes, in 2 years (Wagner, 2015; the Biomarkers Safety Consortium 2015).
- **Safety:** By combining clinical trial experience and data, PPPs can improve safety in drug development. The Cardiac Safety Research Consortium is a PPP that specifically focuses on advancing cardiac safety knowledge for new and existing therapeutics. Improvements in safety are critical to the advancement of new therapeutics (Cardiac Safety Research Consortium (2015).

3.2.2 System Outcomes

The system outcomes we examined are increased capacity for product development, increased number of products, and decreased cost of translation. While there is early

evidence that these system outcomes are being achieved (for example, dozens of new tools and 21 new therapeutics have been developed), partnerships in general have not yet asserted that they have directly reduced the cost of drug development. Initiatives by the C-Path hold promise for developing efficiencies in medical product development.

3.2.3 Impact Outcome

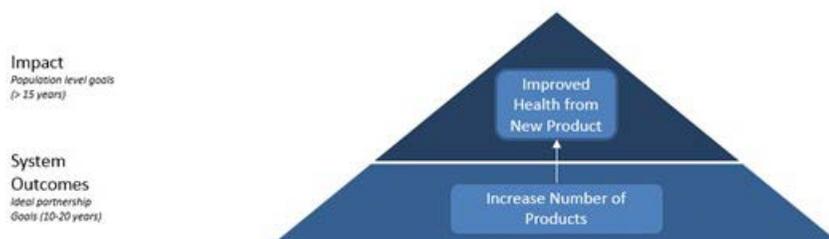
To the extent that patients realize benefits from a new therapeutic treatment or prevention, one can assume that the health of the affected population is improving with the support of new products and findings from PPPs. For example, over 300 million people in malaria endemic areas have received one of the anti-malaria therapeutics developed by Medicines for Malaria Ventures (MMV).

3.3 Precursors to Success

The ultimate success of all product development and enabling technologies PPPs is to improve the health of a population through the development of new tools and products. It often takes PPPs more than 15 years to assess whether they have improved the health of a population, thus making it difficult to evaluate their ultimate success. Therefore, the analytical framework allows us to examine pathways from activities, to outputs, to intervention outcomes, and to system outcomes that would logically lead to the ultimate impact of improved health. Assessing a partnership's accomplishments along this pathway allows for an intermediary evaluation of a PPP's success. Of note, inputs are generally not evaluated but are acknowledged as necessary resources to conduct partnership activities. In this section we describe the relationships between the levels of the analytical framework, working through the levels in pairs.

3.3.1 Success Pathway for Product Development Partnerships

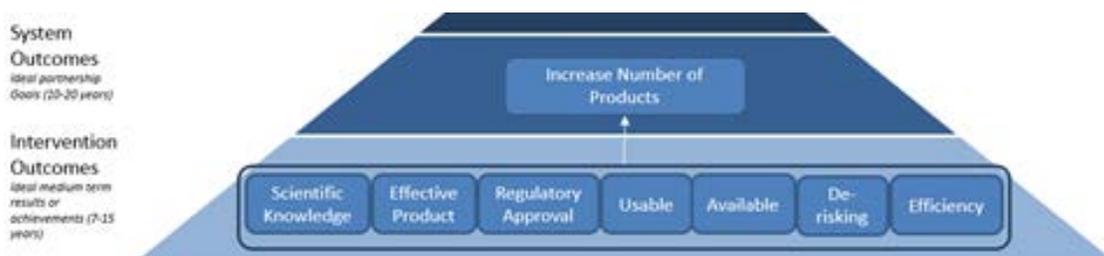
System Outcomes → *Impact*



The logical pathway to a PDP's desired impact (improved health from a new product) would involve an increase in the number of products on the market for the affected population. For example, DNDi developed Nifurtimox-Eflornithine Combination Therapy (NECT), the first drug developed in over 25 years, to treat human African Trypanosomiasis (HAT). Since its

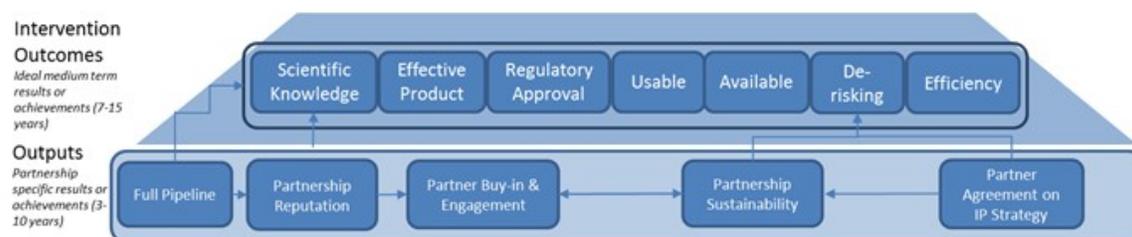
development, the WHO has added NECT to their Model List of Essential Medicines, and it has been made available in 13 African countries. The Democratic Republic of Congo has attributed improved health in their population from NECT as it accounts for over 90% of the prescribed treatment for HAT.

Intervention Outcomes → System Outcomes



System outcomes are facilitated by the achievement of intervention outcomes, which are generally achieved at least 7 years after a partnership's inception. Products are more likely to be developed and used if the expertise of multiple partners, such as academics and pharmaceutical partners, goes into the design and cost is shared across the partnership (de-risking). Further, improved scientific knowledge allows a deeper understanding of the disease course and may illuminate which compounds are more likely to succeed in clinical trials. A product will likely only be used if it achieves an improvement in efficiency, effectiveness, and or ease of use. Moreover, a drug will likely only be used if it has received regulatory approval and is available in the countries of interest. For example, NECT, developed by DNDi, was as effective as other treatments for human African Trypanosomiasis (HAT). However, NECT was easier to administer, safer, and more cost effective, making it a preferable drug. Likely due to the inclusion of NECT on WHO's Essential Medicines List, African countries were more likely to adopt NECT as a standard of protocol for the treatment of HAT, thus ensuring it was widely available in the country.

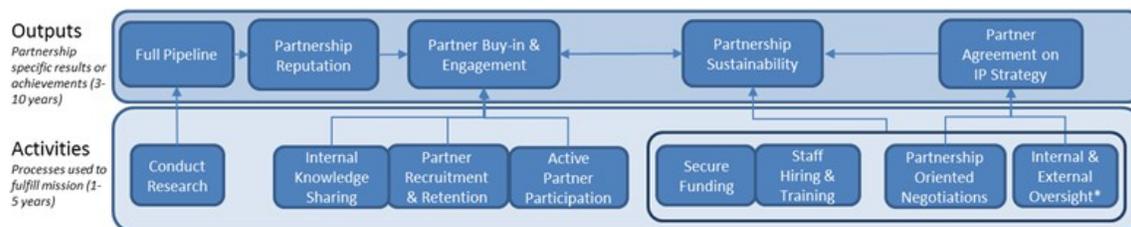
Outputs → Intervention Outcomes



The completion of outputs facilitates the pathway to intervention outcomes for PDPs. Logically, a full pipeline would produce drug candidates that would receive regulatory approval and would fulfill intervention outcomes such as a more effective or efficient drug. Further, the publishing of the development and clinical trials (partnership reputation) of a drug candidate improves the scientific literature base (scientific knowledge) and may

improve the identification of future drug candidates. The output of partnership sustainability leads to the de-risking of a product, since a partnership with a strong financial, in-kind, and committed base of partners ensures the cost and project oversight are shared among multiple partners. For example, MMV currently has approximately 17 funders, with funding pledged through 2017, thus enabling them to have sustainable financial backing to continue clinical trials and move products to approval and adoption.

Activities → Outputs



Outputs are a result of the completion of activities presented in the Analytical Framework. We describe outputs and associated activities that facilitate achievement of those outputs below. In order to achieve a full pipeline, PDPs often engage in developing an extensive project plan with clear objectives, milestones and defined roles for each partner, begin discussions with regulatory bodies, and establish a process for identifying and selecting contract research organizations (conduct research). To establish the output of partnership reputation, PDPs will publish articles, present abstracts, speak at events with stakeholders, and engage in other dissemination activities. Improving a partnership reputation also paves the way for the output of partnership buy-in and engagement in the PDP. Further, PDPs who facilitate platforms to share internal knowledge help partners to stay informed, thus preventing partner disengagement. In addition, PDPs who provide avenues for partners to stay active and engaged, such as presenting at stakeholder forums or leading a working group, can be expected to have higher partner retention rates.

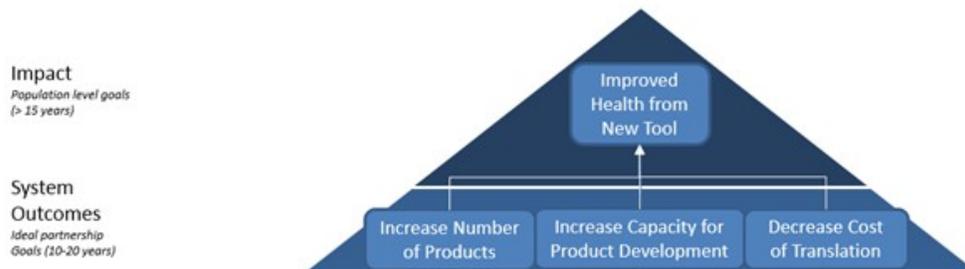
The output of partnership sustainability has a reciprocal relationship with partner buy-in and engagement, as a partnership is more sustainable if it has a strong base of active partners and partners will likely stay engaged if the partnership has a sustainable base. The activities of staff hiring and training and secure funding feed into partnership sustainability by ensuring an adequate financial base and team of staff to accomplish the partnership’s objectives. Finally, the partnership agreement on IP strategy facilitates partnership cohesion that allows for a sustainable relationship among partners.

Finally, the output of partner agreement on IP strategy is facilitated through the activities of partnership-oriented negotiations and oversight. Incorporating partners in decision-making processes and oversight bodies enables them to be engaged when partnership agreements, such as IP, are formed. Having partner buy-in at these levels can provide an avenue for

partners to compromise on IP policy, thus reducing the likelihood of disagreements once IP is developed. For instance, IMI’s ND4BB-ENABLE partners decided in the beginning to establish an IP policy in which the royalties would remain with the generator; however, any partner that improves upon it would also receive some compensation. Partners from this partnership have stated that this model of IP agreements has allowed for greater partner cohesion and collaboration.

3.3.2 Success Pathway for Enabling Technology Partnerships

System Outcomes → Impact



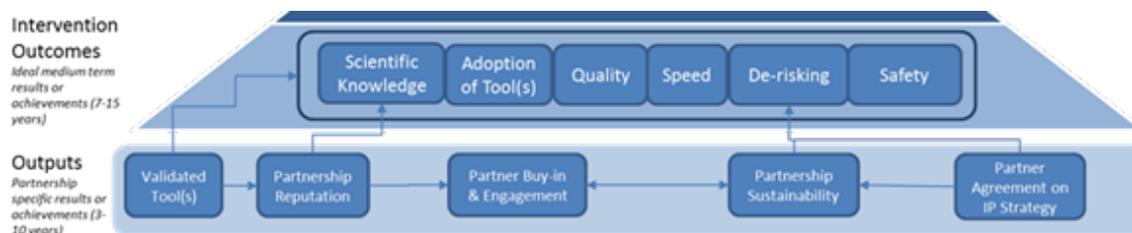
The logical pathway to an ETP’s desired impact (improved health from a new tool) would involve the combination of the system outcomes (increased number of products, increased capacity for product development, and decreased cost of translation). Increased number of products may be achieved through the development of tool(s) which then, in turn, facilitate product development activities. These tools may increase the capacity of product development by making product development more certain, improving timelines, and making regulatory approval more rapid. Further, increasing the efficiency and effectiveness of product development may decrease the overall cost of translation. For example, the development of novel biomarkers by the FNIH Biomarkers Consortium has increased the capacity of the I-SPY 2 breast cancer clinical trial to develop cancer treatments faster and at a reduced cost. Since these system outcomes often take at least 10 years to achieve, most PPPs in this analysis have yet to achieve them, as 90% of ETPs are less than 10 years old.

Intervention Outcomes → System Outcomes



System outcomes are facilitated by the achievement of intervention outcomes, which are generally achieved at least 7 years after a partnership's inception. Tools are more likely to be developed and used if multiple partners' expertise goes into the design and cost is shared across the partnership (de-risking). To be used in product development activities, tools need to (1) be sensitive and/or specific (quality), (2) be known by a variety of players (adopted), (3) improve safety of drug development process (safety), and (4) be developed in a timely manner (speed). Further, improved scientific knowledge allows a deeper understanding of the disease course and may illuminate which compounds are more likely to succeed in clinical trials. An example of an ETP achieving intervention-level outcomes is the Cancer Research Institute's Cancer Immunotherapy in partnership with the Association for Cancer Immunotherapy, and Stanford University, who developed the Minimal Information About T cell Assays (MIATA) project. The MIATA tool seeks to improve cancer immunotherapy development (a system outcome) through making data interpretation and comparison of t-cells clearer by the development of a set of uniform set parameters to examine T cell assays.

Outputs → Intervention Outcomes



The completion of outputs facilitates the pathway to intervention outcomes for an ETP. Logically, the completion of the design of a tool leads to the validation and adoption of the tool, which could be an improvement over current tools in quality, speed, and safety. A tool will likely only be competitive if it is an improvement over existing tools. Further, the publishing of a tool's development process (partnership reputation) improves the scientific literature base (scientific knowledge) and may help improve the identification of drug candidates. The output of partnership sustainability leads to the de-risking of a tool. A partnership with both strong financial and in-kind commitment from their partners de-risks the development of the tool through ensuring the cost and project oversight is shared among multiple partners. IMI-PReDiCT, focused on creating in vitro platforms for target validation and drug discovery, works with 21 partners spanning pharmaceutical companies, universities, and research institutes. IMI-PReDiCT has published videos from partners that state the benefit of working with other partners across sectors has improved the quality of the tools they are developing. Further, with sustainable financial backing and in-kind

resources from IMI, the project enabled rapid identification of potential models that it hopes to develop into a full package soon.

Activities → Outputs



Outputs are often a result of the completion of activities presented in the Analytical Framework. To develop the output of validated tools, ETPs often engage in developing an extensive project plan with clear objectives and milestones and allotting defined roles to each partner (develop and assess tools). To establish the output of partnership reputation, ETPs will publish articles, present at conferences, present at events with stakeholders, and engage in other dissemination activities. Improving a partnership reputation also paves the way for the output of partnership buy-in and engagement in the ETP. Further, ETPs that facilitate platforms to share internal knowledge allow partners to stay informed, thus preventing partner disengagement. In addition, ETPs that provide avenues for partners to stay active and engaged, such as presenting at stakeholder forums or leading a working group, would logically have higher partner retention rates.

The output of partnership sustainability has a reciprocal relationship with partner buy-in and engagement, as a partnership is more sustainable if they have a strong base of active partners, and partners will likely stay engaged if the partnership has a sustainable base. The activities of “staff hiring and training” and “secure funding” feed into partnership sustainability through ensuring an adequate financial base and team of staff to accomplish the partnerships objectives. The partnership agreement on IP strategy facilitates partnership cohesion that allows for a sustainable relationship among partners.

Finally, the output of partner agreement on IP strategy is facilitated through the activities of partnership-oriented negotiations and oversight. Incorporating partners in decision-making processes and oversight bodies enables them to be engaged in development of partnership agreements (e.g., IP policy).

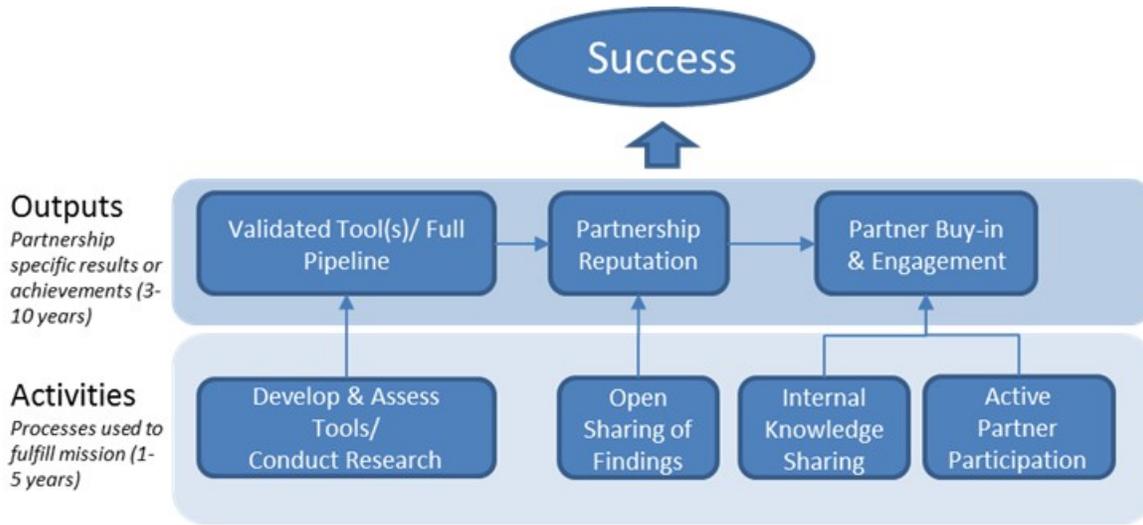
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4. SYNTHESIS OF FINDINGS—CONSIDERATIONS FOR PARTNERSHIP SUCCESS

4.1 General

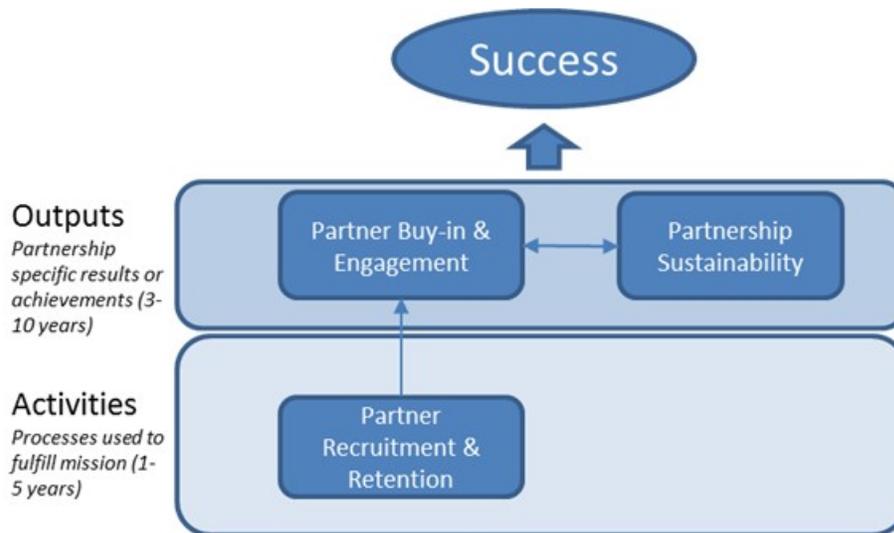
During the literature review analysis, we did not assign directionality or value statements to the process findings of inputs, activities and outputs. We simply gathered information about the characteristics of those constructs. After all of the information was gathered, we synthesized the activities and outputs as they compare to partnerships that were considered the most and least successful. As previously mentioned, inputs are usually assumed to be a component of the type of logic model used for our framework and rarely analyzed (Lavinghouze et al., 2013). While success in one of these areas does not guarantee success, certain relationships appear to correlate with success, which are examined below.

4.1.1 Broad Goals and Small Successes



As noted by our experts in the roundtables, partnerships have broad goals such as developing tools or conducting research, but it is also important to have small, measurable steps (short-term successes or milestones) at the inception of the partnership. These early successes can provide the partnership with internal and external credibility and allow the partners to feel more deeply engaged and to envision ways to accomplish larger, longer-term goals together.

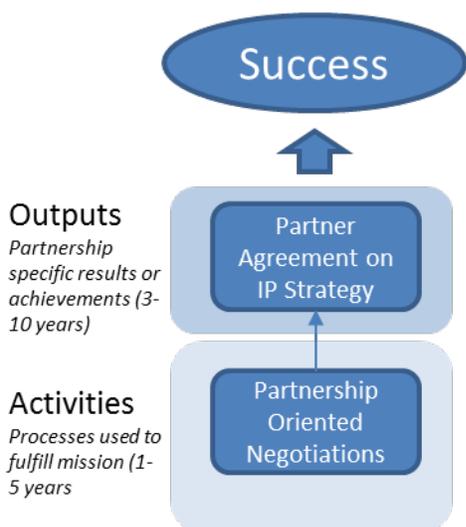
4.1.2 Diverse Stakeholder Inclusion



One key factor in successful partnerships is the inclusion of diverse stakeholders together at the formative partnership planning stage, with critical attention to the desired representation. Industry, government, donors, regulatory bodies, and non-profits/other stakeholder groups all have a particular role for the formation of the partnership. In setting the priorities for the partnership, it is important to engage industry as an essential participant from the beginning. While inclusion of more partners did not necessarily emerge from our literature review as an indicator of success, partnerships with diverse partner representation and deep commitment from those partners did tend to have more success. In addition, early multi-sector inclusion is crucial prior to partnership launch to ensure sufficient funding, partnership agreement on agenda and objectives, and allocation of responsibilities. Examples include:

- Innovative Medicines Initiative (IMI) spent 3+ years meeting with the European Federation of Pharmaceutical Industries and Associations and the European Union to develop a unified agenda and plan before its official launch (IMI, 2010).
- Global Health Innovative Technology (GHIT), initiated in 2013, started with support from the Japanese government, five industry-based partners, and the Bill and Melinda Gates Foundation. Since GHIT's launch 1 year ago, they have funded over eight projects from preclinical to Phase 2 projects and are ramping up for their third call for proposals (GHIT, 2013).

4.1.3 Negotiating Early Agreements

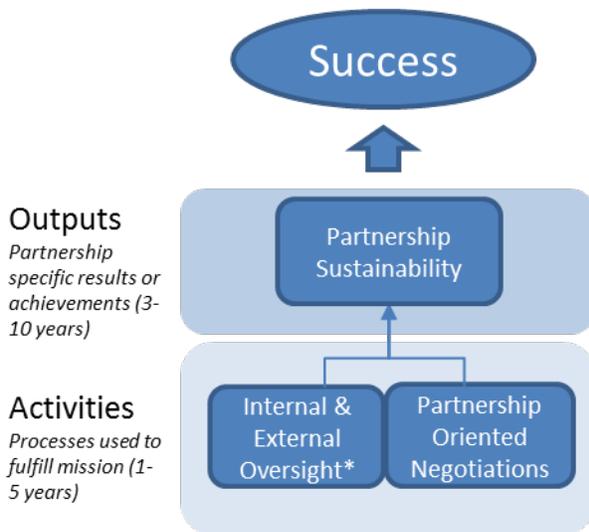


Setting up initial agreements appears to be crucial for partnership success and minimizing challenges in the future of the partnership. Agreements can include IP agreements, publishing agreements, or data sharing agreements. Building these agreements together ensures buy-in from partners obtained from individual representatives all the way through senior leadership. Several expert roundtable participants observed that over the past 5 years, both the pharmaceutical industry and academia have become more open to collaboration and developing win-win agreements. Examples of effective agreements are:

- *Collaborative IP agreements* are effective for stimulating more industry participation.
 - For example, the IMI ENABLE Partnership, a PDP, has used a very successful collaborative approach in which a lead compound submitted by a pharmaceutical company may be modified by a partnership research organization to generate a promising drug candidate. The IP remains with the pharmaceutical company as generator of the IP, but organizations that improved on the IP are compensated. This innovative approach to IP agreements has been an important factor in establishing an impressive 32 partners, including major pharmaceutical companies, in the initial year of operation.
- *Agreement on rules of engagement, including interaction* among partnership members and each member's responsibilities; these agreements should go beyond a memorandum of understanding.
 - For example, the European and Developing Country Clinical Trials Partnerships (EDCTP) are required to develop both a partnership agreement and an implementation agreement specifying each participant's responsibilities. As the umbrella management and oversight organization, EDCTP requires each partnership to submit all partnerships and implementation agreements to EDCTP for review.

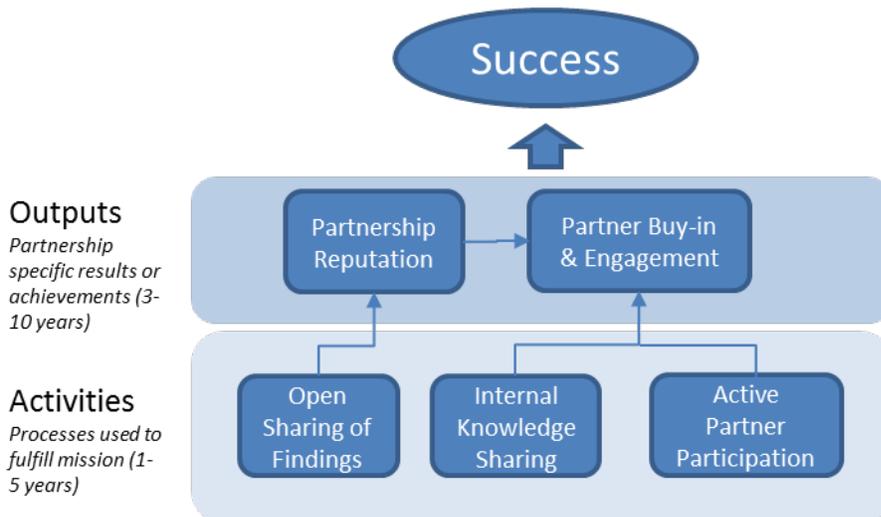
ETPs reported that their primary focus on precompetitive research requires a minimal IP framework. This approach in ETPs has worked well and has facilitated access to developments by a broad range of partners.

4.1.4 Partnership Flexibility



Although it is important to work in a collaborative process to establish initial partnership agreements, several roundtable experts noted that it is also important to have flexibility built into partnerships to regularly revisit milestones and agreements. Some partners may change over the years, and opportunities to adjust agreements to meet the needs of new partners or new priorities in existing partners are critical.

4.1.5 Harness Synergies

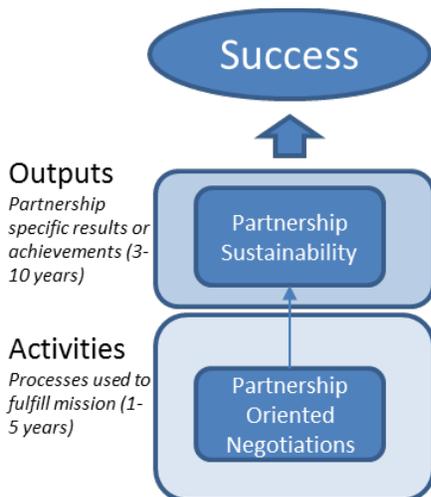


Partnerships should consider approaches to harness synergies within and across partnerships in related as well as different therapeutic areas: For example:

- Build mutual benefits for multiple partner goals (e.g., share control arms in trials).
- Share best practices among participants.
 - For example, scenarios were described in which pharma has shared with academia their systematic process for assessing screening results to select hits to advance to leads, providing examples of how the process was used.
- Establish best practices and re-use key elements of IP agreements and other agreements after successful implementation.
- Add partners incrementally instead of building new partnerships (seek to improve existing infrastructures instead of re-invent the wheel).
- Develop and/or use a central agency with administrative, regulatory, and legal agreement expertise to support multiple partnerships rather than each partnership developing internal capability.
- Hold frequent team meetings—every 2 weeks, for example—to foster open communication needed to identify possible efficiencies as well as problem areas that could be best addressed by all partners.

To foster new ideas, some roundtable participants suggested hosting ‘think tank’ forums within their partnership and with other partnerships to share best practices and identify possible synergies within and across partnerships. They noted that these open discussions cultivate an atmosphere of pre-competitive trust and collaboration. The result can be creative solutions that no one participant could have developed. For example, they may identify resources such as expertise, data, and facilities, as well as funding that could help the partnership achieve its goals more efficiently and effectively.

4.1.6 Mutual Goals



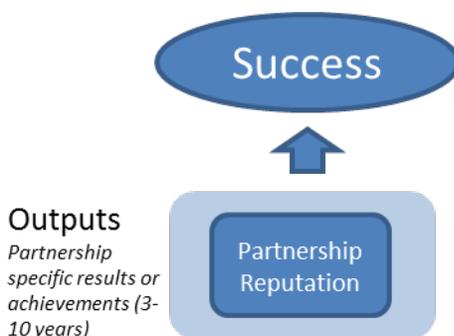
Each partner should contribute to the goals of the partnership in a way that highlights that partner's strengths. Partnerships can foster partner buy-in through mutual goal/agenda setting that builds on the strengths of partners. In order to foster buy-in, our literature review reveals that some partnerships do the following:

- Being strategic in the number of partners within their partnerships.
 - For example, too many or too few may inhibit the partnership's ability to accomplish goals.
- Requiring partner dues.
- Requiring equitable representation on governing boards.

Expert roundtable participants emphasized that one should not assume that all partnership members share a common perception of partnership goals and success. A clear vision of the goals of the partnership must be developed in an open, direct dialog among the partners across sectors.

A critical activity suggested for clarifying goals of a partnership is the development of a target product profile that includes factors across the value chain from therapeutic efficacy and safety to manufacturing, cost, and supply chain considerations.

4.1.7 Passing It Forward

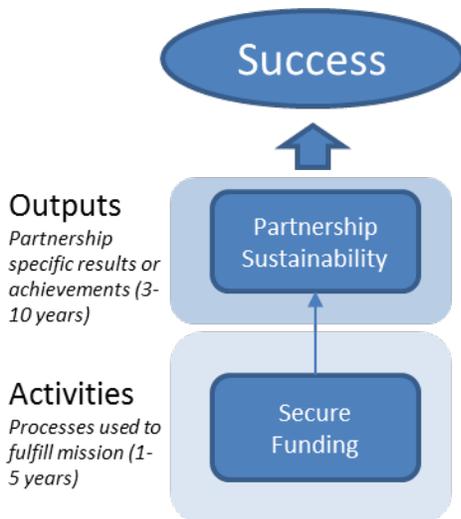


With a large number of new partnerships forming, personnel from more established partnerships could mentor members of newer partnerships to increase efficiency and reduce redundancy. Mentoring new partnerships can be achieved in many different ways. For example:

- Develop toolkits that outline early partnerships' agreements or directly mentoring a new partnership.
- Members of mature partnerships become members of newer partnerships' governing boards.

Sharing this knowledge is an important element to the success of an overarching management entity such as the FNIH or IMI. In the roundtable discussions, however, these organizations cautioned that no two partnerships are alike. While some principles and policies can be shared to great advantage, each new partnership will have unique requirements that should be addressed in a way that best serves that partnership.

4.1.8 Funding Considerations



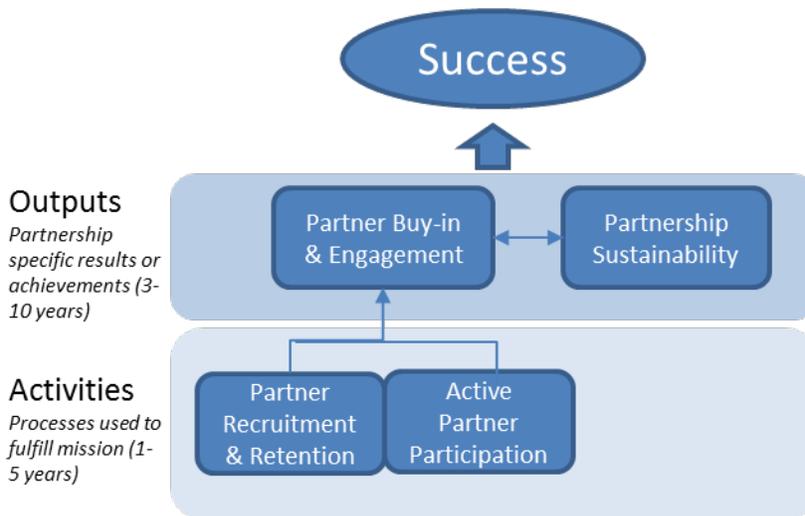
Partnerships should seek diverse and sustainable funding in an effort to prevent undue dependence on one funder. According to our literature review, some partnerships strategize to not have more than 25% from one funder. Other partnerships work toward having some long-term funding within their partnership. The most successful partnerships analyzed could continue their work at its current level of effort for at least 9 months to 2 years without securing additional funding.

Long-Term Funding: Experts cited the constraints of many standard government funding mechanisms that prevent alignment with the needs of partnerships for long-term funding and changing research activities based on product development results. For example, a PDP may need to make a 3- to 4-year commitment for a large scale clinical trial, but government funding may be uncertain over the extended period of the trial. Additionally, serious industry engagement will require evidence of long-term funding sources for the collaboration. In the IMI model, industry provides 50% of the funding while the European commission provides the remaining 50%. This established commitment to funding of approved partnerships, pending successful progress, provides industry with the confidence to invest in the activity.

Milestone Payments: While long-term funding is important, some funders use milestone payments to ensure the progress of the partnerships. These milestone payments can be helpful in establishing goals for new partnerships. In addition, it is important to have a clear understanding of the level of involvement the funder has in driving the agenda, governance, and goals of the partnership.

Diversity in Funding Sources: Among the most successful partnerships analyzed, an average of 10 funders supported each partnership. However, many newer partnerships (less than 5 years old) that demonstrated promise for success only had 3-6 funders. All of these successful partnerships had experienced substantial financial growth throughout their partnerships' history; although, not every individual year saw a growth in financial resources for successful partnerships. While the number of funders and success are highly correlated, it is difficult to determine the cause and effect relationship of these factors.

4.1.9 The Value of Engagement and Commitment



Among the most successful partnerships, we noted a deeper level of partner commitment and buy-in. Partners contributed in a variety of ways. For example, successful partnerships:

- Were more likely to acknowledge and to be sustained by both in-kind and financial resources. Examples of in-kind resources included donated lab space or materials.
- Have members representing diverse sectors (industry, academic, non-profit and government), who often co-authored publications and co-presented at press releases or conferences.

These diverse contributions by the partners reflect a deeper engagement within the partnership; this multifaceted commitment is important to the ongoing success of the partnership.

4.2 Unique Considerations

Different types of partnerships have different needs. Although some common elements are found across successful partnerships, PDPs and ETPs have unique considerations that must be taken into account when assessing rationale for success or failure to achieve their goals. In addition, within a central management entity (i.e., an 'umbrella' organization) such as FNIH, C-PATH, or IMI, each partnership has unique issues that should be addressed in its formation, goals, and partnerships. The most effective approach was described as one that builds on common parameters and best practices while also understanding and addressing the unique considerations.

4.2.1 Product Development Partnerships

PDPs emerged because there was a unique public health need to develop treatments that are often less appealing for for-profit companies to develop independently. These partnerships often develop treatments that otherwise would not be developed for conditions that are rare or short-course treatments. Moreover, because of the high risk of failure in developing drug candidates, it is critical to the success of the partnership to have a full pipeline of treatment candidates. According to RTI's literature review, PDPs face a unique challenge because PDPs have longer timelines and major funding requirements for large-scale clinical trials. Interestingly, only 8% of PDPs are working within an umbrella organization and all of these are relatively new partnerships. The oldest PDPs are managed as independent entities with multi-sector representation.

4.2.2 Product Development Partnership Case Study: Cures Within Reach

Cures Within Reach is a medical repurposing partnership. Through a network model, Cures solicits, vets, and secures funding for pilot clinical trials and final preclinical research to test approved drugs in new therapeutic areas (Cures Within Reach, 2015).

Formation and Partners: Cures Within Reach was started in 2005 (launched from the private foundation Goldman Philanthropic Partners with the name Partnership for Cures and renamed again in 2012 to Cures Within Reach). Its mission is to support drug, device, and nutraceutical repurposing, primarily addressing diseases for which no effective treatment is available. Therapeutic areas have included oncology and CNS. The partnership now includes over 60 members comprised of academia, patient advocacy groups, and major pharmaceutical and biotech companies (Cures Within Reach, 2014).

Outputs: Cures Within Reach has overseen over 50 projects thus far. For example, they facilitated the repurposing of sirolimus to create treatments for the deadly childhood disease

autoimmune lymphoproliferative syndrome, and then 5 other pediatric autoimmune diseases. This unique partnership has successfully repurposed at least 10 medical products that are either being used clinically or now being tested in much larger clinical studies and is actively engaged in expanding its reach.

Cures within Reach has found that their average time from initiating a repurposing clinical trial to off-label patient availability is between 18 to 36 months. Further, between 10-30% of their repurposing trials result in a new treatment. Maintaining budgets of under \$500,000 per project, this partnership has been reported as a model partnership for efficient and affordable drug development (Murad, 2014).

Key Factors for Success: They have attributed their success in this unique model to some of the following (Cures Within Reach, 2015):

- Adhering to their repurposing research model that involves sending out Request for Proposals among academic and biotech partners and utilizing a network of scientific advisors and independent reviewers to review proposals
- Ensuring all proposals adhere to the following screening criteria:
 - target populations in which there are significant unmet medical needs
 - utilize drugs, devices and nutraceuticals approved for human use
 - complete in less than 36 months and for less than \$500,000, and
 - culminate in publication
- Developing research roadmap with projects with quarterly aims and milestones
- Funding is released based on the project progress with aims and milestones
- Developing a health care savings report from the repurposed drug to encourage buy-in from investors, usually philanthropists and disease specific organizations.
- Seeking to include stakeholders, such as patient advocacy groups and key opinion leaders, at the onset of a partnership to communicate progress and disseminate clinical findings.

4.2.3 Enabling Technology Partnerships

As synthesized from the literature review findings and expert roundtable discussions, ETPs are not as dependent on a therapeutic area to contribute to successes in drug development. For example, a partnership generating knowledge about biomarkers that indicate a drug likely will cause liver damage could benefit many different therapeutic areas. ETPs will most often have shorter timeframes and can be nimbler in their activities than a product development effort focused on regulatory approval of a new therapeutic. It is perhaps for these reasons that more ETPs are being developed in recent years, concurrent with a reduction in the number of new PDPs emerging. There are other unique findings for ETPs as they relate to central management entities (i.e., umbrella organizations). Of all ETPs, 42%

are housed within an umbrella organization. Further, of all the partnerships that currently exist within an umbrella organization, 88% are ETPs. Of the partnerships under an umbrella, 40% have successfully completed a tool; whereas, only 24% of partnerships not under an umbrella organization have completed a tool.

4.2.4 Enabling Technology Partnership Case Study: Cardiac Safety Research Consortium:

The Cardiac Safety Research Consortium (CSRC) is an ETP developed in 2006 to advance scientific knowledge of cardiac safety among new and existing medical products. They work to inform regulatory processes, standards, definitions, and strategies in the field of cardiac safety (CSRC, 2015).

Formation and Partners: CSRC began with a memorandum of understanding between Duke University and the FDA and now has grown to a partnership of more than 50 members from government, regulatory bodies, industry, and academia.

Outputs: CSRC's work is widely cited, and many of their think tank consensus statements and points to consider documents are widely used by researchers outside their partnership. For example, CSRC convened experts from government, academia, professional societies, device manufacturing, and pharmaceutical industry to serve as a research incubator to improve the safety of percutaneous coronary interventions through using antithrombotic drug use and radial artery access (Hess et al., 2013). In 2015, CSRC developed a standardized cardiovascular safety and adverse event case report form to assist with the collection of uniform details of cardiovascular events (Sabol et al., 2015) in clinical trials.

Key Factors for Success: During the expert roundtables, partners from CSRC provided insight on key organizational factors critical to their success. Key factors for success identified by the experts and in the literature review included:

- Partner representation from government, industry, academic, and regulatory organizations from the onset of the partnership. They found multi-sector buy-in lent itself to establishing their credibility among stakeholders. Further, they found that their think tank discussions are richer because of the different perspectives of their stakeholders, resulting in thorough and creative solutions to cardiac safety issues and establishing mutual goals across different sectors.
- Engagement of partners through early 'wins' by accomplishing small tasks in the beginning. These small accomplishments facilitate partners' engagement and build momentum for larger successes in the future.

4.2.5 Umbrella Organization Model

Umbrella organization models are increasingly being used by PPPs, especially among ETPs. Using this model, a larger organizing entity supports the efforts of individual partnerships. This model can be seen with partnerships within the organizing entities such as C-PATH, IMI, FNIH, and Cancer Research Institute. This model allows partnerships to benefit from

organizational efficiencies learned previously from negotiations with other partnerships within the organization. The umbrella organization model provides a range of benefits to the partnerships that include:

- It allows the umbrella organization to set the strategic vision, tasking PPPs to carry out the various components of the vision. Outsiders may be more likely to invest in a partnership with a strong internal structure with an established track record.
- The umbrella organization may provide a proven infrastructure for funding coordination, IP and legal services, and general business management advice that may relieve individual PPPs from investment in these services, thus allowing them to maintain focus on their mission. The umbrella model could provide an efficient approach to sharing resources and knowledge in the establishment and operation of new partnerships.

4.2.6 Hybrid Umbrella Partnerships: Collaboration between Product Development and Enabling Technology Partnerships

Expert roundtable participants agreed that PDPs and ETPs are quite different in their goals and timelines. There is a need, however, for integrated, coordinated efforts between PDPs and ETPs. PDPs need to be clear about the issues they are experiencing with drug development to ensure that ETPs are developing tools that are useful to the PDPs. Ultimately the goal of many ETPs is to support the downstream efforts of developing medical products. As a result, an emerging hybrid umbrella organization model has developed in which the central management entity seeks to oversee both enabling technology and product development partnerships to address a continuum of needs.

4.2.7 Emerging Hybrid Umbrella Organization Model Case Study: New Drugs for Bad Bugs

In 2012, IMI launched a PPP named New Drugs for Bad Bugs (ND4BB), to address antibiotic resistance in Europe, recognizing that a complex system of scientific, business, and regulatory needs must be addressed before new antibiotics can be effectively developed (IMI, 2010). ND4BB is a novel model for partnerships, including within its management umbrella a range of both PDPs and ETPs that are required to achieve success. ND4BB is a Hybrid Umbrella Organization that addresses the need noted by expert roundtable participants to address the product development issues across the spectrum, from enabling research, product development, costs, production, and market economics. Cross-project communication and collaboration is described as a key objective of ND4BB, as each partnership operating concurrently supports the development of antibiotics.

Formation and Partners: In 2013 ND4BB launched COMBACTE, whose goal is to create a pan-European network of clinical sites that will be used to improve clinical trial design, conduct clinical trials, and support surveillance of antibiotic-resistant bacterial pathogens. Additional ETP partnerships within ND4BB, COMBACTE-CARE and COMBACTE-MAGNET, were launched in early 2015 to build upon the work of COMBACTE to further support capacity

building of clinical trial sites and begin clinical trials of drug candidates. Also in 2013, ND4BB launched TRANSLOCATION, another ETP, to conduct research on penetration and efflux on Gram-negative bacteria and develop a framework for sharing data and information across ND4BB. In 2014, ND4BB launched its first PDPs, ENABLE, whose goal is to develop antimicrobial candidates and begin clinical testing on candidates. To address the gaps in the business of antibiotic development and use, ND4BB launched DRIVE-AB, an ETP, in late 2014 to develop new economic models that incentivize the development of antibiotics while also ensuring that the antibiotics are used judiciously. ND4BB intends to develop additional partnerships that gather data on best available treatments for Gram-negative pathogens, develop novel drugs for pneumonia and urinary tract infections, and develop inhaled antibiotics to treat respiratory infections among patients with cystic fibrosis. In its formation, priority-setting and operation, all of the partnerships within ND4BB include active participation by industry, academia and European Union representatives.

Outputs: Thus far, ND4BB has implemented their novel, integrated approach to launch six sub-partnerships, and they are planning an additional partnership to address specific gaps in the discovery, development and commercialization of new antibiotics.

Key Factors for Success: factors that have contributed to the early success of ND4BB include:

- **Agenda and research focus** of ND4BB are set by pharmaceutical partners and supported by government entities. Other partners such as academics, research organizations, and other third parties apply to carry out this work in collaboration with the pharmaceutical partners, thus ensuring buy-in from all critical partners.
- **Address the spectrum of needs** for antibiotic development across product development, enabling technology, and market issues, maintaining communication across this continuum of work in the sub-partnerships.
- **Novel IP policy** in ENABLE stimulates collaboration between academic and industry partners, a critical need in PDPs. Briefly, this policy states that IP generated with ENABLE goes to the initial compound's owner; however, organizations that have a role in generating new IP improving on the original compound will be compensated once the product is successful.

These unique policies and structural factors in the ND4BB model have facilitated rapid progress in addressing antibiotic resistance in Europe.

4.2.8 Partnership Considerations by Therapeutic Area

There are several commonalities and differences noted in partnerships in different therapeutic areas (e.g., infectious disease, cardiovascular disease, and oncology). For example, while infectious disease partnerships tend to focus exclusively on interventions for infectious diseases, partnerships that include a cardiovascular disease focus tend to address diverse therapeutic areas and do not tend to focus solely on cardiovascular disease (Table 4.1). Interestingly, half of all infectious disease partnerships focus on product development

and half focus on enabling technologies. However, over 70% of both cardiovascular and oncology partnerships focus on enabling technologies. Infectious disease partnerships tended to average more oversight bodies. Oversight bodies included governing boards such as regulatory, scientific, ethical, financial, legal, and management/staff oversight boards. Similar characteristics across all 3 therapeutic areas were:

- Average number of funding sources
 - The average without outliers was also calculated. Many partnerships collect dues from their partners, and this method makes the number of funders appear higher than other partnerships that do not collect dues.
- The proportion who are managed by an umbrella organization
- The strong presence of industry involvement at the inception of the partnership.

Table 4.1. Partnership Comparisons by Therapeutic Area

	Infectious Disease	Cardiovascular Disease	Oncology
% of partnerships with sole focus	69%	21%	55%
% who focus on PD	50%	29%	24%
% who focus on ET	50%	71%	76%
Average # of oversight body	3.4	2.3	2.2
Number of Reported Funding Sources	10.6 (if remove two outliers of greater than 50 then average is 6.6)	11.8 (if remove two outliers of greater than 40 then average is 5.6)	7.6 (if remove one outlier of greater than 55 than average is 4)
% of partnerships under an umbrella	22%	21%	31%
Sector responsible for starting partnership*	<ul style="list-style-type: none"> • 22 reported (4 IMI) • Industry: 12 (55%) • Government: 8 (36%) • Academic: 2 (9%) • Third Party: 3 (14%) • Foundation: 1 (5%) 	<ul style="list-style-type: none"> • 11 Reported (1 IMI) • Industry: 8 (73%) • Government: 4 (36%) • Academic: 4 (36%) • Third Party: 1 (9%) • Foundation: 1 (9%) 	<ul style="list-style-type: none"> • 20 Reported (5 IMI) • Industry: 13 (65%) • Government: 7 (35%) • Academic: 3 (15%) • Third Party: 5 (25%) • Foundation: 3 (15%)

* % may be greater than 100 as possible for multiple sectors to start a partnership

4.3 Challenges

Despite the successes of many partnerships, the partnership model still faces barriers and challenges. Some of the challenges cited by the expert roundtable participants include:

- **Funding and financial stability** beyond yearly grant cycles was consistently cited as a major challenge. As stated above (Section 4.1.8), government funding cycles create challenges for long-term support required, especially for PDPs engaged in

clinical trials. Solutions for this challenge include developing a diverse set of funding sources and collaborations. Experts suggested that IMI and GHIT models could be options for continuous engagement and funding of partnerships.

- **Funding dilution** was mentioned as an increasing challenge. With the proliferation of the partnership model and increased number of partnerships in recent years, more requests for funding are presented to the limited number of funding entities. To address this dilution of funding, efficiencies can be achieved through increasing collaborations between partnerships and establishing umbrella organizations to support multiple partnerships.
- **Maintaining partner engagement** over long periods of time and during changes within their organizations. One approach to addressing this challenge is to engage personnel at a high level within the partner organization, in addition to the “working” level staff. This senior management engagement can provide continuity over time.
- **Achieving a common understanding of partnership goals** was often cited as a challenge. For example, pharmaceutical industry, academic, and non-profit organizations may all have different cultures and expectations of the partnership. To address this challenge, expert roundtable participants suggested that early, candid discussions take place in the development of the partnership’s formal agreements. Revisiting the agreements and discussing expectations of all participants was recommended as a best practice at project and management meetings throughout the life of the partnership.
- **Communication across partnerships** through mechanisms such as forums to share best practices would be helpful. These communications and collaborations are, however, sometimes difficult, as each partnership has IP and confidentiality agreements that may constrain communication and data exchange. To address this challenge, roundtable experts recommended that communication with other partnerships be addressed when initial confidentiality and IP agreements are developed. All parties can discuss the benefits of those collaborations and identify those elements of the data and best practices that could be shared. Experts suggested that third party organizations could convene a forum(s) for exchange of information on best practices and possible collaborations between partnerships.
- **Global regulatory diversity** was identified as a challenge, especially for PDPs. The experts suggested a solution of a more global infrastructure for assistance in IRB and regulatory approval would benefit a range of partnerships.

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5. BUILDING ON SUCCESSES

A thorough analysis of partnership models, activities, and outputs supports the conclusion that partnerships are an effective method to advance drug development, especially when industry does not have sufficient financial incentives to be the sole source of development for a product or tool. Partnerships are continually evolving to meet the needs of all sectors involved. Analysis of the literature and expert sources provided the basis for the following considerations that could inform planning and optimize the formation and effective operation of new public-private partnerships. Sections 5.1, 5.2, and 5.3 examine methods or ideas that could improve success rates for partnerships in the planning, formation, and ongoing operations phases of their partnerships' lifecycle.

5.1 Planning

The literature review and the expert roundtable comments provided the following insights on ways to streamline and improve the process of forming new partnerships as well as options for improving current partnerships.

- **Forum on best practices.** Several experts expressed strong support for a forum for presentation and discussion of best practices and trends in medical product partnerships. The output of the forum would be new insights for existing partnerships as well as options for new partnership formation.
- **Partnerships within an existing umbrella organization.** Umbrella organizations such as the FNIH, C-PATH, and IMI have proven effective in engaging industry and creating new partnerships that incorporate the best practices of prior partnerships. The existing infrastructure and efficiency of the umbrella organizations can facilitate the formation of new partnerships.
- **Global partnerships.** The European Commission, in its establishment of the ND4BB entity, recognized the critical need for additional research and product development focused on antibiotic-resistant bacteria. This established partnership provides a model and collaboration opportunity for new partnerships in antibiotic product development.
- **Emerging hybrid umbrella organization model.** Under this model, discussions with industry and the academic research community would provide insights on the therapeutic product as well as the enabling technology needs. For example, improved clinical trial approaches or biomarkers could be important to enhancing the probability of success in a drug development program. If important enabling technology needs are identified that are not currently being addressed, the option of a hybrid model addressing enabling technologies as well as product development might be considered.
- **Option for more flexibility in agreements and funding with private sector partners.** The 2012 White House National Bioeconomy Blueprint mentions challenges faced by U.S. Government agencies in funding initiatives focusing on development of medical therapeutics. (White House, 2012). Concerns were also voiced by this project's expert roundtable participants regarding the challenges

experienced in standard Federal funding mechanisms, especially the limitations of fiscal year funding and expenditure. An option that might facilitate U.S. government funding for PPPs is the Other Transaction Authority (OTA) mechanism, first approved as an element of the Space Act of 1958. Congress later provided OTA to HHS (42 U.S. Code § 247d–7e) and six other agencies, thus demonstrating some confidence that OTA is an effective mechanism whose use should be expanded beyond NASA. The OTA provides great flexibility in creating terms and conditions aligned with a project and project participants. As a result, the OTA enables the agency to be more flexible in developing agreements (Halchin, 2011; Dix et al., 2003). The OTA has been used as a mechanism in creating multi-partner agreements. Combined with traditional grants and contracts, the OTA has the potential to provide continuous funding for drug research and development through clinical trials and production. An additional benefit of the OTA would be the flexibility for a more collaborative public-private development program.

5.2 Formation

The strategies provided in this section reflect the best practices identified in successful PDPs and ETPs that would facilitate an effective formation process. As indicated in the analysis framework for partnerships shown in Figures 2.3 and 2.4, many of the elements critical to the successful formation of a partnership are common to the formation of any organization. For example, in the formation of a partnership or a new company, involvement of talented staff, definition of clear goals, and availability of funding to accomplish those goals are required. Thus, good management practices are critical for successful formation of a partnership, as they are for other organizations. Factors specific to success in partnership formation are:

- **Goal alignment with other or umbrella organizations.** Prior to the formation of a new partnership, identification of existing PPPs and umbrella organizations that closely align with the goals can bring clarity to the unique mission of the proposed partnership. Discussions with the closely aligned existing partnerships can identify synergies, potential collaborations, and, perhaps, a linked partnership to take advantage of the established relationships. Several experts cited a concern regarding the proliferation of new partnerships, indicating that before the launch of a new partnership, perhaps the stakeholders should explore pursuing their goals within an existing partnership.
- **Staff with industry experience.** Including staff within the partnership who have experience working in the pharmaceutical industry will bring important skills and insights on the perspective of the private sector partners and provide confidence to pharmaceutical industry partners that the partnership can understand their goals, approaches, and constraints.
- **Goals with industry input.** Several successful models of partnerships, especially ETPs, attribute much of their success to the major role of industry in setting the partnership's goals. Whether the end product is the commercial introduction of a new therapeutic, industry adoption of an enabling technology, or industry sharing/usage of data, the involvement of industry in setting the goals appears to be critical. These goals can be guided by a target product profile addressing the expected outcome, including regulatory approval, manufacturing, pricing and marketing. An exclusive focus on technical goals without consideration of the other issues could result in a

compromised participation by industry and generation of a product with limited or no commercial interest in moving the therapeutic to market. In addition to the larger, long-term goals, the partnership should set more near-term, achievable goals to develop confidence in the partnership's ability to meet milestones.

- **Diverse partner engagement.** In addition to the engagement of industry, several successful partnerships have cited the importance of engaging regulatory agency representatives in partnership formation and planning process. With this regulatory input, the activities of the partnership can be better focused on an effective outcome and a plan for achieving that outcome most efficiently. Academic researchers will bring scientific perspectives, expertise, and facilities to advance the agenda of the partnership. Government entities can bring resources and expertise in addition to funding.
- **High level representatives in partner organizations.** Engaging senior management of partner organizations has been helpful in maintaining continuity of support throughout long development timelines and provides a source of support when challenges are encountered and changes occur in personnel at the working level of the partners.
- **Open communication.** Established PPPs have cited the importance of frequent and open discussion among partners in both the formation and ongoing operation of a partnership. This communication ensures that the partners understand each other's perspective and agree to a common approach that may represent a compromise by participants to achieve success. The discussion is required to ensure that all partners (1) have a commitment to the goals of the partnership, (2) see the partnership as a win-win, and (3) understand the different sectors represented in the partnership and appreciate their motivations. A practice of including substantial time in partnership meetings for brainstorming has been effective for developing open and candid communication in a "think tank" environment. Partnership participants should not assume other participating organizations share their perspective on a successful partnership outcome.
- **Intellectual property (IP) and publication/data agreements.** Development of IP and publication agreements early in the partnership has been cited as important to preventing later conflicts. A collaborative IP agreement like that recently developed by the ENABLE partnership should be considered by PDPs to stimulate industry participation (see Section 4.2.7). While ETPs are less likely to require extensive IP agreements, the data sharing agreements will be more critical and also should be addressed early in the partnership formation.
- **Diverse funding sources.** Continuity of funding will be critical to establishing the partnership's credibility with industry and its ability to conduct the long-term activities, especially costly clinical trials. As described in Section 5.1, the Other Transaction Authority may be an option to create greater flexibility for funding a partnership. Successful partnerships such as those in IMI are able to attract industry commitment for 50% of the costs because the European Commission has made a commitment to provide the remaining funds required. The Global Health Innovation Technologies Fund combines funding from the government of Japan, the Bill & Melinda Gates Foundation, as well as the pharmaceutical industry.

5.3 Ongoing Operation

Consideration of the key factors described in Section 5.2 for the formation stage of the partnership will lead to an effective partnership framework and culture of communication that will enhance the probability of ongoing success of the partnership. Factors identified as critical to enhancing the probability of ongoing success are:

- **Frequent project meetings.** All sectors engaged in a specific project should meet frequently—once every 2 weeks or once a month, depending on the level of activity. These meetings should include open communication between partners and brainstorming sessions. Frequent interaction will facilitate improved understanding of each other’s objectives and exchange of best practices and will surface concerns early.
- **Open time for brainstorming.** Senior representatives from the partners should meet on a periodic basis—every 6 months is common. During these meetings, in addition to a review of project progress, time should be reserved for open “Think Tank” sessions to facilitate brainstorming on ways to improve and expand the partnership or identify new resources (expertise, new partners) to support the objectives of the partnership.
- **Flexibility for agreements and goals.** Changes in a PPP, especially a long-term partnership, may require modification of the IP, publication, and other policies/agreements due to changes in the external environment or the participating organizations. These changes may also apply to the structure and staffing of the partnerships. A culture of cross-sector respect and communication should allow for discussion of possible changes. In a long-term partnership, changes of these types are not unexpected.
- **Engagement of regulatory agencies.** Several PPPs have mentioned the value of an ongoing dialogue with regulatory agencies. The FDA has been characterized by partnerships as responsive and very helpful to the ongoing planning process.

6. CONCLUSION

Over the past 20 years, partnerships that engage government, industry, and academia have collaborated across the spectrum of research and development activities to develop new medical products. Diversity across these drug development partnerships can be seen in their varied objectives, funding approaches, and operational models. This report examines public and private sector partnerships for drug development across a range of partnership models to determine key factors that contribute to success in realizing the goals of the partnership.

Our analysis identified two types of partnerships, Product Development Partnerships (PDPs) and Enabling Technology Partnerships (ETPs), as well as a new model for organizing these partnerships.

Key success factors common to both PDPs and ETPs include:

- diverse stakeholder inclusion with well-defined roles;
- engagement and commitment through membership in governing bodies, co-authorship of publications, participation in press events, participation in partnership meetings, and direct financial or in-kind contributions;
- mutual goals that highlight partners' strengths;
- early agreements addressing IP, publishing, and data sharing, which facilitates transparency and commitment among partners;
- flexibility in the partnership to regularly revisit milestones and agreements;
- frequent team meetings engaging all participants to identify possible efficiencies as well as problem areas;
- diverse and sustainable funding to prevent undue dependence on one source; and
- specific milestones and early successes identified within the partnership's broad goals, which are important to maintaining funding support and partner engagement.

The success factors unique to PDPs include:

- maintain a full pipeline of drug candidates at different stages of development;
- include staff with pharmaceutical industry experience to assist with the development and regulatory approval process; and
- engage senior management in the partner organizations to facilitate continuity of commitment to their role in the PDP.

Key success factors unique to ETPs include:

- engage industry partners in defining the precompetitive needs that would improve the product development process; and

- operate within an umbrella organization that provides established management, regulatory, and financial systems to minimize overhead costs and start-up delays.

Public-private partnerships have demonstrated the value of bringing together the expertise and resources of government, business, and academic organizations to address important needs in developing new medical products. Over the past 20 years of PPP formation, partnership models have evolved to improve their efficiency and effectiveness in response to changes in the technical, regulatory, and business environments.

Our analysis of partnerships also identified the emergence of a central management entity or “umbrella” organization model used increasingly by PPPs, especially ETPs, to support the efforts of multiple partnerships by providing an infrastructure and an efficient approach for sharing resources and knowledge in the establishment and operation of new partnerships. Examples of umbrella organization models include FNIH, C-PATH, and IMI.

While the original umbrella organization models have focused primarily on enabling technology development, a recent “hybrid umbrella” model has emerged in which both PDPs and ETPs are included within one umbrella organization. The 2012 formation of the IMI umbrella organization, New Drugs for Bad Bugs (ND4BB), was the first hybrid umbrella organization. This umbrella organization took a novel, integrated approach to launch four sub-partnerships that included both product development and enabling technology activities.

An ongoing understanding of the key factors for partnership success can inform the continued evolution of partnerships to enhance their contributions to the development of new medical products.

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