Vol.6, Iss. 1, January 2009 Journal of Business Chemistry

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ISSN 1613-9615

Vol.6, Iss. 1, January 2009 Journal of Business Chemistry

Letter from the Editor

Discussing challenges in the chemical industry for five years

Five interesting years of the "Journal of Business Chemistry" (JoBC) have passed and many more are hopefully lying ahead of us, with the 6th volume currently in your hands. The JoBC is read throughout the world. Even though the `sectorial` focus seems quite narrow – concentrating on the chemical and related industries – the overall approach of the JoBC is rather broad and interdisciplinary. As "chemistry" is interwoven with a multitude of rapidly progressing fields, many topics from nano- or biotechnology to pharmaceuticals and materials have also been covered. Management topics from innovation and portfolio management to REACH regulation and investments have been analyzed and discussed.

The scientific literature had not provided a platform to discuss interdisciplinary topics of science and business in the chemical industry before. The JoBC has tried to fill this gap and to provide such a platform for academic as well as practitioner-oriented discussions on hot topics in the related sectors. The field of chemistry itself becomes more and more interdisciplinary as the boundaries between industrial sectors and sciences are fading away. This trend provides tremendous opportunities but also challenges for practitioners and academics alike and thus creates the need for discussion forums like journals and conferences on how to stay on top or get to the top in a world of radical changes.

This will likely be even more so the case in the near future, with an omnipresent financial and economic crisis around us, that yet has to unfold its total impact. As a large supplier for most of the highly affected industrial sectors, the chemical industry and all its partners are facing challenging and turbulent times. Measures to cut costs, shrinking markets and severe restructurings will be the effect. However, we are confident that the chemical industry will, in the end, be strengthened. Whatever risks and opportunities the chemical industry will face, the need for a discussion platform on business chemistry issues will only increase. The JoBC hopes it can help to share best practice examples and provide detailed academic analyses of how to act and react in an era of fundamental change.

In the light of these effects, which will be likely to affect all of the firms in the chemical and related industries, we are happy to present in this issue articles on the more traditional branches (like the chemical and the pharmaceutical industry) as well as on more recently established areas (e.g. biotechnology or biopharmaceuticals).

In the commentary section two authors present their opinions on the future of the chemical industry. Rudolf Jerrentrup highlights four trends that contribute to changes in the chemical industry. Furthermore, Matthias Hornke takes a closer look at one of the causes and results of those changes: recent M&A activities and trends in the chemical and pharmaceutical industry.

The articles of the research section deal with the supposedly more modern industries biopharmaceuticals and biotechnology. Minna Allarakhia connects the concepts behind open source software and biopharmaceuticals. Based on the well-known example from the software industry, she evaluates how open source models could be used as a mode of entry into the biopharmaceuticals industry.

Anthipi and Anastassios Pouris review research activities in the South African biotechnology sector. In their paper, they establish a framework for benchmarking domestic research activities with other countries, which are leading in the respective areas. Finally, they contrast their findings with the plans issued by the South African government.

In the practitioner's section, Andreas Boller and Markus Keerl discuss the possible effects of REACH on transfer pricing. They present possibilities of how to optimize a firm's transfer pricing setup. Additionally, they link their findings with some more in-depth issues like cost allocation or tax audit strategies.

ISSN 1613-9615

[Journal of Business Chemistry] Vol.6, Iss. 1, January 2009

Now, please enjoy reading the first issue of the sixth volume of the JoBC. We would like to thank all authors and reviewers who have contributed to this new issue. If you have any comments or suggestions, please do not hesitate to send us an email at contact@businesschemistry.org.

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ISSN 1613-9615

Journal of Business Chemistry

Commentary

The Effects of the Financial Crisis on the Future of the Chemical Industry

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The chemical industry is also feeling more and more strongly the effects of the financial crisis and the recession in the important markets of the world. Even so, "horror" scenarios are not appropriate. The marked decrease in the oil price is also having a positive influence on the level of raw material costs and thus on the profitability of downstream industries. The reason why the situation is, nevertheless, critical is, unfortunately, due to the fact that, at the same time, volumes are clearly dropping and production is declining.

The current situation will, therefore, definitely accelerate change in the chemical industry. Behind this change are four important trends:

- Consolidation rates will increase at the same time as globalization remains an issue.
- Product and technology cycles will continue to be reduced; Innovation is and remains a pivot for successful development.
- The industry is well advised to continue to tackle the issue of process optimization – with the added advantage of releasing additional cash.
- The importance of financial investors will be reduced in favor of strategic investors, since it will no longer be so easy to finance attractive leveraged deals.

With regard to these points, the following outlines current trends and developments, using examples of well-known and important market players in Germany.

The end of consolidation and globalization has not yet been reached

Under the impact of the current crisis, specialty chemistry in particular will accelerate its portfolio optimization process and try to hive off operations which do not satisfy profitability demands.

This will become increasingly more difficult next year due to the lower interest from investors. In addition, bank restraint will often make it impossible for financial investors, and also for strategic buyers, to obtain attractive financing for bigger deals in the current situation. In the medium term this will settle down again once a reasonable base of confidence has been established, especially since, even after significant capital destruction, there is enough investment capital still available which wants to be invested in the medium term. One needs to wait and see what the situation is in spring 2009.

At the same time, it should be stressed that globalization is by no means concluded, but is still on-going. As well as looking at economies of scale, commodity manufacturers will also be looking for proximity to their raw materials sources, and premium manufacturers will be looking at those resources which guarantee that their innovation power for differentiation can be maintained and further developed. In addition, globalization demands that enterprises are present in local markets, and so, in the future, the chemical industry has also to be constantly searching for correct positioning in order to cover these markets. Key factors for success here are concentration on core segments, on the one hand, and, at the same time, flexibility and market adaptability, on the other.

High-wage countries will therefore have to develop themselves into producers of products to meet the highest requirements – as is happening daily in other industries. It is crucial here not only to maintain a scientific lead

through innovation, but also to increase the gap; this especially in view of the efforts of developing countries such as e.g. China and India, whose leading chemistry companies will certainly take advantage of the present crisis to penetrate the West and occupy appropriate niches – in particular, as long as they can profit from the current labor costs advantages. At the same time, it is essential for Western companies to develop their position in these developing countries of high market potential and gain a substantial share of the market.

The consolidation process is continuing even in the current situation as is clearly shown by recent BASF developments, which resulted from a slump in orders in the automobile industry. The group, nevertheless, is still standing by its announced takeover of Ciba for 3.8 billion; at the same time, however, it is planning a large-scale production stop with the closure of 80 plants, 40 of which are located in Ludwigshafen. Approximately 20,000 of a total of 95,000 employees are hit by these cuts in production, initially by cutting down overtime or taking a vacation. The fact that directors Hambrecht, Marcinowski and Kreimeyer have bought BASF shares at this time, is proof of confidence in the future of the enterprise, as well as in their own management efficiency. It also shows clearly that chemistry has a positive future even in Western Europe, and that the current situation will doubtless be used to accelerate the necessary processes and adaptation measures in order to have a better standing than ever when the crisis is over.

Placed in a more favorable position in such times are groups such as Bayer, who, in addition to the chemistry business, also focuses on pharmaceuticals, because although this sector is certainly dependent on the rules and regulations governing the health sector and subject to the accompanying increasing pressure on prices, it is clearly affected less by the current financial crisis. Thus, the CEO of Bayer, Wenning, stressed that only sub-group Bayer Material Science (BMS) is affected by current developments and that uncertainty over future economic development is greatest there. In 2002, Bayer began a reorganization of the group which is now paying off; according to the management, approximately 70 % of the business, in particular, the health and nutrition segments, is today less dependent on the economic situation. However, 30 % still hang strongly on the economic situation, and the enterprise is indeed hit by the slump in demand from important customer groups. In the plastic business 18 % of enterprise turnover is made with the automobile industry, 17 % with the furniture industry, 16 % with the electrical and electronic industry, and 14 % with the building industry.

Rapid Cost Reduction and Cash Release are currently in the foreground – Continuous and sustainable process optimization should follow in the medium term

Due to the current situation the chemical industry is feeling an increasing downward pressure on prices and must deal with a marked decrease in quantities. This is particularly the case in specialty chemistry, which is close to consumers. Since this consumer restraint is to be felt most with large acquisitions, the effects are showing up very clearly in the automotive and building industry segments. The current focus is on programs to reduce costs, which lead to a fast improvement in results, and on measures for short term cash release, which improve liquidity e.g. by optimizing the working capital.

Here we will see a divide. While companies which have to carry a high borrowing ratio (e.g. as a result of leveraged financed company takeovers through Private Equity Societies) will clearly address the issue of cash release in the short term, listed societies will stabilize their attractiveness on the market by appropriate cost optimization programs.

Not many companies will have the chance to make themselves more independent of these market dynamics – unlike Altana Chemie. Susanne Klatten, Germany's richest woman, is intending to completely take over and privatize the Altana Chemical Group. The industry sees this as a clear commitment to taking firm hold of the reins. Mrs. Klatten's decision is a very clever business one, especially in the current situation, because Altana stock is available at a very favorable price on the stock exchange. Altana thus wins enough scope to maneuver without losing sight of its strategically aligned growth program. In various press conferences, CEO Dr. Matthias L. Wolfgruber conceded that Altana is also feeling the effects of the economic slowdown, and he assumes that for a short period of time the situation will significantly affect the value chains. A complete takeover by Skion (the Quandt heiress' investment company) would therefore

offer him greater financial scope for planned acquisitions, the more so as the special character of the margin-strong and less cyclic chemistry business with specialties and innovations would make a contribution in coming years to enabling the continuous growth of the enterprise at high profitability. Although the structure as a listed company was not, on the whole, felt to be an obstacle, other capital measures could not be considered in view of the current market price.

With regard to process optimization, a focus on the supply chain will become more important in the medium term. Continuous optimization in the medium term will once again involve raising and realizing business-specific and cross-company potential. The improvement potential involved in the concepts "Order to Cash" or "Lead Time Reduction" will also constitute one of the crucial levers for future competitive differentiation.

Regarding the optimization of processes, the matter of optimal organizational structure has to be addressed in the service sector, in administrative as well as in technical and other areas. In the context of a heterogeneous international production and business structure a close investigation must be carried out to decide which activities are to be centralized and which decentralized. The issue of "Shared services" will also be important in the future and will pose a challenge to management. It is crucial to find the optimal mix of outsourcing and in-house solutions, bearing in mind that outsourcing is not "a universal remedy". In some cases, it has been shown that there are quite elegant in-house solutions, which, even when compared to outsourcing, lead to improvements in quality and performance.

Stringent innovation management secures future success

The success of focused specialists in the chemical industry, such as, for example, Munich Süd-Chemie, with its diversity of buyers, shows that technology is a crucial component of future success, involving consistent development by purposeful internal effort was well as external focused acquisitions. Thus, Munich Süd-Chemie, for example, has drastically improved its competence in the special filter business by the recent takeover of the British materials flow technology supplier Cooksen. A similar objective was behind the aim to take over the foundry chemical business of the Evonik subsidiary Alzchem in Upper Bavaria and the consideration of co-operation with the American enterprise Ashland.

Technological advantages are being increasingly achieved together with the end customers or in partnerships with enterprises from other industries. For example, Süd-Chemie and the plant engineering and equipment construction company Linde announced that they will conjointly develop equipment for the production of second-generation bio-fuels. These are by-products of farming and forestry such as straw, grasses or waste wood. In contrast to conventional bio-fuels, they are not produced from oil or sugary plant components, whose recovery is being regarded with an increasingly critical eye, but from cellulose. The two partner enterprises are bringing together their know-how from different areas for a specific purpose; Süd-Chemie provides the process technology, while Linde proves its competence in plant construction. Together they can now achieve synergy effects which alone could hardly have been realized.

Such a procedure is particularly necessary given that the relative portion of expenditure for research, development and marketing as well as for access to end customers will continue to rise. At the same time, the chemical industry's customers will be increasingly international and it is necessary to follow customers into the respective countries in order to be able to offer local customized solutions. For and in the future, application know-how will play an important role, and network structures, formal and informal, will guarantee presence and efficiency at global level.

An effective and efficient innovation management is one of the basic prerequisites on the road to technology leadership. Purposeful innovation management is not necessarily only a question of on-going creative masterstrokes, but also, and mainly, a clearly defined process. On the one hand, it is important permanently to feed and expand the idea pipeline; on the other hand, enterprises need for this a stringent Stage Gate process, which, by means of clear pre-selection based on firmly defined points, leads the really attractive projects to success. Here, the NPV represents, without doubt, a crucial criterion for the cost-effectiveness of the project. Above all, the period of time needed up to marketing, the "Time-to-Market", is a key to success.

In addition appropriate structures and processes are required in R&D departments and above all, market-focused thinking from employees. Many other industries have alrea-

dy established professional structures in this regard; for the future, in the chemistry sector, it is to be expected that stronger focus will be placed on optimizing the R&D departments in order to establish appropriate processes.

An example such as Süd-Chemie, an enterprise which, when compared with other enterprises, spends an over-proportionate amount more on R&D, shows clearly the success of an appropriate innovation-oriented strategy, which has made an impact even in the crisis. This shows the confidence of the chairman of the board of Munich Süd-Chemie, Dr. Günter von Au, who, in November 2008, delivered a remarkably optimistic view of the coming year, forecasting growth in sales of at least a high single-digit figure. He named his reasons for this as, among other things, the strong presence in Asia and the good business development with new products which have a unique selling proposition (USP). Even if this positive view should diminish somewhat, this example shows, nevertheless, that there are successful strategies for positioning oneself futurably in the high-wage country Germany.

General market dependence remains

With all these things it is necessary to note, however, that for neither large players in the market, like BASF, nor for focused specialists and niche players is it a walk in the park. Thus, Wacker Chemie, for example, reflects the dependence on the market situation or only the psychology of the markets. The stock of the chemical group and semiconductor supplier suffered sensitively in the fall of 2008 from the downwards forecast of a competitor and the subsequent concerns about the profit performance of the Wacker subsidiary Siltronic, after MEMC Electronics Materials, a manufacturer of silicon chips for the solar industry, had to revise downwards its goal for the sales development in the fourth quarter. In the third quarter 2008 the enterprise announced a significant sales increase despite the expected economic slowdown, and for the whole year sales should also increase by significantly more than 10 %. Operational profits should increase further as well.

Broad positioning on its own is not the answer

Even those enterprises which are broadly positioned and also have a substantial part of their business in the building and automobile sectors, will clearly feel the effects of negative market development in these market segments. The current CEO of Evonik, Werner Mueller, has qualified these effects up to now by describing the business model of the integrated industrial group with its three pillars of chemistry, energy and real estate as robust. In addition to the fundamental growth potential in the chemistry segment, the two other business segments, energy and real estate, have stable profit-makers at their disposal. Even so, the situation will slow down. The group can still rejoice that in the third quarter 2008 all three business segments contributed to sales growth and made positive contributions to the results. Due to better selling prices and higher sales volumes in the first nine months the chemistry segment, in particular, could contribute to organic growth of 13 %, the effects of portfolio and exchange rates balancing each other out to a large extent. In the energy segment, behind which hides the former Steag, sales increased by 18 % due to substantially higher coal prices and the corresponding increase in electricity sales. The financial investor CVC has a quarter involvement in Evonik. He has high expectations of an increase in Evonik's appreciation, not least due to the financed, comparatively high purchase price, of his share. This poses a substantial challenge to the group, not least because of the current market situation in important customer markets.

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Commentary

Mergers & Acquisitions (M&A) in the Pharmaceutical and Chemical Industries: A Lighthouse in Choppy Waters

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After record years in 2006 and 2007 that even topped the peak-year 2000, a cooling down of the international market for Mergers and Acquisitions (M&A) could be observed in 2008: Whilst the global transaction volume in 2007 reached about $ 4,400 bn. (2006: $ 3,600 bn.), the total for 2008 is expected to hit about $ 3,300 bn. The main reason for this development can be seen in the financial market crisis and the resulting problems for financial investors to raise outside capital. Consequently, these financial investors account for less then 10 % of the global M&A market and it's up to strategic investors – often family-owned – to fuel the national and international M&A markets. Unlike financial investors, companies (strategic investors) are still able to embark on M&A activities in the $ bn.-range due to their often comfortable solvency situation.

Although it's very likely that we are currently observing the final stage of the so-called 6th "M&A-Wave", it should not be forgotten that the global M&A year 2008 was even stronger than the 5th "M&A-Wave"-peak in the year 2000. Strategic investors in the pharmaceutical and chemical industries accounted for a major portion of the global M&A market during the last years. This article delivers a brief review of M&A in these industries, together with an outlook for the year 2009.

Strong market consolidation

When looking at the big deals in the pharmaceutical and close-by chemical industry, it is evident that after mega acquisitions in 2006 (e.g. Bayer/Schering, Linde/BOC Group, Merck/Serono) and in 2007 (e.g. Akzo Nobel/ICI, Schering-Plough/Organon Bioscience), the year 2008 is once again proving that companies in the chemical and pharmaceutical markets are responsible for a large part of the global M&A volume. In the first half of 2008, the dominant role in the pharmaceutical M&A market was played by transactions with Japanese participation (e.g. Takeda/Millennium, Daiichi Sankyo/Ranbaxy, Eisai/MGI Pharma), accounting for a transaction volume exceeding € 17 bn (refer to figure 1). It is obvious, that in the rather saturated Japanese pharmaceutical market, which holds about 9 % of the global $ 712 bn. pharmaceutical market (year 2007), Japan-based pharma-suppliers are looking for growth opportunities in other geographical markets or are trying to improve their position in biotech and generics. Mega deals dominated pharmaceutical industry headlines at a later stage in 2008, such as those announced by Roche (takeover of US biotech company Genentech for about $ 44 bn.), Fresenius (takeover of US-based APP Pharmaceuticals for about $ 3.7 bn.) and Novartis (planned takeover of US-based contact lens specialist Alcon for € 39 bn.). Next to strategic product-driven considerations, the strong position of European currencies against the dollar supported this development. After the planned takeover of Barr Pharmaceuticals (USA) by the Israel-based global generics market leader TEVA, there are already speculations in the market, that the Germany-based generic producers Stada and Ratiopharm are the next takeover targets, which would lead to a further consolidation of the generic pharmaceutical market - or at least the pharmaceutical market in general.

Although the M&A market start in 2008 for the chemical industry was not as dynamic as that of the pharmaceutical one, the announ-

ced takeover of the US specialty chemistry company Rohm & Haas by Dow Chemical in July 2008 (transaction volume: $ 18.8 bn.) or National Starch by Henkel for about € 3.7 bn. and Ciba by BASF for € 3.8 bn. made clear that chemical players are also going through a re-arrangement phase and taking their chances. However, the strong M&A activity of the chemical industry in 2008 should not delude that, during the last 3-4 months, the financial crisis had massive impact on chemical companies' customers – especially the automotive industry (for example: in the USA, November 2008 car sales with – 37 % were the lowest since 1982). Massive demand reductions are already leading to reduced production in many chemical companies. While disease-linked demand for pharmaceutical products is relatively stable, investments in chemical (derived) products can – to a large extent – be postponed or even completely abstained. This situation over the last 3-4 months is certainly leading to extreme cautiousness regarding M&A in the chemical industry.

Key M&A market drivers in chemical and pharmaceutical markets

The recently observed takeover premiums indicate a clear value creation deal logic. For example, referring to the stock price at announcement date, the takeover premium at the Takeda/Millennium deal was at 53 % and Dow Chemical is willing to pay a premium of about 70 % for the planned Rohm & Haas takeover, to be followed later in 2008 by premiums for example of 32 % for the BASF/Ciba and 42 % for the TEVA/Barr deal. Such high premiums can only be justified by massive cost synergies or revenue/profit-growth expectations. Since revenue synergies are difficult to quantify and most value calculations are therefore based on cost synergies, the reason for such premiums is very often seen in cost synergies in areas such as administration, procurement, sales and R&D. Examples for targeted cost synergies p.a. are $ 750 – 850 mill. for the Roche/Genentech deal, € 240 – 260 mill. for the Henkel/National Starch deal and about € 220 mill. for the BASF/Ciba deal. Since acquisition prices of the above mentioned takeovers were negotiated before the stock market crash in October 2008 the pressure to reach - or even exceed - the targeted cost-synergies is undoubtedly growing. This is especially true given that market-oriented revenue synergies are unlikely to be realized in the current economic slump.

Especially for pharmaceutical companies, the realization of cost synergies is the main approach to further realize high margins, while many patent-related "super margins" will erode during the next years – according to the research company Datamonitor, pharmaceuticals which will lose patent protection between the years 2007 and 2012, will lead to a revenue decrease of $ 115 bn. When "blockbusters" with their $ bn. sales volume disappear, generic pharmaceutical companies will expand their market power and will themselves strive for economies of scale by means of M&A. Moreover M&A is seen as an adequate means to create "critical mass" for costintensive active pharmaceutical ingredient research – on average it costs $ 800 mill. and takes twelve years to develop a new drug. This "Herculean task" can only be achieved by big and financially strong companies. While managing the costs on the production part is hard enough for many companies, additional pressure comes from the revenue part. Governmental efforts target to reduce drug prices in order to unburden the public health care systems. This increased cost pressure implicates further consolidation pressure, also for the generic pharmaceutical industry.

Acquisitions driven by strong revenue growth expectations – or at least substitutions for lost "blockbuster" revenues – most certainly play a major role in the acquisition of biotech companies like Serono, Millennium or Genentech. Likewise, macroeconomical factors such as demographic changes and resulting shifts in the demand structure in the traditional triad regions (USA, Europe and Japan), lead to the necessity to capture new markets.

2009 is predicted to be another strong M&A year for the pharmaceutical industry

Given the above mentioned factors, the pharmaceutical industry will remain under cost pressure. It is therefore assumed that M&A activity in the pharmaceutical industry will continue to be high in the year 2009, in order to meet global market needs and to reduce costs in parallel – this might even be accelerated by the separation of generic business parts and a shift in business models towards companies which are either focused on low-cost generic production or on R&D-intense production of patented drugs.

For the chemical industry, the further development of raw material prices and product

demand will be a key driver regarding the M&A level. Should raw material price levels start to rise again M&A will be an option in order to further reduce costs and to secure profits. Furthermore, low product demand levels might lead to a new arrangement of critical masses in the chemical industry, resulting in M&A activity.

It can be summarized that the current conditions are keeping the M&A wheel turning, not only in the chemical but especially in the pharmaceutical industry and the M&A market volume for the year 2009 stands a good chance to reach a high level again. However, it should not be forgotten that about 2/3 of all transactions do not meet the expectations. Therefore, apart from a careful target-setting and target-selection process, post merger integration (PMI) remains a key issue. A carefully managed PMI with a strong focus on cost/revenue synergy realization, helps to justify the acquisition and to ensure a "happily ever after marriage, once the excitement of the wedding party has worn off"!

Figure 1 Main transactions in the pharmaceutical and chemical industries in year 2008 (partly announced or in planing phase)

Buyer	Country	Target	Country	Deal-Volume (bn.)
Novartis	CH	Alcon	US	€ 39
Roche	CH	Genentech	US	$ 44
Dow Chemical	US	Rohm & Haas	US	$ 18.8
TEVA	IL	Barr Pharma	US	$ 9
Takeda	JP	Millennium	US	$ 8.8
Daiichi Sankyo	JP	Ranbaxy	IN	$ 4.6
Eisai	JP	MGI Pharma	US	$ 3.9
BASF	DE	Ciba	CH	€ 3.8
Henkel	DE	National Starch	US	€ 3.7
Fresenius	DE	APP Pharma	US	$ 3.7

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Research Section

Open Source Biopharmaceutical Innovation- A Mode of Entry for Firms in Emerging Markets

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The open source model provides a valuable framework for collective knowledge production and dissemination. Mirroring the efforts of the open source community that developed Linux, open biopharmaceutical initiatives are enabling companies to access knowledge-based resources critical to drug development. The objective of these initiatives is to preserve the downstream technological opportunities for multiple firms.

As economies in emerging markets enter the biopharmaceutical arena, it is essential that developed economies share not only technological expertise, but also their experiences regarding knowledge production and dissemination. The goals should be to assist these economies to participate on a level playing field with respect to market entry and product development, to protect local knowledge, and ensure fair access to global knowledge as well as technology. Maintaining and building the public domain with particular attention to knowledge that is of benefit to these economies can allow researchers to quickly and cost-effectively access knowledge.

In this paper, two models are developed to understand how open source strategic alliances and open licensing can be used as modes of entry into the biopharmaceutical industry by firms in emerging markets. Case examples and qualitative data are both used to provide a basis for these models.

Introduction

Chesbrough (2003; 2007) explains that innovation has become open through the division of labour. In many industries, the vertically integrated organizational structure where innovation is solely an internal activity is gradually being transformed into a more fluid structure integrating internal and external sources of innovation. For example, companies are finding value through the licensing of intellectual property, the development of joint R&D ventures, or other arrangements to exploit technology outside the boundaries of the firm (Chesbrough, 2003; 2007). In the pharmaceutical industry, giants such as Merck and Pfizer have watched as biotechnology upstarts such as Genentech, Amgen, and Genzyme have exploited external discoveries to become major players in this industry. These companies used an open business model in which ideas move from discovery to commercialization through at least two different organizations. (Chesbrough, 2003).

From a knowledge perspective, in the closed model, human capital is employed within the boundaries of the organization. Knowledge is generated within and belongs to the originating firm. The organization's profit model revolves around the notion that knowledge is discovered, developed, and then embodied within firm-only products (Chesbrough, 2003). Appropriated knowledge is controlled by the originating firm. In the open model, human capital and knowledge are accessed both inside and outside the boundaries of the organization. A firm can profit both from the embodiment of knowledge within internally developed products as well the embodiment of knowledge in products developed by other firms (Chesbrough, 2003).

Open source software development reflects both collaborative production and shared implementation of a technology (Chesbrough et al., 2006). Open source software is considered to be a reaction to the proprietary software model (Lakhani and von Hippel, 2003; Chesbrough et al., 2006). Namely, open source software involves collaborative production and requires free distribution of software source code and the right for others to modify the code. I assert in this paper that open source innovation is a model of open innovation involving collaborative knowledge production and knowledge dissemination with and by participating firms.

Lakhani and von Hippel (2003) discovered in their research three types of incentives driving firm participation in open source software development including: direct utility to the organization from collaborative, open software development e.g., absorptive capacity development and early access to technology; intrinsic benefit from participating in the development of this software e.g., learning a new skill; and signalling one's abilities in a technological arena to one's peers or firms. The open source model has provided a valuable framework for collective knowledge production and dissemination beyond the software community. Mirroring the efforts of the open source community that developed Linux, open knowledge networks and other cooperative strategies are enabling biopharmaceutical companies to access disembodied, upstream, knowledge-based resources critical to downstream drug development (Nelson, 1959; Reichman, 2003).

The Human Genome era has emphasized the notion that biological knowledge is complex. Discovery research no longer simply focuses on individual units of knowledge, but considers the behaviour and relationships of all units of knowledge in a particular biological system from a functional perspective (Kitano, 2001; 2002). Genomes are now being described as consisting of complex, intersecting systems rather than unitary collections of separately functioning structures (Hood, 2000; Dutfield, 2003). In this sense, it is possible to observe many similarities to software development. Software is a complex system, developed from many intersecting components (lines of code). Several developers may be required to generate these intersecting lines of code so that the associated processes can emerge and function. Demarcating the lines of ownership in this case can be an onerous task.

As economies from emerging markets enter the biopharmaceutical arena, it is essential that developed economies share not only technology expertise, but also their experiences regarding collaborative knowledge production, technology transfer, and intellectual property management. The goal should be to assist these economies to participate on a level playing field with respect to market entry and product development, to protect local knowledge, and ensure access to global knowledge as well as technology. Researchers and technology transfer officers must therefore, take greater caution in the patenting and licensing of technologies that have significant application in developing and under-developed markets. Maintaining and building the public domain—with particular attention to knowledge that is of benefit to these economies, can allow these researchers to quickly and cost-effectively access knowledge. Open licensing, geographic-based licensing, and assigning fair-royalties are additional options being employed to assist researchers in developing economies access technologies that address neglected diseases or local health needs (Chokshi et al., 2006).

As biopharmaceutical knowledge has become increasingly high in complementarity, high in applicability, but low in substitutability, open source innovation, particularly when knowledge exists in disembodied form during the upstream phases of research, can provide multiple firms the opportunity to pursue downstream product development activities. From a mode of entry perspective, open source strategies can further assist firms from emerging markets to enter a technological arena without the onerous upfront costs associated with exporting, developing subsidia-

ries, pursuing acquisitions or forming joint ventures, as well as encountering transactions costs associated with the sourcing of and contracting for proprietary knowledge (Antonelli, 2003).

I begin by analyzing models of open source innovation from the information technology (IT) sector. Case examples are provided of the use open source IT innovation in emerging markets. I then provide an overview of how the open source model has emerged in the biopharmaceutical sector since the completion of the Human Genome Project. Open source based strategic alliances and open licensing are discussed as specific mode of entry options for firms. Case examples and other qualitative data provide the basis for the development of models of these modes of entry for firms in emerging markets.

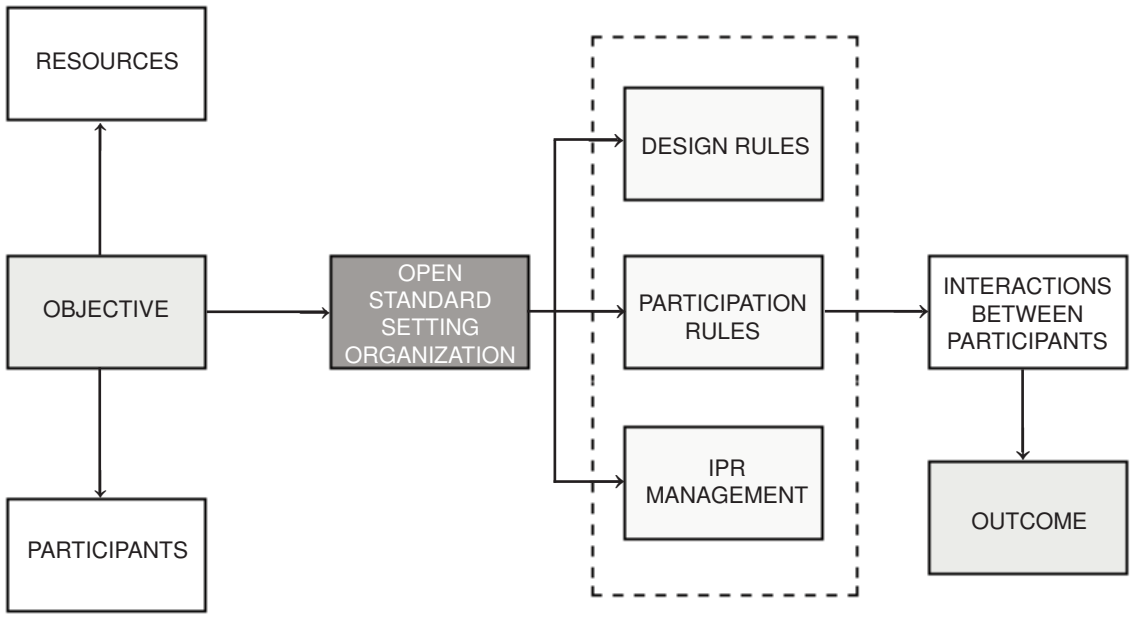
Open Source Models in the Information Technology Sector

Models of cooperation associated with open standard development and open source software development from the IT sector provide us with valuable insight for cooperative biopharmaceutical development. It is important to note that open standard development reflects collaborative technology production between multiple organizations; open source software development entails both collaborative production as well as implementation of a technology.

Open standards are essentially a set of rules for the design of new products. These rules enable coordination between products and components by establishing a common interface to manage their cross-interaction (Chesbrough et al., 2006). Voluntary, non-market standard setting organizations that operate in industries such as software development, where coordination is large, can have a considerable impact on the adoption of a particular technology as an industry standard (Chesbrough et al., 2006).

Open standards create value for consumers by promoting competition between implementations. Firms selling products that implement a standard enjoy less uncertainty associated with the coordination of products (Chesbrough et al., 2006). It is anticipated that firms that produce technologies used to implement a standard, participate in open standard groups to capture the value associated with the development of a new compatibility standard including absorptive capacity development and early access to technology (Cohen and Levin-

Figure 1 Model of Open Standard Development[1]



1) Flow: The objectives impact resources and participants; the Open Standard Setting Organization establishes rules to manage the interactions between participants and in turn determine the outcome in terms of knowledge developed and any associated intellectual property. IPR=Intellectual Property Rights.

thal, 1990; Chesbrough et al. 2006). Figure 1 is a model of open standard development. The objectives of the open standard setting organization will likely impact the resources and participants that are needed and eventually commit to the development of the open standard. Rules are established to not only manage the technology development process, but also decision making processes, and any associated intellectual property. These rules impact the interactions between the participants and the eventual outcome in terms of standard development.

In the management of standard creation, standard setting organizations establish a set of rules and obligations for members as outlined in the charter and bylaws of the organization (Lemley, 2002). Intellectual property rights (IPRs) in open standard development are governed by these rules and address searching for IPRs within member files and or the broader literature, disclosing information within the organization, and licensing of IPR. These rules are essentially designed to prevent members from adopting a standard that entails ex-post hold-ups by patent owners offering a license that likely would not have been accepted ex-ante. Table 1 outlines the intellectual property strategies used in the creation of standards (Chesbrough et al., 2006).

Open source software development reflects both collaborative production and shared implementation of a technology (Chesbrough et al., 2006). Open source software is considered to be a reaction to the proprietary software model, differing from this latter model in terms of intellectual property rights and its production. Namely, open source software involves collaborative production and requires free distribution of software source code and the right for others to modify the code. Two highly visible open source projects are the Linux operating system through the Open Source Development Labs (OSDL) and the Mozilla web browser project. In both cases, firms donate their research to the open source project while exploiting the pooled R&D of the project to enable the sale of related products and services (Chesbrough et al., 2006).

For example, IBM is hoping to take advantage of some of the world's largest untapped information technology (IT) markets—markets not weighed down by existing proprietary technology—by offering innovation around the adoption of open source solutions such as Linux. IBM has found success pushing open source software into emerging markets because governments in these markets often favour Linux over proprietary technology—finding the idea of proprietary software culturally dis-

Table 1 Intellectual Property Strategies Used in Information Technology Standard Creation

IP Strategy	Description	Examples
Contributing IPRs	Royalty-free licensing to promote implementation of standard.	Ethernet
Defensive Patent Pools	Aggregating patents in the public domain.	Cable Labs
Open-source Licensing	Freely licensing any follow-on innovations.	Linux, Apache
Participatory Licensing	Disclosing of patents during standard setting and licensing to implementers.	RSA cryptography patents
Ex-post Licensing	Conducting a search for standard related IPR and approaching implementers about licensing.	Eolas vs. Microsoft BT hyperlink suit
Active Hold-up	Participating without disclosure and then pursuing ex-post licensing.	Rambus
Cross-Licensing Alliances	Cross-licensing that replicates the patent pool.	GSM Semi-conductors
Royalty-generating Patent Pool	Pooling of patents with a centrally administered licensing authority.	MPEG-LA

tasteful (Meredith, 2005).

Linux' unprecedented growth in the Asia/Pacific region has global ramifications. As alternatives to proprietary systems are adopted and expanded worldwide, the viability of Linux as an operating system (OS) standard continues to increase (Meredith, 2005). In June 2003, IBM jointly established a Linux competency center with the Beijing government in China. IBM and the Beijing government established this center for many reasons, including promoting the usage of Linux by helping organizations port applications to a Linux environment, creating end-to-end Linux solutions, as well as providing training for Linux professionals in China (Meredith, 2005).

A second center in Guangzhou, opened in June 2004, provides software testing, project and technology-management services, as well as professional training courses for local software developers. IBM has instituted similar efforts all over the Asia/Pacific region (Meredith, 2005). According to the Korea Times, in May of 2005, IBM had been in talks with South Korean officials and industrialists about promoting the global open source computer operating system (Meredith, 2005). Similarly driven by cost, licensing issues, and technical issues, a number of companies across India are taking a serious look at the world of free and open source software (Meredith, 2005). IBM officials cite that organizations at all levels find it reassuring to be using an open source system—that is, to see the code powering systems and to understand from the outset the technological issues likely to be encountered with downstream product development.

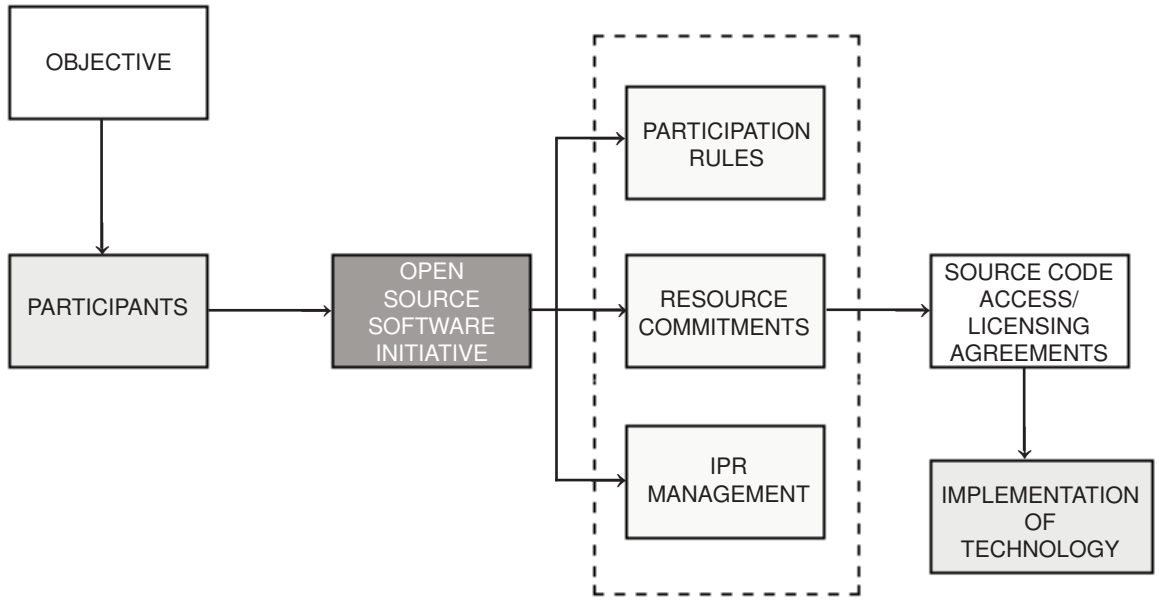
Sun Microsystems likewise, hopes to use the open source model to help developers use cutting-edge technology to innovate and enable the associated countries to move up the worldwide IT value chain. Sun Microsystems provides businesses in emerging economies access to its intellectual property without barriers to adoption, exit, and without barriers of licensing to build their network infrastructure (Sun Microsystems, 2008). Sun Microsystems indicates that governments and educational institutions are warmly embracing open source technologies because countries can move quickly along the IT value chain without the multimillion dollar commitments required to license proprietary technology (Sun Microsystems, 2008).

In February 2008, Sun Microsystems announced its first overseas expansion of its OpenSPARC educational program. The three-year agreement with China's Ministry of Education (MOE) extends to as many as 10 universities in China this year, and trains 150 teachers each year on Sun's OpenSPARC designs. As a consequence, Sun Microsystems claims that its business is driven largely by the adoption of open source technologies at the university level and across governments. This broad adoption is thought to be enabling Sun Microsystems to get onto solid ground in a number of emerging markets (Sun Microsystems, 2008).

Research results from several open source studies at UNU-MERIT (United Nations University – Maastricht Economic and Social Research and Training Centre on Innovation and Technology) further suggest that many countries and institutions have made strides in adopting policies to enhance public access to knowledge. In just four years, Extremadura –one of the poorest regions of Spain—successfully invested in creating a free-software society. The model is now being replicated in other poor regions of Spain, as well as in Latin America. In Africa, the University of the Western Cape (UWC) in South Africa has introduced an open learning model spearheaded by the Massachusetts Institute of Technology. The Commonwealth of Massachusetts also successfully introduced OpenDocument—an Open Standard for office applications—which provides important lessons for other regions and countries across the world (Bergstrom, 2006; UNU-MERIT, 2008). Various initiatives at UNU-MERIT hope to use these lessons to assess the effectiveness of several alternative global mechanisms that have been proposed such as Open Source Science and Open Medicine to boost health research and development and broaden access to affordable drugs for the world's poorest populations respectively (Bergstrom, 2006; UNU-MERIT, 2008).

Figure 2 is a model of open source software development. Once again, the objectives of the open source initiative will determine the type of participants that join. In open source software development, the participants are primarily volunteers who are located across different geographic regions using tools to collaborate in source code development. Rules are established once again to not only manage decision making processes and any associated intellectual property, but also resource commitments including technological donations made to the open source initiative. As a result of any donations and development efforts, users are able to use, change, and improve the software, and to redistribute it in

Figure 2 Model of Open Source Software Development[2]



modified or unmodified form. Various licensing agreements ensure this open access to source code.

The Emergence of Open Source Innovation in the Biopharmaceutical Sector

The International Human Genome Project catalyzed the open-source movement in genomics-based research. Globally dispersed laboratories jointly collaborated to map and sequence the Human Genome. The resulting data were rapidly deposited into the public domain to ensure an open and level playing field for all researchers. Just as in the case of the previously discussed open standard setting organizations and open source software initiatives, leaders of the National Human Genome Research Institute (NHGRI), together with the Wellcome Trust, and academic researchers at the major human genome mapping centres, resolved in February 1996 that all human genomic DNA sequence information generated by centres funded for large-scale human sequencing, should be freely available and in the public domain in order to encourage research and development (Marshall, 1996). NHGRI followed up with an April 1996 policy statement making rapid release of data into public databases a condition for grants for large-scale human genome sequencing (NHGRI, 1996). NHGRI also warned that it would monitor whether grantees were patenting large blocks of primary human genomic DNA sequence and might invoke the exceptional circumstances limitation (to restrict patenting) in future grants (NHGRI, 1996).

A more general statement of Principles and Guidelines for Sharing of Biomedical Research Resources, adopted by the National Institutes of Health (NIH) in December 1999, also attempted to guide NIH grantees in their appropriation activities. The statement outlined that the use of patents and exclusive licenses is not the only, nor in some cases the most appropriate means of implementing the Bayh-Dole Act. Where the subject invention is useful primarily as a research tool, inappropriate licensing practices are likely to thwart rather than promote utilization, commercialization, and public availability (NIH, 1999).

Open source innovation has also flourished in bioinformatics—where software code

2) The objectives determine types of participants; the Open Software Initiative establishes rules to manage the interactions between participants and the resources to be committed to the initiative; these rules also result in establishment of access/licensing agreements and in turn determine the eventual implementation of the technology.

and databases are traded and pooled on a mutual sharing basis. Researchers indicate that the BioPerl project for example, allowed the development of tools during the Human Genome Project to facilitate the interchange of data amongst laboratories who kept their research in dissimilar formats (Stein, 1996). BioPerl, BioJava, and BioPython—now organized together as the Open Bioinformatics Foundation (OBF), make their work available under standard open source licenses (OBF, 2008). The Bioinformatics Organization further encourages collaborations in bioinformatics development, maintains computational resources, and promotes open access to materials and methods for bioinformatics research and education throughout the world (OBF, 2008).

These efforts in the public sector have similarly encouraged the private sector to promote and participate in open source initiatives. The Single Nucleotide Polymorphisms (SNP) Consortium brought together ten of the world's largest pharmaceutical firms. Consortium members recognized the SNP map as a precompetitive, research tool. The Consortium committed to developing a SNP map to assist researchers to identify the multiple genes associated with complex ailments such as cancer, diabetes, vascular disease, and some forms of mental illness. The competitive members viewed the map as a tool to be jointly developed and shared, with open access to the Consortium's data guaranteed for the public at large. Specifically, the rules established at the outset determined not only knowledge production processes but also included an agreement to relinquish any property rights to the knowledge generated within the Consortium—thereby avoiding any downstream holdup issues (Davies, 2001).

Then in October of 2004, Novartis, the Broad Institute of MIT, and Harvard announced a joint project to decipher the genetic causes of type 2 diabetes. The collaboration reflected the mission of the Broad Institute to bring together researchers to solve complex problems requiring multi-disciplinary teams and that are difficult to solve in the traditional (isolated) laboratory setting (Lawler, 2004). Companies typically demand that data created in cooperative ventures be kept away from competitors. However, Novartis argued that the benefits of openness would outweigh those of secrecy, and the company placed the genetic variation data it collected on a public web site. While the team did not file patents on the database, it did allow others to patent new therapies or diagnostic tests based on the public information (delaying appropriation to downstream activities) (Lawler, 2004). Novartis' decision is a signal of an emerging change in attitude toward the appropriation of all forms of biological knowledge—reminding us of reaction that encouraged the development of the open source software model. It is worthwhile to note that in each of the above case examples, organizations are not only benefitting from division of labour typically associated with open innovation (i.e. via collaborative knowledge production), but are also freely accessing knowledge from both inside and outside the boundaries of their own organization (i.e. via adherence to the open source model).

Open Source Biopharmaceutical Innovation as a Mode of Entry

Choosing a mode of entry into a new market and for the purposes of this paper a new technological arena, is a critical decision faced by firms. Firms can choose from a variety of modes, including exports, licensing, wholly owned subsidiaries, acquisitions, and different types of joint ventures. Other modes include subcontracting, associations, and consortia (Malhotra, 2003). In the choice of mode of entry, the knowledge to be transferred is a key issue considered by firms. Namely, protection of knowledge from the threat of opportunism is a primary driver of entry mode choice (Malhotra, 2003). However, it is interesting to observe, that many biotechnology and pharmaceutical companies are promoting and engaging in alliances that are committed to open source drug discovery via cooperative knowledge production and cooperative knowledge dissemination. In the sections that follow, I consider both open source based strategic alliances—namely the consortium structure and open licensing as modes of entry into the biopharmaceutical arena.

Methodology and Context

The data presented in this paper are sourced from a previous study conducted by the author and colleagues. Allarakhia et al. (2008) analyzed 39 open source biopharmaceutical consortia including the likely participants in such initiatives, the rules for participation, the focus of knowledge production activities, and the management of joint knowledge assets. These consortia were visible and significant in their achievements, thereby enabling the

researchers to 1) accurately analyze interactions over a reasonable period of time, 2) analyze the policies established with respect to knowledge production and dissemination, and 3) retrieve adequate literature sources for the study. Literature sources analyzed included peer-reviewed journal articles by consortia members or third-party researchers, press releases, consortia websites, publications, and presentations. The researchers also substantiated the data by surveying consortia directors.

It is anticipated that the analysis extended in this paper will allow for an understanding of the structures associated with open source biopharmaceutical initiatives and the development of a model similar to those developed for open standard setting organizations (Figure 1) and open source software initiatives (Figure 2). This model should incorporate how rules and organizational structures encourage entry by firms into such initiatives and in turn the technological arena, how learning is encouraged for participating firms, and how knowledge is disseminated so that firms outside the open source initiative can pursue product development opportunities—that is, either at no cost or minimal cost.

In the biopharmaceutical industry, many new drugs hinge upon advances in molecular biology and genetic engineering. As a result, research activity that adheres to the molecular biology paradigm requires network-like alliances between academic institutions, biotechnology companies, and traditional drug manufacturers (Bower and Whittaker, 1992; Powell et al., 1996; Blumenthal et al., 1997). The genomics era has highlighted the need for partnerships that are broad and cross institutional as well as national boundaries. The breadth of upstream research to be conducted to ensure successful drug development, particularly in a decade marked by shrinking pipelines and blockbuster drug patent expirations, has reinforced the need for knowledge-based networks (Reid et al., 2001). Hence, Allarakhia et al. (2008) studied open source based consortia including geographically dispersed participants to understand knowledge production processes in these alliances as well as knowledge dissemination strategies including open licensing employed by consortia members.

Open Source Based Strategic Alliances as a Mode of Entry

As the pharmaceutical industry further transitions into the current post-genome paradigm, the nature of biological knowledge, namely the complementary nature of upstream biological knowledge, its complexity in terms of function, and its breadth of application, will encourage the formation of strategic alliances to ensure equitable access to knowledge for future product development. Strong early-mover advantages in drug development rest on the ability to rapidly identify, access, and integrate new combinations of knowledge (Antonelli, 2003; Grant and Baden-Fuller, 2004).

Biology knowledge is complex and derives from a variety of scientific and technical disciplines. The molecular level of analysis, the computational nature of discovery research, and the global scale of research, all provide evidence that the drug discovery and development paradigm has changed dramatically. To manage the uncertainties of drug discovery, a new model of cooperation is emerging— the open source consortium (Kitano, 2001; Chokshi et al., 2006). These networks of collaboration are supported by information and communication technologies and are enabling researchers from a variety of disciplines and laboratories to generate and validate biological and chemical knowledge. In these consortia, the issues of data-sharing and intellectual property are closely related. As Chokshi et al. (2006) discuss, consortia must decide in advance what data should be released to the public to ensure equitable downstream access to the data and open opportunities for the development of products; alternatively, in some cases, it may also be necessary to ensure, through the appropriation of data, that downstream incentives for product development are maintained for consortia members. Rules and policies will determine which option should take precedence in a project and/or consortium. In the sections that follow, I analyze these rules across the 39 selected biopharmaceutical consortia.

Participant Type. In their analysis, Allarakhia et al. (2008) determined that researchers from academia were present in all 39 consortia; researchers from non-profit research organizations also participated in 34 consortia. In 17 cases, there were government researchers and/or there was government participation via consortium catalyzation or the

provision of monetary support. Interestingly in 22 cases, private sector firms were involved to a significant extent (Table 2, see appendix 1). In 6 of these cases, private sector participants were directly or significantly responsible for catalyzing the initiative—namely, the SNP Consortium, the Novartis-Broad Initiative, the Accelrys Combinatorial Chemistry Consortium, the Accelrys Functional Proteomics Consortium, the Accelrys Nanotechnology Consortium, and the Agilent-Industry Open Microarray Design Program (Davies, 2001; Cassier, 2002; Lawler, 2004; Agilent, 2007; Accelrys, 2007). Although 32 out of the 39 consortia were funded by public sources (primarily via government grants), 15 were jointly funded or sponsored by private organizations; and 4, namely the Accelrys Consortia and the Cancer Vaccine Consortium were funded primarily by the private sector participants.

Structure of Open Source Consortia. The decision to participate in open source initiatives is affected by the degree of accessibility to the associated knowledge. Open access ensures that knowledge is available to all researchers for downstream activities regardless of participation in the initiative. In this case, the possibility of free-riding exists by outside firms who can enjoy the disclosed knowledge at little or no cost (Gintis et al., 2001). Closed access in contrast ensures that knowledge is only available to those contributing members within the alliance; therefore, the ability for a researcher or firm outside of the alliance to pool internal knowledge with that from the closed pool may not be possible or at a cost that will vary with the market power of the closed group. All but 3 of the consortia used an open access alliance structure. The Accelrys Combinatorial Chemistry Consortium, the Accelrys Functional Proteomics Consortium, and the Accelrys Nanotechnology Consortium were all closed access consortia—ensuring that knowledge was only available to consortia members (Accelrys, 2007); (Table 2, see appendix 1).

Rules for Participation. In terms of participation, 18 consortia established rules regarding membership. Offering monetary commitments, making formal commitments to the mandate and policies of the initiative, or licensing products used within the initiative, were signals of cooperation used when joining these consortia (Table 2, see appendix 1).

While the majority of consortia allowed members with the requisite research experience to join voluntarily, 7 of these 18 initiatives used formal invitations or applications, steering or executive committees, or by-laws to determine membership. Where formal commitments were required, as for the International Regulome Consortium, participation by-laws and agreements tended to address both admission policies as well as exit policies.

Ten consortia required a monetary commitment as part of membership; out of this group, 2 required the maintenance of grants and 8 required up-front membership fees. In open access initiatives such as the SNP Consortium, large upfront payments were made to support research (Davies, 2001). In other instances, such as the International Structural Biology Consortium, membership fees were paid, as verified by the director in our survey. These membership fees entitled a member access to beta-version software, experimental instruments, and technology developed by associated research labs and institutions.

Both monetary fees and software licenses were required to join the Accelrys Consortia. As Accelrys software formed the basis of the consortium project, in order to take part in and obtain the benefits of the project work, members were required to maintain licenses to a number of products which formed the core of consortium technology (Accelrys, 2007).

Focus of Knowledge Production Activities. In their analysis, Allarakhia et al. (2008) determined that almost half of the 39 consortia were focused on genomic or proteomic research; an additional 7 consortia were focused on systems-based research. Interestingly, some of the consortia progressed further downstream, developing tools to support molecular biology-based drug discovery or chemistry-based drug discovery; in some cases, consortia were focused on pre-clinical and clinical research. However, only two initiatives, the Biological Innovation for Open Society (BIOS) and the Cancer Vaccine Consortium were focused on downstream biological product development (Sulston, 2006; Sabin, 2007).

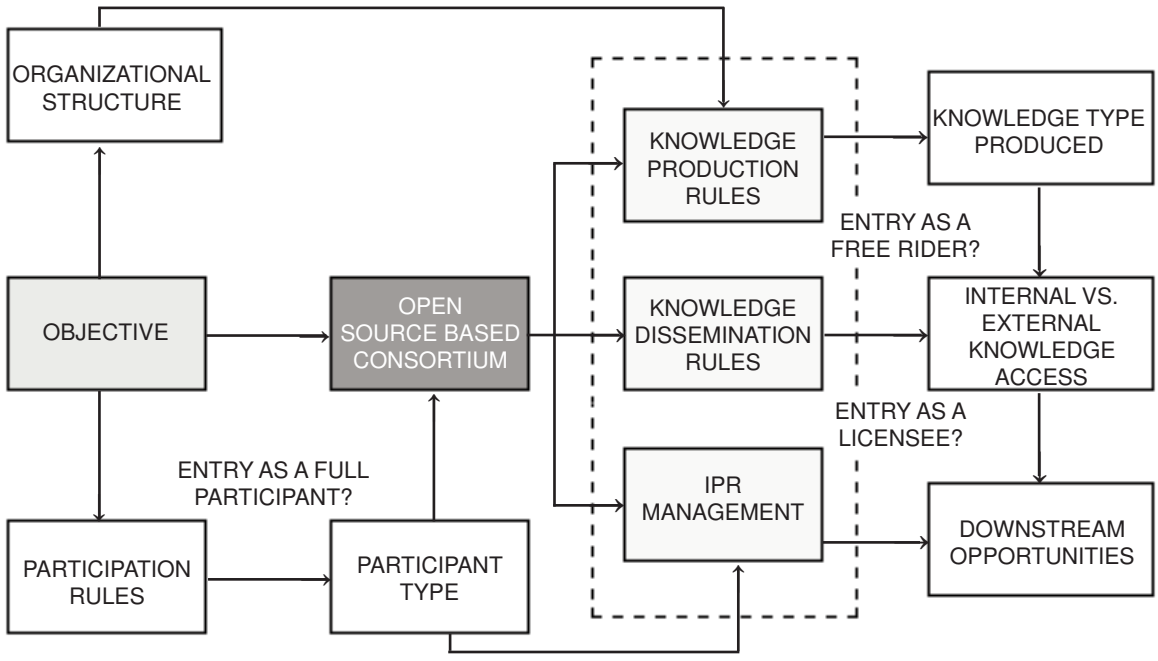
Rules for Knowledge Dissemination. In most cases, data were released almost immediately with complete access provided to members and the public at large. Data were maintained within large data repositories with the objectives of standardizing data and creating linkages between repositories developed within the consortium and between external repositories. For example, 30 consortia used or planned to use databases to provide access to upstream genomic, proteomic, systems, biochemical, or cell biology information. These consortia addressed the open dissemination of data as part of their rules for sharing of

information with members and the public at large. In addition, 22 consortia used peer-reviewed publications to provide validated information to the public (Table 3, see appendix 2).

Allarakhia et al. (2008) were further able to determine that in the case of 16 consortia where tools, biomaterials, or reagents were either a direct outcome or a by-product of consortia member research, rules existed that addressed the sharing of these items with members or the public at large. These rules advocated sharing of materials for consortium research, ensuring access to open repositories where animal models were housed, or providing for the wide dissemination of materials for the public at large; only in a few cases was access to tools ensured for members only (Table 3, see appendix 2).

I contend that the above study provides insight for firms considering entry into the biopharmaceutical entry. Specifically, in terms of mode of entry into the biopharmaceutical arena, firms from emerging markets can enjoy many of the benefits associated with participation in open source based consortia. These benefits include early access to knowledge, absorptive capacity development, and cost sharing during knowledge production activities. However, firms from emerging markets may have limited resources available and should be aware of the structure and rules associated with the consortium before committing these resources. The objectives of the open source consortium in terms of knowledge production and dissemination will determine both the most effective organizational structure and the types of participants that will join. The organization of knowledge production activities will impact not only accessibility to knowledge but also the learning experience for any firm. An awareness of participant type—public or private sector—can enable for a determination of motivation with respect to participation and likely adherence to the open source model. Rules for participation should be understood at the outset as a monetary commitment may be required to join the consortium; in this sense, participation rules can determine which firms can join the consortium as a function of resource avai-

Figure 3 Open Source Based Consortium Model and Mode of Entry Options[3]



3) Flow: The objectives of the open source consortium determine both organizational structures to manage knowledge development activities, as well as the necessary partici pation rules; Participation rules determine the types of organizations that can join including the ability for firms from emerging markets to join as full participants; The con sortium establishes rules to manage knowledge production (learning in this case is determined by the established organizational structures), knowledge dissemination, and the management of any associated intellectual property; Knowledge production rules determine the type of knowledge produced; Knowledge dissemination rules deter mine which participants can access the knowledge including emerging market firms inside and outside the consortium; IPR management rules impact which firms can pur sue downstream product development opportunities including the ability for firms from emerging markets to license consortium knowledge/technology.

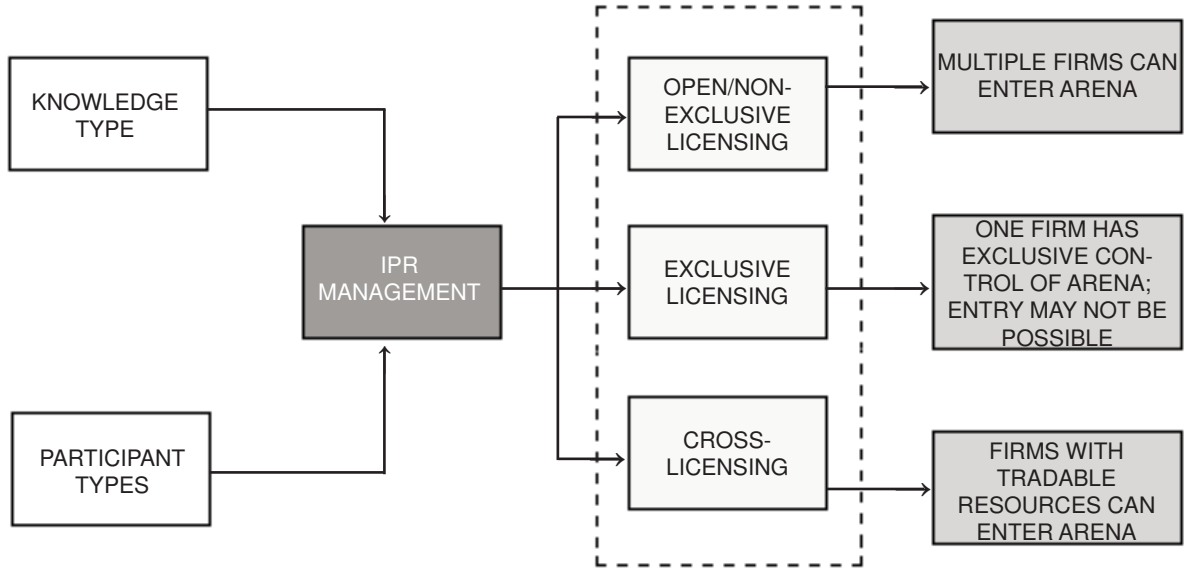
lability. Rules regarding knowledge access—ranging from open access for members only, to open access for members and the public at large, to open licensing, will further drive the decision to join the consortium. Depending on the knowledge access policy, a firm may be forced to join the consortium in order to access critical knowledge, a firm may choose to free-ride and access knowledge without any resource commitments to the consortium, and/or choose to access knowledge as a licensee (see Figure 3).

Open Licensing as a Mode of Entry

The choice of exclusively licensing or non-exclusively licensing a patent is a function of the characteristics associated with the knowledge, the desire of the patent holder to maximize revenue from disembodied versus embodied knowledge, and the desire to diffuse the knowledge versus develop the knowledge (Arora and Fosfuri, 2003; Foray, 2004). For example, the decision to sell disembodied knowledge in the form of patents and licenses can complement or substitute for the sale of embodied knowledge. Substitution occurs when the profits from the sale of disembodied knowledge are greater than those from the sale of embodied knowledge (Antonelli, 2003; Arora and Fosfuri, 2003). Specifically, when the costs of internal coordination of the knowledge are larger than the transaction costs associated with the market for technical knowledge, or when special assets are required to progress further downstream, the patent holder may choose to maximize revenue through a licensing strategy, specifically an exclusive licensing strategy (Teece, 1986; Antonelli, 2003; Arora and Fosfuri, 2003).

Complementarity between the sale of disembodied knowledge and internal embodiment occurs when knowledge possesses high applicability and it is possible to operate in different markets from other licensees of the knowledge (Teece, 1986; Arora and Fosfuri, 2003, Foray, 2004; Scotchmer, 2004). In this case, a non-exclusive licensing strategy can ensure that multiple participants can pursue several streams of research. Furthermore, cross-licensing is a useful innovation management strategy when knowledge exhibits high levels of complementarity (Shapiro, 2001). With downstream activities dependent on the recombination of a variety of knowledge, the cost of coordination including accumulation of the full range of required knowledge may be too high for one innovator (Antonelli, 2003;

Figure 4 Impact of IPR Management on Entry Options[4]



4) Flow: The characteristics of knowledge and participant types (including their motives) will impact how IP is managed; Options include open licensing, exclusive licensing, or cross licensing; Each option has an associated impact on the opportunity for firms to pursue downstream product development opportunities.

Burk and Lemley, 2003). Namely, the capabilities of the one innovator may only cover a portion of the research domain. Consequently, innovators may find it profitable to engage in cross-licensing for knowledge. However, the ability for each innovator to access knowledge depends on the amount and type of proprietary knowledge each one is able to contribute in any bargaining event (Antonelli, 2003).

In Figure 4, I contend that both knowledge type—disembodied versus embodied—as well as participant type—private or public sector—will impact the intellectual property rights management strategy adopted. Open or non-exclusive licensing with or without royalties will encourage multiple firms to enter and/or stay within a technological arena. In contrast, exclusive licensing will enable one firm to enter and possibly maintain control of a technological arena (Walsh et al., 2003). In the case of cross-licensing, only firms with tradable knowledge assets may be able to bargain for other knowledge assets and in turn, enter or stay within the technological arena. It is important to note that the ability to enter and stay in a technological arena will also depend on the substitutability of knowledge assets. For example, the existence of non-infringing work-around solutions will encourage a licensor to provide non-exclusive licenses (Allarakhia et al., 2008; Antonelli, 2003).

In their study of biopharmaceutical consortia, Allarakhia et al. (2008) found that consortia differentiated between disembodied knowledge in the form of raw data and embodied knowledge created by consortia members in the form of tools, biomaterials, and reagents. Although disembodied data was mandated in most cases for almost immediate release, tools, biomaterials, and reagents could be appropriated and licensed to consortia members and the public at large. Appropriation activities were regulated by the provision of rules regarding licensing terms. Supporting data and materials sharing policies provided by the NIH, the Wellcome Trust, the Creative Commons, the Biological Innovation for Open Society, and even private sector firms such as Open Biosystems, enabled for relatively easy access to disembodied and embodied knowledge created within consortia (Table 3, see appendix 2).

From the consortia analysis, Allarakhia et al. (2008) were able to identify various licensing agreements employed to widely disseminate embodied knowledge as well as copyrighted material (Table 4). In each instance, the objective was to ensure that multiple firms would have the incentive to enter and remain within the technological arena.

Non-exclusive license. Many instances were found of non-exclusive, royalty-free licenses used to disseminate knowledge generated by consortia members. In one instance, a limited use license provided researchers with a limited, non-exclusive, non-transferable right to the product (with no right to resell, repackage, or further sublicense). For example, the purchase of products distributed through this licensing agreement did neither include nor carry any right or license to use, develop, or otherwise exploit products commercially (Open Biosystems, 2007). In the case of one consortium, members could offer royalty-free licenses for tools and data to project team members, and royalty-free licenses for non-commercial use to others (Biomarkers Consortium, 2008).

MIT license. DopaNet's Molecular Pages is a collection of annotated quantitative biotechnology data. DopaNet Molecular Pages are available under the terms derived from the MIT License (Le Novère and Donizelli, 2004). The MIT License, also called the X License or the X11 License, originated at the Massachusetts Institute of Technology, and is a license for the use of certain types of computer software; essentially, a non-copyleft (licenses that use copyright law to give permission instead of forbid) free software license. The license allows a user to deal with the software without restriction, including without limitation the rights to use, copy, modify, merge, publish, distribute, sublicense, and/or sell copies of the software (Open Source Initiative, 2007).

Creative Commons license. The International Molecular Exchange Consortium applies the Creative Commons Attribution License. This consortium is a group of major public interaction data providers sharing curation efforts and exchanging completed records on molecular interaction data. The Creative Commons offers licenses that enable researchers to keep their copyright but allow others to copy and distribute the work provided that credit is assigned and only in accordance with specified pre-conditions including attribution plus non-commercial use only, attribution and non-derivative use, or attribution and dissemination to others that follow the same conditions set by the original researcher (Creative Commons, 2007; International Molecular Exchange Consortium, 2007).

CAMBIA-Biological Open Source. The Bio-

logical Innovation for Open Society (BiOS) is an initiative of the Center for Applications of Molecular Biology in Agriculture (CAMBIA) with the objectives to develop new means for cooperative invention, improvement, and delivery of technologies for life sciences. The licensing strategy promoted by BiOS hopes to encourage entry into a technological arena with a focus on those researchers and firms in neglected markets. Specifically, it is anticipated that open source agricultural research will enable innovation by small biotechnology companies. This will enable the development of locally suited technologies, reduce dependence on giant agribusiness conglomerates, and facilitate research on crops suited for local conditions in the developing countries (Thomas, 2005).

Under a BiOS-compliant agreement, the user must agree to conditions that encourage cooperation and development of the technology in order to obtain the right to use the technology, instead of royalties or other conditions that discourage creation of products (Sulston, 2006). The conditions include a provision that licensees cannot exclusively appropriate the fundamental essence of the technology or improvements (BiOS Initiative, 2007). The base technology remains the property of the entity that developed it, but improvements can be shared with others that support the development of a protected commons around the technology; participants who agree to the same terms obtain access to improvements and other information, such as regulatory and biosafety data (BiOS Initiative, 2007). To maintain legal access to the technology, users must agree not to prevent others who have agreed to the same terms from using the technology and any improvements in the development of varied products.

Patent pool. It is anticipated that the Knockout Mouse Project will require the resolution

Table 4 Intellectual Property Strategies Used in Biopharmaceutical Innovation

IP Strategy	Description	Examples
Open Data Access	Rapid release of data into public databases; Original research articles are also freely available online within six months of publication.	Human Genome DNA sequences; Open Access journals
Non-exclusive License	Non-exclusive, royalty-free licenses; Not commercially exploitable.	Open BioSystems; Biomarkers Consortium
MIT License	Licenses that use copyright law to give permission instead of forbid, usually permission to copy, use, modify, and share.	DopaNet Molecular Pages
Creative Commons License	The Creative Commons offers licenses that enable researchers to keep their copyright but allow others to copy and distribute the work provided that credit is assigned and only in accordance with specified preconditions.	International Molecular Exchange Consortium
Biological Open Source License	The user must agree to conditions that encourage cooperation and development of the technology in order to obtain the right to use the technology, instead of royalties or other conditions that discourage creation of products.	BiOS
Patent Pool	Researchers from various organizations and institutions controlling critical patents agree to the formation of a patent pool.	Knockout Mouse Project
Geographic-based License	Geographic-based restrictions with respect to patenting and licensing.	MalariaGEN

of several intellectual property claims involving both the production and use of knockout mice. The Knockout Mouse Project is an initiative that aims to generate a comprehensive and public resource comprised of mouse embryonic stem (ES) cells containing single deletions (knockouts) of every gene in the mouse genome—essentially research tools to understand the role of genes in biological processes. Hence, researchers from various organizations and institutions controlling such patents have agreed to the formation of a patent pool of mouse knockout technologies to enable the development of these stem cells (Austin et al., 2004).

Geographic-based licensing. The Grand Challenges in Global Health, which funds MalariaGEN, has developed the Global Access Strategy. This system requires grantees to prepare both a strategy for commercialization of research and an intellectual property management policy. Key provisions of the Global Access Strategy include a requirement that the principles of the strategy apply to licenses and contracts that use intellectual property of the consortium; that downstream licensees of the consortium's intellectual property not apply for secondary patents in the developing world that would prevent access to affordable health care solutions; and a stipulation that prohibits exclusive licensing of the consortium's intellectual property except in cases where it is necessary to provide a marketing incentive (Chokshi et al., 2006).

Discussion

The ability to join an open source initiative will be tempered by informal and formal rules of participation. With formality, entrance costs may be used to facilitate research and development activities as well as to signal cooperation and commitment to the initiative (Kollock, 1998; Gintis et al., 2001). The role of such entrance costs or rules for participation is to create trust through a visible signal. For example, committing resources in advance including monetary fees makes other participants in the initiative, and future researchers who are considering participation, aware of a researcher's cooperative intentions (Gulati et al., 1994). The decision to participate in any initiative is also affected by the degree of accessibility to the associated knowledge. Open access ensures that knowledge will be available to all participants in future downstream research regardless of participation (Gintis et al., 2001). Closed access in contrast, ensures that knowledge is available only to contributing members within the initiative.

In terms of property rights, Ostrom argues these rights do not emerge spontaneously from a common property system. Private property rights depend on the existence and enforcement of rules that define who has a right to pursue which activities involving a resource and how the returns from that activity will be allocated (Ostrom, 1989). For example, the use of binding agreements can ensure cooperation during knowledge dissemination. Therefore, in the management of open source initiatives, the research outcomes to be disseminated, the format for dissemination, and the knowledge to be privatized, should be clearly understood by all the participants. Internal rules or mechanisms used to promote cooperative behaviour can include: formalizing the requirements to join the knowledge network, ensuring frequent interactions, encouraging communication between participants, punishing defection, and setting the boundary for access to knowledge. An authority that regulates access to knowledge can ensure that a fair and efficient knowledge governance strategy is indeed used.

If and when knowledge is appropriated through the filing of patents, rules should further encourage licensing that provides the greatest collective value to the initiative members and/or the public at large. For example, many of the consortia analyzed by Allarakhia et al. (2008) advocated the use of royalty-free non-exclusive licenses. Where technology can be substituted through non-infringing workaround solutions, a patent holder will also have an incentive to offer a non-exclusive license, rather than face competition without any possible compensation for his/her initial discovery. Alternatively, in cases where the market for technology is relatively small with technology having zero standalone commercial value, a patent holder may need to offer a non-exclusive license to ensure that a downstream developer will use the technology in products, thereby enabling the patent holder to reap the rewards of his/her original discovery.

From a mode of entry perspective, open source initiatives can level the playing field for new entrants into a technological arena. Organizations from emerging markets adhering to the open source model should equally ensure that the public domain of knowledge is not only sustained, but also augmented.

Public-sector and private sector organizations from such economies can institute policies that preserve the public domain of knowledge, enable the formation of open source initiatives for standard or technology development, encourage the use of open licensing strategies for appropriated knowledge, and the use of clearinghouses that can manage knowledge and technological assets—ensuring broad dissemination and adoption of these assets. Table 5 outlines these issues and the rules or associated solutions that can be used to manage open-source-based initiatives.

Conclusion

Rising costs, technological complexities, and shorter life cycles have put pressure on companies and their internal innovation processes. Chesbrough (2003) discusses that open business models can enable biopharmaceutical companies to leverage external resources and human capital to save time and money during the innovation process. The open business model further allows companies to generate revenue through the licensing of technologies that cannot be fully exploited within an organization and through the in-licensing of technologies that are discovered outside the boundaries of the organization (Chesbrough, 2003). Therefore, managers of firms in developed and in emerging markets alike should seek out these opportunities presented by open innovation—including participating in open source based innovation.

For firms in emerging markets, open source based innovation presents a cost-effective means to learn about a domain and the corresponding product development opportunities. These firms can then use the experience gained from participation in open-source-based innovation to make an informed decision regarding the investment into product development. In the biopharmaceutical industry, as product development includes expensive clinical trial testing and regulatory approvals, an informed decision needs to be based on the firm's resource availability across the biopharmaceutical value chain as a function of a particular technological opportunity—perhaps even the need to continue participating in open innovation during product development.

The practical lessons learned from this paper, however, indicate that firms from emerging markets with limited resources will have to carefully evaluate the objectives of an open-innovation- (including open source) based community and/or network. The objectives can include the creation of pure knowledge or even embodied knowledge in the form of tools and products. Ultimately then, firms hoping to enter a biopharmaceutical arena will have to analyze where they are located on the learning curve and what they hope to gain through participation in an open-innovation-based community. Organizational structures will then determine how firms can participate in any learning and knowledge development processes. Specifically, the distance from knowledge development activities and any supporting organizational structures that seek to mini-

Table 5 Managing Open-Source-Based Innovation

Open Source Management Issue	Rules, Options, Solutions
Participation in an Open Source Initiative.	Participation Rules; Entrance Costs to Signal Commitment.
Structure of Initiative—Open or Closed Access. Participation Rules; Binding Agreements.	Participation Rules; Binding Agreements.
Organization of Knowledge Production Activities.	Project, Technology, and/or Geographic Based Teams.
Encouraging Cooperation During Knowledge Production.	Enabling Frequent Interactions and Communication; Punishing Defection e.g. Costs Associated with Defection; Regulating Authority.
Encouraging Cooperation During Knowledge Dissemination.	Public Databases; Internal Rules and External Guidelines Regarding Appropriation and Licensing; Patent Pools; Clearinghouses to Manage Knowledge and Technology.

mize this distance, will determine how much learning by doing and using firms will experience. This learning by doing and using will be of particular relevance to firms from emerging markets. Finally, the mechanisms used to disclose and share knowledge will impact whether firms can indeed move down the biopharmaceutical value chain. It is therefore anticipated that open-innovation-based communities with clear rules, leadership, and transparent processes will be more productive—avoiding any surprises for firms with limited resources contemplating participation.

In terms of future research, it is essential to analyze new case studies involving emerging market firms and their participation in open innovation communities. These case studies should seek to look at the evolving models of open innovation as the number and type of participants change, as the objectives with respect to innovation evolve, and as the complexities associated with knowledge structures increase so that knowledge management becomes paramount. This analysis should further seek to understand any geographic-based issues hampering technological innovation by firms in emerging markets and how to eventually position these firms to meet both global and local product needs through open innovation.

References

Accelrys Nanotechnology Consortium (2007): www.accelrys.com, accessed 6/2007.

Agilent-Industry Open Microarray Design Program (2007): www.agilent.com, accessed 6/2007.

Allarakhia, M., Kilgour, D. M., Fuller D. (2008): *Modeling the Incentive to Participate in Open Source Innovation*, The R&D Management Conference, Ottawa, Canada, June 17-20, 2008.

Antonelli, C. (2003): Knowledge complementarity and fungeability: Implications for regional strategy, *Regional Studies*, **37** (6-7), pp. 595-606.

Arora, A., Fosfuri, A. (2003): Licensing the market for technology, *Journal of Economic Behavior & Organization*, **52** (2), pp. 277-295.

Austin, C.P. et al. (2004): The Knockout Mouse Project, *Nature Genetics*, **36** (9), pp. 921-924.

Bergstrom. L. (2006): *Open source and open medicine take centre stage at UN research symposium*, EurekAlert, accessed November 2008.

Biomarkers Consortium(2008): www.biomarkersconsortium.org, accessed 11/2008.

BiOS (2007): www.bios.net, accessed 6/2007.

Blumenthal, D., Causino, N., Campbell, E. G. (1997): Academic-industry research relationships in genetics: A field apart, *Nature Genetics*, **16** (1), pp. 104-108.

Bower, J. D., Whittaker, E. (1992): Global R&D networks: The case of the pharmaceutical industry, *Journal of Industry Studies*, **1** (1), pp. 50-63.

Burk, D. L., Lemley M. A. (2003): Biotechnology's Uncertainty Principle, in: *Perspectives on Properties of the Human Genome Project*, Elsevier Academic Press, San Diego CA, pp. 305-354.

Cassier, M. (2002): Private property, collective property, and public property in the age of genomics, *International Social Science Journal*, **54** (1), pp. 83-98.

Chesbrough, H. W. (2007): Why Companies Should Have Open Business Models, *MIT Sloan Management Review*, **48** (2), pp. 22-28.

Chesbrough, H. W. (2003): The Era of Open Innovation, *MIT Sloan Management Review*, **44** (3), pp. 35-41.

Chesbrough, H. W., Vanhaverbeke, W., West J. (2006): *Open Innovation: Researching a New Paradigm*, Oxford University Press, Oxford.

Chokshi, D. A., Parker, M., Kwiatkowski, D. P. (2006): Data sharing and intellectual property in a genomics epidemiology network: Policies for large-scale research collaboration, *Bulletin of the World Health Organization*, **84** (5), pp. 382-387.

Cohen, W.M., Levinthal, D.A. (1990): Absorptive Capacity: A New Perspective on Learning and Innovation, *Administrative Science Quarterly*, **35**, pp. 128-152.

Creative Commons (2007): creativecommons.org, accessed 6/2007.

Davies, K. (2001): *Cracking the Genome: Inside the Race to Unlock the Human DNA*, The Free Press, New York, NY.

Dutfield, G. (2003): *Intellectual property rights and the life sciences industries: A twentieth century history*, Ashgate Publishing Limited, Burlington VT.

Foray, D. (2004): *The Economics of Knowledge*, MIT Press, Cambridge, MA.

Gintis, H., Alden Smith, E., Bowles, S. (2001): Costly Signaling and Cooperation, *Journal of Theoretical Biology*, **213**, pp. 103-119.

Grant, R. M., Baden-Fuller, C. (2004): A knowledge accessing theory of strategic alliances, *Journal of Management Studies*, **41** (1), pp. 61-84.

Gulati, R., Khanna, T., Nohria, N. (1994): Unilateral commitments and the importance of process in alliances, *MIT Sloan Management Review*, **35** (3), pp. 61-69.

Hood, L. E. (2000): *The university office of technology transfer: The inventor/researcher's view*, CASRIP Symposium Publication Series, No. 5, CASRIP, University of Washington, Seattle WA.

International Molecular Exchange Consortium (2007): imex.sourceforge.net, accessed 6/2007.

Kitano, H. (2002): Systems biology: A brief overview, *Science*, **295** (5560), pp. 1662-1664.

Kitano, H. (2001): Systems biology: Toward systems-level understanding of biological systems, in: Kitano, H. (ed.), *Foundation of systems biology*, MIT Press, Cambridge, MA, pp. 1-29.

Kollock, P. (1998): Social dilemmas: The anatomy of cooperation, *Annual Review of Sociology*, **24**, pp. 183-214.

Lakhani, K. R., von Hippel, E. (2003): How Open Source Software Works: Free User-to-User Assistance, *Research Policy*, **32** (6), pp. 923-943.

Lawler, A. (2004): Broad-Novartis Venture Promises a No-Strings, Public Gene Database, *Science*, **306**, p. 795.

Le Novère N., Donizelli M. (2004): The Molecular Pages of the Mesotelencephalic Dopamine Consortium (DopaNet), *BMC Bioinformatics*, **5**, pp. 174.

Lemley, M. (2002): Intellectual Property Rights and Standard-Setting Organizations, *California Law Review*, **90**, pp. 1889-1981.

Malhotra, N. (2003): The Nature of Knowledge and the Entry Mode Decision, *Organization Science*, **24** (6), pp. 935-959.

Marshall, E. (1997): The battle Over BRAC1 goes to court, BRAC2 may be next, *Science*, **278** (5345), pp. 1874.

Meredith, L. (2005): *BRIC by Brick; IBM looks to open source in emerging markets*, SearchDataCenter, February 24 2005.

NHGRI (1996): *NHGRI Policy Regarding Intellectual Property of Human Genomic Sequence*, NHGRI, April 9 1996.
Nelson, R. (1959): The simple economics of basic scientific research, *Journal of Political Economy*, **67** (3), pp. 297-306.
OBF (2008): www.open-bio.org, accessed 11/2008.
Open Biosystems (2007): www.openbiosystems.com, accessed 6/2007.
Open Source Initiative (2007): www.opensource.org, accessed 8/2007.
Ostrom, V. (1989): Some Developments in the Study of Market Choice, Public Choice and Institutional Choice, in *Handbook of Public Administration*, New York, NY.
Powell, W. W., Koput, K. K., Smith-Doerr, L. (1996): Inter-organizational collaboration and the locus of innovation: Network of learning in biotechnology, *Administrative Science Quarterly*, **41,** pp. 116-145.
NIH (1999): *Principles and Guidelines for Sharing of Biomedical Research Resources*, NIH, December 23 1999.
Reichman, J. (2003): A contractually reconstructed research commons for science and innovation, in: *The Role of Scientific and Technical Data and Information in the Public Domain*, The National Academies Press, Washington DC, pp. 141-160.
Reid D., Bussiere, D., Greenway, K. (2001): Alliance formation issues for knowledge-based enterprises, *International Journal of Management Reviews*, **3** (1), pp. 79-100.
Sabin (2007): www.sabin.org, accessed 6/2007.
Scotchmer, S. (2004): *Innovation and Incentives*, MIT Press, Cambridge, MA.
Shapiro, C. (2001): Navigating the Patent Thickets: Cross-Licenses, Patent Pools, and Standard-Setting, in A. Jaffe, J. Lerner and S. Stern (eds.), *Innovation Policy and the Economy*, NBER.
Stein, L. (1996): How Perl Saved the Human Genome Project, *The Perl Journal*, available at www.bioperl.org/wiki/How_Perl_saved_human_genome, accessed November 2008.
Sulston, J. (2006): Staking claims in the biotechnology Klondike, *Bulletin of the World Health Organization*, **84** (5), pp. 412-413.
Sun Microsystems (2008): www.sun.com, accessed 11/2008.
Teece, D. J. (1986): Profiting for technological innovation: Implications for integration, collaboration, licensing and public policy, *Research Policy*, **15** (6), pp. 785-805.
Thomas, Z. (2005): Open source agricultural biotechnology, *Current Science*, **88** (8), pp. 1212-1213.
Walsh, J. P., Arora, A., Cohen, W. M. (2003): Effects of research tool patents and licensing on biomedical innovation, in: *Patents in the Knowledge-Based Economy*, The National Academies Press, Washington DC, pp. 285-340.
UNU-MERIT (2008): www.merit.unu.edu, accessed 11/2008.

Appendix 1

Table 2 Analyzing Consortia Structure, Participants, and Rules for Participation

Consortium	Alliance Structure	Significant Participants	Participation Rules
Affymetrix-National Alliance for Autism Research; Est. 1994	Open	A,N,G,P	MC (Grants), Selection
Agilent-Industry Open Microarray Design Program; Est. 2005	Open	A,N,G	Based on Consortium
Alliance for Cellular Signalling (AfCS); Est. 2002	Open	A,N	
Beta Cell Biology Consortium (BCBC); Est. 2001	Open	A,N,G	
Biological Innovation for Open Society (BIOS); Est. 2004	Open	A,N,P	
Cancer Vaccine Consortium; Est. 2002	Open	A,N,G,P	EC
Cell Migration Consortium; Est. 2001	Open	A,N	SC
Collaborative Cross; Est. 2005	Open	A,N,G	
Combinatorial Chemistry Consortium; Est. 1996	Closed	A,P	MC, License
Consortium for Functional Glycomics (CFG); Est. 2001	Open	A,N,G	Application
DopaNet; Est. 2002	Open	A,N,G	
Functional Proteomics Consortium; Est. 2000	Closed	A,P	MC, License
HepatoSys; Est. 2004	Open	A,N,P	Invitation
Human Epigenome Consortium; Est. 2003	Open	A,N,P	
Human Genome Consortium; Est. 1990	Open	A,N,P	
International Genomics Consortium; Est. 2004	Open	A,N,P	
International HapMap Project; Est. 2002	Open	A,N,P	
International Molecular Exchange Consortium; Est. 2005	Open	A,N	
International Regulome Consortium; Est. 2004	Open	A,N,G,P	By-laws
International Rice Functional Genomics Consortium; Est. 2003	Open	A,N	
International Rice Genome Sequencing Project; Est. 1997	Open	A,N	
International Sequencing Consortium; Est. 2002	Open	A,N,G	
Knockout Mouse Project; Est. 2006	Open	A,N	
MalariaGEN; Est. 2005	Open	A,N,G	
MitoCheck Consortium; Est. 2004	Open	A,N,G,P	
Mouse Genome Sequencing Consortium (MGSC); Est. 2000	Open	A,N,G,P	MC
Mouse Models of Human Cancers Consortium (MMHCC); Est. 1999	Open	A,N,G,P	MC (Grants)
Nanotechnology Consortium; Est. 2004	Closed	A,P	MC, License
Novartis Institutes for Biomedical Research-Broad Institute Alliance; Est. 2004	Open	A,P	
Osteoarthritis Initiative; Est. 2001	Open	A,N,G,P	
Public Population Project in Genomics; Est. 2004	Open	A,N,G	MC
Receptor Tyrosine Kinase (RTK) Networks Consortium; Est. 2005	Open	A,N,G	EC
Research Collaboratory for Structural BioInformatics (RCSB); Est. 1998	Open	A	
RNAi Consortium (TRC); Est. 2005	Open	A,N,P	MC
Single Nucleotide Polymorphisms (SNP) Consortium; Est. 1999	Open	A,N,P	MC
Structural Genomics Consortium; Est. 2003	Open	A,N,P	MC
SYMBIONIC; Est. 2004	Open	A,N,P	
TB Structural Genomics Consortium; Est. 2000	Open	A,N	Application
The Lipid MAPS Consortium; Est. 2003	Open	A,N,G,P	

A=Academic; N=Non-Profit Research Institutes; G=Government (including Government Funding Agencies and Government Laboratories); P=Private Organization; MC=monetary commitment (upfront fees, membership fees, maintenance of grants); EC=Executive Committee; SC=Steering Committee.

Appendix 2

Table 3 Analyzing Consortia Rules Regarding Knowledge Dissemination

Consortium	Rules or Mechanisms used to Disseminate Data	Rules Regarding Sharing of Tools, Biomaterials, Reagents
Agilent-Industry Open Microarray Design Program	Based on Consortium Rules	Based on Consortium Rules
Alliance for Cellular Signalling (AfCS)	Database Deposit; Publication	Reagent Sharing for AfCS Research
Beta Cell Biology Consortium (BCBC)		Freely Distributed to Academics for Non-Commercial Use
Biological Innovation for Open Society (BIOS)		Royalty Free, Non-Exclusive Licenses Among Participants
Cancer Vaccine Consortium	Publication	
Cell Migration Consortium	Database Deposit; Publication	Royalty Free, Non-Exclusive Licenses for Non-Commercial Use
Collaborative Cross	Database Development	Repository; Open Subscription to Mouse Repository
Combinatorial Chemistry Consortium	Exclusive Access to Data	Exclusive Access to Licensed Software
Consortium for Functional Glycomics (CFG)	Database Deposit; Publication	Material Sharing for Consortium Research; Royalty Free, Non-Commercial Use
DopaNet	Database Deposit; Publication	
Functional Proteomics Consortium	Exclusive Access to Annotated Data	
HepatoSys	Database Development; Publication	
Human Epigenome Consortium	Database Deposit; Publication	
Human Genome Consortium	Database Deposit; Publication	
International Genomics Consortium;	Database Deposit	
International HapMap Project	Database Deposit; Publication	
International Molecular Exchange Consortium	Database Deposit/Management	Creative Commons Copyright Licensing Advocated
International Regulome Consortium	Database Deposit; Publication	
International Rice Functional Genomics Consortium	Database Development	Sharing of Materials
International Rice Genome Sequencing Project	Database Deposit; Publication	
International Sequencing Consortium	Database Deposit	
Knockout Mouse Project	Database Development	Public Repository for Biomaterial; Patent Pooling Advocated
MalariaGEN	Data Management Addressed	Restricted Licensing; Geographic Restrictions
MitoCheck Consortium	Database Development	
Mouse Genome Sequencing Consortium (MGSC)	Database Deposit; Publication	

Appendix 2 continued

Table 3 Analyzing Consortia Rules Regarding Knowledge Dissemination (continued)

Consortium	Rules or Mechanisms used to Disseminate Data	Rules Regarding Sharing of Tools, Biomaterials, Reagents
Mouse Models of Human Cancers Consortium (MMHCC)	Database Deposit; Publication	Repository for Biomaterials; Reagent Distribution through Open Biosystems
Nanotechnology Consortium	Exclusive Access to Data	Exclusive Access to Licensed Software
Novartis Institutes for Biomedical Research-Broad Institute Alliance	Database Deposit; Publication	
Osteoarthritis Initiative	Data Repository	Research Tools Wide Available; Limited Materials Priority Distribution
Public Population Project in Genomics	BioBanks-Database; Publication	
Receptor Tyrosine Kinase (RTK) Networks Consortium	Database Deposit; Publication	
Research Collaboratory for Structural BioInformatics (RCSB)	Data Bank; Publication	
RNAi Consortium (TRC)		Distribution through Sigma Aldrich and Open Biosystems
Single Nucleotide Polymorphisms (SNP) Consortium	Database Deposit; Publication	
Structural Genomics Consortium	Database Deposit; Publication	
SYMBIONIC	Database Development; Publication	
TB Structural Genomics Consortium	Database Deposit; Publication	
The Lipid MAPS Consortium	Database Deposit; Publication	

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Research Section

Biotechnology Research in South Africa: A Benchmarking Exercise

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Biotechnology has been identified as a priority area for the national innovation system in South Africa. Since 2003 new structures have been established in the country in order to enhance biotechnology research and innovation in accordance with the "National Biotechnology Strategy". Recently and for the first time in the country's science policy history, the Department of Science and Technology published the "Ten Year Plan 2008-2018" which sets quantitative objectives for the national system. The effort of this article is to benchmark the country's research related to biotechnology in order to provide the foundations for the monitoring of the evolution of the field and the accomplishment of the broad objectives set by the Department of Science and Technology. The international comparisons identify a number of management challenges and policy concerns and the extent of efforts required so that the South African biotechnology innovation system meets the objectives set by the Government.

Introduction

Biotechnology is internationally believed to be the next revolutionary scientific endeavour in the history of humanity. Researchers suggest that the same way that steam power and the railway and more recently information and communication technologies have revolutionized society, biotechnology will change the way we live and we think about living organisms and society (Freeman and Soete, 1997).

Biotechnology as a research domain opens up the way for new applications in healthcare, agriculture, food production, environmental protection, development of materials and chemicals, and new scientific discoveries. The new technologies regenerate old industries and create new businesses offering skilled jobs that sustain knowledge-based economies and produce economic growth.

The economic prospects led a number of countries to develop relevant policies and provide incentives for the promotion of research, development and innovation and as a consequence a number of studies have been undertaken monitoring and assessing the performance of biotechnology in those countries (European Commission, 2003; Reiss, and Dominguez-Lacasa, 2005).

The South African government supports biotechnology and encourages home grown research. A recent report identifies that South Africa exerts leadership and provides the example for the adoption and acceptance of biotech crops in the African continent and globally (James, 2007). South Africa is classified as the only country in the African continent and one of the 14 biotech mega-countries in the world. Countries are classified as biotech mega-countries when they grow 50,000 hectares, or more, of biotech crop. Furthermore, a multi-criteria survey identified that an approving climate of opinion prevails towards biotechnology in the country (Pouris, 2003b).

Moreover the recently published "Ten Year Plan" of the Department of Science and Techno-

logy sets the vision that South Africa should be "among the global top ten nations in the world in terms of the pharmaceutical, nutraceutical, flavour, fragrance and bio-pesticide industries" by 2018 (DST, 2007).

The purpose of this study is to identify the state of biotechnology research in the country in quantitative terms (specific and measurable objectives required by the management by objectives set by the government) in order to inform relevant policy in South Africa.

More specifically the effort is to identify the research performance of the country in biotechnology research over time and in comparison with a number of target countries. The results of the investigation can constitute the benchmarks for monitoring of the evolution of the research in the field and the accomplishment of the objectives set by the Department of Science and Technology.

Methodological Issues

Any analysis in the field of biotechnology faces a number of methodological hurdles. The challenges arise from the character of biotechnology. Biotechnology is used for producing existing products in new ways, identifying new product opportunities (as in drug discovery), and for producing new products that could not be commercially produced before (as with many large molecule therapeutics and some genetically modified plant varieties). The wide range of uses for biotechnology means that it is a generic technology with applications in many different economic sectors.

The OECD has developed both a single definition of biotechnology and a list-based definition of different types of biotechnology (OECD, 2006). The single definition defines biotechnology as "the application of science and technology to living organisms, as well as parts, products and models thereof, to alter living or nonliving materials for the production of knowledge, goods and services."

The OECD list-based definition of biotechnology includes a number of techniques such as genomics, sequencing of proteins and peptides, cell and tissue culture.

The above definitions underline the fact that biotechnology is a particularly research intensive domain. The European Commission states (European Commision, 2002):

"The life sciences revolution was born in, and is fed and nurtured by, research. Public research laboratories and institutions of higher education are at the core of the science base interacting also with enterprise based research and that of other private bodies. The success of any knowledge-based economy rests upon the generation, diffusion and application of new knowledge. Investments in research and development, education and training and new managerial approaches are therefore of key importance in meeting the challenges posed by life sciences and biotechnology."

The high research intensity of the sector justifies our emphasis on the use of scientometrics techniques as a tool for evaluation purposes. Countries with weak biotechnology research capacity and hence weak publication profiles will undoubtedly be weak in the innovation spectrum of the biotechnology sector.[1]

The ISI databases (Science Citation Index Expanded, Social Sciences Citation Index and Arts and Humanities Citation Index) were identified as the most appropriate for the objectives of the investigation. The ISI databases are used extensively for similar studies in biotechnology (DST, 2007) ,and other scientific disciplines (Braun et al., 1997).

The combined databases cover comprehensively the most prestigious journals in the world in all fields of research endeavours and constitute a unique information platform for the objectives of this effort.

Furthermore, in South Africa universities receive subsidy from the Department of Education according to the number of publications in ISI journals (and in an additional departmental list) and universities provide incentives to their researchers to publish in ISI journals. Consequently those journals cover adequately the South African research effort.

The databases classify the articles to different scientific disciplines according to the character of the journals in which they appear. Following the example of VINNOVA (VINNOVA, 2003) the following scientific disciplines were considered

1) We also considered the use of patents as relevant indicators. However, South Africa has a non-examining patent regime (patents are registered without examination for novelty and/or usefulness) and very few South Africans apply for biotechnology related patents in the USPTO and EPO probably because of the high costs.

as constituting the biotechnology literature: Biochemistry and Molecular Biology; Microbiology; Biotechnology and Applied Microbiology; Genetics and Heredity; Cell Biology; Virology; Neurosciences; Chemistry Medicinal; Biophysics; Engineering Biomedical and Developmental Biology. While the associations and linkages of the above disciplines with biotechnology are well known, it is worth clarifying the presence of neurosciences and developmental biology in the set. Modern molecular biology and cell biology methods have been used in neurobiological research in association with older methods for the past two decades. More recently, however, neurosciences are interlinked with novel technologies such as genomics and differential gene expression methods. Similarly, developmental biology has emerged as a promising new field. The focus of developmental biology is the identification of the mechanisms underlying embryonic development of tissues and organs and specifically genes which are involved in promoting differentiation and growth of different tissue types and in controlling organ development.

The developed database was analyzed in order to identify South African researchers publishing biotechnology related research. South African authors have been identified on the basis of their addresses in the published articles.

The results of the analysis are compared with the performance of a number of countries which are recognized as leaders in the field of biotechnology. The choice of the comparator countries is made in order to provide an indication of the current state of the country's research vis-a-vis the vision that has been set by the country's Government. (The Scandinavian countries, Singapore and Switzerland are among the leading countries in the world in the field of biotechnology and South Africans often use Australia and Brazil for comparative purposes).

Biotechnology and Related Research in South Africa

Analysis of the ISI databases identified 6,006 articles in biotechnology disciplines with at least one South African author for the period 1995-2006. "Biochemistry and molecular biology" is the most prolific discipline contributing 1,601 publications during the period (see table 1). Microbiology and biotechnology & applied microbiology follow with 1,049 and 1,009 publications respectively. The column total shows the actual number of South African articles and it is less than the sum of the horizontal cells in the table. This is happening because articles may be classified to more than one scientific discipline.

Table 2 shows the growth in the number of publications in the various biotechnology disciplines from the beginning of the period (1995-1998) to the end of the period (2003-2006). Neurosciences exhibit the largest growth (265 %) albeit from a small basis (20 publications per year). Virology and developmental biology follow from similarly small initial bases. The growth of the total number of biotechnology articles over the period was 64.5 %. During the same period the total number of publications from South Africa increased from 18,206 (1995-1998) to 22,473 (2003-2006) – an increase of 23 %. It is noticeable that the relative prolific disciplines (e.g. microbiology and biotechnology & applied microbiology) will need more than 10 years in order to double their size.

Table 3 shows the relative emphasis placed in the most prolific biotechnology disciplines in comparison to selected disciplines in South Africa. The emphasis is estimated as the ratios of disciplinary publications to the total number of publications from the country during the most recent period 2004-2007 (August) and during the period 1995-2006.

The table shows that environment, plant and animal research attracts substantially more attention than the biotechnology related disciplines. These findings reconfirm our previous finding (Pouris, 2003a) that "the active South African disciplines (that is, those with publication rates above the national average of 0.5 %) are those involving its natural wealth, that is, ecology/environment, geosciences, plant and animal sciences, and space science (astronomy)". Comparison of the research emphasis in the two periods indicates that the biotechnology related disciplines (with the exception of neurosciences) had only marginal improvements. It is worth mentioning the substantial drop in emphasis in medicine, general and internal.

Figure 1 shows the extent of collaboration of South African researchers in the biotechnology related disciplines and at the national level (as it is estimated by the ratio of collaborative articles to total number of local articles). Collaboration in biotechnology research follows the broad national patterns with USA being the main collaborating partner followed by England and Germany.

Table 1 South African Publications in Biotechnology Related Disciplines

Year	Biochemistry & Molecular Biology	Neuro-science	Genetics & Heredity	Cell Bio-logy	Biotechnology & Applied Micro-biology	Bio-physics	Virology	Biomedical Engenee-ring	Medical Chemistry	Development Biology	Micro-biology	TOTAL
1995	101	18	55	49	62	11	20	5	20	7	63	**411**
1996	95	18	71	50	62	9	19	4	25	2	48	**403**
1997	104	24	63	57	64	15	33	5	22	2	63	**452**
1998	117	22	59	49	65	16	37	5	26	2	78	**476**
1999	137	32	66	42	70	12	41	4	26	2	69	**501**
2000	111	49	74	50	78	20	43	3	39	9	89	**565**
2001	144	39	77	70	77	15	53	6	35	8	115	**639**
2002	162	48	76	54	77	14	37	10	34	9	83	**604**
2003	140	50	67	39	109	17	55	8	35	10	104	**634**
2004	164	81	66	52	83	19	47	7	44	5	102	**670**
2005	164	69	57	66	127	15	81	8	47	8	115	**757**
2006	162	100	65	58	135	18	71	11	41	8	120	**789**
TOTAL	**1,601**	**550**	**757**	**636**	**1,009**	**181**	**537**	**76**	**394**	**72**	**1,049**	**6,901**

It should be noted that collaboration in biotechnology related disciplines is substantially higher than the national average.

The second issue that we examine is the identification of the sources of biotechnology research in the country. Table 4 shows the main South African producers of biotechnology related research. The University of Cape Town with 1,329 publications (22 % of the total) appears to have been the major contributor of biotechnology research in the country since 1995. The universities of Stellenbosch and Witwatersrand follow having contributed 17.5 % and 16 % of the total number of publications respectively. Absent from this list

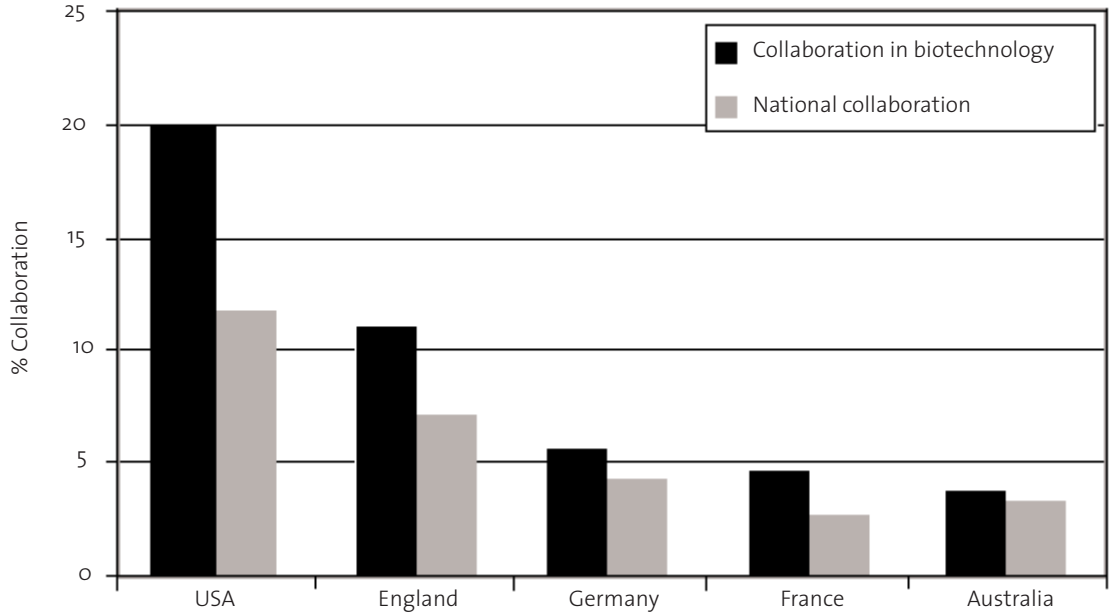
Table 2 Growth in Biotechnology Disciplines

Discipline	Publications per Year Average, 1995 - 1998	Publications per Year Average, 2003 - 2006)	Growth %
Biochemistry & Molecular Biology	104.2	157.5	51.1
Neuroscience	20.5	75.0	265.8
Genetics & Heredity	62.0	63.7	2.7
Cell Biology	51.2	53.7	4.8
Biotechnology & Applied Microbiology	63.2	113.5	79.6
Biophysics	12.7	17.2	35.4
Virology	27.2	63.5	133.4
Biomedical Engeneering	4.7	8.5	80.5
Medical Chemistry	23.2	41.7	79.3
Development Biology	3.2	7.7	140.6
Microbiology	63.0	110.2	74.9
TOTAL	**354.5**	**583.2**	**64.5**

Table 3 Disciplinary Emphasis in South Africa (2004 - 2007)

Discipline	Emphasis 2004 - 2007	Emphasis 1995 - 1996
Plant Sciences	5.9	5.2
Medicine, General & Internal	4.3	6.5
Ecology	3.7	3.5
Environmental Sciences	2.7	2.4
Zoology	2.7	2.7
Biochemistry & Molecular Biology	2.7	2.7
Microbiology	2.1	2.3
Veterinary Sciences	1.9	1.8
Geosciences, multidisciplinary	1.9	1.9
Astronomy & Astrophysics	1.9	2.1
Biotechnology & Applied Microbiology	1.9	1.7
Neurosciences	1.3	0.9

Figure 1 Extent of Collaboration in Biotechnology -related Research and Nationality



are the country's research councils (i.e. Medical Research Council, Agricultural Research Council, CSIR and MINTEK) which contribute less than three percent of the country's research publications in the field each. Similarly absent are studies from industrial establishments in the country.

The two companies with certain presence are SAPPI with 17 publications over the period and the South African Breweries with 14 publications. Table 4 also shows the biotechnology emphasis within the various institutions. Biotechnology emphasis is estimated as the ratio of the number of biotechnology related articles to the total number of articles produced by the researchers of the institution. It should be expected that in institutions with high emphasis in biotechnology the relevant researchers have more power to influence university decisions than in institutions with low relative emphasis. The University of Stellenbosch is identified as the most biotechnology-intensive institution in the country with 16 % of its publications being related to biotechnology research.

The third issue we investigate is related to South Africa's performance in biotechnology research vis-à-vis the performance of a number of other countries.

Table 4 Main Contributors to Biotechnology Research: SA 1995-2007

University	Publications	% Contribution in Country	Emphasis within institution
University of Cape Town	1,329	22.0	11.4
University of Stellenbosch	1,057	17.5	16.0
University of the Witwatersrand	970	16.0	10.0
University of Pretoria	671	11.1	8.7
University of KwaZulu-Natal	463	7.6	7.5

Table 5 (see appendix 1) shows the number of publications from a number of countries in the disciplines related to biotechnology during 2006. South Africa produces substantially smaller numbers of publications than the other countries – even though there are countries with substantially smaller populations (e.g. Singapore and Finland with populations around 5 million). South Africa compares favourably with Singapore only in the fields of microbiology and virology.

South Africa needs to increase its output by factors ranging from three to five if it wishes to compare favourably with those countries.

The suggested increase can be the result of a redirection/redeployment of human resources from other scientific disciplines or the result of an enlargement of the whole of the scientific system. Table 6 (see appendix 2) shows the research emphasis (number of biotechnology related articles as a percentage of the total number of articles from the country) placed on the various biotechnology related scientific disciplines in South Africa and the comparator countries. In comparison to other countries South Africa does not place enough research emphasis in biochemistry and molecular biology, cell biology, biophysics and developmental biology. In those disciplines South Africa should double its emphasis in order to be within the comparator counties' norms. On the other hand South Africa places a comparative over-emphasis on virology and it is within the standards of the comparator countries in biotechnology & applied microbiology and microbiology.

Conclusions

This article sets the objective to identify the state and trends of biotechnology research in South Africa in order to provide the context in which the government has set the objective of South Africa being among the global top ten nations in the world in the field by the year 2018.

Academic research, as is manifested in publications, is of particular importance for the field of biotechnology as empirical studies supported by the European Commission show that "policies to create and sustain the knowledge base are crucial for commercialisation but the reverse is not true" (European Commision, 2003; Reiss; Dominguez-Lacara, 2005).

Our findings are as follows:

- South Africa has a growing biotechnology research system. During the most recent ten year period there was an average growth in biotechnology related publications of 64 % while the growth in the country's publications has been 25 %.
- In comparison to leading countries in biotechnology research South Africa needs to increase its research publications by a factor of three in order to produce a similar volume of knowledge in the field.
- The South African research system overemphasises the macro-aspects of plant sciences, animal sciences and environmental related sciences in comparison to biotechnology related disciplines.
- Three universities – University of Cape Town, University of Stellenbosch and University of Witwatersrand– have produced more than 50% of the country's publications during the last ten years. An important finding is that the country's research councils (i.e. CSIR, MRC, MINTEC, ARC etc.) produce a minimal number of publications in the field of biotechnology.
- South Africa pays half as much emphasis on biotechnology related disciplines as the comparator countries. Exceptions are the disciplines of biotechnology and applied microbiology and of microbiology which are within the standards set by the comparator countries.

The above findings have a number of policy implications. The South African government will have to establish a number of policy measures in order to accelerate the growth of knowledge production in the field of biotechnology. This can be achieved firstly by re-directing researchers to the fields of biotechnology, for example, through different value bursaries and research grants, and secondly by expanding the research system. The above-mentioned analysis indicates that the biotechnology research system can be doubled in size without having to expand the total research system. After that doubling, however, the country's research emphasis will be within the comparator countries' norms and further expansion may be achieved through growth of the total research system. In this context, it should be emphasized that South Africa follows a pluralistic approach in the management of its national research system. There is no differentiation in the research support of various disciplines, policy instruments are introduced without assessing their impact on other areas of importance, govern-

ment departments follow their own policies - sometimes neutralizing other departments' policies - and similar. Redirecting the university research system towards biotechnology related disciplines will require a fresh thinking and the development of powerful policy instruments by the Department of Science and Technology.

It is interesting to discuss the differences which arise when the relevant size of countries (population or GDP) is taken into account. For example, comparison of the absolute number of publications produced annually indicates that South Africa needs to increase its relevant production rate by a factor of three in order to be comparable with the other leading countries. However, when we estimate the required increase for comparability taking into account the population size of the various countries (number of publications per capita) we find that South Africa requires a growth by a factor of ten. In this context the absolute number of publications is indicative of the size of the research system that may be required in order to have a viable and effective biotechnology research system. If the successful countries can support a biotechnology innovation system with a particular size biotechnology research system, other countries could emulate those countries with similar size bio-research systems. A caveat that should be mentioned is the extent of concentration of the bio-research system. The performance of the innovation system, under ceteris paribus conditions, may be different in a country with five million people than in one with fifty million people, even though both may have the same size research systems. The difference will be the effect of the dispersion of research in the larger country. Successful research and innovation require a certain critical mass and proximity which may not be always available in relatively larger countries. It will be important to identify the critical mass required, say within a particular institution, in order to have a successful biotechnology group.

The finding that the country's research councils (government contract research organisations) make a minimal contribution in terms of publications in the field of biotechnology is also of policy importance. Research councils in South Africa (functioning as contract research organisations) boast their involvement in the field and their successes which range from DNA fingerprinting of plant cultivars to increase by 188 % of the size of the knob of ginger and from the development of pearl millet resistant to downy mildew to the development of BACOXTM gold bioleaching technology. Their absence from the publication arena, however, may be interpreted as meaning that their "researchers" are not in the research front. If this assertion is correct, research councils in South Africa run the danger that they will eventually become uncompetitive internationally with adverse consequences for their technology transfer activities and their contribution to the country's research system.

In concluding it should be emphasized that the management by objectives (setting targets) that has been introduced in South Africa has a number of advantages. Probably the most important benefits are the inducement of the monitoring and benchmarking of the national system of innovation and the governmental focus on particular disciplines and technologies. The last issue has been identified by OECD as one of the major weakness in science and technology policy in South Africa.

References

Braun, T.; Schubert, S.; Zsindely, S. (1997): *Nanoscience and nanotechnology on the balance, Scientometrics,* **38** (2), pp. 321–325.

Dalpe, R. (2002): Bibliometric analysis of biotechnology, *Scientometrics,* **55**, pp. 189–213.

DST (2007): *Innovation Towards a Knowledge-based Economy –Ten-year Plan for South Africa 2008-2018.* Department of Science and Technology, Pretoria.

European Commission (2002): *Life Sciences and Biotechnology – A Strategy for Europe.* Communication from the Commission to the European Parliament, the Council, the Economic and Social Committee and the Committee of the Regions Com 27 Luxembourg.

European Commission (2003): *Efficiency of Innovation Policies in High Technology Sectors in Europe (EPOHITE),* Final Report from STRATA Accompanying Measures, EUR 20904.

Freeman, C.; Soete, L. (1997): *The Economics of Industrial Innovation.* MIT Press, Cambridge, MA.

James, C. (2007): *Global Status of Commercialised Biotech/GM Crops: 2006. International Service for the Acquisition of Agri-Biotech Applications,* ISAAA, accessed at URL: http://www.isaaa.org, March 2007.

Molatudi M.; Pouris A., (2006): Assessing the Knowledge Base for Biotechnology in South Africa: A Bibliometric Analysis of South African Microbiology and Molecular Biology and Genetics Research. *Scientometrics,* **68**(1),

pp. 97-108.
OECD (2006): *OECD Framework for Biotechnology Statistics.* Organisation for Economic Cooperation and Development, Paris.
Pouris, A. (2003a): South Africa's Research Publication Record: the Last Ten Years. *South African Journal of Science,* **99**, pp. 425–428.
Pouris, A. (2003b): Assessing Public Support for Biotechnology in South Africa. *South African Journal of Science,* **99**, pp. 513-516.
Reiss, T.; Dominguez-Lacasa, I. (2005): *Indicators for benchmarking biotechnology innovation policies.* Fraunhofer ISI, Karlsruhe.
VINNOVA (2003): *Swedish Biotechnology- Scientific Publications, Patenting and Industrial Development.* Swedish Agency for Innovation Systems, VA2003:2.

Appendix 1

Table 5 Bio Publications in Selected Countries 2006

Countries	Biochemistry & Molecular Biology	Neuroscience	Genetics & Heredity	Cell Biology	Biotechnology & Applied Micro-biology	Biophysics	Virology	Biomedical Engenee-ring	Medical Chemistry	Development Biology	TOTAL
Australia	1,441	1,536	617	1,315	509	258	211	214	143	151	6,395
Brazil	1,025	952	393	402	367	232	183	93	200	91	3,938
Denmark	692	496	242	270	240	140	50	59	82	33	2,304
Finland	491	365	262	204	163	151	50	75	47	29	1,837
India	1,373	536	243	386	819	346	133	44	511	49	4,440
Korea	1,672	812	250	712	101	446	77	160	414	54	4,698
Singapore	371	216	108	192	167	123	45	111	26	21	1,380
South Africa	**162**	**100**	**65**	**58**	**135**	**18**	**71**	**11**	**41**	**8**	**669**
Sweden	1,320	844	424	507	356	351	137	124	107	86	4,256
Switzerland	1,193	1,000	380	655	319	288	111	167	153	95	4,361

Appendix 2

Table 6 Emphasis on Biotechnology Research- SA and Selected Countries 2004-07 (in %)

Countries	Biochemistry & Molecular Biology	Neuroscience	Genetics & Heredity	Cell Biology	Biotechnology & Applied Microbiology	Biophysics	Virology	Biomedical Engeneering	Medical Chemistry	Development Biology
Australia	3.87	3.54	1.89	2.84	1.31	0.75	0.56	0.37	0.35	0.49
Brazil	4.95	4.13	1.99	1.83	1.65	0.97	0.68	0.41	0.90	0.34
Denmark	6.21	3.61	2.12	2.52	2.34	1.51	0.46	0.45	0.73	0.35
Finland	4.86	3.62	2.69	2.01	1.75	1.43	0.58	0.57	0.40	0.33
India	4.40	1.30	0.81	1.33	4.40	1.27	0.38	0.16	1.72	0.19
Korea	5.45	2.20	0.87	2.64	3.01	1.49	0.22	0.49	1.48	0.34
Singapore	4.63	1.99	1.32	2.53	2.13	1.24	0.57	1.31	0.45	0.41
South Africa	**2.76**	**1.27**	**1.14**	**1.07**	**1.88**	**0.30**	**1.18**	**0.15**	**0.77**	**0.13**
Sweden	6.14	3.99	2.16	2.54	1.72	1.79	0.63	0.47	0.47	0.40
Switzerland	5.60	3.85	1.76	2.90	1.39	1.39	0.63	0.73	0.73	0.43

Journal of Business Chemistry

Practitioner's Section

REACH Effects - Opportunities and Risks for Transfer Pricing

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1 Introduction

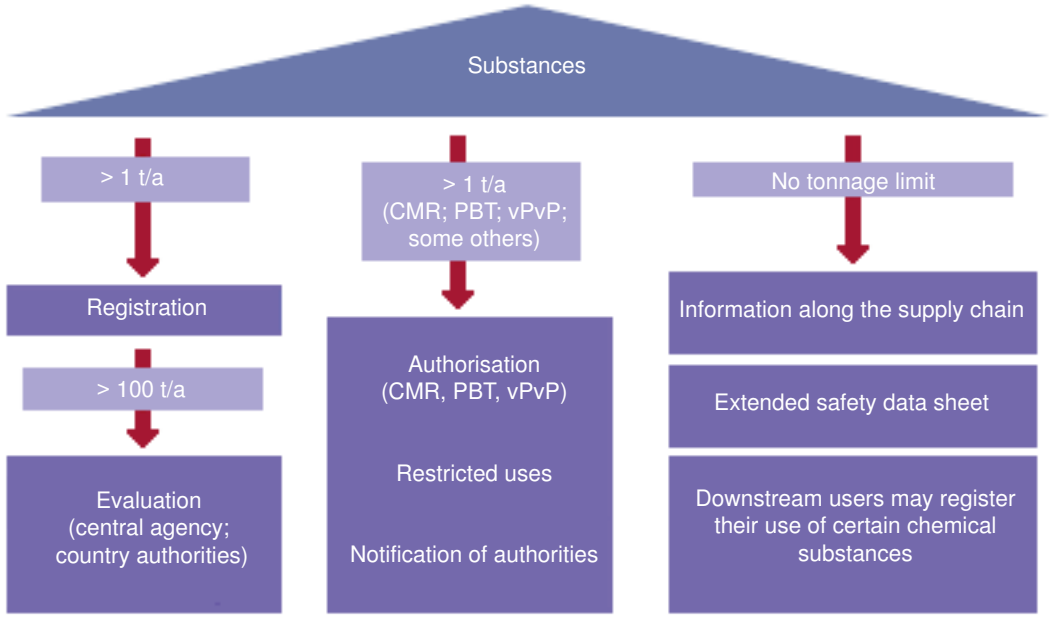
This article gives a general background to the REACH regulation and reflects on the possible impact of REACH on Transfer Pricing opportunities and risks. REACH stands for Registration, Evaluation and Authorisation of CHemicals. Since REACH may provide some opportunities for improving the Transfer Pricing setup of multinational enterprises (MNEs), this article summarises good Transfer Pricing practice with respect to REACH and its potential effects on operations. It furthermore raises interdependencies between REACH and Transfer Pricing topics like cost allocation, base shifting, remuneration of R&D, remuneration of Only Representatives, tax audit strategies, Advance Pricing Agreements, Mutual Agreement Procedures, Transfer Pricing documentation and Transfer Pricing guidelines.

2 Background to REACH

As of June 1st, 2007 the EU 27+3 (27 EU member states plus Norway, Iceland and Liechtenstein) chemicals legislation changed dramatically. In the upcoming years about 30,000 chemical substances, which are either produced or imported into the EU 27+3, will have to be registered with the newly created European Chemicals Agency (ECHA) in Helsinki. The rules of REACH apply to all substances imported or manufactured. The instruments of registration and evaluation form one pillar of REACH, authorisation and restriction of use for substances of high concern form the second pillar and the information flow along the supply chain the third pillar (see figure 1).

- The first pillar "Registration" indicates that all substances in volumes of over one ton per year (1t/a) must be registered by the importers or producers. Also covered in the first pillar are the evaluation tasks to be performed by the authorities under REACH: evaluation of testing proposals and compliance check by the ECHA and substance evaluation by the Member States Competent Authorities. Evaluation under REACH (Title VI of the REACH Regulation) defines the assessment of registration dossiers (examination of testing proposals and compliance check of registrations) and substances. The main objective of the examination of testing proposals is to check that reliable and adequate data are produced and to prevent unnecessary animal testing. The purpose of checking a registration dossier for compliance is to ensure that the legal requirements of REACH are fulfilled and the quality of the submitted dossiers is sufficient, the safety assessment is suitably documented in a Chemical Safety Report (CSR) as required in the REACH regulation, the proposed risk management measures are adequate, and that any explanation to opt out from a joint submission of data has an objective basis. Substance evaluation aims to clarify any grounds for considering that a substance constitutes a risk to human health or the environment. Evaluation may lead to the conclusion that action should be taken under the restriction or authorisation procedures or that risk management actions are to be considered in the framework of other appropriate legislation. Information on the progress of evaluation

Figure 1 Three Pillars of REACH



proceedings is made public.

- The second pillar "Authorisation, Restriction and Notification" applies to all substances of very high concern (SVHC) in quantities of one ton and more per year (1t/a). Title VII of REACH (articles 55-66) covers the criteria for inclusion of substances into the SVHC category. The SVHC category includes carcinogenic, mutagenic or toxic for reproduction (CMR), persistent, bioaccumulative and toxic (PBT) and very persistent and very bioaccumulative (vPvB) substances. The substances which are subject to authorisation can be found in annex XIV of REACH. This annex currently includes a list of 15 substances but is subject to periodic additions. For these substances, an extended communications regime, including end-users, applies. Restrictions in use as well as notification of articles containing such substances can have far reaching consequences for the manufacturers or importers and thus may impact the global use pattern of such substances.
- The third pillar of REACH "Supply Chain Communication" applies to all substances and has no inherent lower tonnage limit. Part of the responsibility of manufacturers or importers for the management of the risks of substances is the communication of information on these substances to other professionals such as downstream users or distributors. In addition, producers or importers of articles must supply information on the safe use of the articles to industrial and professional users, and also to consumers on request. This important responsibility applies throughout the supply chain to enable all parties to meet their responsibility in relation to management of risks arising from the use of such substances. The supplier of a substance or a preparation must provide the recipient of the substance or preparation with a safety data sheet compiled in accordance with Annex II (article 31) and even has the duty to communicate information down the supply chain for substances on their own or in preparations for which a safety data sheet is not required (article 32).

With these instruments REACH regulates the production, the import and the use of chemical substances in the EU 27+3 market.

The REACH regulation entered into force on June 1st, 2007. The time to implement is quite short. In order to assure a full consideration of the requirements into the standard

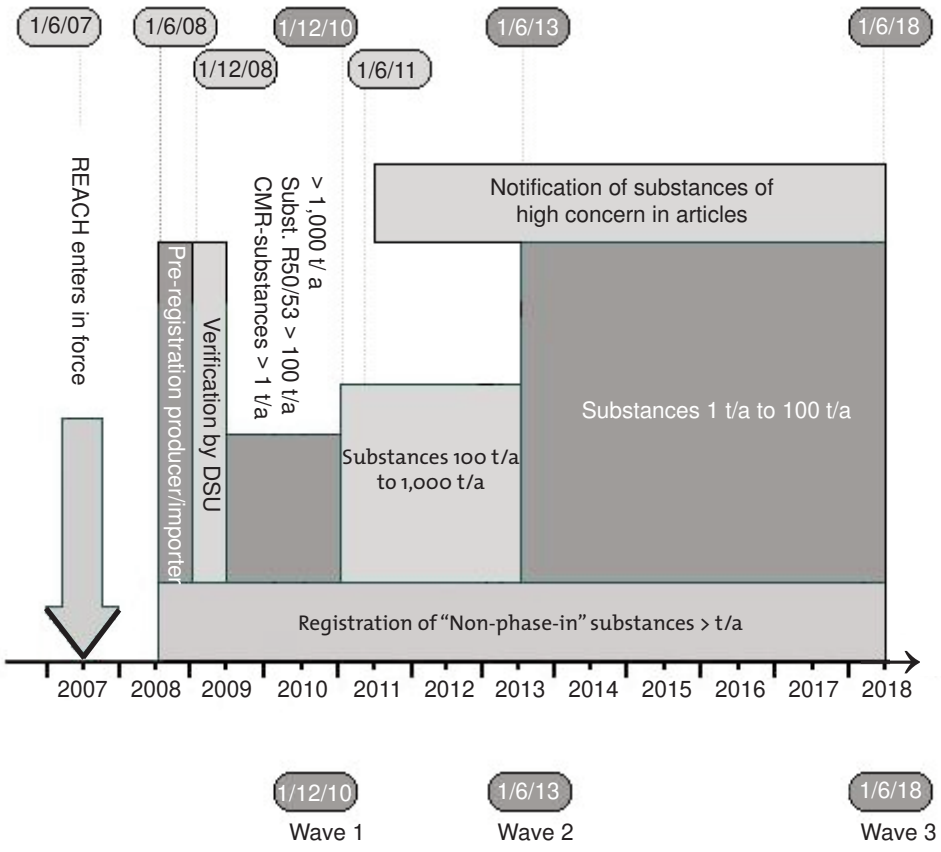
operating procedures of the industry, the people responsible for the supply chain need to participate fully. Communication with downstream users and ensuring supply of strategically important raw materials – both on the producing/importing end as well as on the following elements of the value chain – play a decisive role in the effects REACH will have on an enterprise. Identifying both, the opportunities and the risks that REACH poses, is crucial. The relevant consequences for the supply chain managers are both the increased risk in the supply chain stability and the opportunity in the increased communication.

The protection of health and the environment was the foundation of the work on the legislation. However, all the tests, the two-way communication and the inquiries into the use and exposures require a huge amount of work for all participants in the value chain. Over the next eleven years (see figure 2) there are three waves of registrations after the pre-registration in the second half of 2008. First, substances produced or imported in quantities over 1,000 tons/annum (t/a), substances with aquatic impact over 100 t/a and CMR-substances (carcinogenic, mutagenic or toxic for reproduction) over 1 t/a have to be registered by December 1st, 2010. The second registration wave concerning substances between 100 and 1,000 t/a ends on June 1st, 2013. Only in 2018 will all the other substances with volumes over 1 t/a and below 100 t/a need to be registered.

2.1 Complete reversal of the burden of proof

The most direct effect of REACH lies in the reversal of the burden of proof. Now, the industry must document exposure to humans or the environment during normal or reasonably foreseeable conditions of use including disposal of substances in chemical safety assessments

Figure 2 Timeline of REACH



and the chemical safety report (CSR). All substances with yearly production or import of over 10 tons must be registered with the CSR. This requires a communication of uses and potential exposure in both directions of the supply chain. The identified uses of a substance need to be included in the safety data sheet (SDS).

Over the coming eleven years the pre-registration, tests and registration of the estimated 30,000 substances are required. Approximately 1,500 of these will be subjected to an intense authorisation procedure due to their CMR properties, because of their assessment result in the classification as persistent, bioaccumulative and toxic (PBT) or very persistent and very bioaccumulative (vPvB). REACH distinguishes between substances on their own, in preparations and in articles. With the registration the allowed uses as well as the restrictions are available in a central database for the public and the authorities. For the first time it will be possible to build up a detailed picture of where chemicals are used and to show the material flows.

2.2 Extra costs built into the system

REACH will undoubtedly cause extra costs for many players. Currently, the producers and importers are screening their portfolios for the impact of REACH on their costs. The occasion to streamline the portfolio is one factor that has already been identified. No clear indication has yet developed on just how many substances will drop out and not be registered. However, for each individual substance the downstream users will incur a significant cost. The development of alternatives and the qualification of new products with certified uses in the next step of the chain (e.g. as aircraft component, or in a flame retardant function) may cost millions.

Since all steps of the value chain are reviewing their portfolios, the stability of the supply chains is tested to quite an extraordinary extent. Some fear that between 5 % and 20 % of the substances they currently use in their products will not be available or will not be registered for their uses. The likelihood of substance withdrawal is higher for substances in the low tonnage bands and with low margins. Even producers of substances with no obligations to register must be aware of potential downstream exposure issues if they are used in combination with hazardous substances.

REACH requires that consumer products are labelled if substances authorised under REACH are contained in them. Therefore, one possible scenario is the complete elimination of consumer products containing substances with authorisation requirements by large retail chains in some product categories. If this is to occur, many of these substances may be used in much smaller amounts and therefore the fixed costs of the production plants may have to be distributed on a much smaller product base.

2.3 Fundamental differences between producers and downstream users

The regulation differentiates clearly between the role of producers and importers and the role of downstream users (see figure 1). While downstream users are required to implement risk management measures, vendors are now required to supply only to customers where they can be reasonably certain that sufficient risk management measures are taken. For substances with authorisation requirements a rather strict control of this requirement might be introduced.

2.4 The influence of REACH on the supply chain manager

As soon as the downstream user requests the inclusion of his use in the list of allowed uses, the timeframe for inclusion or exclusion in the SDS is one month. If the vendor determines that for health and environmental reasons a certain use cannot be permitted (article 14 REACH regulation), he needs to inform the ECHA as well as the downstream user. Additionally, it has to be documented in the SDS that this particular use is not allowed.

2.5 Opportunities and risks of REACH on the supply chain

With all the preparation needed to comply with REACH, the data and information for substance use in preparations and articles must be gathered. A state-of-the-art response of a company consists of a team of experts from management, regulatory affairs, safety, health and environment, research and development, strategic purchasing, operations, supply chain management and customer facing functions. These multi-disciplinary teams have to identify opportunities and risks along the supply chain. The costs of REACH can be quite significant for specialty chemicals producers. Inclu-

ding these costs in Transfer Pricing considerations may have a significant impact on the bottom line. For this reason, the supply chains in various industries are actively analysed for optimisation potential. On the basis of increased communication – both from customers and suppliers – these efforts may have positive impact on the entire value chain. The early involvement of supply chain experts is highly recommended. Integrating the preparation for REACH into the daily business in a balanced manner requires careful allocation of resources.

The reactions to the entry into force of REACH vary from complete apathy to hyperactivity. Top-management leadership, stringent project management and an integrated team are a few of the critical factors to REACH compliance. Special attention needs to be focused on substances in danger of elimination and on suppliers unable or unwilling to comply with the REACH requirements. The communication in both directions along the supply chain needs to be established early and utilised for a competitive advantage.

3 REACH effects on Transfer Pricing

As mentioned above REACH was not properly taken into consideration by many MNEs and international business in general in the downstream industries since REACH was already drawn up in the years leading up to 2006. Few MNEs prepared themselves properly; others waited for 2008 to react. In the last months not only directly affected MNEs in the chemical industry but also downstream users like the pharmaceutical industry and the plastics industry intensified their efforts to evaluate REACH dependencies and REACH impacts on their operations. Beyond that, REACH effects on Transfer Pricing strategies and operational Transfer Pricing are still seldom assessed in detail.

Since REACH may provide some good opportunities for improving the Transfer Pricing setup of MNEs and international business, this section summarises good Transfer Pricing practice with respect to REACH and its possible effects on operations. This section raises interdependencies between REACH and Transfer Pricing topics like cost allocation, base shifting, remuneration of R&D, remuneration of Only Representatives, tax audit strategies, Advance Pricing Agreements, Mutual Agreement Procedures, Transfer Pricing documentation and Transfer Pricing guidelines.

3.1 Cost allocation

Costs caused by REACH compliance activities of MNEs within the chemical industry can reach significant amounts as mentioned above. They may be allocated to several different entities within an MNE performing functions such as:

- Group headquarter services (e.g. legal services or patent services)
- Division headquarter services
- Purchasing, supplier management
- Manufacturing/tolling
- Downstream user
- Research & Development (R&D)
- Intellectual Property Rights management
- Distribution/Marketing & Sales
- Syndicate management

How to allocate the REACH costs from a Transfer Pricing perspective is driven by the arm's length principle, laid down in article 9 of the OECD Model Tax Convention. The arm's length principle is the international transfer pricing standard that OECD member countries have agreed should be adopted for tax purposes by multi-national enterprise (MNE) groups and tax administrations. Transactions between affiliated companies comply with the arm's length principle when conditions imposed are comparable to those that are or would be imposed by independent enterprises dealing with comparable transactions in comparable circumstances.[1]

The arm's length principle treats the members of an MNE group as operating as separate, independent entities. The focus is on the conditions which would have been obtained between independent enterprises in comparable transactions and comparable circumstances. The OECD guidelines provide detailed descriptions of methods that are used to apply the arm's length principle. These methods fall into three categories:

- Traditional transaction methods
- Transactional profit methods (or profit based methods)
- Other unspecified methods

Traditional transaction methods compare actual prices or other less direct measures, such as gross margins, on third party transac-

1) The OECD guidelines state the following: "[When] conditions are made or imposed between ... two [associated] enterprises in their commercial or financial relations which differ from those which would be made between independent enterprises, then any profits which would, but for those conditions, have accrued to one of the enterprises, but, by reason of those conditions, have not so accrued, may be included in the profits of that enterprise and taxed accordingly."

tions with the same measures on the controlled party's transactions. Three methods can be listed:

- Comparable uncontrolled price method (CUP)
- Cost plus method (CPLM)
- Resale price method (RPM)

A transactional profit method, on the other hand, compares the overall net operating profits that arise from intra-group transactions to the net operating profit earned on comparable transactions carried out by independent companies. The transactional profit methods for the purposes of the OECD guidelines are:

- Profit split method
- Transactional net margin method

The transactional profit methods are generally considered to be less precise and reliable than the traditional transaction methods. Nevertheless, they may be applied as a result of practical difficulties in finding suitable information for the application of the traditional transaction methods.

3.1.1 At cost or cost plus mark-up

The question could be raised, as to whether REACH costs should be invoiced with cost plus mark-up (CPLM) or at cost. From an arm's length perspective, the invoicing of REACH costs at cost and without any mark-up could be justified if an independent third party would be willing to enter into such a transaction. This could apply, for example, where the REACH costs are marginal in comparison to the sales and costs of the operational business. Alternatively, significant cost savings for the provider of the REACH services could justify invoicing at cost. This could be the case if the provider performs the REACH services on his own behalf and on the behalf of associated companies and/or third parties. The savings with respect to the own costs of the provider could be realised due to respective economies of scale resulting from the provision of services for associated companies and/or third parties.

3.1.2 Cost allocation keys

Different allocation keys may be applicable to the cost allocation to entities performing different functions, bearing different risks and providing different assets within the value chain. Possible REACH cost allocation keys could be:

- Distribution between different entities of a MNE on the basis of their:
  - Contribution to the Added Value
  - Percentage of sales
  - Production volumes
- Allocation of all REACH costs with respect to one chemical substance to the:
  - Owner/Licensor of Intellectual Property Rights
  - Licensee of Intellectual Property Rights
  - R&D entity

The REACH principle "No Data – No Market" (REACH regulation article 5) widens the scope of possible cost allocation keys to the above as it considers the whole value chain to be subject to REACH compliance. As a result, REACH costs may be allocated within a MNE to different entities all over the world, not necessarily restricted to the REACH region EU 27+3.

3.1.3 Cost qualification

REACH costs may be qualified by local tax authorities from a tax perspective in different ways:

- They may be seen as deductible expenses.
- They may be qualified as building a capitalised asset in the balance sheet that can be amortised within the asset depreciation range. How long is a respective asset depreciation range with respect to a chemical substance? Does it depend on the product life cycle or is it defined as a lump-sum-range notwithstanding the specific chemical substance in question? Such questions may be governed by local tax law.
- They may be assessed as non-deductible and not building a capitalised asset. Due to article 5 "No Data – No Market", REACH may be interpreted as a "license to operate"(Temme and de Loose, 2008). This could prevent tax deductions in certain countries. Obviously, only a few countries deny tax deductions. Consequentially, companies will achieve tax benefits due to REACH costs incurred.
  If a deduction of expenses or of a capitalisation is possible, tax effects may differ between tax figures in the past and future forecasts of each MNE and its entities. In this respect tax planning effects like tax rate differences and interest effects have to be considered in detail.

According to the prospective huge cost volumes in question, the deductibility of REACH costs in different entities within a MNE may have significant tax effects.

3.1.4 Regional REACH cost allocation

The significant tax effects of REACH costs can be illustrated with the following scenario (See figure 3 and figure 4), covering four MNEs (A, B, C, D). MNE D has the lowest economies of scale[2] and therefore realises the lowest gross profits per ton (t) of its production sold to the market. Assuming that the Non-EU 27+3-price is the price before REACH influences the market price for chemical substance X, MNE D is still profitable.

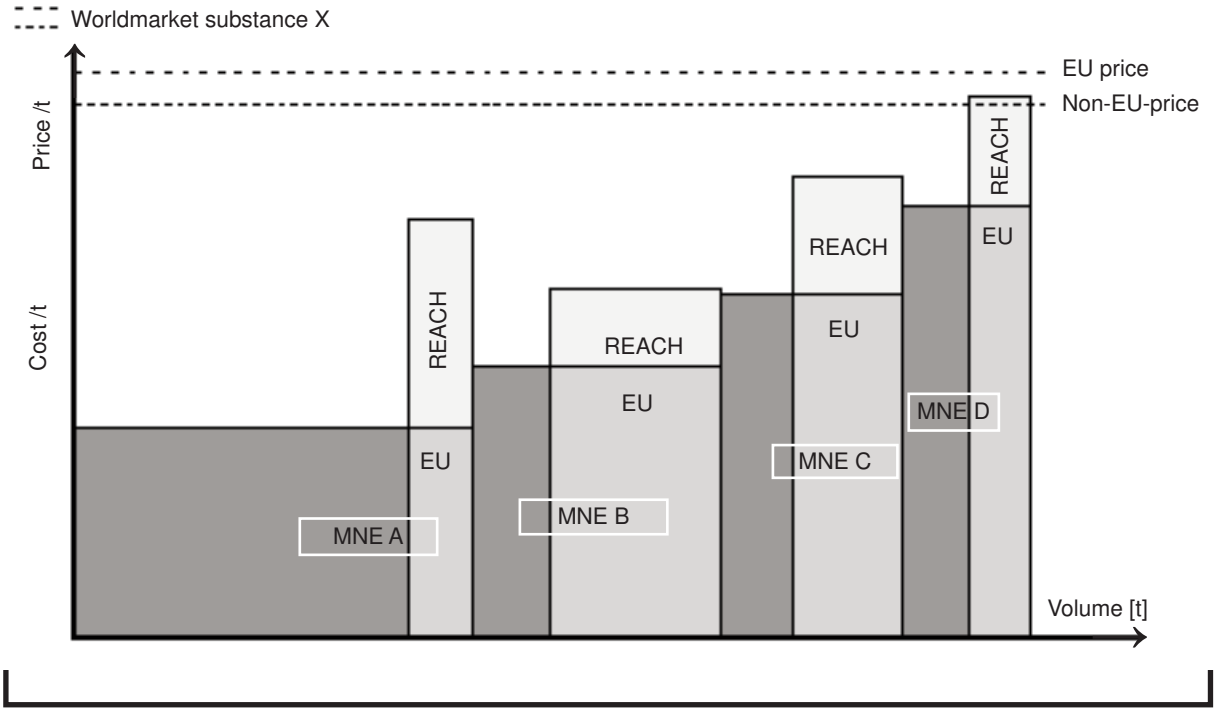
The enforcement of REACH changes the cost structures of all MNEs. The absolute cost increase per substance is assumed to be identical for all MNEs as far as they market/produce substance X in the same tonnage/volume defined in the REACH regulation. But all MNEs have different actual volumes distributed to the EU 27+3-market. Therefore, their cost increase per production ton differs, as shown in Figure 3. The absolute costs per manufacturer are assumed to be in the same tonnage band for manufacturers A, B and C. Manufacturer D however is in a lower tonnage band and therefore has smaller overall costs due to REACH requirements.

As a result, MNE D in our example presented in Figure 3 faces total costs higher than the Non-EU 27+3-price. Therefore, it may be forced to continue activities in the REACH region with losses, trying to reduce cost base in the long run or hoping for an increase of the market price to the EU 27+3-price, as indicated in Figure 3. Assuming that the market price for substance X within the REACH region does not increase to a EU 27+3-price higher than the Non-EU 27+3-price as indicated in Figure 3, MNE D may be forced to stop activities in the REACH region if it does not see any potential for future cost reductions. This would allow MNE D to avoid REACH costs completely.

3.1.5 Global REACH cost allocation

Alternatively, the profit-loss situation with respect to each of the MNEs could be described in a different way if REACH costs are seen to be deductible not only within the REACH region, but

Figure 3 Regional REACH cost allocation



2)Economies of scale have the following effect: a decrease of the production volume results in higher costs per produced ton in particular due to worse procurement conditions and fewer process improvement experiences.

also in other entities around the world. An economic argument could be that the above mentioned economies of scale of a MNE depend on the production volume worldwide. Consequently, the costs for the production per ton would increase for MNE D as far as necessary to force MNE D to stop producing substance X at all because its new costs per ton are higher than the market price. The global REACH cost allocation model is presented in figure 4.

This model allocates the REACH costs of each MNE with respect to a chemical substance X among all markets/manufacturing entities involved in the business with substance X using the above outlined cost allocation keys.

3.1.6 Statement

From an arm's length perspective, as considered by the OECD, the allocation of functions performed, including associated risks borne and assets provided, should answer the question if and to what extent regional or global REACH cost allocation is applicable in each individual case. The economic environment, in particular the influences on the competitive situation and achievable economies of scale, may have significant impact on the REACH cost allocation. As REACH costs are very much linked to the REACH region through the "No Data – No Market" principle, at least a portion of these costs should be allocated to entities within the REACH region. But the more a MNE as a whole is dependent on the continuation and further development of business relations into the REACH region and the more its entities outside the REACH region benefit from activities within the REACH region, the more they should participate by bearing the respective costs incurred. Therefore, global allocation of REACH costs (figure 4) is favourable.

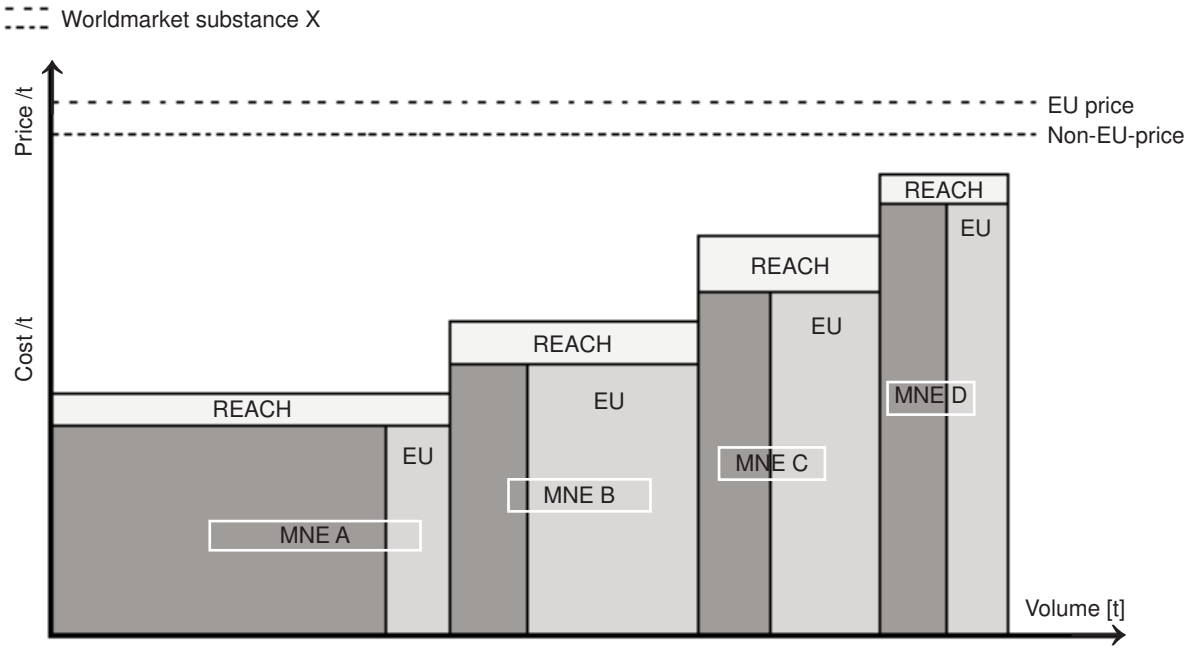
3.2 Opportunities and risks of REACH on Transfer Pricing

Opportunities and risks of REACH on Transfer Pricing cover several topics from Transfer Pricing planning to operational Transfer Pricing. This articleresents a selection of Transfer Pricing topics with REACH relevance and describes Transfer Pricing aspects indicating possible solutions.

3.2.1 Impacts on base shifting

The implementation of REACH and the enforcement of the respective rules may affect competitive environments and encourage MNEs in the chemical industry or downstream users in reassessing their operations on a broad basis, including Tax Efficient Supply Chain Management (TESCM). New regulative requirements like

Figure 4 Global REACH cost allocation



REACH are central occasions and primary characteristics for TESCM. Figure 5 shows a matrix with the columns "key factors" and "central occasions" which may indicate potential for TESCM. The y-axis of Figure 5 groups the entries in both columns as primary characteristics for TESCM or other potential indicators for TESCM.

The in-depth analysis of the implications of REACH from a Transfer Pricing perspective may show that REACH can be an unexpected but very welcome occasion for restructuring projects rescheduled in the past. The advantages for restructuring projects may be caused by the REACH costs having significant impact on the valuation of transfer packages and on the calculation on respective arm's length exit charges. These effects may change the above mentioned rescheduled restructuring projects, especially if the break-even was only missed slightly.

3.2.2 Remuneration of R&D

As some substances may not be authorised by the ECHA, REACH is expected to accelerate the intensity of R&D activities within the chemical industry to develop substances.[3] Downstream users may also develop new manufacturing methodologies to substitute dangerous substances or those no longer authorised. Depending on the extent of changes with respect to R&D within the value chain this may not only increase the R&D costs but also change remuneration models, including royalties for licences or patents. If the R&D activities and REACH compliance are executed by the principal entity, its remuneration with the residual profit will not be significantly affected. In cases of contract R&D or contract REACH compliance services, REACH may exclusively increase the cost basis but not affect the arm's length mark-up on the respective costs. Questions may be raised with respect to the arm's length remuneration of Only Representatives.

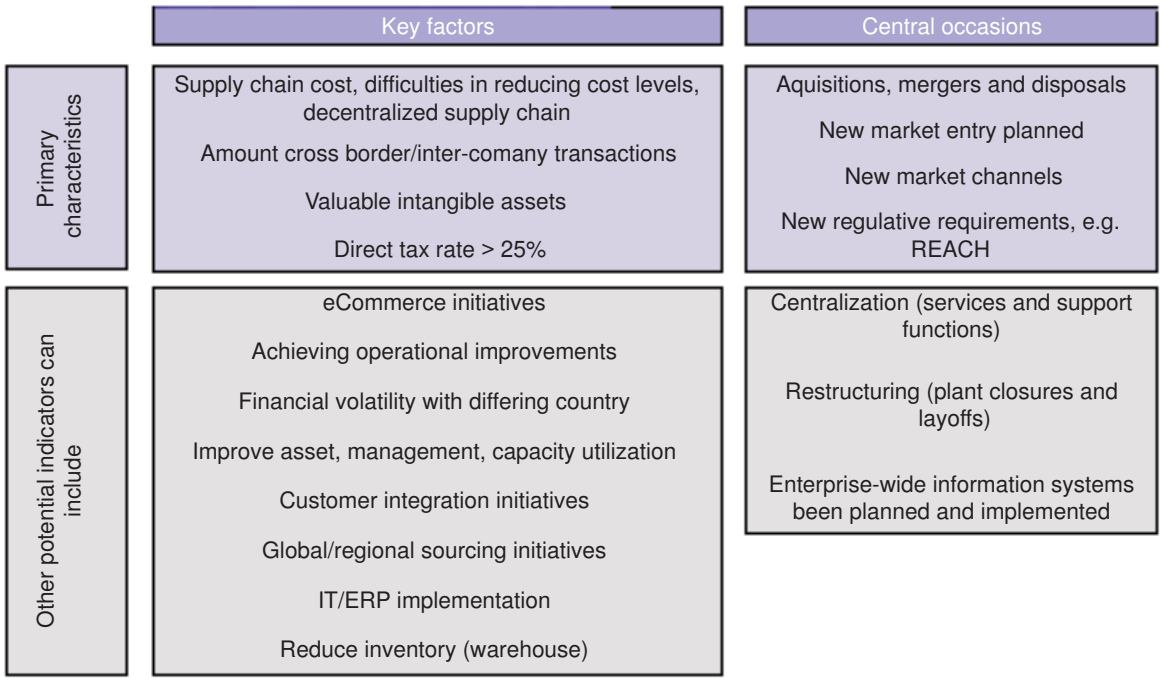
3.2.3 Remuneration of Only Representatives

According to Article 8 of the REACH regulation, company groups may appoint an EU 27+3 subsidiary as an Only Representative for a group manufacturer of chemical substances located outside EU 27+3.

How should such Only Representatives be remunerated from a Transfer Pricing perspective to meet the generally accepted arm's length principle?

The ECHA outlines the activities and respon-

Figure 5 TESCM more often suitable as expected



3) ECHA listed 15 substances identified as such of very high concern in late October 2008 that will become subject to the authorisation phase of the EU's REACH program.

sibilities of Only Representatives of manufacturers of chemical substances located outside EU 27+3 in the paper "Guidance on registration" (ECHA, 2008), as follows:

An only representative is fully liable for fulfilling all obligations of importers for the substances he is responsible for as a registrant. These do not only pertain to registration but also all other relevant obligations such as pre-registration, communication in the supply chain, notification of substances of very high concern (SVHC), classification and labelling and any obligations resulting from authorisations or restrictions etc. (see Art. 8(2)).

The only representative registers the imported quantities depending on the contractual arrangements between the "non-Community manufacturer" and the Only Representative.

REACH does not distinguish between direct and indirect imports into the EU and therefore such terms are not used in this guidance. It is essential that there is a clear identification of:

- who in the supply chain of a substance is the manufacturer, formulator or producer of an article;
- who has appointed the Only Representative;
- which imports the Only Representative has responsibility for.

As long as the above conditions are met, it does not matter what are the steps or supply chain outside the EU between the manufacturer, formulator or producer of an article and the importer in the EU.

It should, however, be pointed out that the use of the Only Representative facility creates the need for exact documentation on which imported quantities of the substance are covered by the Only Representative registration and which imported quantities are not. The only representative will need this information to fulfil his obligation under Article 8(2) to keep available and up-to-date information on quantities imported and customers sold to. Moreover, the importer will also need to know whether a concrete quantity of the substance in a preparation is covered by the registration of the Only Representative of the substance manufacturer, as he would otherwise be subject to a registration requirement himself. This documentation will need to be presented to the enforcement authorities upon request.

The registration dossier of the Only Representative should comprise all uses of the importers (now downstream users) covered by the registration. The Only Representative shall keep an up-to-date list of EU customers (importers) within the same supply chain of the "non-Community manufacturer" and the tonnage covered for each of these customers, as well as information on the supply of the latest update of the safety data sheet.

For phase-in substances the Only Representative will have to pre-register the substance in order to benefit from the extended registration deadlines and will subsequently become participant of the Substance Information Exchange Forum (SIEF) (see section 3.4 of the Guidance on data sharing).

Subsequently, the first answer to the question, how REACH Only Representatives should be remunerated from a Transfer Pricing point of view, may be: REACH Only Representatives provide authorisation, registration and evaluation services to other group companies. These services are comparable to other routine services provided within the group and therefore should be remunerated accordingly. A usual remuneration method could be the cost plus method, remunerating the cost incurred by the service provider plus a profit mark-up. The definition of such profit mark-ups is usually supported by benchmarking studies, showing profit mark-ups of independent service providers comparable with respect to the kind of services provided considering functions performed, risks assumed and assets employed.

But the activities of an Only Representative are not restricted to services such as monitoring, testing or applying for authorisation, evaluation or registration. Furthermore, Only Representatives are responsible and liable for the fair and true presentation of SDS and all other data necessary for the communication with the ECHA. The corresponding responsibilities may still be classified as routine services. Those may be remunerated with routine profits defined similarly to the ones for other standard services.

With respect to any further obligations against third parties like ECHA or EU 27+3 customers tax authorities may tend to identify the coverage of non-routine risks by Only Representatives. Consequently, tax authorities may assume the remuneration with cost plus a low profit mark-up does not meet the arm's length principle. In REACH terminology: "REACH Only Representative remuneration may not reach an arm's length remuneration level". Therefore, caution is recommendable with a simple roll-out of ordinary intercompany management services agreements not reflecting possible significant differences of the business model implemented with respect to functions performed and risks borne.

Depending on the individual cases and especially the degree or volume of risks covered by the Only Representative a non-routine remuneration or a routine remuneration with a higher

profit mark-up may be applicable and feasible.

Alternatively, REACH Only Representatives may be protected against liabilities resulting from future claims for damages in an appropriate way. This could be implemented in intercompany REACH Only Representatives agreements. As a consequence, a routine remuneration may be feasible and applicable for the Only Representative.

Furthermore, an assessment of possible differences between functions performed and risks assumed compared with other intercompany services agreements is strongly recommended. Such assessments could show the transferability of other remuneration models already applied within the group. Sophisticated assessments and proper documentation of the remuneration models for REACH Only Representatives and their economic background could ease future tax audit defence significantly. Otherwise, adjustments, interest payments and penalties may result in the future.

3.2.4 Assessment of REACH costs in tax audits

For many years local tax authorities have been tangibly strengthening their focus on Transfer Pricing, in particular on management services fees, and therefore MNEs should be prepared for future assessments of large cost pools such as REACH costs. These assessments get more probable in cases of:

- Material tax rate gaps
- Poor Transfer Pricing documentation
- Lack of benchmark studies in place
- Non-existence of reliable cost allocation agreements
- Huge cost pools
- Low profitability and/or loss making periods

3.2.5 APA, MAP, documentation and guidelines

REACH may also be a relevant factor to be considered during Advance Pricing Agreement negotiations with respect to the secondary clauses governing the application of an Advance Pricing Agreement within its validity period. It should be considered at an early stage of tax planning if an Advance Pricing Agreement (including a roll-back) approach or a Transfer Pricing documentation and tax audit approach (including possible future mutual agreement procedures) is more feasible for the MNE and its individual Transfer Pricing situation. The quality of such decisions at an early stage depends very much on the deep understanding of strategic Transfer Pricing risk allocation, Transfer Pricing risk assessment and Transfer Pricing risk management.

As a consequence, the following should be assessed in detail:

- Transfer Pricing risks involved
- Impacts on Advance Pricing Agreements already in place including possible prolongation negotiations or necessary modifications
- Need for new Advance Pricing Agreement due to REACH impacts
- Impacts on benchmarking strategies for the future
- Necessities for adaptations of cost accounting for REACH purposes
- Opportunities for base shifting and restructuring
- Defendable cost allocation strategies

If REACH leads to significant operational changes in the business models of a MNE or its divisions, this may cause the need for a detailed Transfer Pricing documentation of such extraordinary business transactions to prevent or manage future issues in tax audits. Such documentation should report the relevant considerations and their visible impacts on the Transfer Pricing methodology applied.

Last but not least, Transfer Pricing guidelines in place may need modifications for REACH purposes if the general considerations are not applicable on REACH transactions.

4 Conclusion

The introduction of REACH urges MNEs and international business in general to assess their Transfer Pricing risks from a REACH perspective and simultaneously affords several Transfer Pricing opportunities. In particular, the field of operational Transfer Pricing and other such crucial Transfer Pricing planning topics should be assessed in detail. A REACH Transfer Pricing assessment may cover remuneration of Only Representatives, cost allocation, Transfer Pricing documentation, Transfer Pricing guidelines, remuneration of R&D, base shifting, Advance Pricing Agreements, tax audit strategies and Mutual Agreement Procedures. When dealing with all elements of REACH, one should not only consider the operational and communications aspects but also take a broader view of the need for involvement of tax and accounting specialists.

References

ECHA (2008): Guidance on registration, in: *Guidance for the implementation of REACH*, May 2008, version 1.3.

EU (2006): REGULATION (EC) No 1907/2006 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 18 Decem-

ber 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC, in: Official Journal of the European Union, 30 December 2006, pp. 1-849.

KPMG (2005): *REACH - further work on impact assessment: A case study approach*, A study for UNICE/CEFIC Industry Consortium, DG Enterprise & Industry and DG Environment.

KPMG, TNO, SIRA Consulting (2004): *The consequences and administrative burden of REACH for the Dutch Business Community*, October 2004.

OECD (2005): Articles of the model convention with respect to taxes on income and on capital, as of 15 July 2005.

Temme, M., de Looze, R. (2008): REACH out to tax you, REACH implementation, in: *Specialty Chemicals Magazin*, **28** (1), pp. 30-31.