6. Social Motivations and Incentives in Ex Situ Conservation of Microbial Genetic Resources

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Innovation in life science depends on Public Service Microbial Collections (PSMCs) for facilitating acquisition of and access to existing microbial research materials through a worldwide network of centralised deposit and access services.[1] Microorganisms are critical to maintaining the health of other life forms that depend on them for energy recycling, nutrients and minerals, while conversely, causing infectious disease when they overlap with susceptible hosts.[2]

1 Scott Stern, *Biological Resource Centres: Knowledge Hubs for the Life Sciences* (Washington, DC: Brookings, 2004).

2 The authors are grateful for the fruitful collaboration with Philippe Desmeth (BCCM), Dr. David Smith (WFCC), Lucy Hoareau (MIRCEN) and Julia Hasler (MIRCEN). Special thanks to all collection staff that shared their expertise, especially Dr. Dagmar Fritze (DSMZ), Dr. Francois Bimet (Pasteur), Pierre-Alain Fonteyne (formerly at BCCM-IHEM), Dr. Matthew Ryan (CABI), Dr. Camacho (USCNCMCC), Dr. H. Marie-Daniel (BCCM/MUCL), Prof. R. Mutters (MCCM), F. Van-Hove of the Belgian collection BCCM/MUCL as well as Dr. Alexandre Bartsev (OECD), and Dr. George Garrity. Financial support was provided by Belgian Science Policy of the Belgian Government through IUAPVI/06, Department of Land Economy at the University of Cambridge, the Cambridge European Trust, the CT Taylor Fund and St Edmund's College, Cambridge.

The World Federation of Culture Collections (WFCC) is a network of over 500 public culture collections that are publicly available for research.[3] It is the WRCC's historical mission to organise the collection, authentication, maintenance and global distribution of cultures of microorganisms and cultured cells. Through the culture collections network, cultures are distributed and made available for research and development under marginal distribution costs, often with the possibility to further distribute the cultures to qualified third parties (for example, the standard agreement of the European Culture Collection Organisation). This results in major benefits for the development of downstream applications in important sectors such as biofuel production, plant symbionts and biocontrol agents providing environmentally sound alternatives to fertilizers and pesticides in agriculture and probiotic bacteria in the diary industry.[4] The use of certified materials from culture collections diminishes the cost from mistakes in cumulative research[5] and decreases the search costs for finding appropriate materials.[6] Therefore, the socio-economic benefits of the investment in public culture collections are substantial.

At present, the situation of exchange of biological materials within a global commons, which prevailed during the early days of the emergence of the modern life sciences, is facing a set of important challenges. The commoditization even of upstream research resources may hamper some of the most promising new scientific opportunities made possible by current advances in high throughput screening and increasing availability of full genome sequencing of entire microorganisms.[7]

The most important concern regarding culture collections is the quality management of their holdings and the associated costs. This does not only include biosecurity related issues, but also problems of cell contamination and misidentification. The German DSMZ collection (Deutsche Sammlung

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3 See http://www.wfcc.info.

4 Jerome H. Reichman, Tom Dedeurwaerdere and Paul A. Uhlir, *Global Intellectual Property Strategies for the Microbial Research Commons* (Cambridge: Cambridge University Press, forthcoming 2012).

5 Jeffrey L. Furman and Scott Stern, "Climbing Atop the Shoulders of Giants: The Impact of Institutions on Cumulative Research", NBER working paper 12523 (National Bureau of Economic Research, 2006).

6 Douglas Gollin, Melinda Smale and Bent Skovmand, "Searching an Ex Situ Collection of Wheat Genetic Resources", *American Journal Agricultral Economics*, 82 (2000), 812–27; and Bert Visser, Derek Eaton, Niels Louwaars and Jan Engels, "Transaction Costs of Germplasm Exchange Under Bilateral Agreements", FAO/Global Forum on Agricultural Research Document, No. GFAR/00/17–04-04, Dresden (2000).

7 See Reichman, Dedeurwaerdere and Uhlir (forthcoming 2012).

fur Microorganisms) estimates that approximately 20% of all cell lines used in tumour research are misidentified, and thousands of studies based on faulty cell lines have been published. This problem is not as acute for all types of microbial materials. There have been efforts to develop systematic tests for cell culture identification and certified standard reference cultures at the collections, meaning that microbiologists have been able to limit their exposure to contamination. As a consequence, quality management standards, such as ISO (International Standards Organisation) certification of collections or certification standards of Biological Resources Centres play an important role in the exchange of ex situ microbial material.[8]

A second important concern is the capacity problem of the collections and the related problem of making the appropriate conservation choices. Because of the high cost of isolation and the extraordinary scope of the microbial diversity, the main efforts have been on the collection and identification of the diversity of the microbial species with known scientific and commercial value. However, only a tiny percentage of microbial diversity has even been identified—probably less than 1%—and only a small fraction of this known diversity can actually be effectively cultured. The rest is in situ and part of it will remain that way for a very long time. Researchers are still going back to collect in situ for local microbes to be studied and bring them in the public culture collection system in ways that we do not hear about—for example, in the plant breeding world. Moreover, the situation of the public culture collections is characterized by a high level of interdependency between the various countries involved. The largest public culture collection, with approximately 25,000 strains, holds less than 2% of the total number of strain holdings of the WFCC members and only an estimated 1.5% of the total biodiversity of unique strains holdings in the WFCC collections. Intense collaboration and exchange amongst culture collections is a necessary consequence of this situation.

Social and industry needs in relation to the culture collections raise important coordination and collective action problems that have been dealt with mainly through public sector involvement in the financing of their operations. The reason for this is the evident public good nature of many of the microbial strains, such as the investment in collecting and conserving general purpose microbial resources used on a non-exclusive basis in scientific research, or the conservation of reference strains used for

8 See *OECD Best Practice Guildelines for Biological Resource Centres* (Paris: OECD, 2007), available at http://www.oecd.org/dataoecd/7/13/38777417.pdf.

quality management and biosecurity controls.

With the biotechnology revolution, however, new actors have gained influence over the microbial actors network.[9] Technological advances have increased the value of microbes by creating new commercial applications such as pharmaceutical drugs based on micro-organisms, and by lowering the uncertainty of product success. Market oriented social planners in the USA and elsewhere realized the opportunity to diminish time laps between basic research findings and commercialized products (Bartsev, Pers. Comm.). In the mid 1980s, financial pressure among PSMC mounted under rapidly accumulating stocks of microbes and governments' finances were put under increasing stress.[10] Hence the conditions existed for private cost sharing of public collections as a way for industry to access the microbe flow and to diminish time lags between innovation and consumer products.[11] A new climate of business orientation started to influence some social planners and public collections, adopting more formal exchange practices and quality management through certification, even for upstream research tools such as those held in the network of the public culture collection. The management of these new markets directly developed on the basis of public domain assets further added to the complex set of challenges that the culture collections already have to face in the global context.

To understand how this transformation of the publicly accessible research infrastructure affects the governance choices of the culture collection, we conducted a series of interviews in order to address the following research questions: Who are the actors that shape the governance choices of the public culture collections? What distinguishes the basic research tier of the publicly accessible research infrastructure from the emerging commercial tier within the PSMCs? How are the governance problems of coordination for providing essential research materials on the global scale addressed by these two tiers? A preliminary set of in-depth structured interviews were conducted with the staff of five microbial collections in Europe and Latin America. Based on the insights of these interviews, we conducted shorter structured telephone interviews with members of a large number

9 Alex Weedon, "Implementing the Microbial Commons: Legal and Institutional Perspectives", discussant presentation at the Microbial Commons conference, Ghent, Belgium (11 June 2008).

10 Dwight Baker, "Microbial Diversity and Pharmaceutical Industry Culture Collections" in *Genetic and Functional Diversity of Agricultural Microorganisms*, ed. by Jun-ichi Kurisaki, et al. (Tsukuba, Japan: National Institute of Agrobiological Sciences, 2005), pp. 56–61.

11 Furman and Stern (2006).

of collections worldwide, and a large-scale survey of member collections of the WFCC. The results highlight, firstly, the multifunctionality and public good properties of micro-organisms for users in both basic research and product development of, for example, pharmaceutical drugs. Secondly, they show that a two-tier system is developing of one traditional, more scientifically oriented kind of PSMCs, and another, more commercially oriented tier.

1. Analysing actor networks in the World Federation for Culture Collections

Actor Network Theory will be used to contrast the governance attributes of the research sector and analyse the policy implications of the two-tier regime in the PSMCs: the basic research tier with a set of governance attributes characterized by informal exchanges and reciprocity amongst researchers on the one hand, and the emerging commercial tier which has recourse to the use of formal contracts and certification of management standards.

The inherent interdependence among actors causes a complex system of interests and incentives. Actor Network analysis can be used to disentangle and simplify the different motivations in these networks.[12] In this framework, all actions are viewed as being interrelated, within and between networks. It is by inducing other actors to act in a special way that the influence is achieved, for example, by persuading other actors to enrol in the network, and to gain the right to speak on behalf of other actors. Successful "translation" happens when actors accept their roles; translation fails when it cannot overcome heterogeneous preferences and motivations. For the purpose of this study the term actor is used for non-humans in the sense of Strathern (1999), i.e. anything mobilised in the course of action. Here we consider individuals, organisations, microbes and even policies to be actors in order to acknowledge their influence on the microbe flow.

The data for studying the actor networks was gathered in close collaboration with the WFCC, which is the largest international collaboration organisation of PSMCs and United Nations Educational Scientific and Cultural Organisation's (UNESCO) Microbial Resources

12 Michel Callon, "The Sociology of an Actor-Network: The Case of the Electric Vehicle", in *Mapping the Dynamics of Science and Technology*, ed. by Michel Callon, John Law and Arie Rip (London: Macmillan, 1986), pp. 19–34.

Network (MIRCEN) with 22 member collections in industrialised and developing countries.

A survey based on a written questionnaire was organized amongst members of WFCC and MIRCEN and completed by in-depth personal interviews. 119 collections returned the written questionnaire and 12 follow-up personal interviews were organised. The written questionnaire specifically addressed the distribution patterns of the culture collections to other actors in the actor networks and aimed to quantify the relative importance of the commercial tier as expressed through the importance of formal Material Transfer Agreements and the adoption of International Standards Organisation (ISO) certification. The personal interviews with staff and researchers at the culture collections were focused on a selection of six collections in European countries, which are representative of different degrees of use of formal contracting and adherence to ISO certification. They were chosen within a relative homogeneous policy context (Europe), in order to better assess the impact of the adoption of commercial practices on the conservation and distribution choices in the PSMCs. They were completed with two interviews with officials of the umbrella organisations (WFCC and ECCO) and four interviews in developing countries to check the consistency of the results in a wider geographical context.

2. The importance of the basic research tier and the commercial tier

This section presents the analysis of the governance choices for conservation and distribution of microbial genetic resources in the PSMCs. It focuses on the identification of the players in the two major actor networks that play a role in the publicly available science infrastructure: the basic research tier and the commercial tier. The next section will analyse how these major actor networks increased or decreased in importance and assess their role in the governance choices on conservation and distribution of microbial materials.

The first question that needs to be asked concerns the role of the various actors in the organisation of conservation and distribution of strain holdings. This question was addressed in our survey amongst the WFCC members, the results of which are presented in Figure 1. The results show the significant number of new strains coming directly from in situ settings into the culture collections (37% from own collecting activities in the field

by the culture collections, and 27% from research laboratories in academia and hospitals who principally do their own collecting), the dominance of public sector transactions (77% to entities that are largely public) and the importance of reciprocity amongst collections (16% of new material comes from other public culture collections and 9% of existing material goes to other public culture collections).

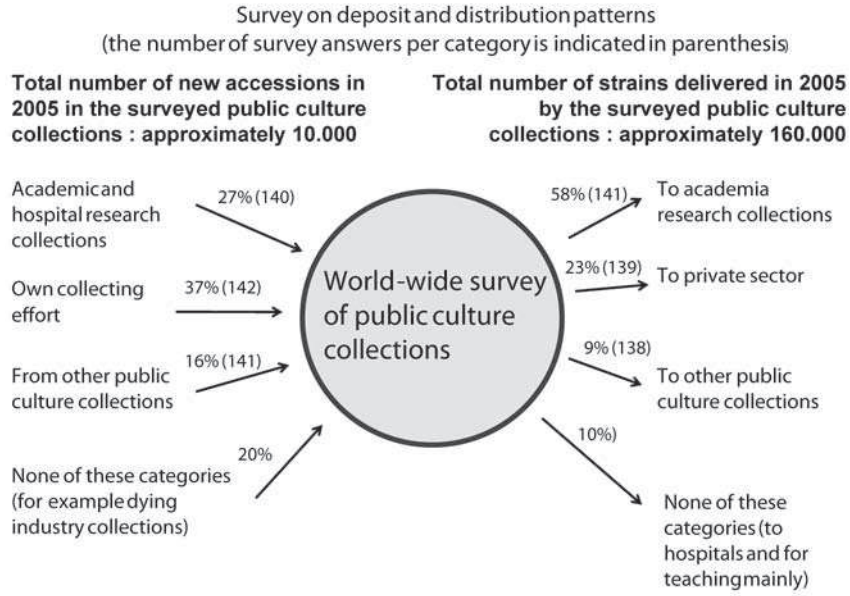

Figure 1. Providers and users of microorganisms in PSMCs

A socio-technical actor network is built around these transactions, which connect the main actors to the various user groups and ensures their influence. The quantitative survey already shows some of the direct mechanisms of influence of the main actors, mainly by mechanisms of direct reciprocity between collections and researchers. Not only do the collections help each other to complete the gaps in their own reference holdings, but they also allow other collections to further redistribute strains that they provide to them, insofar as the other collection has the capacity and the intent to do so. The influence of the industry appears clearly as an important client of the culture collections' strains.

Even if the industry client is not the most important recipient of the strain holdings, it is a vital one, because it provides a complementary income

stream to the collections, which would otherwise be entirely dependent on public funding. Moreover, the selling of strains is often complemented by other services such as identification services for industry and research contracts. The results of the survey show that of all the funding streams other than core funding, the selling of strains (both to public and private institutions) topped the supplementary income streams, followed by contract research, other services and lastly income from patent and safety deposits.

The industry clients exercise their influence not only through bringing an income stream to the collections, but also through the indirect mechanisms which are the standard procedures, technical tools and cognitive approaches imposed in the actors' networks. The original quantitative survey that was conducted for this study showed the importance of the procedures that are imported from commercial practices and adopted by the research sector. 40% of the interviewed collections received some or all of their strains through some formal agreement, either through material transfer agreements, accession forms or other contracts. Therefore, formalization is still not the major practice in the PSMCs but the major international collections obtain the vast majority of their materials through contracts and the trend is clearly in the direction of more formal contracting. A 2009 semi-structured questionnaire on exchange and distribution patterns in PSMCs shows similar results and confirms the increase in formal transactions. Amongst a group of 43 culture collections from Europe (20), America (11), Asia (5), Australia (5) and Africa (1) more than 50% used formal means of transaction in most of the cases (that is, written agreements in their accession and distribution forms); 25% never used formal means and the remaining group used them only occasionally.[13] These results were equally distributed over OECD and non-OECD collections that participated in the survey. Another indicator of the adoption of commercial standards for exchange is the use of ISO certification of management procedures. 13% out of 113 collections that answered this question of the survey had adopted the ISO certificate. The survey shows that the proportion of collections adopting certification is still substantially less than their involvement in

13 Tom Dedeurwaerdere, Maria Iglesias, Sabine Weiland and Michael Halewood, "The Use and Exchange of Microbial Genetic Resources for Food and Agriculture", Background Study Paper of the Commission on Genetic Resources for Food and Agriculture, 46 (2009); and Tom Dedeurwaerdere, "Global Microbial Commons: Institutional Challenges for the Global Exchange and Distribution of Microorganisms in the Life Sciences", *Research in Microbiology*, 161 (2010), 414–21.

scientific collaborative networks such as the European Culture Collection Organization (ECCO) or the Global Biodiversity Information Facility (GBIF). However, it is fair to say that the recourse to certification is also increasing in the culture collections' community.

3. Social motivations and incentives in the Actor Networks

Based on these results, further in depth interviews were conducted to analyse two different categories of motivations among PSMCs, in one public sector driven regime of managing and distributing microbes, and in an emerging business-oriented regime. The resulting conflict is studied through the lens of how to organise the exchange of micro-organisms based on reciprocity or based on market-based exclusive license contracts.

3.1 The traditional role of PSMCs within the research infrastructure

An important role of public collections is to distribute its microbial holdings, to make them available for present use in science or applied research or hold them as option value for future uses. For instance, traditionally microbes have been transferred free of charge to all users, including to teachers for educational purposes. This is a way to minimise transaction costs in exchanges among relatively few participants, i.e. taxonomists and researchers within, for example the same university, or in different organisations in one single country. Relatively homogeneous aims within those networks facilitate the creation of trust. The "glue" that motivates such microbe transactions is based on relationships, with high informal excludability, reputation based sanctions, and scarce use of private property rights.

In the traditional actor network, social planners support the network through financial incentives, principally core funding to enable day-to-day operation, and ear-marked support to, for example, major research projects. Financial support to traditional PSMCs is provided by governments through host organisations or through competitive grants from many different types of donor organisations including multilateral organisations such as the European Commission. Of the 423 collections registered in WFCC, the majority are university supported (42%) and

government supported (41%), with the remaining collections supported by semi-governmental organisations (8%), being private collections (4%), supported by industry (1%) and inter-governmental organisations (1%). This support is generally complemented by revenues from products and services (Smith, Pers.Comm.). Hence microbial collections are influenced by a broad set of incentives, stemming from the PSMCs' founding principles (e.g. public or for profit), type of users (e.g. researchers but also university lecturers using microbes for teaching, hospitals, academia or private sector), and the intended use of the microbes including agriculture, pharmaceutical products and bioremediation.[14]

3.2 Market creation in the public sphere

In order to secure appropriate governance of PSMCs it is important to have updated information about who funds microbe collections and for what purposes. Notably, funding for PSMCs is provided increasingly by industry and auto financing (WFCC 2005).

The complex activities of PSMCs create the need for investment in expert staff and sophisticated storage equipment. The cost of creating a new collection of about five thousand microbe strains is approximated to US$1 million, excluding the substantial costs of storage, maintenance and use.[15] As a consequence of the high costs of creating and operating collections, closures, mergers and grandfathering of abandoned collections is common.[16]

In fact the largest collections of microbes are held by the industry itself.[17] However, starting in the mid-1990s, the pharmaceutical industry has changed its basic research focus, and closed or outsourced many of its in-house collections (Garrity, Pers.Comm). Small niche public service collections provide specialised services to the industry under conditions of relative secrecy. As a consequence, property rights to microbes are changing and there may be concerns that resulting new profit incentives turn collections away from the objective of conserving sufficiently large stocks of general purpose biological materials available for exploratory and basic research.[18]

Technological advances have increased the value of microbes. This is a result of higher and more predictable value from new commercial

14 Furman and Stern (2006).
15 Baker (2005).
16 Ibid.
17 Furman and Stern (2006).
18 David Smith, "Culture Collections Over the World", *International Microbiology*, 6 (2003), 95-100.

applications in, for example, pharmaceutical drugs. With the biotechnology revolution, starting in the 1970s, three new actors gained influence over the microbe actor network: new technology, private industry, and a more business oriented way of organising public sector activities.[19] Market-oriented social planners in the USA and elsewhere realised the opportunity to diminish time laps between basic research findings and commercialised products (Bartsev, Pers.Comm.). Growing stocks of microbes made PSMCs costlier to maintain, and government budgets faced increasing stress in general.[20] A new climate of business orientation started to influence some social planners and public collections. Hence the conditions existed for private cost sharing of public collections, which gave industry access to the microbe flow and diminished time lags between innovation and consumer products.[21] Figure 2 synthesises what is shown to be the emergence of a new network, which created a two-tier system in the governance of microbes.

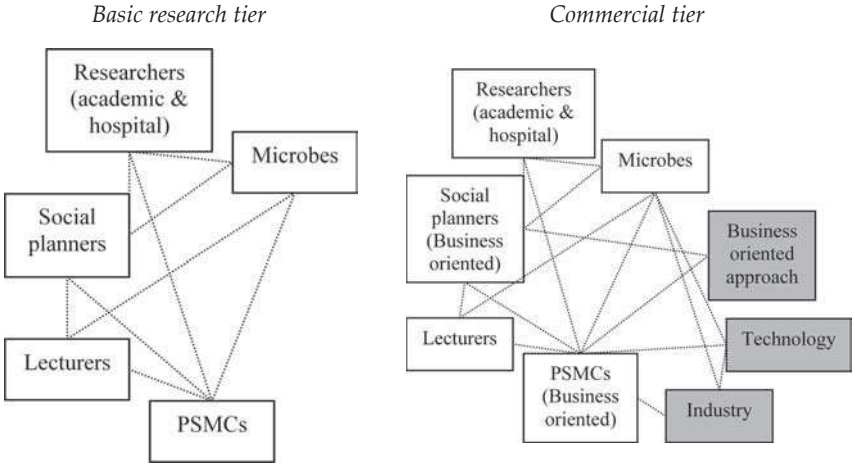

Figure 2. The two-tier actor network that translates the microbe flow in basic and applied research (shaded boxes represent new actors in the second tier)

In Table 1, the two tiers are characterised with respect to their salient attributes. Although in reality the features of the two tiers are often mixed within one collection, the dichotomy is a useful way to understand the incentives and the way PSMCs choose to govern their exchange of micro-organisms. The

19 Weedon (2008).
20 Baker (2005).
21 Furman and Stern (2006).

basic research tier has strong influence from the public sector, is rather homogenous and open, and quality signalling is based on social networks. In contrast, the commercial tier is influenced by industry and adopts a more formal and closed approach to management of the collection's holdings.

Governance attribute	The basic research tier	The commercial tier
Attributes of micro-organism transactions		
Incentives for microbe transactions based on:	Reciprocity	Markets (Fee)
Compliance mechanism for microbe transactions based on:	Social networks (reputation)	Legalistic principle (formal property rights)
Institutional attributes of the public collection		
Strong source of influence from:	Public organisation	Industry
Microbes distributed mainly to:	Public organisations	Industry
Group heterogeneity among PSMCs and demanders:	Low	High
Collaboration with other public collections is:	Open	Closed
Signalling of organisational quality is:	Social network based	Formal (ISO)

Table 1. Attributes of the microbe actor network with respect to management of micro-organisms, of the basic research tier and the commercial tier

Standardisation of management procedures is another business oriented governance mode.[22] Actors outside the traditional networks of PSMCs have difficulty in ascertaining quality of, for example, high quality microbe transfers, since they lack the social networks through which to verify the

22 Paul Milgrom and John Roberts, *Economics, Organization and Management* (Englewood Cliffs, NJ: Prentice Hall, 1992).

quality of any given PSMC. Hence standardised procedures to signal the organisational quality (ISO certification) is a way for the industry to inform their choice of PSMC from which to obtain microbes and services. This emerging quality system has been endorsed by some collections, such as DSMZ, while others continue to use informal signalling associated with the traditional actor network.

3.3 Implications for provision of public goods

This section builds on the salient attributes of the two tiers' motivations, roles and resulting ways of organising their interaction, with the view to evaluate briefly their role in microbe conservation as global public goods. In general, regarding the conservation of microbes, the issues of agreeing and building capacity for conservation of option value, monitoring of microbe populations to adapt the conservation choices, and quality control appear to be of particular relevance (e.g. Smith, Pers. Comm.; Baker 2005). PSMCs' individual efforts need to be aligned to global conservation of diversity of microbes, rather than investing in overlapping conservation efforts which generate a small total conserved diversity. In this respect, for those microbes that hold particularly strong public good properties, market signals may provide inappropriate guidance for conservation.

Coordinated action, as in the basic research tier, is well placed to manage such public good properties in contrast to markets.[23] However, heterogeneity and group size can negatively affect the scope for collective action in the coordination among PSMCs internationally. Hence, the entrance of new actors may increase the cost of certain kinds of coordination. Not only has the described entry of industry but also increased international interconnectedness emphasised this vulnerability of the basic research tier. Therefore, while the basic research tier has capability to manage public goods, this capability may become reduced by increased group heterogeneity.

However, the commercial tier has the facility to manage heterogeneous agents by deploying a standardised mode of transactions (in contrast to industry's likely difficulty in accessing trust-based networks). In the light of increased heterogeneity among microbe users it would appear that a formalised mode, based on formalised property rights and fees, is

23 Robert Cook-Deegan and Tom Dedeurwaerdere, "The Science Commons in Life Science Research: Structure, Function and Value of Access to Genetic Diversity", *International Social Science Journal*, 188 (2006), 299–318; and Charlotte Hess and Elinor Ostrom, "A Framework for Analyzing Governance and Collective Action in the Microbial Commons", paper presented at workshop on exploring and exploiting microbiological commons, Brussels (7–8 July 2005).

well-aligned to the emerging needs of servicing different users and possibly to decrease lead times between basic research and applied products.

In sum, the basic research tier is well placed to manage information flows needed for the overall coordination of the conservation efforts, while the commercial tier can contribute with formal measures of microbe transfers, and ascertain administrative quality.

In this chapter we have studied the suitability of different institutional designs to manage the conservation of and access to micro-organisms worldwide. Traditionally, microbes have been managed by publicly funded microbial ex situ collections. However, commercial users have come to influence the governance of the flow and diversity of microbes in ex situ collections.[24] By using Actor Network Theory, we argue that the resulting phenomenon can best be described as market creation in the public sphere. Pharmaceutical and other biotechnology firms introduce market incentives, based on formalized property rights. This has important implications: while such commercial co-financing of the microbial flow secures short term input to applied research and product development, the question remains how the collections' long term strategies to meet societal needs are affected. The risk, of course, is that short term market incentives encroach on longer term conservation priorities. Hence, instead of as now having the commercial tier increasing its influence of the basic research tier, the social planner must strengthen the basic research tier in a way that does not impede many of the attributes of market orientation that lead to high effectiveness.

24 See, for example, Reichman, Dedeurwaerdere and Uhlir (forthcoming 2012).