School of Management

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THE EMERGENCE OF CROWDSOURCING AND OPEN SOURCE MODELS IN DRUG DEVELOPMENT

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Abstract

Contemporary cases of crowdsourcing (CS) and open source development (OS) related to drug development have been selected and studied. Contemporary examples of CS/OS from within and outside of the pharmaceutical industries have been presented to give a background and suggest possible benefits and problems. The main criteria for selection have been that the case must seek to advance drug development and must use crowdsourcing or open source as a mechanism. The cases found in our search show a large diversity in terms of application, usage, and possible implications for the pharmaceutical industry. We found that crowdsourcing within a scientific problem context produced good results, but that open source initiatives were either poorly financed and not successful or focused on neglected diseases made possible through strong backing by non-profit organizations. An analysis of which the pharmaceutical companies where that showed activity on the platforms identified R&D-intensive and biotech companies as the most active. Contract research organizations (CROs) and generics manufacturers (GMs) showed almost complete absence. We argue that GMs are not likely to be interested in this kind of R&D, but CROs are an untapped resource. Finally we propose a hypothetical model that takes into account all the findings from our study and the literature. This model is based on a limited type of open source with a limited number of partners making use of the untapped CRO resource through crowdsourcing.

Key Words: open innovation, crowdsourcing, open source, drug development

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1 INTRODUCTION

The idea of open innovation (OI) or the ”free revealing of innovation” is not a completely new phenomenon. It is a well recognized way of innovating within the development of medical equipment, semiconductor process equipment, library information systems, and sporting equipment (Baldwin & von Hippel 2011). What exactly is open innovation? According to Henry Chesburgh, it is a paradigm that assumes that businesses both can and should use external ideas as well as internal ideas, and internal and external paths to market, when seeking to advance their technology (Phillips 2012).

One factor behind the increasing importance of open innovation is the rising numbers of knowledge workers and their mobility which makes idea protection increasingly difficult for firms. This mobility combined with a growing availability of venture capital has helped to spawn off new firms and commercialize ideas that historically would be locked within existing firms. Another contributing factor to the emergence of OI is the recent advancements in computing and communication technology that has lowered communication costs, allowed for modularized systems where multiple parties can contribute independently, and facilitated collaborative online platforms (Chesbrough & Appleyard 2007).

Online platforms for collaboration and sharing are also the foundation for an emerging open innovation phenomenon, *viz* crowdsourcing (CS). Crowdsourcing is an activity where organizations broadcast problems to a large number of individuals outside of the organization using online platforms (Ekins & Williams 2010). Furthermore, the advent of internet and software development has revealed a huge potential in combining open innovation and software creation through online activities (Baldwin & von Hippel 2011). This phenomenon, known as open-source software development, has revealed the power of open-source (OS) development can have when used in a suitable environment.

In traditional innovation within the pharmaceutical industry, R&D has historically been an internal process and a strategic asset to create barriers for market entry. Furthermore, there is a built in conflict between two main features that makes innovation particularly difficult. On the one hand the company has to be very big to allow funding of R&D projects and to bring new chemical entities (NCEs) through all the stages of development and clinical trials to the final marketing. On the other hand, large companies are generally less efficient at producing new candidate drugs as hierarchies and slow bureaucracy prevent quick and flexible research and decision making. Given that approximately only 1 in 10000 candidate substances tested in the laboratory eventually become a commercial drug (PhRMA 2011), a slow innovation process is likely to significantly hamper new product development. This problem has in recent years mostly been resolved by mergers and acquisitions where the big pharmaceutical companies simply buy promising leads from smaller companies and take them through the very expensive late stages of development (IMAP 2010).

The opposite of the traditional closed innovation process within the pharmaceutical industry would be an open innovation model where firms commercialize external (and internal) ideas by opening up the research and ideation process to external parties. Chesbrough (2003) argues that a fundamental shift is now happening from closed innovation models where the firm controls the innovation process to an increasingly open innovation model where the boundaries between the firm and the surrounding environment are more fluid. This shift presents opportunities for firms to unlock unused potential, but also presents challenges in terms of managing the innovation process and intellectual properties.

As there are few examples of open innovation phenomena such as crowdsourcing and open source development in the pharmaceutical industry there is a need to research and further add to the knowledge in this area. An analysis of the few examples that do exist should be a suitable starting point in this process.

1.1 Problem Discussion

During the drug development process a lot of basic research on biological target systems is duplicated in different labs, where a lot of effort is put into hiding new discoveries from competitors. Furthermore, during the development of other more lucrative drugs, it is likely that researchers stumble upon discoveries that could be beneficial in the development of drugs for the treatment of diseases with less potential in terms of future revenue. Unfortunately there is an option value in keeping this knowledge in-house instead of sharing it; the value of making that information proprietary in the future should there be new circumstances that make this information useful in the development of a more lucrative drug. There is also a cost associated with disseminating this knowledge should the will exist; it takes an active effort to gather up the information and present it to the research community in a standardized way that can be useful to fellow researchers.

This importance of making use of such hidden or lost knowledge is underlined by the trend of a declining number of novel medicines reaching the market in the EU. The number has fallen from an average of 40 per year between 1995 and 1999 to 27 per year in the 2000s. This decline has caused the European Union Commission to worry enough about the state of the pharmaceutical industry to initiate a sector inquiry into the pharmaceutical sector in the EU. They found some disturbing results in regards to the use of patent protection:

> "(the inquiry) *found that originator companies engaged in so-called 'defensive patent strategies'. Defensive patents are not foreseen to be used for innovation but primarily pursue the purpose of blocking the development of a new medicine from a competitor. The sector inquiry also showed that, in such cases, originator companies do not intend to pursue these patents in order to bring a new or improved medicine to the market.*"
>
> (European Commission 2008)

This could be interpreted as that much effort which could be invested into projects creating value for society in terms of new drugs instead goes into blocking the efforts of others. This is virtually antipodal to the idea of open innovation.

In order to get new drugs out on the market a long and costly process of drug development has to precede launch. The cost of developing a drug has risen tenfold from 1975 to 2005 (PhRMA 2011). This is mainly due to that the tightness of government controls have increased tremendously in recent years which raises the total cost and increases the lag time between the first discovery of a lead compound and when profits are earned (Bátiz-Lazo & Holland 2001). To take the drug through all the phases that are required before approval of the drug could cost as much as 1.3 billion dollar for the average drug (DiMasi & Grabowski 2007).

As a direct result of the costly development of new drugs, the best way to make money for many of the existing pharmaceutical companies is to spend their capital on the marketing of existing drugs rather than in R&D to develop new drugs (Angell 2004). According to Angell "*drug companies increasingly promote diseases to fit drugs, rather than the reverse*". This notion is supported by data showing that the big pharmaceutical companies spend a lot more money on advertising than on R&D. For example, in the 1990s the top 10 drug companies in the world consistently spent about 35% of sales on marketing and administration, and only 11% to 14% on R&D (ibid). A way to get more novel products on to the market could thus be to reduce the total R&D expense for new products and thereby increase the willingness of the companies to spend money on R&D at the expense of marketing old known compounds.

Whether or not open innovation could offer a way around some of these issues remains to be seen, but it was suggested by Chesbrough and Appleyard (2007) that a new emerging area beyond IT for open innovation could be in the development of drugs that are otherwise generally considered to be non-profitable if developed through more traditional in-house R&D. Furthermore, a study by Lakhani et al. (2006) suggest that openness and crowdsourcing (termed broadcast search in the study) can result in a higher resolution rate for scientific problems. The study included 166 scientific problems from 26 different firms from various industries including agrochemicals, biotechnology, chemicals, and pharmaceuticals. These findings indicate that there is potential gain in openness even in an R&D heavy sector such as the pharmaceutical industry.

Currently there are only a few studies on how open innovation and crowdsourcing is used in connection with drug development. Moreover, the concepts seem to be used interchangeably and there seem to be some confusion as to what really constitutes open innovation, crowdsourcing, and open source development. We therefore aim to explore this area further to find out how open innovation in general, and crowdsourcing and open source development in particular, is used in the drug development today and how the activities are categorized by the participating parties themselves.

1.2 Research Question

With this paper we aim to explore how and by whom open innovation, crowdsourcing, and opens source development is used in drug development today.

1.3 Research Objective

There are relatively few studies on how and by whom open innovation (OI), crowdsourcing (CS), and open source development (OS) are used in drug development. Our objective is therefore to explore how these activities are used in this context in order to better understand how OI/CS/OS could contribute to a more efficient drug development in the pharmaceutical industry. Our study will be exploratory to its nature and we will based on our findings discuss implications and possibilities for the industry as well as suggest future areas of research.

1.4 Thesis' Structure

The thesis will start with a *Background* section where relevant literature is covered to provide the framework for the discussion of OI/CS/OS. Contemporary examples of OI/CS/OS within and outside the pharmaceutical industry will be used to build the context within which our analysis will be performed. Furthermore, a short review of the pharmaceutical industry is also included in the background section, with a more comprehensive analysis of the pharmaceutical industry appended as *Appendix A* for the interested reader. For data collection we will use an exploratory field study to gather information from a selected number of platforms that we consider to be relevant. The method and criteria for selection and how the data was gathered and analyzed are detailed in the *Method* section. This is followed by *Platform Introductions* where overviews of the selected platforms are presented to provide the reader with some background before any further data presentation or analysis. The results from the data collection are then gathered and presented in tabular form in the *Results* section. The analysis of the data is presented in a separate *Analysis* section where the different platforms are categorized according to the definitions that we have arrived at and compared with each other depending on their classification and what kind of comparisons we find add to the knowledge in the field. The thesis ends with a *Conclusions* section and suggestions for future research.

2 BACKGROUND

2.1 Open Innovation

Open Innovation can be defined as a model where businesses use external ideas, as well as internal ideas, and internal and external paths to market, when seeking to advance their technology (Phillips 2012). It is important to realize that open innovation is the foundation on which specialized platforms such as crowdsourcing and open source development rests.

Gassmann & Enkel (2004) argues that open innovation can be categorized into three core processes; the outside-in process where the firm's knowledge base is enriched through integration of external parties and sourcing; the inside-out process where the firm increases profits by bringing ideas to the market, selling IP (intellectual properties), and multiplying technologies by transferring ideas to external parties; and the coupled process where the outside-in and inside-out process are coupled by working in alliances with external parties.

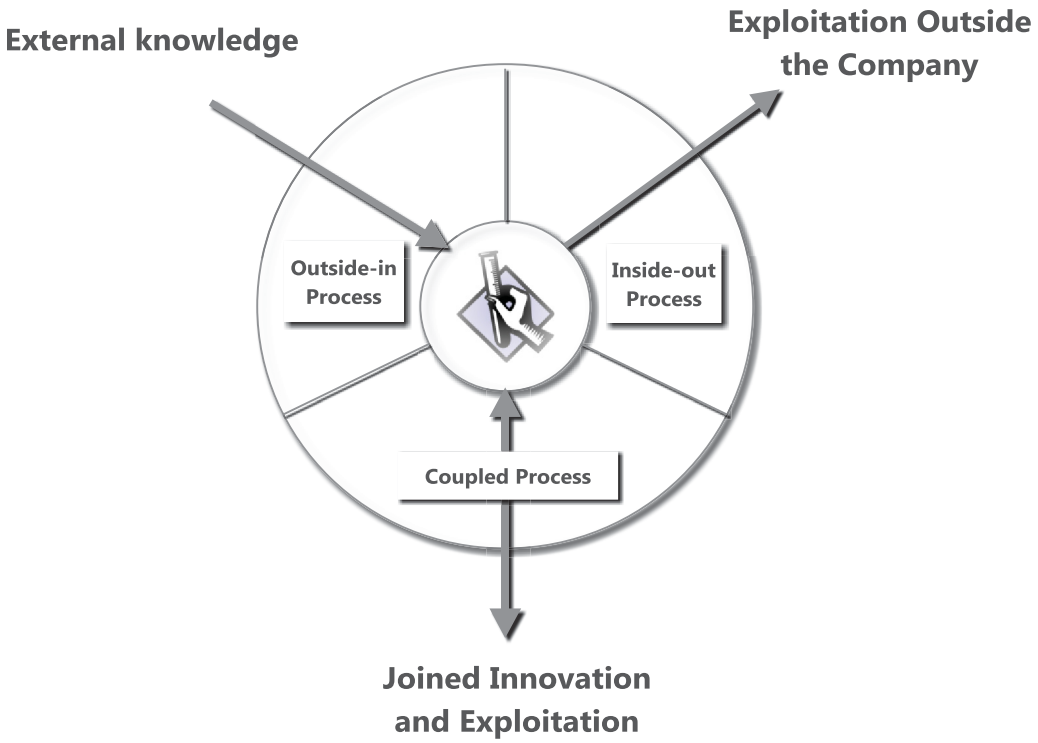

Figure 1 The three innovation types according to Gassmann & Enkel (2004). The locus of innovation within the company is illustrated with a test tube.

The focus of our research is on outside-in processes where a firm's knowledge base can be enriched by external parties and sourcing, specifically by using the crowdsourcing mechanism to broadcast problems to an external heterogeneous group of individuals and organizations or by using an open source development model where open access to data, open collaboration across organizational and geographical boundaries, and open rules accelerate the innovation process.

Although several researchers argue that there is a continuous shift from closed to open innovation models it does not mean that all industries are part of the shift or ever will be (Chesbrough 2003). Chesbrough argues that industries can be placed on a continuum from closed to open in relation to innovation. Industries like the nuclear-reactor industry can be considered using a closed innovation model whereas the film industry that innovates through a network of alliances and partnerships largely uses an open model. In the drug development industry only a few examples can be found where an open innovation model has been adapted, although several studies suggest benefits given that a suitable model could be adapted that connects and gives incentives to all parties (Lakhani et al. 2006). Furthermore, there are many different types of open innovation, all off which might not be suitable for a complete drug development process.

One parameter that has been pivotal in changing the strategy direction towards open innovation platforms is the rapid decline in communication costs. This has together with modular designs allowed for an efficient development process. When working with open innovation, creating a structure of modularity is crucial because it provides the possibility of co-operating both independently and parallel without too much time-consuming correspondence. The modular design architecture is realized through an interactive online structure which allows users to participate in the development and innovation process at a very low cost. This was not possible before the advent of the World Wide Web. Furthermore, working on an online module-based platform will make communication not only more efficient but also less likely to include errors due to ease of retraction.

The modularity has also made possible a strategy that has been employed successfully in highly competitive industries. This strategy has been to use a selective approach to the openness, where open modules are shared for collaboration while at the same time other modules are closed. This approach has been shown to be beneficial in many respects and a well known example of this strategy is the development of the Linux software (Henkel & Baldwin 2009). By this approach, the firms can better control and customize IP issues, stimulate value creation, and take advantage of beneficial side effects. However, in the pharmaceutical industry, research indicates a stronger conviction regarding the importance of IP issue & patent protections (ibid).

The very foundation of open-innovation is based on the attraction to participate for users, and the sustenance of their participation. Each firm will need to develop and customize their own form of open-innovation. By assembling a form where both open and owned invention have their places, firms can start to adopt the open-innovation trend. From a cost perspective, there is evidence of diminishing design and communication costs when employing an open-innovation strategy (Baldwin & von Hippel 2011). Furthermore, the work of Baldwin and von Hippel (2011) indicates that the will of participating in a collaborative work is closely connected to the value creation. The value creation in this context is the splitting of the design costs in-between the different parts, while at the same time still giving all parties access to the full benefits of the final design.

In open innovation through a user-community, development is normally concentrated to the "*most advanced and motivated lead-user segment*" (von Hippel 2001). This can be formalized as shown in equation 1. The performance, motivation, and ability variables in the equation are valid for individuals as well as for groups.

$$Performance = f(Motivation \times Ability) \qquad \text{(Equation 1)}$$

(Locke, Mento & Katcher 1978; Klehe & Anderson 2007)

This indicates that the successful implementation of open innovation within drug development probably relies on attracting the most able, arguably to a large extent found within the R&D intensive big pharma companies (see Appendix A), and making sure that the incentives are big enough to motivate them and to sustain their participation.

From the literature, two main types of human motivation can be distinguished, *viz.* intrinsic and extrinsic motivation (Amabile 1993). Intrinsic motivation is based on the will of doing it "for its own sake" (for personal satisfaction or just for fun) and the extrinsic motivation which requires a reward separated from the initial task, e.g., a monetary reward or something that is perceived as carrying other value for the individual doing the work (Kanfer, Chen & Pritchard 2008). Intrinsic motivation can also include the satisfaction of getting recognition by a crowd and displaying their capacity to potential employers. However, studies have indicated that in order to be motivated, individuals generally expect some sort of financial compensation (Dahlander & Wallin 2006).

In open-innovation in general, previous research has found three main motivators for the individuals: career concerns, payment, and personal need for innovations. Given the complexity of biological mechanisms and considering the large R&D departments and research group collaborations usually operating within the pharmaceutical field, the basic setting might be very different as compared to, for example, open source software (OSS) development. In software development isolated individuals largely contribute to the development and incentives that are successful there might not be so easily translated to the drug development sector.

A prerequisite for successful open innovation, regardless of ability and motivation, is efficient ways of communication and sharing of data and results. Finding, designing and developing an intuitive platform which supports the scientific way of work is important to increase the chances of a positive outcome. Currently we are facing problems emerging from the absence of contemporary computational methods and virtual tools that can ensure an efficient access to the data produced by isolated laboratories, universities, and scientist (Matt Todd 2010). As suggested by Mat Todd (2010) in his speech "*How Can we Crowd-source Chemistry to Solve Important Problems?*" at Google, there is a global need of developing an intuitive virtual tool, providing easy access to raw research data from all global contributors.

Besides being necessary for communication tools, computers can through progress in the area of advanced computer simulation software, be able to speed up the process of drug development and at the same time cut development costs. However, "wet" chemistry, i.e. practical lab chemistry, is not likely to become obsolete in any near future. There is thus a need to create tools to share protocols and lab journals as well as a need to create interconnected clusters of simulation software. Whether this can successfully be done using a single platform, or if it is best done thorough several platforms with different designs remains to be seen.

Baldwin and von Hippel (2011) point out that a reevaluation of the traditional approach to intellectual property (IP) rights may be called upon to account for the increase in open innovation activities. Their findings show two primary economical benefits of open innovation as compared to a more traditional IP dependent innovation. First, the avoidance of the costly and difficult process of protecting IP and second the opportunity for spin-offs beneficial to the revealing inventor such as "*enhancement of reputation, positive network effects and obtaining a cheaper source of supply*" (ibid). However, the need to retain some form of confidentiality agreements and IP protection despite an increasing use of OI activities is expressed by Ekins and Williams;

> *"….breed a new class of researcher without affiliation, who has allegiance to neither company nor research organizations. They test their hypotheses with data from elsewhere, they do their experiments through a network of collaborations, they may have no physical lab; while a shared cause may not be essential, confidentiality agreements and software may unite them as a loose cooperative"*
>
> Ekins & Williams (2010)

Where open innovation activities in an industry such as the pharmaceutical industry will end up in terms of modularity, incentives, computer/IT tools, and IP protection is impossible to know beforehand. However, a close look at how these issues are handled within the first tentative platforms that are operational today may give some clue as to which direction it is heading.

2.2 Crowdsourcing

The term crowdsourcing refers to a participative online activity where an organization proposes to a group of individuals of varying knowledge and heterogeneity, via an open call, the voluntary undertaking of a task (Estellés-Arolas & González-Ladrón-de-Guevara 2012). The term was coined in 2006 by Jeff Howe in an article in the technology magazine Wired (Whitford 2008). Crowdsourcing covers a wide range of contemporary activities, including content contribution to Wikipedia, open-source development of the operating system Linux, collaborative design and funding of products at Quirky.com, user-designed garments at Threadless.com, and open product improvement platforms such as Ideastorm.com by IBM (Poetz & Schreier 2012).

Crowdsourcing can be classified as a part of the open innovation field. Whereas open innovation signifies a broader paradigm where organizations use external ideas as well as internal idea when seeking to advance their technology (Phillips 2012), crowdsourcing refers to a specific activity where an organization uses online communication to broadcast a problem to the external parties. Within a laboratory or firm, problem solvers mainly use previous experience and knowledge to solve problems which limits the potential solution space and search for solutions. Broadcasting the problem to a larger more heterogeneous group of "outsiders" can counteract the negative effects of "local search". The basis for this is the hypothesis that knowledge is widely and unequally distributed in society (Lakhani et al. 2006).

By utilizing online platforms to source for knowledge and solutions, the "local search" is widened to a "global search" tapping into a larger and more heterogeneous group of problem solvers. In line with this, the study by Lakhani et al. found that the most significant effect on a scientific problem being solved was the presence of heterogeneous scientific interests amongst scientists submitting solutions (ibid).

A survey done in 2011 of 32 crowdsourcing providers by the organization Crowdsourcing.org indicates that the enterprise crowdsourcing industry is still in its infancy but is growing at an accelerated rate with an estimated 375 million USD in revenue in 2011 (Crowdsourcing.org 2012). This growth is mainly driven by the adoption of crowdsourcing within the internet services, media and entertainment, and technology sectors that contribute with 67% of the industry's revenue (ibid).

The report suggests five categories of crowdsourcing: ideation-based tasks, expertise-based tasks, freelance services, software services, and micro-tasks. Expertise-based tasks has the most dominant position with 37% market share with the other categories sharing approximately equal market shares of 15-16% (Crowdsourcing.org 2012, see Figure 2). Ideation-based tasks are defined as online workers engaging in the creative process of generating, developing and communicating new ideas (ibid). This covers all the stages from innovation, development, to actualization. In contrast to other categories, ideation is most

focused on large (over 1 billion USD revenue) and medium size enterprise (100 million to 1 billion USD revenue) clients.

Expertise-based tasks are completed by online workers that are recognized as reliable sources of techniques and skills, or status and authority, by their peers, or possess knowledge based on familiarity in a specific field that can be both practical and theoretical (Crowdsourcing.org 2012). In the context of drug development research, the scientists and researchers involved are usually highly educated and possess knowledge within the specific field. Based on the categorizations above we argue that the tasks completed in drug development research can largely be categorized as expertise-based but there could also be cases at the early stages where ideation is a more suitable category.

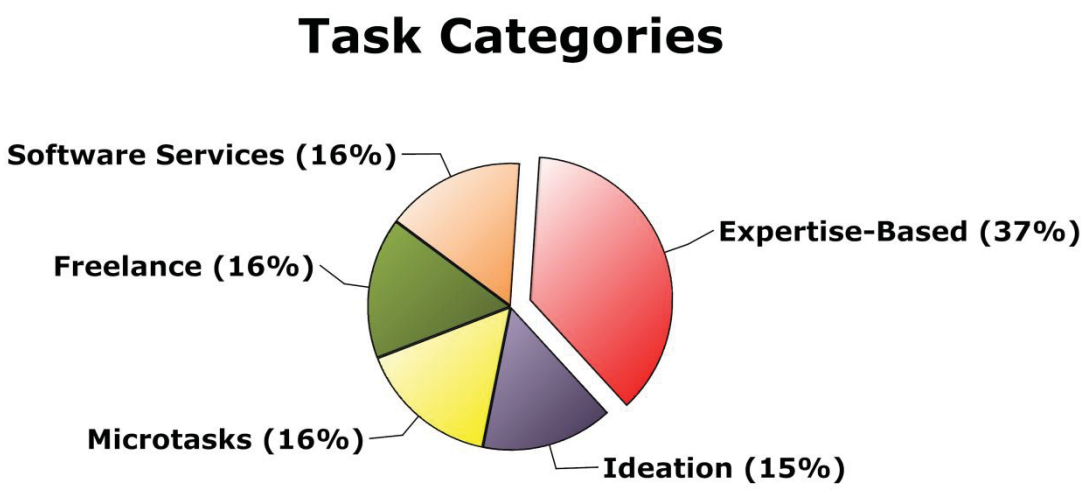

Figure 2. The five categories of crowdsourcing and their proportion in the 32 companies surveyed by crowdsourcing.

Contrary to common beliefs, a survey indicates that crowdsourcing is not a transfer of low-skill jobs to low-cost locations, instead more than half of the crowdsourcing workers live in North America and Europe and are overall well educated (Crowdsourcing.org 2012). In the survey it is argued that crowdsourcing emerged into the market as a part-time, second income opportunity for workers to join the global workforce and that most workers (77%) have a primary job. The majority (60%) of the workers are male and between 18-40 years old. Males are more prevalent in software services and expertise-based work while females are in majority in micro-tasks (ibid). The ideation category is shared equally between genders.

In connection to innovation, there has been much debate as to what degree users, "the crowd", really can contribute with novel and promising ideas compared to experienced professionals. Bennett and Cooper (1981), for example, argue that a truly creative idea for a new product “is very often out of the scope of the normal experience of the consumer.”

However, a more recent study by Poetz and Schreier (2012) provides an important initial indication that crowdsourcing initiatives among users can actually outperform professional in-house activities for the generation of new product ideas, at least under certain conditions. Poetz and Schreier argue that the ability of users to come up with promising ideas depend on the underlying industry or product category and if the knowledge needed to generate an idea is complex and/or costly to acquire, users are less likely to engage in developing their own ideas.

In the context of scientific problem solving, such as in the pharmaceutical industry, a study by Lakhani et al. (2006) suggest that openness and crowdsourcing (termed broadcast search in the study) can result in a higher resolution rate for scientific problems. The study included 166 scientific problems from 26 different firms from various industries including agrochemicals, biotechnology, chemicals, consumer products, and pharmaceuticals. The majority of firms had tried to solve the specific problem within their laboratories prior to broadcasting, but without success (ibid). The problems were broadcast to over 80 000 independent scientists via the online innovation and science problem platform Innocentive.com. In Table 1, all the 166 problems included in the study are shown by category.

Table 1. The 166 problems from the study by Lakhani et al. (2006) divided into disciplines.

Discipline of Problems Posted	Number of Problems	Solution Requirements: Theoretical|Reduction to Practice (%)	Average Award Value (USD)	Average Number of People Expressing Interest	Average Number of Sub-missions	Number of Problems Resolved	Solving Rate (%)
Life Sciences							
Biochemistry	11	27|73	33181	269	5.7	0	0.0
Molecular Biology	7	43|57	15000	116	3	2	28.6
Biology	7	71|29	14571	236	9	5	71.4
Toxicology	3	67|33	12500	80	1	2	66.7
Structural-Diversity	2	50|50	14000	228	4	1	50.0
Chemistry and Applied Sciences							
Synthesis	71	30|70	37408	223	9	22	31.0
Formulation	27	66|44	24666	220	10	8	29.6
Analytical	16	50|50	25375	314	13	1	6.3
Polymer	13	54|46	26884	254	8	1	7.7
Materials Science	4	50|50	25000	335	11	3	75.0
Other	5	60|40	22676	464	35	4	80.0
Total	166	42|58	29689	240	10	49	29.5

The results show a 29.5% resolution rate for the problems that previously had remained unresolved in the firms' laboratories. Furthermore, as Table 1 shows, there is a large category dependent variance in the solving rates. In the biochemistry category there is a zero percent solving rate, whereas there is a 71.4 percent solving rate in the biology category. Altogether this shows that revealing information and opening up the problem solving process can be a beneficial strategy for firms in R&D-heavy industries, such as the pharmaceutical industry, but care must be taken as to the nature of the problem when predicting solving rates.

To conclude the section on crowdsourcing, crowdsourcing is an open innovation activity that is not just in its infancy, it is producing high solving rates and is a steadily growing 375 million USD revenue industry (2011). However, it seems like crowdsourcing is best applied to ideation and small well defined problems and tasks. It is more likely to be (and is already) successful for solving smaller "chunks" of research outsourced by a company as part of their research rather than by itself producing new drugs.

2.3 Open Source Development

Open source is a term derived from the software world, where it describes software whose source code is publicly available and freely redistributable. The source code is the “recipe” that programmers write to specify the desired operations of a computer or other programmable entity; a step-by-step description that defines what the software does.

Open source development is a type of crowdsourced problem broadcasting activity and consequently both a form of crowdsourcing and open innovation. However, Masum and Harris (2011) argue that instead crowdsourcing can be seen as a limited type of open source activity that in the context of open source can be termed "open input" with a goal of harnessing the input from innovators worldwide to solve challenges. Furthermore, in line with our previous discussions, they argue that open innovation is a broader approach where organizations bring in external ideas and make underused internal ideas more available externally, to evolve business models and collaborations (ibid).

The idea of open source with its origins in the software development industry has gained increasing attention from other industries and fields. A study by Masum and Harris (2011) explores the usage and possibilities of open source in research targeted towards neglected diseases in the biotech/pharmaceutical industry. Based on applications and literature, they suggest that open source for research in neglected-diseases can be seen as involving three practices: open access to data, open collaboration across organizational and geographical boundaries, and open rules that enable or mandate various forms of openness.

The findings by Masum and Harris (2011) suggest that pharmaceutical open source activity for research in neglected-diseases is heavily weighted towards the discovery (or precompetitive) stage of R&D, with little activity in the development stage and none in the stages of clinical trials and filing (see Figure 3). They argue that this is largely related to the greater investment required, reduced rewards for collaboration, and stronger incentives to hold exclusive IP rights at the later stages. Furthermore, their findings show a large variety of projects with no single model for open source as an alternative to traditional R&D (ibid). The different initiatives each use some aspects of the open source model but none includes all of them.

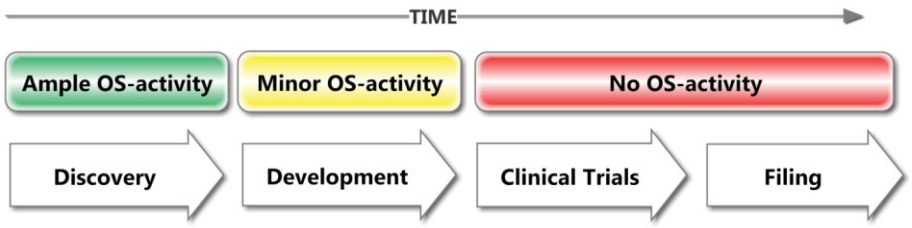

Figure 3. The open source (OS) activity through the different stages of drug development according to Masum & Harris (2011)

Finally, Masum and Harris conclude that most initiatives found rely on donors and government funding. This is related to the costs involved at the stages after R&D including manufacturing, regulatory, and distribution costs where private capital would be needed to continue development. Thus, there is a correlation between the types of funding and particular R&D stages where the open source model is more viable. As a conclusion, they state that currently it is not known if viable open source models can be applied to later-stage drug development and delivery, and how such models would combine private and public funding.

A key challenge in developing open source models is the question of intellectual property. The challenge is to ensure that follow-on and collaborative innovation is not hindered, while also making sure that investors receive value for the large investments needed to introduce new treatments on the market (Masum & Harris 2011). In the words of of Harry Thangaraj of St. George's University, London;

> "*Until the patent quagmire can be resolved, no amount of investment can solve health (patent) problems through open source initiatives...*"
>
> (Harry Thangaraj in Masum & Harris 2011)

Årdal et al. (2011) points out a large difference between the successful open source software development and open source drug development in that drugs are ideas that need to be patented, not original work that is protected by copyright. Furthermore, patents cost much money, copyright does not.

Masum & Harris (2011) argue that open source can offer some solutions to this dilemma by giving incentives to innovate without patents by tapping into a distributed community to do research in "small chunks" based on the modularized system introduced by Linux and others. This can be applicable for the earlier, more virtual, stages of R&D while it's unclear if distributed collaboration can be done on lab-based work or clinical trials (ibid). Another key aspect is the incentives for participation. Most existing initiatives rely on grants to fund their operations where the funders impose rules for collaboration and participation. Masum and Harris (2011) suggest that there is a possibility to expand this form of funding further. In an alternative method without grant funding to cover costs, the question of incentives become critical and can be separated between personal and organizational incentives.

Årdal et al. (2011) concludes in their systematic review on open source models applied to drug discovery that drug discovery is indeed modularized in that it consists of a strictly managed process of basic research, target identification and validation, lead identification, and lead optimization. The process is depicted in Scheme 1, Appendix A. The modularization means it does meet the basic criteria needed for a viable open source model, but the patent problems and the lack of potential profits needed to earn back

money invested in the research make it more or less only suitable for neglected diseases with a strong sponsor organization behind the platform.

In section 2.1 we covered possible reasons and motivations to participate in open innovation for the individual. On an organizational level, in the context of open source, the reasons could according to Masum and Harris include (ibid):

- **To develop proprietary products through knowledge and tools from precompetitive collaboration.**
- **By showing high level of innovation, the organization becomes more competitive when seeking grants or funding.**
- **To undermine competitors by creating an open source alternative.**
- **To make money through innovative business models.**
- **To market the organization to employees, policy makers, governments, and the public as an innovative organization**

Given that the field of open source is so new, especially in the pharmaceutical industry, there has been virtually no research on the estimated benefits of the model for business and society. This is a critical aspect since estimation of benefits can strengthen the argument for open source models by showing that it could be beneficial for companies to participate and also benefit society as a whole.

Masum and Harris (2011) argue that economic modeling could be one strategy to estimate potential cost savings. Examples could include reduced duplications of research, reduced costly drug trials where information exists elsewhere that it will not work, faster regulatory processes, and filling knowledge gaps. Here, the concept of "value tracking" could be a method which would involve an online platform that cumulates actual uses of open source platforms, data or technology. Another issue is how to create metrics to estimate the value of the model. Such metrics could include "*creating knowledge for future innovations, reducing disease burden, making money for investors, rewarding researchers, and achieving economic development in R&D industries*" (ibid).

For any platform to produce any usable results, a functional quality control system ensuring that the provided data are of high enough quality is required. Unfortunately all such systems cost money, again highlighting the problem of funding. A strong sponsor organization as a core project management team that reviews the results together with an advisory board is one possibility which is used in the context of neglected diseases (Årdal et al. 2011). As previously discussed, a module-based systems similar to that used in open source software development would decrease the risk of contribute or providing wrongly achieved data and would facilitate retraction.

One idea presented is to use pharmaceutical journals to set the standards to be used in the platform databases. However, there is one large difference between how quality control is achieved today and how it would be achieved in an OS environment. The science

world today works exclusively from the system of peer-reviewing before publication whereas an OS environment would have to consist of peer-reviewing after publication/posting, i.e. real-time reviewing. A positive effect of the real-time peer-reviewing in an OS environment would be that time-delays and excessive filtering of criticism against established practices could be avoided. On the other hand, if care is not taken, this could be at the expense of scientific rigor.

To conclude the section on open source development, open source development is an open innovation activity that can be regarded as a part of crowdsourcing or vice versa. Regardless of how one chooses to look at it from a definition point of view, open source drug development would be a more complete process than the crowdsourcing of specific tasks. Because of this, problems associated with funding, IP rights, and developing models to calculate the benefits for investors and society arise. Open source drug development is, as opposed to crowdsourcing specific scientific problems, not yet an established practice and many problems have to be solved before it can be a viable alternative to closed in-house innovation. The only viable models today seem to be for neglected diseases with a strong sponsor organization behind that can manage and fund the projects.

2.4 The Pharmaceutical Industry

2.4.1 Overview

A major problem in the development of new drugs is the high research and development (R&D) costs and the relatively short period in which to earn back the capital that was once invested into the project. The industry as a whole is very profitable; the average return on invested capital between the years 1992-2006 for the US pharmaceutical industry was 31.7 percent, placing it among the top four industries (Porter 2008). The profit margin is also large, in 2002 for example, the top 10 drug companies in the United States had a median profit margin of 17%, as compared to only a 3.1% average for the rest of the industries on the Fortune 500 list (Angell 2004). However, this does not guarantee success for any given company as sustained prosperity is in most cases tied to successful innovation and can be difficult to achieve.

Many companies have prosperous periods when they have managed to get a big seller drug, a blockbuster drug, out on the market. However, the drug is only protected by patents for a limited amount of time, after which the revenues steadily decline for the originator of the drug. The patent protected period for new drugs is 20 years, but these 20 years include the time from first registration through phase I-IV clinical testing, formulation, and finally marketing and selling (PhRMA 2012). This process takes on average 10-15 years with the result that the actual period to make money on the drug usually is only in the order of a decade (DiMasi, Hansen & Grabowski 2003). Moreover, there is likely to be a waste of scarce resources within the pharmaceutical industry as a lot of companies pursue the latest "hot" targets parallel to each other, thereby duplicating research. From a resource perspective sharing of initial research in identifying targets and tentative leads should be beneficial to all participants and increase the number of drugs that reach the market to the benefit of the public.

For further reading on the pharmaceutical industry and the different types of companies, please refer to *Appendix A — The Pharmaceutical Industry*.

2.4.2 The Pharmaceutical Industry and Intellectual Property Rights

The pharmaceutical companies rely heavily on patents and are adamant that extensive protection of the intellectual property (IP) rights is essential to generate enough revenue to support the R&D necessary for the development of new drugs (Henry & Lexchin 2002). Patents are the legal protection for inventions, such as the new candidate drugs discovered by the pharmaceutical companies. The idea is that this protection allows a company time to recover their significant investment in R&D. Furthermore, in return for such protection, a patent-holder discloses to the world the patented research and the science underlying the invention. As a consequence, important scientific information behind new drugs become available immediately to researchers worldwide (PhRMA 2012).

If a process could be discovered that shortened the time for the first stages of drug development and/or introduced intellectual property rights at a later stage, this has the potential to significantly increase the exclusiveness time for the company and should thus be an incentive to participate in such processes.

For further reading on intellectual property strategies please refer to *Appendix A — The Pharmaceutical Industry*

2.4.3 Open Innovation and the Pharmaceutical Industry

According to Gassmann and Enkel (2004) the pharmaceutical industry has in many cases adopted an inside-out process by selling IP rights and multiplying technologies by transferring ideas to other firms (see Figure 1, page 5). Examples include the firms Novartis Pharma, Pfizer, and Roche, all of which have transferred substances initially aimed for one ailment to another. Examples of such drugs are Viagra, Botox, and Erythropoitin (EPO).

Coupled innovation processes can be found in the pharmaceutical industry where biotechnology gives input to pharmaceutical R&D (Gassmann & Enkel 2004). The study by Gassmann, Reepmeyer & von Zedtwitz (2004) reports 400 to 500 new alliances every year from 1996. An example is the firm Eli Lilly that formed an alliance with Genentech to start development of recombinant human insulin, resulting in the first biotechnology based product which was subsequently released in 1983. Gassmann & Enkel (2004) argue that the objectives of pharmaceutical firms using a coupled process are to set standards or a dominant design for their products to take a leading position in the market.

Open innovation strategies in the pharmaceutical industry are thus not only about outsourcing internal innovation activities; it is rather to adapt a more flexible multi-layered innovation strategy to increase innovativeness and firm value (ibid). This can include a variety of activities from crowdsourcing, commercializing patents, scanning and integrating new technologies, and forming alliances during periods. However, the focus of this work is on the outside-in process rather than on the inside-out or coupled processes, i.e. on the process where the firm's knowledge base is enriched through integration of external parties and sourcing by means of crowdsourcing or open source development.

3 METHOD

3.1 Research Approach

We have designed the research as an exploratory field study. Given the explorative nature of our research question we argue that this design allows us to broadly explore the various instances of crowdsourcing and open source in the pharmaceutical industry to find similarities, draw conclusions, and generalize our results.

The unit of analysis in our research design is the system that connects open innovation and crowdsourcing to drug development. Yin (2009) argues that the definition of the unit of analysis is related to the initial research questions. In this study, the initial research question is how open innovation and crowdsourcing are used in drug development today. Thus we argue that the system that connects crowdsourcing and open source to drug development is the appropriate unit of analysis since it allows us to explore who are participating, how they participate, what the incentives are, how intellectual property is handled, how the system can benefit the industry, and what the managerial implications might be.

3.2 Population and Sampling

Contemporary cases of crowdsourcing and open source development related to the drug development process have been selected. The main criteria for selection have been the following:

- **The case must seek to advance drug development**
- **The case must use crowdsourcing or open source as a mechanism**

Based on these criteria we have searched existing academic literature and online sources to identify candidate cases. The search was not a strict systematic review based on predetermined search paths (Cook, Mulrow & Haynes 1997), but a more loosely defined search through a host of search engines and through reference tracking in previous articles or online publications. Google and Google scholar was the preferred search engines, but other search engines such as ISI Web of Knowledge and SciFinder were also used. Furthermore, we did not only include peer-reviewed academic papers, but included all types of sources that we found pertinent to the study. This, we believe, gives a wider picture that is more likely to pick up on opinions that have not yet found their way into academic papers, albeit perhaps at the expense of some scientific rigor.

As a next step, the identified cases have been evaluated based on the following criteria:

- **Available information -** Is there information available that is reliable and updated?
- **Activity -** Is the system active and in use today?
- **Importance -** Has the system attracted interest from the pharmaceutical industry, academia, and other organizations in terms of participation, funding, or partnerships?

These criteria have been evaluated based on the available information published online and in academic journals. For example, the case candidate "The Tropical Disease Initiative" matched all initial criteria but when accessing their web site it was shut down and no further information could be found at the time of study. Based on the additional criteria, the case was excluded. The selected platforms are listed in Table 2 below and are presented in more detail in section Case Introductions.

3.3 Data Sources and Data Collection

To guide the data collection process a data collection protocol was designed. The collection process is illustrated in tabulated form in Table 2.

Table 2. An overview of the guidelines for data collection in the study.

Overview	**Explore how crowdsourcing and open source is used in drug development in the following cases (selected based on criteria above):** ➢ Arch2POCM ➢ Open Source Drug Discovery (OSDD) ➢ PatientsLikeMe ➢ The Synaptic Leap ➢ Innocentive ➢ FoldIt ➢ OpenWetWare (OWW) ➢ Transparency Life Sciences (TLS)
Procedures	➢ Browse web site for available information to get an initial overview. ➢ If system has an online interactive component, register as a user. ➢ After registration, browse system to retrieve additional information about research projects, users, functionalities, and general activity. ➢ Use search engines to identify other online sources (academic & non-academic) that presents information relevant to the case study. ➢ Based on search, retrieve additional information based on study questions.
Questions	**Study questions:** ➢ Who are the funders and participators in the platforms? ➢ How do participants collaborate in the platform? ➢ What are the incentives to participate? ➢ How is intellectual property managed?
Report guide	**Based on the study questions, write a report in the following format:** ➢ Platform Introductions – Introduce the platforms to give necessary background knowledge for the reader. ➢ Results – Present 4 tables, each summarizing the answers to the four questions above. ➢ Analysis – Categorize the platforms, compare and analyze them according to the Data Analysis as outlined in section 3.4

A case study protocol is one way of increasing the reliability of case study research, according to Yin (2009), and even if our study is not formally a case study such a protocol has formed the basis for our investigation. The data has been collected based on a set of questions on one level: Level 2 (asked of the individual case) (ibid). Multiple sources of evidence have been used in the studies as summarized in Table 3.

Table 3. A summary of the evidence used in the case studies.

Documentation	➢ Public information on web site ➢ Meeting reports ➢ Evaluations of platform
Archival records	Organizational records (organizational charts and budgets presented publicly on web site)
Participant-Observation	Register as user in system, use functionalities and browse information

The evidence has been collected following the case study protocol and subsequently categorized based on the type of evidence.

3.4 Data Analysis

We categorized the platforms as either crowdsourcing (CS) or open source (OS) based on the literature definitions. The platforms were then compared within each class, i.e. CS platforms are compared with CS platforms and OS with OS. Then the CS platforms as a class were compared to the OS platforms.

We also looked at the participating pharmaceutical companies and categorized them as research-based (RCs), generics manufacturers (GMs), biotech companies (BCs), and contract research organizations (CROs). The most active classes were identified and the reason for this was analyzed.

Finally we end the analysis section with a general discussion that summarizes our findings and those available in the literature and we developed our own proposition for a future open innovation model that would entail both crowdsourcing and open source elements.

4 PLATFORM INTRODUCTIONS

In this section a brief overview of each platform is presented to give a more complete picture of the participants and to aid the reader in the subsequent *Results* and *Analysis* sections.

4.1 Arch2POCM

Arch2POCM is a US-based public-private partnership aiming to accelerate drug development by conducting Phase II clinical trials on pioneer therapeutic targets (Norman et al. 2011). The platform refers to itself as a crowdsourcing initiative and the name is derived from the word archipelago, here signifying a heterogeneous group of biomedical researchers, and POCM, proof of clinical mechanism – the goal of the initiative (ibid). The platform aims to initiate independently funded crowdsourced experimental medicine studies in academic labs and pharmaceutical companies (Arch2POCM 2012). The platform is currently in its infancy and in the process of obtaining a commitment of funding from private and public partners

Arch2POCM will focus the research on four areas: oncology, immunology, autism and schizophrenia. Autism and schizophrenia were selected because they represent societal burdens, but are poorly understood and are thus highly risky areas for drug discovery (Arch2POCM 2012). Research in the oncology and immunology areas will focus on pioneer targets correlated with epigenetic function and chromatin biology that are relatively new fields of research.

According to Arch2POCM (2012), the participating users are academicians, pharmaceutical companies, regulatory scientists, public funders, and patient advocacy groups. From academia the following partners have indicated that their scientists will be able to participate: University of California (San Francisco), the University of Toronto, Massachusetts General Hospital, the Karolinska Institute, and Oxford University. According to Arch2POCM, funds will come from a combination of public funding from governments, private philanthropists and private sector funding from pharmaceutical and biotechnology companies.

From the pharmaceutical industry the following organizations have assisted in the creation of Arch2POCM's governance operations model and target lists: Boehringer Ingelheim, Gilead Sciences, GlaxoSmithKline, Johnson&Johnson, Merck & Co, Pfizer, Hoffmann-La Roche, Sanofi-Aventis, and Takeda. From the governmental side the US Food and Drug Administration (FDA) and the European Medicines Agency (EMEA) have indicated support for the initiative and an interest to play an active role. The platform does not include the general public in the innovation model.

The first step in the innovation process is to establish the pioneer targets that will be the focus of the research.

> *"The target List will be generated by aggregating the votes of Arch2POCM's Members: Members will select from a broad list of potential targets prepared by public and private sector scientists and clinicians. All targets on the broader list must meet the following requirements: novel with no clinical precedent for the indication being studied; not proven to be technically intractable and having appropriate tools available for use. Ideally, the Arch2POCM targets would be supported by genetic links to the disease."*
>
> (Arch2POCM 2012)

For each target two test compounds will be advanced. The next step is that Arch2POCM funds research at affiliated sites (i.e., academic, regulatory, pharmaceutical partner, or consortium labs, clinical sites, and contract research organizations) that will carry out the science (Arch2POCM 2012). Finally, the resulting test compounds needs to be approved by the Scientific Committee and their structures will be placed into the public domain.

> *"Arch2POCM will make non-GLP and/or GMP stage-appropriate quantities of the test compounds available to the scientific community for research and development purposes"*
>
> (Arch2POCM 2012)

Arch2POCM is based on an open (termed precompetitive) crowdsourcing model where data generated would be publicly available without patent claims (Norman et al. 2011). Although there would be no patent protection on the test compound, patent legislature for small molecule development candidates gives data exclusivity periods of 5-8 years Additionally, pharmaceutical organizations not joining the platform have the opportunity to develop proprietary molecules based on the findings and create new drugs. The pharmaceutical organizations involved would have the opportunity to purchase the test compounds and the investigational new drug (IND) database generated to continue clinical development and commercialize the findings.

4.2 Open Source Drug Discovery (OSDD)

Open Source Drug Discovery (OSDD) is based on an open source model and is open for anyone to contribute.

> "*The strength of OSDD model is that it is open to all. University and college students, and established scientists alike can contribute. All we seek is a person with a burning desire to solve challenging problems in drug discovery.*"
>
> (OSDD 2012b)

The online collaborative platform focuses on the early stages of discovery. At the following development stage OSDD collaborates with industry/contract research organizations and other publicly funded organizations (OSDD 2012a). In the final phase, drugs that come out of the OSDD platform will be made available like generic drugs. Figure 4 below illustrates the process:

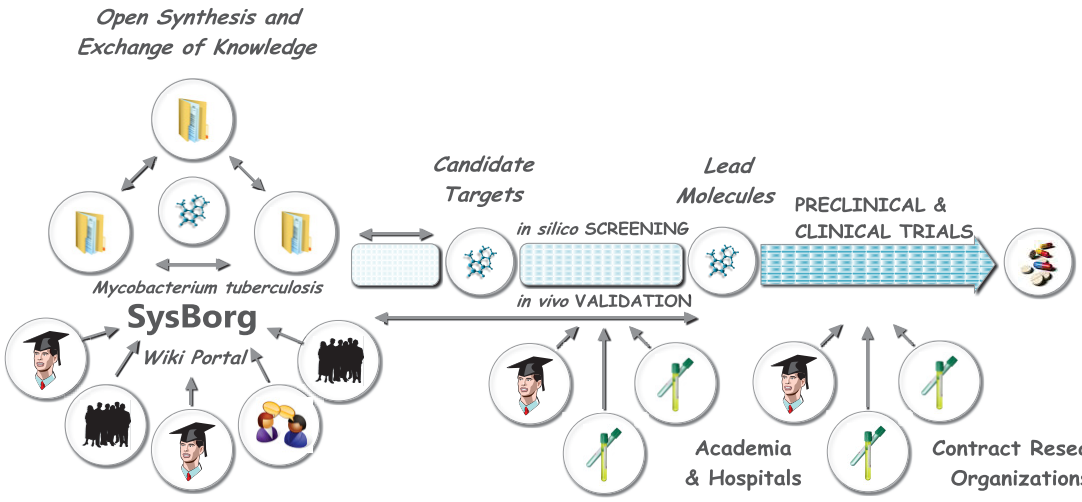

Figure 4. A schematic representation of the drug discovery and development process through OSDD. The illustration is drawn after an original available at www.osdd.org

OSDD is a platform initiated and funded by Council of Scientific and Industrial Research (CSIR) in India and was launched in 2008 (OSDD 2012a). CSIR is an industrial R&D organization founded 1942 and is one of the largest publicly funded research organizations in the world. CSIR has been an important force in driving India's pharmaceutical industry. OSDD is supported by funding from the government of India with an overall total budget of 35 M USD. The funds raised will be used for doing quality control and tests (OSDD 2012b). It will also be used to reward contributors and fund scholarships. The vision is to provide affordable healthcare to the developing world by creating a platform where researchers can collaborate and solve problems associated with new therapies for neglected tropical diseases such as malaria, tuberculosis and leishmaniasis. The first selected target for OSDD is tuberculosis.

OSDD has partnerships with CSIR associated laboratories, universities and academic institutes, and private partners (OSDD 2012b). Only one of the major pharmaceutical companies, AstraZeneca, is participating, the rest being India based biotech companies and contract research organizationss. However, OSDD states on their official webpage that they are looking to seek partnerships with generics manufacturers when they are getting closer to the final drugs as these companies are the most likely to be able to make a profit from a drug without holding any IP rights to it (OSDD 2012b).

From academia, OSDD has partnerships with a number of universities and academic institutes based in India including for example University Of Delhi and Bangalore University. From the general public, anyone can theoretically participate. For non-scholars monetary contributions are a possible option. However, no information has been found if this has happened so far. Contributions that can be made in the platform include:

- **In-kind donation of databases**
- **Laboratory access and/or sharing of technological capabilities**
- **Computing time/bandwidth/computation resources**
- **Acknowledging OSDD contributors by way on monetary or in-kind rewards.**
- **Contribution of resources/datasets/molecule libraries**

OSDD is based on an online collaborative platform, called Sysborg, where ideas, data and resources can be exchanged (OSDD 2012b). Anyone can register and get access to information and functionality on the platform. Tools and resources in the platform include for example: TBrowse (Largest integrative genomic resource on Mtb H37Rv), CRDD (comprehensive resource for drug discovery) and OSDDChem (database of molecules with anti-tuberculosis drug-like properties).

OSDD claims that in the case of tropical diseases the market based incentive mechanisms do not operate (OSDD 2012a). Further, they state that:

> "*Patents as a mechanism to ensure Return on Investment (ROI) from the market fail to play the role it plays as a driver of innovation in the pharmaceutical industry. In the absence of a market size that attracts the interests of the pharmaceutical industry, Intellectual Property (IP) Rights as a legal system has limited role to play in fostering innovation in tropical diseases. Therefore the OSDD approach to drug discovery and development is IP neutral.*"
>
> (OSDD 2012a)

Since affordability and accessibility are key concerns for OSDD, they state that:

> *"the only successful market based model ensuring both is the generic drug industry business model where the market competition is driving the prices to affordable levels and makes competitors seek extended market reach ensuring accessibility."*
>
> (OSDD 2012b)

Thus, anything that is developed within OSDD will be available to the developing world in open source, generic mode without price monopolies. Further, OSDD states that:

> "*Once a drug is approved for use by the regulatory agencies, OSDD will depend on the business model of generic drug industry which made drugs affordable in the*

developing countries. OSDD developed drugs will be available for any industry player with appropriate manufacturing practices to distribute the drugs to the market. The market competition will ensure accessibility and affordability."

(OSDD 2012b)

OSDD acknowledges that there will be instances when a contributor working in an open source environment would like to file patents. However, OSDD claims that these patents should not hinder the principles of affordability and accessibility, quality control, and that subsequent innovations remain openly accessible (OSDD 2012b).

4.3 PatientsLikeMe

PatientsLikeMe is a US-based health-information sharing website for patients (PatientsLikeMe 2012a). PatientsLikeMe is a for-profit business and was co-founded in 2004 by three MIT engineers: brothers Benjamin and James Heywood and longtime friend Jeff Cole. Five years earlier, their brother and friend Stephen Heywood was diagnosed with ALS (Lou Gehrig's disease) at the age of 29 and the platform was the founders attempt to help brother and friend (PatientsLikeMe 2012b). The platform allows patients to share personal information and health data in an online community. The principle behind the business concept is shown in Figure 5.

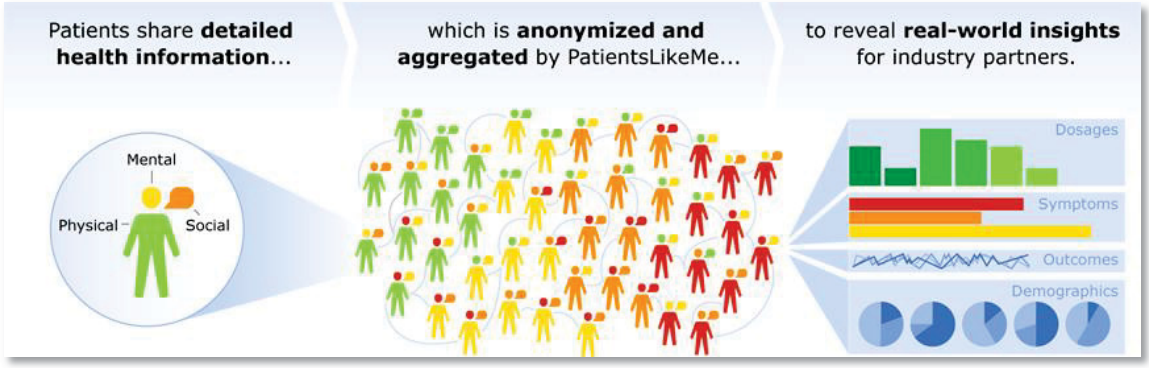

Figure 5. An illustration of the business idea forming the basis for PatientsLikeMe. Illustration taken from (PatientsLikeMe 2012c)

The business model is based on selling the information patients share about their experience with a disease to companies that develop or sell products (including drugs) to patients. According to their website, PatientsLikeMe has over 150 000 registered users with over 1 000 conditions (PatientsLikeMe 2012d). The company has four investors: Commercenet (incubator), Omidyar Network (investment group), Collaborative Seed and Growth Partners LLC (technology investment firm), and Invus LP (investment firm) (PatientsLikeMe 2012a). The main participating group is patients from the general public. The platform is free to use for patients. The other participating groups are termed partners

and are non-profits, from academia, from research centers, or from the commercial sector (PatientsLikeMe 2012e).

Outside of buying data generated by the platform, there is no information if and how participating companies from the commercial sector actively collaborate on the platform. The participating non-profits are all dedicated to curing a specific disease or ailment such as the Accelerated Cure Project for Multiple Sclerosis, a national non-profit organization dedicated to curing MS by determining its causes (PatientsLikeMe 2012e). Participating research centers are also mainly dedicated to specific diseases, the majority of them to the disease ALS, but also covering a broader portfolio of research such as Oxford University MND Care & Research Centre (PatientsLikeMe 2012e).

Participating universities include King's College London, Palo Alto University and The University of Wisconsin (PatientsLikeMe 2012e). The participants from academia are both university and non-university affiliated researchers. Participating companies include large companies from all categories except CROs. Examples include: Novartis Pharmaceuticals Corporation, Merck and Abbott Labs (PatientsLikeMe 2012e). Participating non-profits, research centers and universities publish research reports, presentations, studies and information on the site for patients to read and participate in, but it is not clear from the website if these partners get access to the data generated by the platform.

Patients participate and collaborate by continuously publishing information about themselves related to their condition. The information published is background information about the person, the condition, the diagnosis, and daily journals. Daily journals for example include general mood, quality of life, treatments, and weight. The majority of information published is available for other users to see. Patients can communicate between each other and in forums on the site, as well as take part of research published by partners of the platform.

Information published on the platform is protected by the Digital Millennium Copyright Act. Copyright owners that believe user submissions or other content on the platform infringes upon their copyright need to notify the administrators of the platform and start a legal process (PatientsLikeMe 2012f). There is no information if the aggregated data that is sold has any intellectual property protection but we would argue that it's not likely since the information cannot be classified as intellectual property.

4.4 The Synaptic Leap

The Synaptic Leap (TSL) is a non-profit organization incorporated in the US. The platform's is based on an open source model with its mission "*to provide a network of online research communities that connect and enable open source biomedical research.*" (The Synaptic Leap 2006a). The platform stresses the importance of open source activities within “wet chemistry”, i.e., actual practical laboratory work and not only computer simulations.

The open source model used is termed "Open Source Drug Discovery" and is summarized as six laws (The Synaptic Leap 2006a):

- **First law:** All data are open and all ideas are shared
- **Second Law:** Anyone can take part at any level of the project
- **Third Law:** There will be no patents
- **Fourth Law:** Suggestions are the best form of criticism
- **Fifth Law:** Public discussion is much more valuable than private email
- **Sixth Law:** The project is bigger than, and is not owned by, any given lab. The aim is to find a good drug for malaria, by whatever means, as quickly as possible.

TSL provides an online community platform where participants can register and share information. Additionally, other forums are used to spread information including Twitter, LinkedIn, and a blog. To document research findings, an open-source online electronic lab notebook is used. The platform is based on the principle that there will be no patents on the findings done within the platform.

TSL is operated on a part-time volunteer basis by experts and scientists in biomedical research, IT, and law. The research communities initiated by TSL focus on tropical diseases including: malaria, schistosomiasis, toxoplasmosis and tuberculosis. One of the driving forces behind the platform is Dr. Matthew Todd, a lecturer in organic chemistry at the University of Sydney.

The platform was founded in 2006 through a web site created where research projects were posted. Initially there was little activity on the platform. TSL states that one of the initial customers and partners was the Tropical Disease Initiative but there is no information on the details of this partnership (The Synaptic Leap 2006b). In mid-2008, one of the projects (to optimize the treatment of schistosomiasis drug praziquantel, or PZQ) was funded by a partnership between the World Health Organization (WHO) and the Australian Government which made it possible to assign resources and setup a more sophisticated online platform for documentation and collaboration and a so called core team dedicated to the project (ELN) (Woelfle et al. 2011). Another project where TSL has played a role is a pilot project in open source drug discovery from the Medicines for Malaria Venture (MMV) that has been funded by Australian Research Council Linkage. The project uses findings placed in the public domain in 2010 by GlaxoSmithKline and other pharmaceutical companies (The Synaptic Leap 2006b).

From the pharmaceutical industry, research-based companies including Dutch-based CRO Syncom BV have contributed with research. Additionally, professionals from the industry have contributed with input on the TSL web site. The report by Woelfle et al. (2011) states that from the 100 comments posted on the web site regarding the PZQ-project since January 2010 until beginning of 2011, 60 came from participants not in the core team. Of these 60 comments, 42 were from industry and 16 from academia.

4.5 Innocentive.com

The Innocentive platform is a US-based crowdsourcing pioneer that enables organizations to solve their key problems. By using a challenge driven innovation methodology and the involvements of their millions problem solvers, they have created an efficient and well-known sustainable innovation platform. Awards are paid out to solvers for solved challenges. Dwayne Spradlin, their CEO, has referred to the platform as "*the E-Bay of innovation*" (Spradlin 2010). According to Spradlin, by offering a huge number of solvers (in 2010 approximately 12 million Solvers were registered) and by providing them with the right incentives and tools to contribute, solutions to the posted problems are developed faster, with more cost efficiency, and with less risk as compared to the traditional way of "trial & error" development (ibid).

People can choose to work as a Solver or as a team-Solver. For those who choose to work as teams *Team Project Rooms* (TPR) are available for some challenges. While not all challenges come with the capability to set up a TPR, all challenges can be solved by teams. The only difference is that in Challenges without TPRs, the solvers will be responsible for negotiating with the peers and making their own arrangements in terms of award sharing (Innocentive 2012a). A typical process from developing a challenge to awards given is illustrated in Figure 6.

Figure 6. An illustration showing the typical timeline for a challenge posted on Innocentive.com. Illustration taken from (Innocentive 2012b)

As the world's largest problem solving marketplace, they now work for clients such as Booz Allen Hamilton, Eli Lilly & Company, Life Technologies, NASA, Nature Publishing Group, Popular Science, Procter & Gamble, Roche, Rockefeller Foundation, The Economist, government and nonprofit organizations. The range of awards is from 500 to >1 million USD based on the complexity of the problem and nature of the challenge. The platform has an average success rate of 50 percent for solving posted challenges (Innocentive 2012c). A study by Lakhani et al. (2006) on the results from this platform is also covered in section 2.2 (page 9).

Innocentive is very clear about its intellectual property handling. Only the Seeker who posts a challenges and Innocentive have access to see solutions (Innocentive 2012d). Both Seekers and Solvers are obliged to sign intellectual property agreements, and in some cases the Seeker remains anonymous to the Solver, but never to Innocentive. Innnocentive provides three different agreements depending on the specific challenge (ibid). For ideation challenges the rules are crystal clear, you give up your rights to the idea when submitting. For the other two theoretical challenges you first of all are granting the Seeker a temporary 90 day exclusive license for the intellectual property rights contained in your submission. The final IP rights are dependent on the kind of reward you are offered as outlined in Table 4.

Table 4. The intellectual property agreements for Innocentive's challenges (Innocentive 2012d).

Theoretical-Licensing Challenge:	If a Seeker grants you the full award amount for a Theoretical-Licensing Challenge, you agree to provide a perpetual, non-exclusive license to the Intellectual Property Rights contained in your submission. If offered a partial award, you have the option to reject it and retain your Intellectual Property Rights.
Theoretical-IP-Transfer or Reduction to Practice (RTP) Challenge:	If a Seeker grants you the full award amount for a Theoretical-IP-Transfer or Reduction to Practice Challenge, you agree to transfer all Intellectual Property Rights contained in your submission. If offered a partial award, you have the option to reject it and retain your Intellectual Property Rights.
Ideation Challenge:	By submitting to an Ideation Challenge, you agree to provide the Seeker with a royalty-free, non-exclusive perpetual license to use the ideas contained within. This agreement is NOT contingent on receiving an award, however Ideation Challenges do guarantee that the award will be paid out in full to participating Solver(s). Solutions to Ideation Challenges should not contain content owned by a third party."

4.6 FoldIt

FoldIt is an online computer game that enables people to contribute to scientific research by folding proteins. The game is an experimental research project developed by University of Washington's Center for Game Science in association with the University of Washington's Department of Biochemistry (FoldIt 2012). An example of a protein folding can be seen in Figure 7.

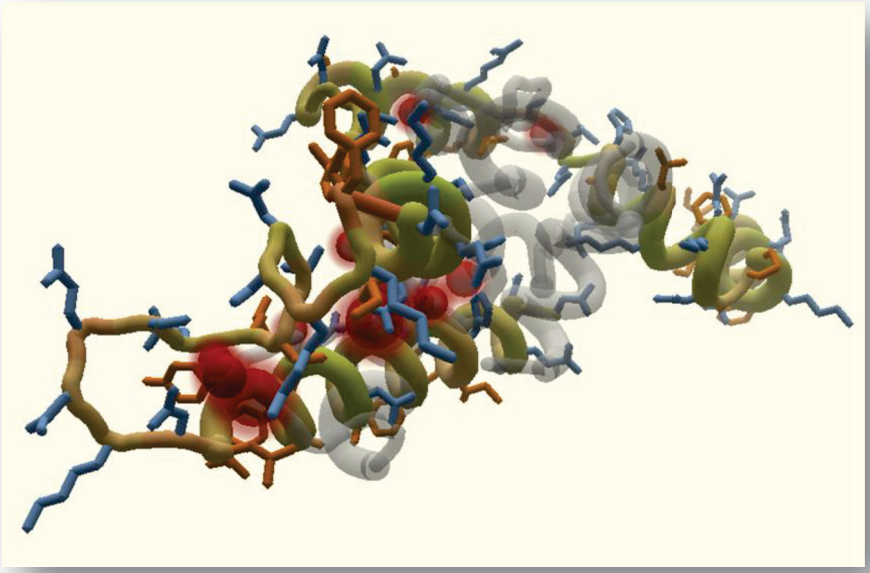

Figure 7. A screen shot of the puzzle solving offered by FoldIt. Picture taken from (FoldIt 2012)

The main participating group is the general public. The general public can register on the site and download an application and solve 3D-puzzles based on the protein structures. The solutions are aggregated by the platform and the best solutions are analyzed by researchers. The structure of proteins are highly complex, and "knowing the structure of a protein is key to understanding how it works and to targeting it with drugs" (FoldIt 2012). The solutions generated can then be used to solve real problems with the aim of targeting diseases. Additionally, users can chat, message and communicate via forums on the platform.

There are no monetary rewards in the platform. However, the platform has a game design where participants are rewarded with points and virtual awards for achievements. FoldIt has complete rights to use the data generated by the platform. The majority of data is logged with the exception of some private chat channels and messaging. No policy regarding open access to the data generated is available currently.

4.7 OpenWetWare

OpenWetWare (OWW) is a port of the open-source community of Wiki and has as its goal to support research, education, publication, and discussion in biological sciences and engineering. Their aim is to create collaborations among researchers, students, and others who have interest in open science. OWW is a sub-division of the Bio Brick's Foundation, which is a public-benefit organization with a mission to advance synthetic biology to the benefit of all people on the planet.

"there are not too many suitable wikis around and indeed, one of the purposes of publishing in a wiki would be to have all relevant information in one freely accessible spot, rather than in zillions of journals as in the paper-based world"

(OpenWetWare 2012).

The way they are trying to fulfill their mission is to provide a platform where scientists all over the world, in a standardized manner, can upload their lab notebooks and working protocols. This reduces the amount of wasted effort in the world by not having scientists, a valuable resource, reinventing the wheel over and over again. OWW uses a threefold strategy to reach their goal, they aim to:

- **Lower the technical barriers** to the sharing and dissemination of knowledge in biological research.
- **Build a community of researchers** in biology and biological engineering who values, practices, and innovates the open sharing of information.
- **Integrate OpenWetWare** into existing and future reward structures in research.

The platform reaches out to researchers and groups who are working in biology & biological engineering. They can contribute to an open product development by adding research results to existing protocols, or to start new lab protocols. The platform also provides the user interface to share information through a forum, connecting labs and groups from all around the world. Dozens of labs and hundreds of researchers covers all steps of the research cycle, except for funding and formal publishing (OpenWetWare 2012). As the OpenWetWare Lab is a port of the open-source community of Wiki, there are no potential IP regulations posted on the web. No official industry partners are listed on the official homepage of OWW.

4.8 Transparency Life Sciences (TLS)

TLS is a patient-centered for-profit company that develops new medications to help people with chronic diseases. They involve patients in the clinical trial design process so that studies are tailored to fit the patients, not only the scientists, needs. According to their webpage, TLS is the world's first drug development company based on open innovation with the goal of developing medicines for unmet medical needs. This is accomplished by acquiring promising drug compounds, designing studies via crowdsourced methods, and conducting those clinical studies with "unmatched productivity" (TLS 2012). This platform reaches out broadly to physicians, researchers in academia, and researchers in the pharmaceutical industry. However, more importantly, it reaches out to patients who can participate in clinical studies.

The TLS' platform uses a division between protocol challenges for the researcher and protocol challenges for the patients. Incentives of participation for the patients and their physicians involve the benefit of participating in a new clinical trials ecosystem. As TLS intend to recruit patient on a low-cost basis, resources can be allocated elsewhere. Patients who meet the inclusion criteria will have the opportunity to take part in the trials themselves which will offer a sense of control over their own ailment.

For the pharmaceutical industry TLS provides benefits such as an enhanced clinical trials speed with reduced cycle times and access to improved future trial planning. However, it is important to keep in mind that the trial planning that TLS offers are paid for by participating companies so they are in fact buying a service at market price, not contributing to open innovation in its true sense.

5 RESULTS

5.1 Who are the Funders and Participators in the Platforms?

Table 5. The findings from the participation data analysis.[a]

Platform	Listed Participant types	Funding
Arch2POCM	Academicians, pharmaceutical companies, regulatory scientists, public funders, government agencies, and patient advocacy groups	Funds will come from a combination of public funding from governments, private philanthropists and private sector funding from pharmaceutical and biotechnology companies.
OSDD	Researchers at CSIR associated laboratories, universities and academic institutes, private research centers, and industry partners	The core funding of OSDD is from the Government of India.
PatientsLikeMe	Patients from the general public as the major participants group. The platform is free to use for patients. The other participating groups are termed partners and are non-profits from academia, research centers, or the pharmaceutical companies.	For-profit business.
The Synaptic Leap	Universities, WHO, government agencies and other non-commercial official organizations, pharmaceutical companies	In specific projects non-commercial official organizations are participating, e.g. World Health Organization (WHO), the Australian Government, and the Australian Research Council Linkage. Otherwise funding poor and unclear.
Innocentive	Companies from various industries as paying customers, individuals with various backgrounds as solvers.	For-profit business.
FoldIt	General public, researchers and students	UW Center for Game Science, UW Department of Computer Science and Engineering, UW Baker Lab, DARPA, NSF, HHMI, Microsoft, and Adobe
OpenWetWare	Researchers and research teams	The public-benefit organization The BioBricks Foundation.
Transparency Life Sciences	Researchers, physicians, pharmaceutical companies, and patients.	For profit business.

[a] The companies and other organizations listed are limited to those that are listed as official partners according to the official homepages of the platforms.

5.2 How do Participants Collaborate in the Platforms?

Table 6. The findings from the collaboration data analysis.

Platform	Collaboration
Arch2POCM	Pioneer targets established; for each target two test compounds will be advanced; funds research at affiliated sites and phase II clinical trials.
OSDD	Online collaborative platform, open to anyone, focused on the early stages of discovery. In the final phase, drugs that come out of the OSDD platform will be made available like generic drugs.
PatientsLikeMe	Patient online community; aggregated data is sold to partners.
The Synaptic Leap	Online collaborative platform; a number of specifically funded projects that coordinates resources. Additionally, other forums are used to spread information including Twitter, LinkedIn and a blog. Discovery phase.
Innocentive	Problems are published for solvers to present solutions to, individually or in group.
FoldIt	Anyone can contribute with solutions; findings are used by research teams. Additionally, users can chat, message and communicate via forums on the platform. Early stages of discovery.
OpenWetWare	Online community where research findings are published; focused on the early stages of discovery.
Transparency Life Sciences	Based on "challenges" for researchers and patients, usually in the form of a test for patients designed by researchers. The online protocol works as a live document which everyone has access to. As people contribute it quickly iterates into a full-fledged clinical protocol.

5.3 What are the Incentives to Participate?

Table 7. The findings from the incentives data analysis.[a]

Platform	Incentives		
	For companies	**For academia**	**For others**
Arch2POCM	A positive return on investment through precompetitive collaboration	No information given	No information given
OSDD	In a not too distant future generics manufacturers should be able to make money from the developed drugs according to the web page.	The possibility to secure funds for research projects through the OSDD platform.	No information given
PatientsLikeMe	To get access to rich research data from patients suffering from the conditions the company is targeting.	Getting aggregated data that can prove valuable for research	**For patients**: The incentive is entirely non-monetary, i.e., the hope of better treatment for themselves and future sufferers. **For non-profits:** Lobby incentives; directing attention to a particular illness.
The Synaptic Leap	No information given	**For researchers directly funded by the platform**: To secure funds **For researchers not directly funded by the platform**: Peer recognition is mentioned as one incentive and also joining a bigger cause.	No information given
Innocentive	Innovative cost-efficient solutions; rewards only awarded for problems solved and not for unproductive R&D.	N/A	**For individuals:** Monetary reward, recognition.
FoldIt	No information given	Getting aggregated data that can prove valuable for research	For the fun of it
OpenWetWare	**For the individual scientist:** Shortening of laboratory procedures by using other scientists' finished protocols can lead to faster results and thus more funding.	**For the individual scientist:** Shortening of laboratory procedures by using other scientists' finished protocols can lead to faster results and thus more funding.	N/A
Transparency Life Sciences	Enhanced clinical trials speed with reduced cycle times and access to improved future trial planning. A service paid for.	**For the individual scientist:** Meet researchers from around the globe and exchange information. **For the solver:** Monetary rewards or credit points.	**For the patient:** By participating they can increase the likelihood of getting better treatments in the future. **For the solver:** Monetary rewards or credit points.

[a]Only the incentives explicitly listed on the official web pages are included.

5.4 How is Intellectual Property Handled in the Platform?

Table 8. The findings from the IP data analysis.

Platform	Intellectual Property Considerations
Arch2POCM	Data generated would be publicly available without patent claims The pharmaceutical organizations involved would have the opportunity to purchase the test compounds and the investigational new drug (IND) database generated to continue clinical development and commercialize the findings.
OSDD	Available to the developing world in open source. OSDD acknowledges that there will be instances when a contributor working in an open source environment would like to file patents. However, OSDD claims that these patents should not hinder the principles of affordability and accessibility, quality control, and that subsequent innovations remain openly accessible (OSDD 2012b)
PatientsLikeMe	No patents on the findings done within the platform.
The Synaptic Leap	The platform is based on the principle that there will be no patents on the findings done within the platform.
Innocentive	Innocentive is very clear about its intellectual property handling. Only the company who posts a challenge and Innocentive has the access to the solutions. Three forms of IP agreements that mainly benefit the company.
FoldIt	No information given
OpenWetWare	Open source Wiki. No potential IP regulations posted on the web.
Transparency Life Sciences	N/A

6 ANALYSIS

6.1 Crowdsourcing or Open Source?

In line with the findings of Masum & Harris (2011) on open source and the pharmaceutical industry our findings show a large diversity in terms of application, usage, and possible implications for the pharmaceutical industry. However, some general patterns emerge when examining the findings.

Our first step in the analysis was to categorize the activities on the platforms into crowdsourcing and open source activities according to the consensus of our literature review in the background section. The data underlying this classification is available in Table 5 to Table 8 in the Results chapter. The categorization is displayed in Table 9. Our rationale for these classifications is outlined in the paragraphs immediately following the table.

Table 9. Categorization of the studied platforms into crowdsourcing (CS) or open source development (OS).

Platform	CS	OS	Comments
Arch2POCM		✓	Early and limited type of pre-competitive type of OS with only invited participants from the industry. Refers to itself as a crowdsourcing initiative.
OSDD		✓	Governmental financed. Truly OS. Has the potential to develop new drugs from scratch to approved and ready product.
PatientsLikeMe	✓		CS of later stage drug development; collection of trial results from different patient-groups.
The Synaptic Leap		✓	Creating an OS bank to open-up "the silent knowledge" between universities etc. No defined stage of drug development. Currently no reasonable potential for a complete drug development.
Innocentive	✓		Pure CS, with incentives and well defined tasks. Very diverse tasks that is likely to span over several stages of drug development.
FoldIt	✓		A narrow niche of CS, focusing on assembling and designing molecules.
OpenWetWare		✓	A broad information bank, providing OS discoveries and protocols. More of an interactive, comprehensive practical laboratory handbook than a drug development platform.
Transparency Life Sciences	✓		In the same CS category as Patients-Like-Me. Platform based on interaction with patients participating in clinical trial studies.

In the comments column, comments regarding the degree of openness of OS initiatives and the potential of an OS platform to cover a complete drug development program are added. As described in the background section, crowdsourcing per se is a too narrow kind of open innovation activity to cover a complete drug development program in its current

shapes and any comments pertaining to the potential of the platforms categorized as CS to cover a complete drug development process is therefore left out.

This categorization is important in our further analysis since these kinds of open innovation activities differ markedly in their current implementation and in their possible future roles for different parts of the drug development process. Furthermore, there is some literature available where open source activities within the pharmaceutical industry has been reviewed and analyzed whereas there is less information available regarding crowdsourcing within the same context.

An aspect that made our analysis difficult is how the definitions of crowdsourcing, open innovation, and open source overlap. In some cases such as Arch2POCM (2012), the term crowdsourcing is used to explain the model whereas OSDD and TSP uses the open source terminology. This brings the analysis to a core question of what the "crowd" really entails. Participants in the Arch2POCM platform are not simply a heterogenous group of people; they are various organizations from academia, the pharmaceutical industry and other areas that form a highly organized partnership to address a structural problem in the industry. A participating individual in this context has little to add unless armed with a relevant educational background or funds. This is why we categorized Arch2POCM as a limited type of OS activity rather than a crowdsourcing activity (Table 9).

In contrast we have examples like Innocentive where the heterogenous "crowd" of individual problem-solvers is the key driver of the platform. Here the view of crowdsourcing as a form of "open input" in the context of open source (Masum & Harris 2011) matches our findings perfectly and Innocentive thus, to us, is a perfect example of true crowdsourcing.

A comparison of the tasks performed and the platform model (CS or OS) being used showed that the size and the level of modularization of the problem showed a clear correlation to the model being used. For problems that are more isolated and smaller in scope, the crowdsourcing mechanism appears to be more applicable. The clearest examples of this are Innocentive and FoldIt that relies solely on the crowdsourcing mechanism to find solutions for isolated problems. The success of innocentive illustrated by their high solving rate for scientific problems shows that successful crowdsourcing models are already in use today. The reason for that success, as suggested by Lakhani et al (2006), could be that the company posting the problem increased the solution space and thereby included groups that for different reasons are not feasible to add to the staff directly. In the open innovation model suggested by Gassmann & Enkel (2004) this represents an outside-in process where external resources can increase the value of the company and these platforms are thus indeed covered by the outside-in focus that we set out to explore.

The pure crowdsourcing cases clearly deviate from the open source model where one aspect is that contributed data is shared openly. For example, Innocentive largely leaves it

up to the company submitting the problem to define the rules for how intellectual property is handled (Table 8, page 37). This offers support to the idea that it is useful to separate the activities into two distinct classes, CS and OS.

In the case of FoldIt, the purpose of the crowdsourcing mechanism is different than in the case of Innocentive since it covers the earlier stages of basic research on proteins with a novel approach. It therefore appears logical that this initiative comes from the academic field since the possible findings that can be commercialized are uncertain and lies far ahead in the future (Table 5, page 34). The characteristics of FoldIt stand in stark contrast to those of Innocentive, a privately owned for-profit business, whose main target group, is companies from various industries with specific problems of commercial nature (Table 5, page 34). The problems posted on the Innocentive platform are clearly defined, isolated entities that are a smaller part of the full innovation process of a company. They can be anywhere in the innovation process from ideation to later stages research. However, examined from the perspective of the five categories of crowdsourcing (Crowdsourcing.org 2012), Innocentive mainly covers ideation- and expertise-based tasks whereas FoldIt can be classified as covering micro-tasks.

Another pattern emerging when looking at the platforms we termed as CS platforms is how the crowdsourcing mechanism is being applied. As defined by Estellés-Arolas (2012) crowdsourcing refers to a participative online activity where an organization proposes to a group the voluntary undertaking of a task. Two different applications can clearly be identified where one adheres to this definition whereas the other differs in terms of application but not in the underlying mechanism. Innocentive and FoldIt could be seen as platforms that adhere to the definition whereas PatientsLikeMe and Transparency Life Sciences differ. In the latter cases, the value of the crowd for the organization is not its problem-solving ability or the voluntary undertaking of a task in its strictest sense; rather it is the aggregate input of real life data from the crowd that creates the value for the organization (Table 7, page 36). The crowdsourcing mechanism in these cases is used indirectly to solve problems by aggregating data whereas the former two directly use the crowd to solve specific problems.

The crowdsourcing approach in its current shape does not appear to offer an alternative path to the model used today when developing new drugs in the pharmaceutical industry. Instead it is one specific mechanism that can be used as part of a firm's open innovation strategy.

In contrast to this, two of the platforms we categorized as open source activities, OSDD and Arch2POCM, clearly aims at finding alternative ways for new cures for diseases that covers more than specific problems along the development cycle. Not surprisingly, both these platforms are initiated mainly or solely from the public sector and rely partly or solely on public funding of various forms (Table 5, page 34). It appears that the industry itself does not have enough incentives to find alternative models for innovation; instead external forces need to drive these initiatives. This is in line with the findings of Årdal et al (2011)

that points the crucial role of a strong sponsor aiming at finding a cure for a specific disease (in most cases a neglected disease) in creating an OS platform that shows any promise in generating a new drug.

Also, as pointed out in the case of open science and collaboration by Woelfle et al (2011), when collaboration is a basic requirement, a central organization is needed that serves as the driver of the initiative to attract and maintain interest and direction.

The last two cases we classified as open source activities, The Synaptic Leap (TSL) and OpenWetWare (OWW), are for different reasons not really close to covering a complete drug development process. In the case of OWW, this is easily explained because it was never their intention. Instead they could be regarded as more of an interactive, comprehensive practical laboratory handbook than a drug development platform (Table 9). In the case of TSL they have received some funding for specific projects targeted at specific diseases from World Health Organization (WHO), the Australian Government, and the Australian Research Council Linkage (Table 5, page 34), but they are generally poorly financed. From the available information the outcome is so far poor, thus again reinforcing the hypothesis that strong funding is necessary to produce any tangible results from an open source initiative in the context of drug development (Årdal et al. 2011).

6.2 Type of Companies Presently Active on the Platforms

We deemed it interesting to find out what kind of companies that is presently active within these platforms to find a pattern. As was detailed in Appendix A it is possible to divide he modern pharmaceutical industry into different subgroups with markedly different strategies and cost structures, generics manufacturers (GMs), R&D intensive companies (RCs), biotech companies (BCs) and contract research organizations (CROs).

The examples of pharmaceutical companies that are involved in the platforms are shown in Table 10. It is obvious that RCs and BCs are involved to a larger extent than both GMs and CROs. Looking from an R&D-input perspective this is of course logical as the research to be posted on open innovation platforms, when they still are in their infancy, must spring from R&D activities that to the largest extent is performed by RCs and BCs (see Scheme 1, page 54, for an overview of the drug development process). If we on the other hand look at it from the aspect of commercialization, the GMs are the companies that should have the easiest task of making money out of it, because they have the supply chain and structure that allows for fast and cheap manufacturing of drugs that are developed without patent rights. The Indian platform OSDD also points this out (OSDD 2012b).

As GMs are mostly interested in the finished patent-free products, they can be expected to get more involved over time as these platforms mature and marketing of the spawned products are getting closer. CROs are by definition only performing research when somebody is paying them and are only involved when major donations and contributions have been made by governments, health organizations, or charities.

Table 10. Categorization of the pharmaceutical companies contributing to the different platforms.[a]

Platform		Research-based Company (RC)	Generics Manufacturer (GM)	Biotech Company (BC)	Contract Research Organization (CRO)
Arch2POCM	Boehringer Ingelheim	✓			
	Gilead Sciences			✓	
	GlaxoSmithKline	✓			
	Johnson&Johnson	✓			
	Merck & Co	✓			
	Pfizer	✓	✓		
	Hoffmann-La Roche	✓		✓	
	Sanofi-Aventis	✓		✓	
	Takeda	✓	✓		
OSDD	LeadInvent			✓	✓
	Premas Biotech			✓	
	TCG LifeSciences			✓	✓
	AstraZeneca	✓	✓		
PatientsLikeMe	Abbott Laboratories	✓		✓	
	Acorda Therapeutics			✓	
	Avanir Pharma.			✓	
	Biogen Idec			✓	
	Merck & Co	✓			
	Novartis Pharma.	✓	✓	✓	
	Sanofi-Aventis	✓		✓	
	UCB			✓	
The Synaptic Leap	Syncom BV	✓		✓	✓
Innocentive	Various[b]				
FoldIt	N/A				
OWW	N/A				
Transparency Life Sciences	Various[b]				

[a] Information about official business partners are taken from the organizations' official webpages; Only partners clearly indicated as for-profit organizations active in drug development have been included.

[b] The companies buying services at market price from crowdsourcing platforms are many and diverse and are excluded from this table as they are not the focal point of the associated discussion.

6.3 Summarizing Discussion

For organizations in the pharmaceutical industry, incentives vary depending on the platform (Table 7, page 36). From our point of view, the most interesting platform that could potentially generate leads for diseases other than neglected diseases, Arch2POCM, is based on a precompetitive model where later commercialization after additional in-house development would be the incentive. From literature there seem to be a consensus that the only viable business model to date to produce drugs for other diseases than neglected diseases with strong sponsor organizations behind is a precompetitive open source model (Årdal et al. 2011). Norman et al. (2011) argues that commercial development of the results from the test compound can have a strong positive return on investment because clinically validated new targets are associated with a higher likelihood of success. These initial clinical validations would previously have been associated with large uncertainty carried solely by the company.

From the individual's perspective there are varying levels of intrinsic and extrinsic motivational factors involved (section 2.1, page 5). From FoldIt in one end, where no monetary rewards are given and the key motivation is the intrinsic enjoyment of solving puzzles, to Innocentive in the other end where direct monetary rewards are offered. For researchers, a combination of factors including peer recognition, funding, network effects and personal development can be found in the majority of platforms. However, literature does indicate that to sustain participation from a large enough number of solvers a monetary reward is generally required (*vide supra*). As suggested by Lakhani et al. (2006), the opportunity to extend the search for solutions to a larger, more heterogeneous group and thus extending the solution space is the key driver behind the success of crowdsourcing platforms. This is perhaps best exemplified by Innocentive where the focus is on single well defined problems and where the company behind the challenge has the right to control intellectual property.

The findings by our study and from other sources about important factors in open innovation activities such as crowdsourcing and open source development in drug discovery can be summarized as follows:

- **Crowdsourcing is more mature and producing better results than open source in the context of scientific problem solving.**
- **Open source platforms need strong financial sponsors.**
- **The crowd needs to be as wide and including as heterogeneous members as possible**
- **The drug development process can be modularized**
- **Monetary rewards are import for sustained participation**
- **The most able individuals and organizations must be persuaded to participate**

- **Precompetitive open source development is the most likely way to give enough incentives for the big pharmaceutical companies to participate**
- **There are different kinds of crowdsourcing platforms based on slightly different principles and that are effective at different stages in the drug development process; in the early ideation processes, as expertise-based problem solving, and as a tool to gather huge amounts of patient data in the final stages.**
- **Mostly RCs and BCs active on the platforms**

6.4 Our Own Suggestions

We have attempted to synthesize a possible future way forward that takes into account most of the criteria mentioned in the previous section. The idea is to create a hybrid platform where a limited open source approach similar to Arch2POCM would form the basis. This platform would not be a true open source platform because the results would only be available to the existing partners that are funding the platform. The crowd is thus limited to the partners. The exclusiveness will increase the willingness of the participating companies to provide sufficient funds. Given the precompetitive nature, findings can be commercialized at later stages to allow for the participating parties to make money in competition with each other and thus circumvent the patent quagmire.

In our eyes, the existing Arch2POCM suffers from several drawbacks; it does not include a heterogeneous crowd and it does not offer monetary rewards. The way to get around this problem would be to operate a crowdsourcing platform within the limited open source platform, with monetary rewards for solutions, and thereby broadcast the problems to a much wider solution space.

We propose that this solution space now could include contract research organizations (CROs) as well, a group that shows very little activity on the platforms according to our analysis (Table 10, page 42). We hypothesize that a lot of underused capacity, perhaps mostly in emerging countries such as India and China, now could be used as a valuable resource. Their incentive would be to be able to work on problems that they currently do not have enough experience and reputation to be able to get on contracts. They can build a reputation by solving problems, avoid the fear of failure as failure is never exposed (important according to Årdal et al. 2011), work on problems that they think their unique expertise and underused capacity would suit best, and do all of this without any problems relating to patents because this modular work is almost identical to the contract research they are already performing and their business model does not rely on patents.

What the next stage for crowdsourcing and open source within drug discovery will be remains to be seen, but we are confident that there will be future development within this area as there are opportunities to better exploit the widely distributed problem solving capacity around the globe.

7 CONCLUSIONS

We have searched the internet for examples of crowdsourcing and open source initiatives that could potentially contribute to more efficient drug development. We identified eight such platforms that show a large diversity in terms of application, usage and possible implications for the industry. There is some ambiguity as to how crowdsourcing and open source development should be defined, but we classified four as crowdsourcing cases and four as open source cases. We found that crowdsourcing in general produced good results, but that open source initiatives were either poorly financed and not successful or focused on neglected diseases made possible through strong backing by non-profit organizations. However, one example stood out as particularly interesting. Arch2POCM is an initiative between big pharmaceutical companies, non-profit organizations, and governments that is based on precompetitive cooperation. This example, although interesting, suffers from a limited solution space in our opinion. An analysis of which the pharmaceutical companies where that showed activity on the platforms identified R&D-intensive and biotech companies as the most active. Contract research organizations (CROs) and generics manufacturers (GMs) were almost completely absent. We argue that GMs are not likely to be interested in this kind of R&D, but CROs are an untapped resource. Finally we proposed a hypothetical model that took into account all the findings from our study and the literature. This model is based on a limited type of open source with a limited number of partners making use of the untapped CRO resource through crowdsourcing.

8 LIMITATIONS

This thesis is limited to the context of crowdsourcing and open-innovation in the pharmaceutical industry. Other examples and references are presented in the text, but only to provide the reader with a clearer understanding of the phenomenon. It does not necessarily mean that the findings from the other industries are applicable to drug discovery. The pharmaceutical industry faces very high upfront R&D costs and act in a high risk environment encumbered by regulatory constraints and time consuming procedures. These parameters set this industry apart somewhat from other industries where open innovation and crowdsourcing have been successfully implemented.

The search was not a strict systematic review based on predetermined search paths (Cook, Mulrow & Haynes 1997), but a more loosely defined search through a host of search engines, through reference tracking in previous articles and online publications. Furthermore, we did not only include peer-reviewed academic papers, but included all types of sources that we found pertinent. This, we believe give a wider picture that is likely to pick up on opinions that have not found their way into academic papers, but maybe at the expense of some scientific rigor.

All papers and all material were not fully read by all co-authors. For example, one author was assigned to digging deeply into open source while the others were looking at crowdsourcing and innovation in the pharmaceutical industry, respectively. The synthesis was then done collectively through personal communication and the important sources of the other authors findings were read by the other authors, either in full or partially.

9 FURTHER RESEARCH

Arch2POCM is a highly interesting case because it is based on a public-private model. When this platform has matured a little more, studying it should provide valuable knowledge as to the future direction of crowdsourcing and open innovation in drug development.

Our suggestion of a hybrid model with crowdsourcing combined within a limited pre-competitive type of open source would be interesting to research further.

By spreading the risks (research capital spent) and accept a collaborate model, the NPV of the new drug could be positive even if the lack of patent protection reduces the gross revenue. This could be possible because not only do the companies save resources in drug discovery, they will experience a significant cost reduction in the IP area where filings and protection from infringements is associated with high costs. These mechanisms would need further research and metrics and models would have to be created to allow for better predictive abilities.

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Appendix A — The Pharmaceutical Industry

The Key Players

The modern pharmaceutical industry can be divided into different subgroups with markedly different strategies and cost structures. Three such groups can be identified (Bátiz-Lazo & Holland 2001); (a) companies that focus of low-cost lean supply chain production of generic drugs. Generic drugs are drugs where the patents have expired and where there is free competition to produce the drug. (b) R&D intensive large corporations relying on a few blockbuster drugs for the financing of their operations, and (c) biotech companies that produce new drug candidates using the knowledge gained through the emergence of genetic engineering. The biotech companies mainly use larger biomolecules that have to be produced by biological means, such as transmutations and fermentations.

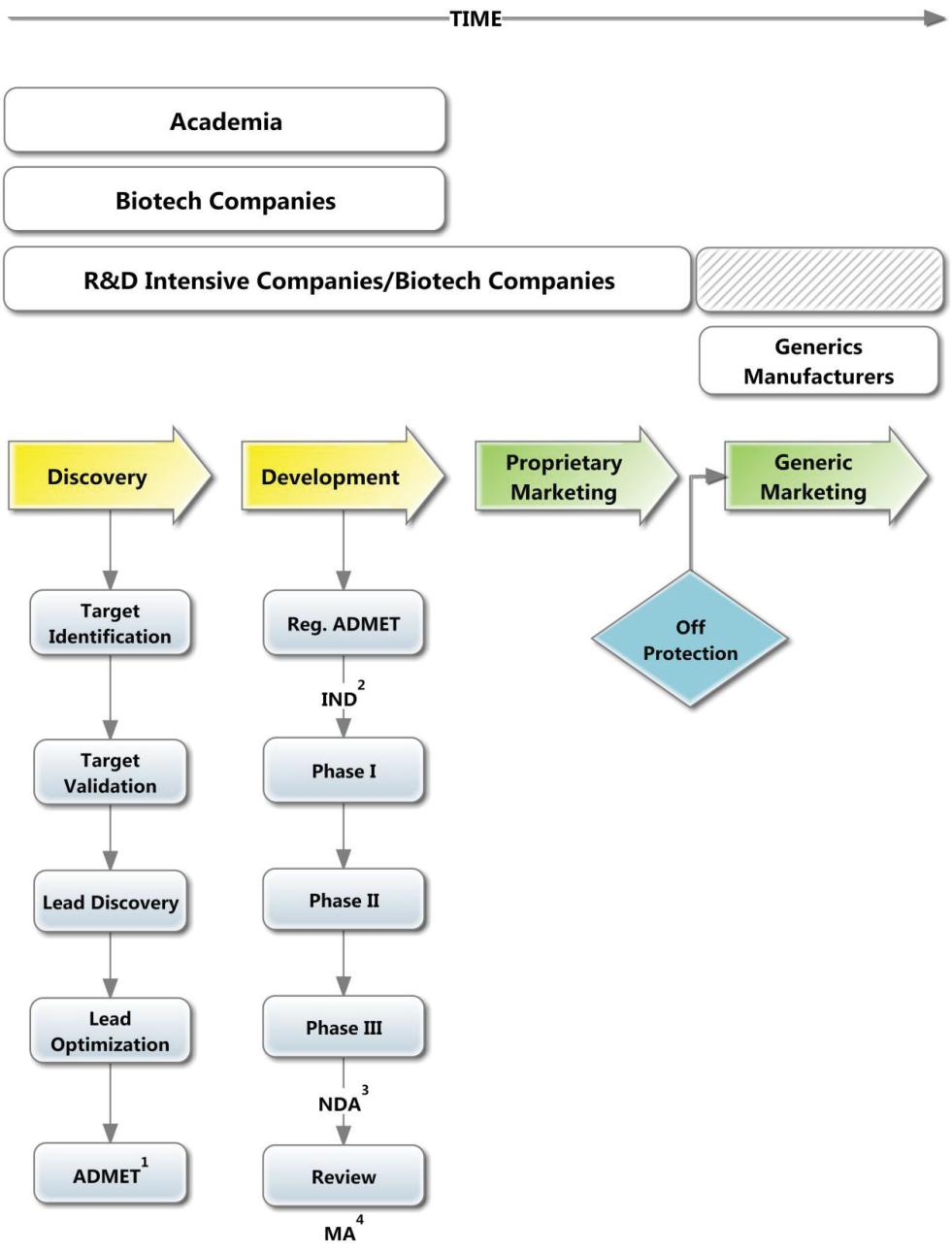
Research-based companies (RCs) and generics manufacturers (GMs) are differentiated by their manufacturing efficiency and R&D costs. RCs often spend large sums on R&D and suffer from low utilization, high fixed costs and low productivity, whereas GMs, on the other hand, have low R&D expenses and a very lean, efficient, manufacturing (Bátiz-Lazo & Holland 2001). This clear strategy separation has led to that those large pharmaceutical companies that own both over-the-counter (OTC) and generics businesses generally operate them separately, often under a different company name. Similarly, those that have acquired biotechnology companies (BCs) normally leave them to operate fairly autonomously (ibid).

For virtually all types of research that can be performed in-house there is an external supplier of R&D that the research can be outsourced to instead. These are known as Contract Research Organizations (CROs) and can either have a small molecule focus like the RCs or a biotech focus like the BCs.

The barriers to entry differ between the three categories. The largest barrier is present for the small molecule pharmaceuticals market, i.e., the market where the big pharma companies make large profits. The profit for these companies largely depends on their blockbuster drugs, such as Nexium, Lipitor, Plavix, etc., and these require years of research and heavy investments to produce (IMAP 2010). Blockbuster Drugs are defined as drugs where annual global turnover for that medicine exceeds US$ 1 billion (European Commission 2008).

The smallest barriers to entry can be seen in the generics industry, which is focused on producing pharmaceuticals where the patent period has expired and doing this as cheaply as possible. However, to get access to the really big profits, blockbuster drugs have to be developed that under patent protection can bring in billions of dollars before competition from the generics business hampers the profits (ibid), although the viability of this business model in the future have been questioned by some (Henry & Lexchin 2002).

A schematic picture of the development process and the involved pharmaceutical companies can be seen in Scheme 1.



Scheme 1. The entire process from basic research by academia to the release of generics by generics manufacturers. The concept for the scheme is taken from (IMAP 2010).

A factor hampering the development of completely new drugs through innovation today is that it is easier to develop “me too” drugs when a new blockbuster drug has become available. “Me too” drugs are drugs that are very similar to the original drug, but that have been changed slightly chemically just enough to evade existing patents (Angell 2004). The manufacturers can also claim that these modifications have added an extra benefit for the patient in terms of tolerability, dosage, or effect, thus making it more likely that the doctor or patient will choose this over the original drug (Bátiz-Lazo & Holland 2001). The truth is probably that they are actually worse than the original in many cases, but this is never studied clinically as all new drugs are tested against placebo and not competitors (Angell 2004).

Innovation within the Pharmaceutical Industry

Traditional innovation within the pharmaceutical industry have turned out to be a balance act where size is necessary in order to have the financial muscles necessary to take a new drug through all the stages of development, but where size is inversely related to innovativeness, flexibility, and creativity. Furthermore, the high costs associated with drug development and the short time in which to earn back the money invested leaves little room for the development of drugs that are not used to treat lucrative life-style associated problems in the western world such as diabetes, obesity, high blood pressure etc. (Henry & Lexchin 2002).

Approximately only 1 in 10000 candidate substances tested in the laboratory eventually become a commercial drug (PhRMA 2011). This problem has in recent years mostly been resolved by mergers and acquisitions where the big pharma companies simply buy promising leads from smaller companies and take them through the very expensive late stages of development. This could be done either by buying the entire company or just the drug candidate along with all of the documentation. A third option can be to enter a licensing agreement where buyer can commercialize the drug, but have to pay a royalty to the original owner of the drug patent (IMAP 2010).

The multitude of mergers and acquisitions has during the last 20 years blurred the line between RCs, GMs, and BCs. Furthermore, the acquisition of GMs by RCs has actually led to that the originator companies themselves introduce generic substitutes for their own branded products through one of their own affiliated GMs (IMAP 2010). This is shown in Scheme 1 as a dashed block next to the “R&D Intensive Companies” block. The fact that the Biotech companies rarely are able to take a drug through all the stages of development themselves without the backup of larger RCs is illustrated in the same scheme by the inclusion of them together in one block. In Table 11, the strategies for some of the major pharmaceutical companies are listed.

Table 11. The business strategies of the major pharmaceutical companies.[a]

Diversification Strategy	Focus Pharma Players
Abbott	Amgen
Bayer	Astra Zeneca
GSK	Eli Lilly
Johnson & Johnson	Pfizer
Merck Schering Plough	
Novartis	
Roche	
Sanofi-Aventis	

[a]The classification is taken from IMAP (2010).

A diversification strategy in Table 11 signifies that the company is expanding the scope of their operations, i.e., moving from being a pronounced RC company to an umbrella company holding a lot of subsidiaries with varying business foci. The main business focus of such subsidiaries could be for example be: OTC drugs, vaccines, eye care, medical devices, branded generics, generics, etc. (IMAP 2010).

The result from the costly development and the somewhat slow R&D within the big pharmaceutical companies is that a lot of the innovation actually takes place at smaller firms. Some of them have the intention to bring the product all the way to the market themselves, but eventually most of them run out of cash and decide to make their profits by selling the rights to the candidate drug. This was the case for many biotech companies in the nineties (IMAP 2010).

In order to spur on innovation targeted at tropical and orphan diseases, the American Food and Drug Administration (FDA) instituted the "Orphan Drug Act" in 1983. This initiative has enabled the development and marketing of more than 350 drugs and biologic products for rare diseases in USA. In contrast, the decade prior to 1983 saw fewer than 10 such products come to market (FDA 2012). This initiative has thus to some extent stimulated innovation within a field where profits generally are lower, but drugs for tropical diseases can only be included in the concept orphan drugs in the EU, due to a wider definition, not in the US (Bergeå 2002). As a consequence more effort is put into the research and development of drugs where there might only be a few thousand sufferers while drugs for tropical diseases such as Leishmaniasis, with an estimated 12 million sufferers and with an estimated 2 million new cases each year, get stuck in the R&D pipeline because there is no profit in it for the big pharmaceutical companies (Strom 2006; WHO 2012).

In has been concluded by medical writer Cliff Mintz (2011) that there is general agreement in the industry analyses performed on the pharmaceutical that there is a need for transformation in how big pharma companies act in order to remain productive. These changes include pursuing:

- **An improved R&D productivity**
- **A continuation of drastic cost-cutting measures**
- **A strategy to rapidly garner market share in emerging markets.**

While some analysts contend that conventional M&A strategies can address these issues, there is a growing consensus that fundamental changes to big pharma's innovation and business models are necessary to ensure its survival.

The Pharmaceutical Industry and Intellectual Property Rights

A new drug is only protected by patents for a limited amount of time, after which the revenues steadily decline for the originator of the drug. The patent protected period for new drugs is 20 years, but these 20 years include the time from first registration through phase all phases of development (PhRMA 2012). This process takes on average 10-15 years with the result that the actual period to make money on the drug usually is only in the order of a decade (DiMasi, Hansen & Grabowski 2003). However, the huge profits tied to patent rights encourage the pharmaceutical companies to circumvent the 20 year timeline. This can be accomplished through the use of several techniques known as "evergreening" (Henry & Lexchin 2002). For example, in the United States under current law, FDA has to put a hold on a generic version of a drug for 30 months after a patent suit is filed, or until the matter is decided in court (Barrett 2010). Other techniques include (Henry & Lexchin 2002):

- **The introduction of new formulations** which are marketed heavily before the generic version of the drug is released.
- **Second-medical-use patents** for drugs nearing the end of their basic patent life. This means that the originator company can register an old drug for a new application which can give them several years of exclusivity in the new application.
- **Repeated patent infringement suits**, which trigger an automatic 24–30 month delay in processing of the generic product claims in Canada and the USA.
- **Collusion with generic manufacturers** to keep products off the market.
- **A company can manufacture and patent a near-identical product** that has no real therapeutic advantage over the original agent. A well-known example of this is esomeprazole, an enantiomer of the top-selling proton-pump inhibitor omeprazole.

The vast amount of resources spent on filing patents, protecting them, and then circumventing them make you wonder if these resources could be put to better use for society while at the same time allowing the pharmaceutical companies to make decent profits.