Contents

Voorwoord Ten geleide en plaatsbepaling

Het model beschreven in dit document (TTL negotiation model), is bedoeld als hulpmiddel om de toepassing van de principes van Maatschappelijke Verantwoord Licentiëren (MVL)[1] bij licentieonderhandelingen tussen kennisinstellingen en bedrijven in de Life Sciences & Health (LSH) sector te vergemakkelijken. Het biedt een raamwerk waarbinnen de MVL principes middels argumentatie en discussie vertaald kunnen worden naar concrete uitwerking. Die vervolgens kunnen worden opgenomen in een licentie, bijvoorbeeld op basis van de MVL-toolkit uit 2020. Het doel is dus uitdrukkelijk niet om uitkomsten voor te schrijven maar om een proces te stimuleren dat de kennisinstelling helpt invulling te geven aan de MVL principes. Dit document is primair bedoeld voor medewerkers van kennisinstellingen.

Het model beoogt kennisinstellingen meer inzicht te geven in wat er nodig is om in een specifiek geval een beoogde toepassing te ontwikkelen. Dit is waardevol bij het bepalen van onderhandelingsdoelen, zowel de bijdragen van de kennisinstelling als de gewenste tegenprestaties. Die doelen worden door onderzoeker, management en kennis transfer organisatie (KTO) bepaald. Dit model biedt een manier om het hiervoor benodigde gezamenlijke beeld te creëren. Het kan de start vormen van de interne discussie om inzicht te krijgen in de mogelijke waardeontwikkeling van een patent (portfolio). Een goede voorbereiding is daarmee een stap in een lang proces naar meer succesvolle kennisvalorisatie.

Een goede voorbereiding is waardevol voor een licentieonderhandeling en kan onderhandelingen versnellen en inzicht te geven voor meer kansen voor andere tegenprestaties dan geld te vinden. Als een kennisinstelling nauwer betrokken blijft en bijdraagt aan de ontwikkeling op basis van de eigen kerncompetenties, zijn er meer typen bijdragen mogelijk. De kennisinstellingen dienen van geval tot geval afwegen welke MVL doelstellingen relevant en haalbaar zijn en welke tegenprestaties daar tegenover staan. Dergelijke tegenprestaties kunnen leiden tot een betere invulling van de MVL principes en voor het bedrijf kan het bijdragen aan de productontwikkeling.

Het toepassen van de MVL principes is geen kwestie van een lijstje afwerken. Het vraagt kennis en ervaring om de betrokkenheid van de kennisinstelling op een relevante en nuttige wijze in te vullen. Daarbij neemt in de regel de betrokkenheid van de kennisinstelling tijdens het ontwikkelingsproces af en die van private partners toe.

Dit model is geen panacee. De kwaliteit van de input en de bereidheid om het te gebruiken, bepalen de mogelijke waarde. Vrijwel altijd zal de uitkomst een grove inschatting zijn van het ontwikkelingsproces, die door de tijd zal veranderen. Dat is echter geen bezwaar als het voor alle betrokkenen helder is dat het een inschatting is en er over kan worden gesproken. Dit model onderkent daarnaast dat een goed beeld van het mogelijke ontwikkelingsproces vaak expertise van derden vraagt. Die kennis kan komen van adviseurs, ervaren ondernemers, investeerders, of anderen. Dergelijke gesprekken dragen verder bij aan inzicht en kennis.

Het model wordt aangeboden op de website van de NFU. Gebruikers kunnen het geheel eenvoudig invullen en op basis van gesprekken, met collega's, experts of de wederpartij, de uitkomsten verfijnen. Deze opzet biedt daarnaast de mogelijkheid om het model op basis van ervaring te verbeteren, bijvoorbeeld door meer toepassing specifieke aspecten op te nemen of aspecten van sub-domeinen in de LSH sector te ondervangen.

[1] https://www.nfu.nl/sites/default/files/2020-08/19.3973_Tien_principes_voor_Maatschappelijk_Verantwoord_Licentieren.pdf

Introduction

A core task of Public Research Organizations (PROs) such as universities and university medical centres is creating societal impact, e.g. by making scientific insights useful to society as part of products or services (valorisation). To accomplish this, the research results need to be transformed into an application (innovation). That is usually done by private partners based on intellectual property (IP) licensed from PROs. For example, in the case of new medicines, biotech and pharmaceutical companies are required to develop and commercialize a product or service.

This process has presented great difficulty for all involved so far, and the situation is becoming even more complicated with the emphasis as described in the Socially Responsible Licensing principles. The commercial partners that are often involved, given their expertise in development and marketing, may not have a thorough understanding of the early stage research or what the PRO can contribute to the further development. And similarly, the PRO needs their expertise, without necessarily understanding what is involved to make products/services based on its research effectively available to society at large.

Now there is a solution. A Technology Transfer License negotiation model (TTL negotiation model) has been created, a series of questions whose answers will provide clarity about the subject of the licensing negotiation. There are many aspects involved, and all of them have to be discussed and considered beforehand by the parties concerned. Having a clear idea of what the PRO has to offer and what the commercial partner needs makes the negotiations smoother and relatively straightforward. This applies to both the preparation of the negotiation with the various PRO stakeholders, as well as the negotiations with a licensee itself. This approach enables the PRO to find opportunities to incorporate Socially Responsible Licensing (SRL) as far as possible into the negotiations.

Let us look in more detail at licences and SRL and the new model to support fair and informed negotiations.

The value of licences is not limited to their monetary return, they can also include other elements that represent value. With that in mind, the Nederlandse Federatie van Universitaire Medische Centra (NFU; Dutch Federation of University Medical Centres) together with other key stakeholders such as the Universiteiten van Nederland (UNL; Universities of the Netherlands) formulated the 10 principles for Socially Responsible Licensing (SRL) in 2019. These principles identify outcomes that may generate such societal value.

However, opportunities to identify societal value for a specific licence are not always straightforward and require preparation and consideration by the PRO. **The model introduces a funnel to assess what is needed to develop a product/service, how PROs can potentially contribute, and identify possible outcomes (SRL type).** It aims to structure and support decision making by the various PRO stakeholders, i.e. researcher, board and technology transfer manager. The model recognizes that these stakeholders will need to work with external experts to generate a sound picture of the potential product and its development.

The model posits that the PRO's continued involvement in the development increases the chance of successful development. A PRO's continued involvement also increases the scope and benefit of the negotiated returns. Involvement can be through support of a (co)-founding principal investigator, scientists engaged in collaborative research, convertible loan or an equity stake in the company. The model recognizes that the PRO's role diminishes over time as the development moves forward, but this continued involvement can benefit the company; the PRO may benefit from the value created by the company and by realizing SRL-type outcomes. This is also relevant for the PRO

as at an early development stage it will be extremely difficult to get a firm commitment on pricing, distribution or availability terms.

The model's premise is that a better preparation reduces friction between parties, increases efficiency and speeds up the licensing negotiations, benefitting all parties involved. Especially when a PRO is willing and able to invest in the development, its expertise can be leveraged to create additional value in the company. As such, this model is part of a PRO's due diligence. It complements existing tools such as the Invention Disclosure Form (IDF) and offers particular benefits when a spin-out is considered.

The key aim of the model is to initiate the internal discussion on value creation of a patent (portfolio) and can serve as an initial step on the long road of more successful knowledge valorisation. It supports the PRO's opportunity and risk assessment of the development process as part of the PRO's internal alignment and decision making. It helps to assess the value of a PRO's contribution in relation to the overall costs and presents possibilities to contribute to the development. This enables the PRO to identify SRL-type outcomes that can realistically be negotiated.

The model will be made available as a digital tool, accessible via a website. The authors and committee hope that this model and the accompanying thoughts, examples and descriptions will improve negotiation quality and benefit PROs, companies and society by increasing the chances of a successful development of products based on scientific insights.

Above all, the inclusion of SRL principles in licence agreements requires awareness and willingness from both parties. We are not in a position to force a level of SRL upon parties, but we strongly suggest being pro-active in incorporating SRL principles in the licence agreements. This tool aims to increase awareness through insight into the development process as a basis for a discussion on SRL principles. The willingness is expected to increase through awareness and insight, but is required from both parties in a negotiation. The authors expect that this tool will contribute to increased SRL. The use of this tool and inclusion of the SRL principles will be part of the development process by the NFU.

Principles

Understanding what adds value requires understanding end-users, development challenges and partner contributions. This understanding allows a realistic assessment of overall contributions and the identification of potential value that can be exchanged. If the value takes a form other than money, a substantiated assessment and robust internal decision making by the PRO should underlie the negotiations. This model facilitates that process. Subsequently, the model's outcomes can be used in the discussion with potential licensees, to align assumptions and manage expectations. A well-prepared partner is a serious partner. Other existing tools used by PROs can also help to assess these challenges and contributions. This model is designed to complement tools such as invention disclosure forms (IDFs).

PROs' prolonged commitment can add substantial value to development, especially in activities or assets related to their core competencies. Access to high-end (joint) research, including improvements to the licensed invention, critical data, equipment, materials, models/assays, patient cohorts and the networks of international experts and key opinion leaders (KOLs) may be far more valuable than the costs incurred by the PRO. By providing these assets as an investment instead of a service, the PRO adds value to the development. Of course, these commitments need to stay within

the boundaries set by law and pre-agreed rules. This includes rules which are designed to protect the PRO, its public funding, and the independence of science in general.

Given the nature of PROs, it is critical to align the various internal stakeholders to improve the speed and quality of decisions related to licensing and start-up formation. When a PRO's researchers, management and knowledge transfer professionals use one and the same model – and in particular, this model – they have a shared understanding of the development process and the opportunities and risks it entails. This shared development picture builds understanding and manages expectations within the PRO, both in licence negotiations and, ideally, when designing research projects. The model can be used when licensing a patent (application) or other intellectual property rights (IPRs) such as copyrights, but can also be used if there are no IPRs, for example related to clinical data.

SRL-type outcomes

To identify potential outcomes of the negotiation that add value to the PRO other than money requires understanding of the specific case and the PRO's interest, as well as the needs, goals and capabilities of the potential licensee. This is contingent on the specifics of the project, for example how well the development process is established, the maturity of the technology, etc. In other words, turning SRL principles into negotiated agreements requires expertise and creativity. For example, the PRO can benefit from local early access to a product/service. In a similar way, support for trials (including clinical ones) or access to equipment or space is likely to add value and provides a way to bind a licensee to the PRO. The wish to focus on the needs of Dutch or European patients can be a reason to provide access to end-user cohorts or relevant data.

Some examples of SRL-type outcomes that can be negotiated in line with SRL principles include, but are not limited to:

1) Faster development to effective availability
2) Wider availability in developing countries
3) Lower costs for end-users
4) Royalties on sales / Milestone payments
5) Research collaboration(s) including public private partnerships and clinical trials
6) Early access to inventions/products in a research setting or to patients in trials
7) Reputation of the Netherlands as a key R&D ecosystem, Dutch KOL recognition
8) Settlement of start-ups/ spin-offs / innovative companies in the Netherlands (*vestigingsklimaat*)
9) Production (development) in the Netherlands
10) Open source access to certain outcomes of the development, e.g. new processes

The model

The model introduces a funnel that provides preliminary insight into the product development needs in a specific case, resulting in a high-level product development plan. It lists activities, costs and risks involved in developing the product/service and the PRO's contribution to that total investment. This is created by the PRO's researchers and knowledge transfer staff. However, to optimally use the model, external expertise will be needed. External perspectives increase the validity of outcomes and broaden the available expertise for discussions and decision making. This will be explained below.

The basis is a qualitative assessment of the 'Opportunity'. This should decide whether continuing to stage two is worth the effort. Although qualitative, the assumptions should be made explicit to

facilitate discussion. The authors and committee believe that a quantitative assessment of the value of a patent application of an early-stage technology requires complex modelling and many assumptions, making the outcome highly speculative. However, if such an assessment is relevant, there are methods to do so, e.g. discounted cash flow, real-option method, etc.

If warranted by the opportunity, detailing the 'Activities' stimulates the PRO to develop a deeper understanding of the actions, assets and expertise required to develop the product/service. The process should facilitate discussion and result in the joint development picture. The underlying assessments and views are as important as the picture itself. It should be grounded in relevant experience to ensure its validity. It is therefore crucial that this process includes external perspectives, e.g. from industry, regulatory bodies and end-users. For example, the research, models and assays that led to the results (IP) may not be relevant for product development. In addition, data generation and documentation within PROs do not always meet the regulatory or industry standards.

To complete the overall picture, assess the 'Costs' and 'Risks'. This assessment is important for two reasons. Firstly, it introduces the value of the earlier research by the PRO and related IPRs in the context of the overall investment required to bring the intended product/service to market. Secondly, this identifies activities that offer the PRO an opportunity to determine what it can contribute to the development. The activities that offer an optimal use of PRO expertise and resources can be an investment to maintain the PRO's involvement in the development. It is those activities that can be linked to SRL-type outcomes during negotiations, as illustrated by the examples in the appendix.

The website

The model will be made available via a website, most likely the NFU website. Users can enter the required information and progress through the specified steps. The tables provided illustrate how the model is presented. The users are prompted with the questions listed in the Appendix Questions. These and additional information about the terminology are ideally made accessible through tooltips. The result is a report to be used in the decision-making process (internal) and negotiations (external). The website will provide examples of SRL-type arrangements, such as those listed in the appendix below, and the background and considerations of the model, for those who are interested. It will be updated and amended based on the experience and needs of the users. Its intended users include researchers and technology transfer professionals of the PROs. It will also aim to be relevant to entrepreneurs, investors, lawyers and other advisors who engage with these PROs in technology transfer arrangements. Rather than being limited to patent licences, it will strive to include relationships involving intellectual property or other assets that are used in university technology transfer.

The website will support the use of the model in four steps. These four steps are described below in order, starting from the opportunity. It can also be useful to approach the question by working backward after setting the objectives to identify outcomes and then requirements of the activities and determine whether such an opportunity exists. The four steps are:

1) Assess Opportunity: if this is sufficiently positive, move to step 2.
2) Fill out Activities, input Risks and Cost assessments; move to step 3.
3) Generate report and discuss outcomes; move to step 4.
4) Set internal objectives and commitment for contribution and SRL goals.

Step 1 requires an assessment made by scoring each topic with plusses or minuses.

Step 2 will require in-depth understanding and expertise related to product development. It is likely that this will take the most time, and involve advice gathered from a diverse set of experts (including external ones). To help determine what activities are relevant, questions have been included in the appendices to this document that warrant reflection by the team members.

Step 3 refers to discussions with all relevant stakeholders and experts involved. This ideally includes the intended licensee to create a shared understanding between the negotiating parties.

Step 4 may occur before or after a partner has been identified and even as early as the research design phase of the project. This last step is key to link outcomes to SRL objectives. To ensure internal alignment, it is advisable that the outcomes are discussed with all stakeholders as part of the negotiation preparation. This avoids issues about commitments and outcomes at a later stage of the negotiations.

The team

This model and the accompanying document were created using the input of a range of experts and sources from both industry and academia. The final version is the result of the efforts by the project team. This team consists of Markwin Velders (Prime Life Science), Vincent van der Wel (Orfenix), Jacqueline Selhorst (ZonMw), Saco de Visser and Benien Vingerhoed (FAST), Hugo van Rooijen (HollandBIO), Arno de Wilde (EQT LS), Corné Baatenburg de Jong (ReumaNederland), Kim Karsenberg (NFU), Joris Heus (Amsterdam UMC, also on behalf of NFU), Christian Staupe (TUe, also on behalf of UNL) and Ivo de Nooijer (AMLUG).

Socially Responsible Licensing assessment model

Opportunity

Score (+/-)

What is the expected use of the product / service?

Expected number of users/customers/patients?

low/ substantial/ high

Expected volume of sales (frequency of use)?

low/ substantial/ high

Is it a technology (platform) that can be easily scaled?

no, products separately developed/ yes, overlap/ yes, high synergy

What is the perceived benefit/efficacy of the product / service?

Is there an unmet need?

similar products exist/ alternatives exist/ no satisfying alternatives exist

What is the ease of use (e.g. level of complexity, side effects, speed)?

worse/ similar/ better

What is the competitive environment of the opportunity?

Are there many similar research and development projects ongoing?

many/ some/ few

Is there investment capital and interest available for solutions in the field?

limited funds/ multiple funds/ many funds

What is the expected development time to reach the market?

How many years are needed to bring the product/service to the end-user?

>8 years/ 3-8 years/ 0-3 years

What is the commitment of the Inventors and/or the research and/or clinical department?

Is/are the inventor(s) committed to remain involved in the development?

no/ yes, limited/ yes, fully

Is the department/institute/faculty committed to supporting development?

no/ limited (e.g. research or staff)/ yes, fully

What is the strategic relevance of the licence/start-up for the PRO itself?

Are key personnel of the PRO involved in the project (e.g. distinguished professors)?

no/ yes (limited)/ yes, very much

Does the technology help strengthen key research areas/themes for the PRO?

no/ yes (limited)/ yes, very much

Does the licence offer the opportunity to link key partners to the PRO?

no/ yes (limited)/ yes, very much

Other key considerations related to the opportunity?

Net assessment of the opportunity:

Activities

1. **Product development**
    1. What steps are needed to develop the product / service from invention / creation to marketable item?

Step 1

Step 2

Step …

2. **Delivery method / manufacturing**
    1. What steps are needed to effectively offer the product / service to its intended end-users?

Step 1

Step 2

Step …

3. **Legal and Regulatory**
    1. Are there any other licences / rights needed to bring the product / service to market?

Answer

    2. What regulations are applicable to the product / service and its development?

Answer

3. Are there laws / rules with regards to market access that are applicable for the product / service, including reimbursement?

Answer

4. What is the expected benefit of the licensed IP, e.g. scope of protection, territory, prosecution status, in light of other existing rights (e.g. Freedom to Operate)?

Answer

5. Are there any other types of rights relevant to market access or exclusivity, e.g. orphan designation, data protection and/or trade secrets?

Answer

4. Customs / Use / Channels

1. How does the end-user access the product/service?

Answer

2. Who determines whether the product is made effectively available to the end-users (and based on what criteria)?

Answer

Costs

	Costs
Product Development Activities	
Step 1: ….	€ …
Step 2: ….	€ …
Step ..: ….	€ …
Delivery method and manufacturing	
Step 1: ….	€ …
Step 2: ….	€ …
Step ..: ….	€ …
Legal / Regulatory	
Step 1: ….	€ …
Step 2: ….	€ …
Step ..: ….	€ …

Risks

	Risk
Product Development Activities	
Step 1: ….	Low / Medium / High
Step 2: ….	Low / Medium / High
Step ..: ….	Low / Medium / High
Delivery method and manufacturing	
Step 1: ….	Low / Medium / High
Step 2: ….	Low / Medium / High
Step ..: ….	Low / Medium / High
Legal / Regulatory	
Answer to question 1	Low / Medium / High
Answer to question 2	Low / Medium / High
Answer to question 3	Low / Medium / High
Customs / Use / Channels	
Answer to question 1	Low / Medium / High
Answer to question 2	Low / Medium / High

Internal report for discussion purposes [EXAMPLE]

Opportunity

It is expected that the product/service will have a ***low*** number of end-users, with a ***high*** sales volume. ***Alternatives exist,*** the developed product service is ***faster / less complicated / has fewer side effects***. ***No*** similar research and development projects are going on. There are ***many funds available and there is great interest from investors*.** The inventors are able and willing to work ***parttime*** on the further development of the product/service. It is expected that the product will reach market in **3 - 8 years.**

Net assessment of the opportunity: ***positive***

Activities	**Costs**	**Risk**
Product Development		
Step 1	€ 100,000	Low
Step 2	€ 1,500,000	High
Step 3	€ 750,000	Medium
Delivery method / manufacturing		
Step 1	€ 100,000	Low
Step 2	€ 1,500,000	High
Step 3	€ 650,000	Medium
Step 4	€ 100,000	Medium
Step 5	€ 2,500,000	High
Legal and Regulatory		
Step 1	€ 200,000	Low
Step 2	€ 300,000	High
Customs / Use / Channel		
Step 1	€250,000	Low
Step 2	€750,000	High

Summary	**Costs**	**Risks**
Total Project Costs and Risks	*€ 8,700,000*	*Medium/High*

Report for Licensing discussion [EXAMPLE]

Opportunity

It is expected that the product/service will have a ***low*** number of end-users, with a ***high*** sales volume. ***Alternatives exist,*** the developed product service is ***faster / less complicated / has fewer side effects***. ***No*** similar research and development projects are going on. There are ***many funds available and there is great interest from investors*.** The **i**nventors are able and willing to work ***parttime*** on the further development of the product/service. It is expected that the product will reach market in **3 - 8 years.**

Opportunity score: 14

Activities	**Costs**	**Risk**	**Party**
Product Development			
Step 1	€ 100,000	Low	PRO
Step 2	€ 1,500,000	High	External
Step 3	€ 750,000	Medium	PRO
Delivery method / manufacturing			
Step 1	€ 100,000	Low	PRO
Step 2	€ 1,500,000	High	PRO
Step 3	€ 650,000	Medium	External
Step 4	€ 100,000	Medium	External
Step 5	€ 2,500,000	High	External
Legal and Regulatory			
Step 1	€ 200,000	Low	External
Step 2	€ 300,000	High	External
Customs / Use / Channel			
Step 1	€ 250,000	Low	PRO
Step 2	€ 750,000	High	External

Summary	**Costs**	**Risks**
Total Project Costs and Risks	*€ 8,700,000*	*Medium/High*

Investment per Party	***Costs***	***Risk***	***%***
6PRO	*€ 2,700,000*	*Medium*	*31%*
External	*€ 6,000,000*	*High*	*69%*

Socially Responsible Licensing goals

1. *Early access for patients*
2. *Research executed in PRO*
3. *Royalties on sales*
4. *Access to product / service in development countries*

Background and considerations.

PRO role and opportunity

A core task of Public Research Organizations (PROs) such as universities and university medical centres is creating societal impact. This includes scientific insights becoming useful to society as part of products or services (valorisation). To accomplish this, the research results need to be transformed into an application (innovation). Sometimes PROs have the ability to do that internally, but in most cases, they need partners to do this efficiently. For example, in the case of new medicines, biotech and pharmaceutical companies are required to develop and commercialize a product or service.

With that aim, PROs frequently collaborate with commercial parties and grant licences to an invention made by their researchers. Nowadays there is a growing awareness that the value of such licences is not limited to their monetary equivalent; socially relevant aspects and values can also be included. With that in mind, the Nederlandse Federatie van Universitaire Medische Centra (NFU) together with other key stakeholders formulated the 10 principles for Socially Responsible Licensing (SRL) in 2019.

The SRL principles state that licences should favour the effective availability of products/services based on the licensed results. The principles identify the aims and interests of PROs to work towards in their licences. The PRO in its turn needs to align its objectives with its partner's. In practice, some of these principles are more complex to implement than others, e.g. because of the type of product/service and the development stage. The principles set the 'why' of licensing. This model adds a 'what', a method to identify elements of value that contribute to achieving SRL objectives. Lastly, the 'how', or examples of wording for SRL licenses, are part of the SRL-toolkit, a clause list created in 2020.

Applying the principles and using the model and tools require a joint effort of the PRO's researchers, management and knowledge transfer professionals. They need to appreciate the value of a product/service developed on the basis of research results, the difficulties to actually develop it, and the relative value of any earlier and potential future contribution. This understanding is important to prepare for negotiations and eventually reach an agreement with a licensee. In the absence of a shared perspective on opportunities and risks (and who assumes them), the negotiations can be frustrating and very time consuming.

There are many ways in which the PRO and its staff can contribute to the development process, before and after the closing of the licensing deal. Although it is likely that in many cases the PRO can contribute only a modest amount to the development, its contribution should not be overlooked. Even if the PRO decides that it cannot or should not contribute to the further development, the preparation will improve the overall negotiations and increase its stakeholders' awareness of possibilities to implement SRL objectives in the licensing agreement. If it sees a way to contribute to a relevant opportunity, the model provides a foundation for a PRO discussion and decision making that will benefit the negotiations.

The core question is the value exchange the development process offers for the licensee. This is where the SRL objectives can be linked to value added by the PRO to the development. Using forms of joint research with shared risks or benefits can be part of the deal. Collaborating in the further development has benefits for the researcher at the PRO and reduces the risks for commercial partners, lowers their exposure and thereby ultimately increases the chances of the invention becoming effectively available.

Appropriate use and implementation of this model will require expert advice from outside the PRO, as the development process is usually not a PRO core activity. Networks, such as those initiated by FAST, or professional service providers can support the process and provide relevant input to the model. The model can also be useful to other stakeholders, such as research funders, including charities, to understand the value of their specific contribution and role. If entrepreneurs and investors understand the framework used by the PRO, this understanding may facilitate negotiations and, in the end, improve the availability of products/services to society.

This document aims to increase awareness and provide assistance to facilitate a successful licensing process in order to put policy and practice on a more level playing field. Choices can be made that create value for future development not only during licensing negotiations but also during the design of research projects. The investment of created value in product development is the ultimate way to achieve the aims set out in SRL. The practice teaches that control over products and licence terms is directly linked to the level of involvement of the licensor in the development process of the product. However, there is no investment without risk. This model therefore also aims to offer a framework to guide the decision for further participation in a future product or service.

Value and valorization

Value is a broad concept. In the context of SRL, it refers to both the economic value of activities, resources, contributions in time and materials to a development process and the partially intangible value of societal benefit of the product/service. Other types of value include creative, aesthetic or scientific ones. Researchers in the LSH field at PROs are constantly investigating new techniques, treatments and methods to diagnose, care for or cure people. These results have value in themselves, e.g. scientific value. However, it is also important that results from this publicly funded research are translated into applications beneficial to society. And although the results of the research performed at PROs are often initially promising, substantial additional research and development are usually needed to turn insights into products/services.

Development requires a myriad of steps that must be completed successfully, including the development of the product/service itself, the capabilities to deliver/manufacture it, the regulatory and legal room to offer it to end-users, and the end-users' or other stakeholders' willingness to use it. All of these elements introduce risks to the process, as most require significant investments and specialized expertise. In some cases, a PRO has all the necessary skills, capabilities and resources and is willing to develop a new product/service 'in house', effectively taking the risk of developing it and creating the total value of the product/service. In most cases, turning research into products/services requires expertise not present within a PRO, for example in manufacturing, regulatory aspects and sales. It may require a way of working not well suited to researchers at a PRO, e.g. a very stringent approach to processes and documentation. In all cases, all the relevant expertise needs to be available to turn research into a commercially viable innovation.

This is where out-licensing can provide a solution, and SRL offers principles to help set the PRO's aims. A cornerstone of SRL is the freedom of parties to negotiate and enter into licensing agreements. The fact that parties can have different aims to do so offers an opportunity to create and add value. The share of value contributed by the PRO will determine its ability to leverage its contribution to achieve objectives that are in line with the 10 principles of Socially Responsible Licensing.

This relative contribution will be limited in many cases. Even if the initial patent applications filed by the PRO are able to support the final product, the development process is likely to require substantial investment. The good news is that there are other opportunities to add value, and the value created in PROs is not solely represented by intellectual property (e.g. patents, copyrights or databank rights). Additional sources of PRO value are the proprietary results of experiments (i.e. pre-

clinical and clinical trials), knowledge, equipment, and expertise of individual researchers and teams, as well as the ability to design and perform specialist research. Moreover, especially in the early phases of development, the role of key inventors and their networks can be very valuable to convince stakeholders. When patients participate early in the development process and/or parties have access to specific patient cohorts, the development process is strengthened.

When engaging in partnership negotiations, PROs should put the value created (actual or potential) in the wider perspective of overall value that needs to be invested. This involves more than the above-mentioned alternative sources of value. For example, the value of early-stage academic patents is often very limited as they were not drafted with in-depth expertise of the relevant application and market. This can have a substantial impact on their value. Thus, PROs need to understand and evaluate the required activities to develop the product/services and their ability to support the research and development if they want to achieve their SRL objectives.

Investing in development

Products and services developed on the basis of research results can follow a multitude of paths from idea to market. Many of those paths end unsuccessfully. There are many factors that determine or influence the development route or outcome. The risks and opportunities can be specific to the product, sector, country, technology, etc. The mix of these factors determines to a large extent what is needed to develop a product/service, how likely it is to succeed, and consequently who is willing to invest time and resources. This can be represented in highly stylized models that help our general understanding but do not show what is actually needed in a specific product, sector, technology, etc.

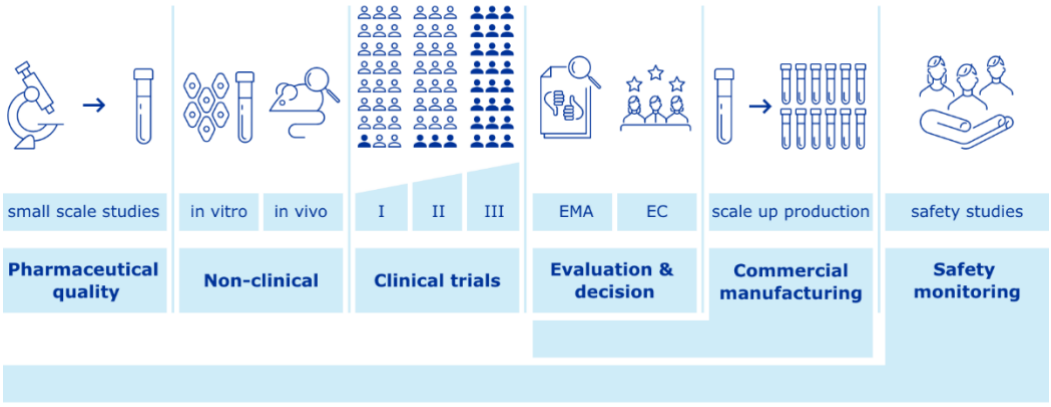


Figure 2 EMA pipeline https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19/treatments-vaccines/vaccines-covid-19/covid-19-vaccines-development-evaluation-approval-monitoring (accessed 13-06-2022)

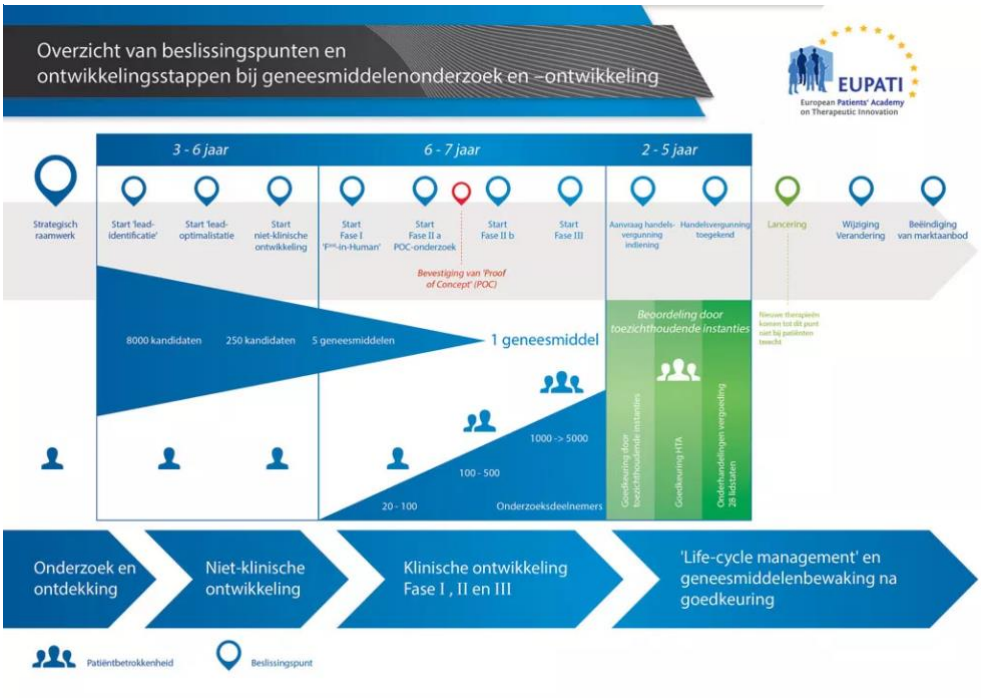
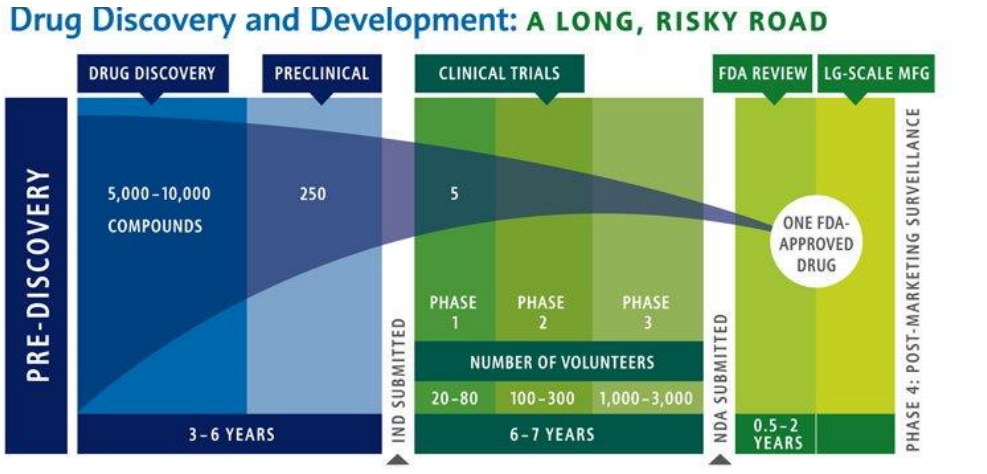


Figure 1 EUPATI Pipeline https://toolbox.eupati.eu/wp-content/uploads/sites/4/2020/07/development-steps-in-medicines-v1_NL.jpg (accessed 13-06-2022)



Source: Pharmaceutical Research and Manufacturers of America

For each of the models and, in hindsight, for each actual product or service, the investments and risks can be determined. When plotting value over time, the result is almost always an S-curve. The curve will differ between projects and even change within a project over time. Thus, they should be taken for what they are: indicative. The core message of the S-curve in product/service development is that the major value increase is in the middle. What the middle is depends on the sector, country, technology, etc. Value tends to increase and risk tends to decrease in a limited number of, usually expensive, steps/phases/actions. Understanding 'the middle' for the specific development route is thus critical.

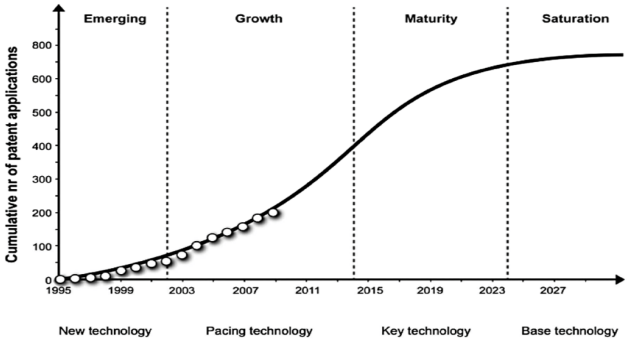


Figure 4 Fernald et al, Limits of Biotechnological Innovation, "Technology and Investment" 2013 (4) 168-178

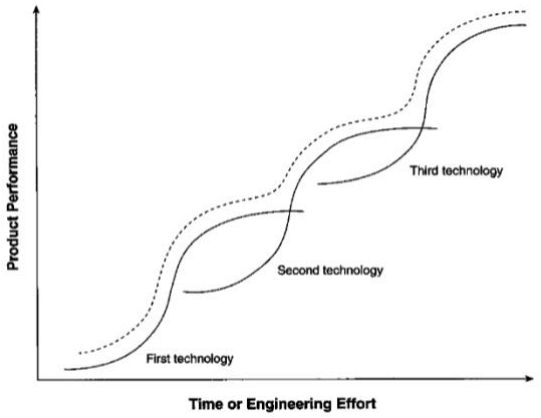


Figure 3 Clayton Christensen, The Innovator's Dilemma, New York 2000.

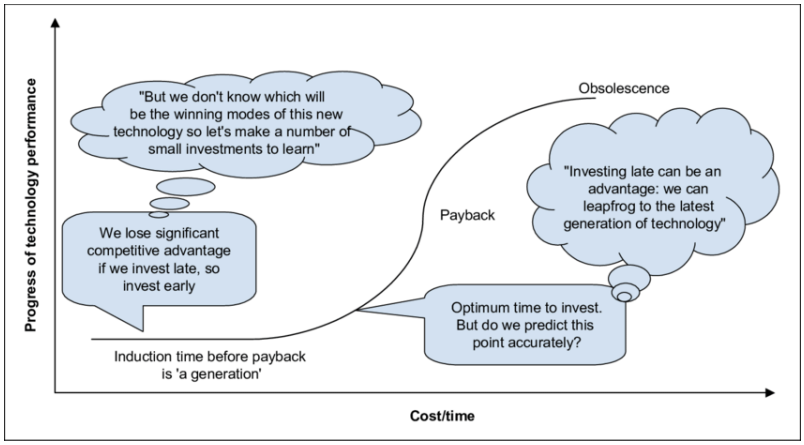


Figure 5 Brown, Target selection and pharma industry productivity: what can we learn from technology S-curve theory?, "Current Opinion in Drug Discovery & Development" 9(4):414-8

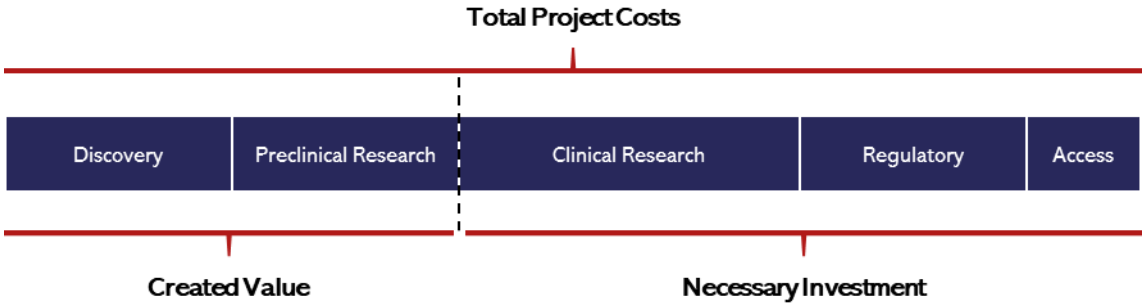
Although the product's increase in value has an inverse relationship with its risk profile, there is a crucial difference. Risk and costs are incurred when the development starts; the value materializes if development is completed successfully. In most cases, little or no income is generated to set off development costs if the product/service does not enter the market. The value is the promise of future income. Consequently, there is a premium on the time and resources that take on the risk to develop the product/service. In other words, investing time and resources while accepting the risks of not recovering the expenditure is the investment. This gives investors their pivotal role in the development process.

Without investments to translate promising results into products/services, the SRL objectives will not exist. Even if the effort is made, it may still fail. But not trying is an automatic failure, and a failure is a loss to society. All of the potential value remains an academic issue in the event of failure

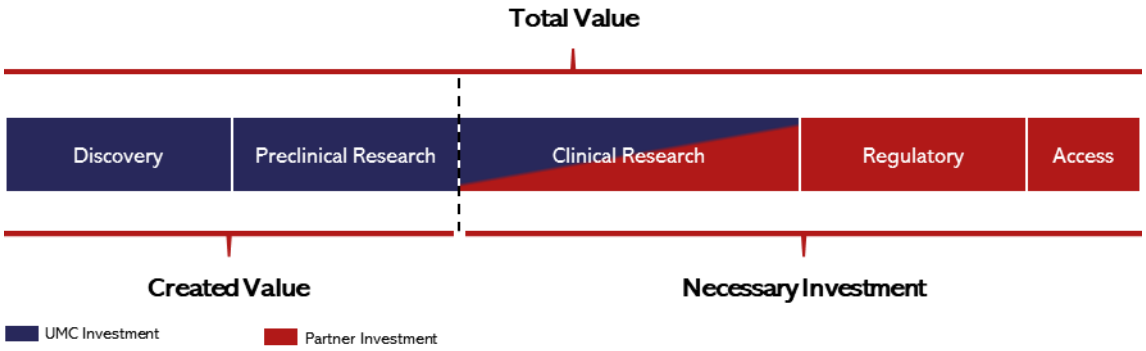
as neither social nor financial value is created. To achieve their aims, PROs must invest in valorisation. What and how much are of course not easy to determine. If the investment is in line with its core mission and competencies, it can be considered an important or logical step in a PRO's valorisation strategy. It helps further a key aim of the PRO and is likely to create value using its core competencies and assets at lower costs than other parties would encounter.

Relative contribution & PRO investment

In almost all cases, PROs are unable, or unwilling, to invest in all of the development needed, i.e. execute all phases of development. This derives from the perspective of risk and from the perspective of its core competencies and assets. Therefore, partners such as biotech and pharmaceutical companies, professional services companies and CROs are needed to contribute. When this process takes place in start-ups, financial investors play a key role by assuming the financial risk for the activities. The start-up team takes the risk of investing their time and talent. All of the investment required forms the Total Project Costs. Some of those investments will already have been made, the PRO Created Value. This may be more or less than the costs incurred by the PRO. The Total Project Costs, minus the Created Value, equal the investment needed ("Necessary Investment").



The outcome reflects the necessary investments to be picked up by the parties willing to invest; in the case of a start-up, this will include the team, the financial investors and potentially the PRO. This is interesting for the PRO because its contribution (Created Value and share of Necessary Investments) in relation to the Total Project Costs determines its leverage. It is this understanding that is the intended outcome of the process and report facilitated by the model. The risk of failure, as well as the money and expertise needed to successfully complete a phase, are components that differ per activity and need to be priced as part of the assessment.



In general, successful completion of phases with a higher risk of failure and greater costs create greater value. Providing resources (including intangible ones) needed to develop the product/service without a return through fees is an investment. This SRL assessment model creates a shared picture of opportunities and risks. It facilitates a shared understanding, both within the PRO and with external stakeholders, about the optimal route forward and how the PRO can add value. It is this contribution that can be leveraged to achieve SRL objectives.

Given the nature and role of PROs, their investment should not be the same type one can expect from a venture capital firm, a large multinational or serial entrepreneur. Not only are they subject to a formal role and legal limitations, they cannot provide those types of contributions as efficiently as specialized partners. However, that does not mean that there are no opportunities to invest. On the contrary, given the role of the other investors mentioned above, the PRO should strive to add value based on its core competencies and capabilities. They are likely to be very valuable and more unique, more sustainable to offer, and easier to commit to as part of a joint effort.

Access to high-end research, critical data, equipment, materials, the networks of international experts can be far more valuable than the costs incurred by the PRO. Similarly, some unique resources may be available, such as proprietary knowledge, access to machines, expert scientists and in some cases access to rare patient cohorts (and their data). Collaborating in the further development reduces the risks for commercial partners, lowers their exposure and thereby ultimately increases the chances of the invention becoming effectively available. It is by understanding the created value and that to be created (and its costs) that enables a PRO to determine how it approaches the subsequent development. Only by adding more value can the PRO claim more benefits or outcomes valuable to itself.

Licensing negotiations and preparations

To achieve the aims of the PRO, i.e. objectives as set out in SRL, requires creativity. By moving beyond a zero-sum approach and searching for opportunities where interests differ, opportunities may be found to create value in the negotiation. This requires creativity and understanding of the different interests and limitations of parties. It is these interests, or more precisely, the perceived conflict between interests, that determine the type of agreement which may be reached. If the interests are sufficiently different, an agreement can be reached whereby the gains of one party do not equal the loss to the other; these are called integrative agreements.

To achieve this, the parties must find new opportunities to capture and distribute value. Often this search requires information or insights that were previously unavailable to one or both sides. A process to find such integrative solutions requires a system in which parties engage in iterative discussions about the development and required activities. It may also require unbundling previous issues to identify individual aspects suitable for discussion and agreement. In addition, it is probably important to drill down to a level of detail relevant to understanding key aspects and considerations.

The topics may then be discussed to identify the differences between the parties needed to construct tradeoffs and offers. The issues which offer high value to one and low cost to the other produce the best opportunities to reach an agreement. This model, and especially the report it generates, facilitates this process by clarifying assumptions. Even if there is only one party interested in taking on the risk of an early-stage development process, as in most early-stage licensing cases, the negotiations will benefit from proper preparation. Even if unsuccessful, the PRO will have gained a better understanding of what is needed. It can use those insights to find new partners or initiate development activities itself.

In any case, preparation is key, both to ensure internal alignment and manage expectations and facilitate efficient negotiations with the potential licensee. On the PRO's side, this requires that researchers, management and knowledge transfer professionals invest time and effort. It requires the use of scarce resources and entails a risk. In other words, the opportunity should be worthwhile to pursue, and the internal stakeholders should be aligned about what is feasible and desirable and what limitations exist. Only with proper preparation and clear roles and boundaries can this

preparation and the subsequent negotiations be concluded in a manner which avoids internal misunderstandings, uncertain mandates, and an unnecessary loss of time.

Appendix Questions

Opportunity-related questions

These questions are intended to help identify the opportunity in broad strokes. The user is strongly advised not to get lost in complicated models or myriads of assumptions about pricing, reimbursement, value, costs, etc. if there are few or no relevant comparators, the time to market is long and/or the technology used requires substantial investments to make it feasible for end-users and the production/delivery of product/service to them.

Market size

The market size is the number of end-users (patients or consumers) who could conceivably use the product.

This does not take into account reimbursement status, market access, production limitations or standards of care of a product.

- How many patients/consumers could use the product to their benefit?
- What is the unmet need of patients/consumers with existing products or services?
- Is the product or service aimed at cure, care or stabilisation of the need?

Market access

The commercial structures and activities needed to effectively market the product.

Apart from regulatory aspects related to market access, the technology, market or capital requirements to effectively market a product have a substantial impact on the best or only route to application and impact. These factors determine the role the licensee can play and what needs to be developed, bought or accessed in some other manner.

- What is a likely business model for the product/service?
- What part of the required activities will the licensee do within its own organization and what part through third parties?
- What other key components or services are required to effectively use the product or service and what is their dependency and accessibility?

Competition

The competitive field for the product or service being developed.

This is likely to change over time. However, the number and size of products and projects reflect the products (actual or potential) in the market that offer an alternative for patients/consumers.

- How many companies are active in the same or a highly similar field?
- How many companies/ researchers work on projects claiming the same or similar benefits?
- How many new products have come out during the last 10 years addressing the same need?

Investors

The activity of investors and deal size in the specific area the product / service is aimed at.

This is dependent on what is considered promising and on what networks of investors are active as investing is generally done in larger consortia when substantial amounts of funding are needed.

- How many investors are active in the field and how many of them are located in the Netherlands?
- How many investors have worked with the PRO and/or the researchers before?
- How many deals (early-stage and other) were done and what was the reported ticket size in the last two years?

Activity-related questions

These questions are intended to help identify the necessary activities to develop, create and offer the product / service. They are intended to prime the review and discussions and provide questions for discussion and further assessment where needed. Please note: these questions cannot be answered fully in many cases, and in cases where it may be feasible to do so, it is questionable whether it is worthwhile to spend the time and money to do so.

Product development

Study design & execution

The design of the study itself and its subsequent execution.

As the research output is conditional on the study design and execution, a key criterion is related to those aspects. The former aspect plays a role in differentiating academic from industrial research, and the value of the findings in either arena; the latter influences the quality of the data and findings.

- What clinically/commercially relevant reference models have been used?
- What end points (clinical) or reference products/service have been used?
- How was the research executed and monitored, e.g. lab journals, number of researchers involved and frequency of changes, method of data capture, for example in line with ICH/EMA/FDA guidelines?

Data quality

The quality and relevance of the research results for the subsequent development.

The development revolves around the available research results and their relevance to it, including technical, regulatory and other hurdles. The value of the initial research results is significant.

- Does the data provide sufficient and relevant information about safety and toxicity (if applicable)?
- Does the data provide insight into efficacy and method of action, e.g. will it work in the relevant context?
- Does the data help to predict the availability/effectiveness (e.g. biological) of the product/service when applied in its intended system?

Resources

The unique or non-catalogue materials or data used in the research that are relevant for the subsequent development.

The resources used to perform the research may play a key role in the development step, initially mostly for corroboration, but they may also be relevant later if they include key product or user-related aspects, either to develop or test the product or related processes (e.g. manufacturing).

- Unique data (sets) used, e.g. data from a rare patient cohort?
- Proprietary materials used, e.g. software or modified organisms?
- Unique or complex equipment or methods used?

Type of technology

The inherent nature of the technology used in the product/service and its use and existence.

The type of technology reflects typology related to its method of action, material nature and physical structure, or similar inherent aspects of the product or carrier. It has many implications for type of partners, regulatory framework, users and method of use, etc.

- Has the technology been used in Life Sciences & Health before?
- What other components or technology (types) are expected to be part of the product/service?
- Are there requirements for use, storage, continued support or waste disposal?

Stage of development

The Technology Readiness Level (TRL).

The stage of development or TRL facilitates discussions, provided the concept is applied diligently. Moreover, the TRL of the product/service is separate from and possibly independent of the TRL of the production and/or delivery methods.

- What is the TRL of the product/service, e.g. (pre-)clinical phase?
- What is the TRL of the likely production method and development process?
- What is the TRL of any ancillary technology required to deploy the product/service?

Technology maturity

The experience with and application of the technology in the context of the patients and users.

The technology maturity can be a determining factor for acceptance and application. Firstly, if a product or service uses a well-known technology which is widely applied, it is easier for users to fit it in their frame of reference and daily routines. Secondly, using a mature technology provides assurance about the type or frequency of adverse effects related to use.

- Is the technology widely accepted in clinical/commercial use, e.g. treatment protocols?
- Is the technology a ‘standard of care’ or some other form of relevant frame of reference?
- Is the technology associated with adverse events (especially recent ones) impacting patients/users/the environment?

Delivery method/manufacturing

Production method

The methods, requirements and conditions to create and deliver the benefit the product/service provides.

For commercial application the production method of a product/service requires standardization and scalability. It is likely that the application of existing processes will evolve during the development or that new ones will need to be developed.

- Are there existing and accessible production methods or do new ones need to be developed?
- Is there sufficient manufacturing capability and capacity (and access to them) to develop and subsequently produce the product/service?
- Are the required raw materials or input expertise available?

Legal and Regulatory

Reimbursement

Whether or not the product is likely to be reimbursed (if applicable) once it has market access.

The reimbursement status plays a key role in assessing the market potential. Assuming the new product is not already on the market in a relevant form, its health assessment involves other aspects as well (unmet need, etc.). Nevertheless, it pays to consider the reimbursement status.

- Are similar products/services reimbursed?
- Are different products/services offering the same or similar benefit reimbursed?
- Is reimbursement required for effective market access?

Regulatory framework

The relevant regulatory framework to be granted market access, from CE marking to pharmaceutical marketing authorisation.

This framework in conjunction with the unmet need determines the speed at which a product may progress to the market. The requirements for regulatory approval impact the clinical or other information to be provided and the complexity of the studies and subsequent process.

- Have similar types of products/services been approved before?
- What international and national standards need to be met and what type of studies are required?
- What safety or efficacy issues have come up before or are expected to come up for the type of product/service?

IP access/Freedom to operate

The freedom to operate concerns the ability to use the IP relevant to the development process without infringing third-party rights.

Although the freedom to operate is a negative assessment, i.e. infringement of other rights, the positive assessment, i.e. what rights are required to effectively apply the rights owned in a manner which enables delivery, is equally relevant (albeit even harder to answer at first).

- What relevant IP is known which is required to use the licensed IP?
- What party or parties may require access or potentially consider the IP blocking their freedom to operate?
- What IP would be needed (ideally) to apply the intended product/service?

Customs / Use / Channel

Segment/channel

The segment refers to the type of patients/consumers and their likely access route to the product/service.

The segment will partially determine who is involved and how the product is used. A prescription product used in a hospital by patients fully cared for by the medical staff is accessed differently than over-the-counter products bought by consumers.

- In what setting is the product/service likely to be used?
- Who initiates use and monitors it, and what treatment protocols apply (if any)?
- Is the product/service an element of a larger product or service?

Integrative potential for the PRO-related questions

These questions are intended to help identify the potential goals and investments a PRO can commit to. They may be expected to be balanced and aligned as the aims and societal benefits the PRO hopes to realize legitimize the investment made.

SRL objectives

What SRL goals are most relevant to the PRO in the given context?

The PRO can have pre-set or project-specific aims based on its policy or the context of the project that inform what it would like to achieve (ideally) in conjunction with effective availability.

- What objectives are set or well suited to the project?
- What in-house developments advance goals or commitments made in other projects?
- What earlier arrangements exist or what prior experience is available regarding SRL goals?

Approval

The willingness to contribute with intangibles to the development of the product/service.

The PRO may provide intangible benefits which speed up the development or uptake of a product and can help to optimize knowledge transfer by fostering close cooperation.

- Are staff members allowed to be involved in the company (outside PRO time)?
- Is there a network of Key Opinion Leaders (KOLs) that can be accessed during the development?
- Is the PRO willing to lend its name and reputation to the development of the product/service?

Conflict of interest

The verification by the parties involved, i.e. PRO and researcher(s), that their intended role or contribution does not lead to an issue.

- What other roles or projects are the PRO and/or staff members engaged in?
- Does the involvement in the project negatively impact the core tasks or responsibilities of the PRO or involved staff members?
- What mitigation strategies and actions are undertaken to manage any potential issues related to or stemming from the perceived conflict of interest?

Investment

The willingness to contribute with assets to the development of the product/service.

The PRO may provide assets which speed up the development or uptake of a product and can help to optimize knowledge transfer by fostering close cooperation.

- Can the PRO provide in-kind investment in staff (e.g. the research team or lead researcher)
- Can the PRO provide data or research relevant to the continued development of the product/service?
- Is the PRO able to invest money in the development (directly or indirectly)?

Appendix Examples of SRL application in Licensing

The following examples are anonymized examples of licensing and development agreements entered into by parties. The details of each case are known to one or more of the authors.

Case 1

Research into human biology can lead to insights into disease pathways and potential ways to treat the disease. Sometimes a well-known chemical entity is shown to have such a beneficial effect. This offers both opportunities and challenges for the researchers and the company that aims to bring a pharmaceutical product to the market. One benefit is, for example, that the substance's toxicological profile is well known, but protecting a well-known substance to a level that merits the investment in clinical development is hard.

In this case, a trade-off was made between support in the clinical development and access to patients, particularly in Europe. The extensive clinical network that linked a number of European research institutes working on the specific disease represented a key asset for the licensee. The benefit to the drug development process was the access not only to research knowledge but also to well-characterized patients in a variety of centres that could perform clinical trials.

The PRO set out to include SRL principles in the licence. Its aim was to ensure effective availability, particularly for patients in Europe. After working together in developing the proposition and licensing negotiations, a suitable solution was found. The US licensee committed to limiting conditions under which the intended product was to be marketed, to ensure effective availability in the European market. In exchange, the clinical network supported the development of the desired drug candidates, both in pre-clinical and clinical development.

Case 2

In an attempt to find specific treatments for rare diseases, existing molecules are increasingly identified as potential treatments and tested in a clinical setting in PROs (known as drug rediscovery). In this case, an investigator-initiated study was performed in a PRO with a molecule that was first registered for its original indication over 50 years ago. Its potential as a safe and effective treatment for a novel, rare indication was tested in a clinical setting. The double-blinded, single-centre clinical trial showed promising results.

At the time that the trial was completed, the introduction of novel and more effective treatments for the original indication of the molecule resulted in the molecule becoming obsolete and being withdrawn completely from the market. As the trial showed promising results, the PRO set out to find an external partner to be able to continue research and development. The primary goal of the PRO was to ensure patient access to the treatment.

In the licensing agreement the PRO negotiated, future access to the medicine was key, including clauses on pricing of the drug once successfully developed. Furthermore, the PRO included clauses on non-shelfing and negotiated continued access to the treatment for the patients of the PRO who participated in the first clinical trial. The PRO and the company entered into an agreement in which the PRO will remain actively involved in the further clinical development of the treatment. The company and the PRO will benefit from each other's expertise and capabilities during the product and regulatory development. Both parties are investing in the research and development of the potential novel treatment, and therefore, after successful development, both parties will share the future financial benefits generated by the commercialization of the product.