Research Policy 45 (2016) 1031–1045

Contents lists available at ScienceDirect

Research Policy

journal homepage: www.elsevier.com/locate/respol

Knowledge integration using product R&D outsourcing in biotechnology

Dzidziso Samuel Kamuriwo*, Charles Baden-Fuller

Cass Business School, City University London, 106 Bunhill Row, EC1Y 8TZ London, United Kingdom

ARTICLE INFO

Article history:
Received 11 November 2012
Received in revised form 15 February 2016
Accepted 26 February 2016
Available online 14 March 2016

Keywords:
Product systems
R&D outsourcing
Knowledge integration
Product systems capability
Inter-firm coordination mechanisms
Biotechnology

ABSTRACT

We build on systems integration literature to explain how and why knowledge integration of non-modular products is based on a strategic choice between internalizing and outsourcing core R&D. The under-researched choice of outsourcing core R&D on an on-going basis appears to face risks of higher transactions costs and loss of control. We illuminate these choices in a comparative analysis of two longitudinal cases that compare an internally focused R&D intensive firm and an externally focused R&D intensive firm; and we show how the externally focused approach can avoid risks by framing non-modular outsourcing as modular even though it is not so and by engaging in a social process of communication to achieve a common agreement between partners concerning the direction of efforts and thus effectively reduce highly iterative knowledge exchange between modules. Our findings add to our understanding of the systems integration literature; the nature of firm product system strategies, as well as firm boundaries in a knowledge economy.

1. Introduction

There is an increasing trend for new products to be developed in networks of specialized firms because the pace of technology development is so fast that no single firm can have the resources to handle all the necessary development in-house (e.g. Powell et al., 1996; Rothaermel and Deeds, 2004; Hobday et al., 2005). In these networks, a focal firm takes on the "role" of product system integrator. This role involves dividing up and allocating innovation and manufacturing tasks along the value chain to network partners or in-house teams and putting in place relevant structures and controls (e.g. Hobday et al., 2005; Brusoni and Prencipe, 2011).

Hitherto, studies of product system integrator roles have focused on modular products. Modular products can be decomposed functionally, spatially and physically thereby defining precisely the link between components in a way that allows interfaces to be specified beforehand (e.g. Brusoni et al., 2001; Hobday et al., 2005; Brusoni and Prencipe, 2011). Modularity facilitates cost effective outsourcing because on-going partner interdependencies can be coordinated efficiently. Roles (that define the part played by each actor) are agreed on the basis of modules; and decision rights are agreed on the basis of accountability or responsibility, and the necessary empowerment achieved module by module. In addition, because module interfaces are fully specified there is timely, relevant and credible communication between module actors (e.g. Sanchez and Mahoney, 1996; Pavitt, 1998; Brusoni et al., 2001). In the case of a modular system, the product system integrator needs a diverse scientific and technological knowledge base sufficient to support the necessary knowledge flows and cross-domain linkages, but not so great as to know everything that is undertaken by partners (e.g. Cohen and Levinthal, 1990; Powell et al., 1996; Prencipe, 1997; Brusoni et al., 2001; Chesbrough, 2003; Padgett and Powell, 2003; Rothaermel and Deeds, 2004; Rothaermel et al., 2006). By knowledge base, we mean the bodies of knowledge or understanding and practice that underpin product design and manufacturing efforts which the product system integrator has mastered i.e. can generate, use or interpret independent of its partners (e.g. Pavitt, 1998; Brusoni et al., 2001).

What is less understood and less researched are the considerable challenges that product system integrators face in outsourcing development work for non-modular high technology products which are underpinned by knowledge which is complex, ambiguous and highly tacit – such as biotechnology drug development (e.g. Rothaermel and Deeds, 2006). By complex knowledge we observe the (large) number of interdependent routines, individuals, technologies, skill sets and resources that must be linked to a particular knowledge asset (Reed and DeFillippi, 1990). Knowledge is ambiguous in the sense that the links between the knowledge and the desired outcome of a commercially viable product are

* Corresponding author.
E-mail addresses: d.s.kamuriwo@city.ac.uk (D.S. Kamuriwo), c.baden-fuller@city.ac.uk (C. Baden-Fuller).

http://dx.doi.org/10.1016/j.respol.2016.02.009

unclear (Simonin, 1999). Knowledge is highly tacit in that it is rarely made explicit in the rapidly changing context of high technology product development (and it may not be possible to make it explicit).

This means that there are challenges to outsource knowledge for non-modular high technology products even when the product development process follows distinct stages along the value chain. The product system integrator has to cope with dense knowledge flows within and across product development stages and across domain linkages (e.g. Padgett and Powell, 2003; Brusoni and Prencipe, 2011); and has to face high coordination costs and a high risk of appropriation or opportunism in alliances (e.g. Chesbrough and Teece, 1996; Cassiman et al., 2005). The development process is also likely to have complex overlapping division of labor, needing regular and costly mutual adjustments that are not easily resolved in an alliance setting (e.g. Padgett and Powell, 2003; Schreiner et al., 2009). Hence in non-modular contexts, it will be difficult to achieve clarity in the role allocations and delegation of decision rights necessary for efficiency in managing on-going partner interdependencies (e.g. Schreiner et al., 2009).

To address the aforementioned challenges, we suggest that a product system integrator has to take a strategic choice which is likely to be influenced by the predominant learning approach it has taken or expects to take with alliance partners (e.g. Grant and Baden-Fuller, 2004; Hoang and Rothaermel, 2010). The first strategic choice requires that the product system integrator internalize and integrate development stages and R&D under hierarchical control for efficient integration and to save on coordination costs and limit expropriation concerns (e.g. Chesbrough and Teece, 1996; Grant, 1996; Cassiman et al., 2005). In this strategy, external engagement by the systems integrator is largely confined to either non-core work, or to specialized or independent knowledge and complementary knowledge required to augment or spur internal efforts (e.g. Chesbrough and Teece, 1996; Cassiman et al., 2005).

In contrast, the second and more externally focused knowledge strategy is that the product system integrator will commit to accessing core knowledge and development externally on an on-going basis and to somehow mitigate the anticipated higher transaction costs and risks of loss of control it faces when engaging external partners for product R&D (e.g. Lorenzoni and Baden-Fuller, 1995; Grant and Baden-Fuller, 2004).

We therefore ask how and why product system integrators who externalize non-modular core R&D knowledge on an on-going basis develop successful products comparable to internally focused product system integrators. Additionally, how and why are they not held back by expropriation and coordination costs concerns?

We study these questions in a research setting of high knowledge intensity – namely biotechnology firms that interact to discover and develop drugs (e.g. Powell et al., 1996; Schweizer, 2005). Our research employs a longitudinal case study approach that compares two biotech specialist drug development companies that are representative of each product system integrator's strategy choices: one that is internally focused in its R&D (e.g. Cassiman et al., 2005); and another that is externally focused i.e. outsources its core R&D on an on-going basis. We examine over seven years, the development of each firm's knowledge, how their partner networks are developed and the coordination mechanisms the two strategies employ to make knowledge integration a success – thereby shedding light on the "role" of a product system integrator.

We find that the externally focused firm's own knowledge base though limited, can be complemented by speedily accessing external partners' knowledge to successfully support innovative product development. The network structure is developed by outsourcing development stages to external partners – a division similar to that which is employed in modular systems. Coordination is exercised sequentially over stages where roles and decision rights are conferred to partners with capacity to undertake core R&D. In order to reduce the amount of knowledge exchange between stages it is helpful to achieve a common agreement concerning the direction of efforts. We hypothesize that this is done through a social process of communication. That is, the main role of communication in this product system is to shape the efforts of partners rather than to transfer knowledge. Communication which builds a common socialization and offers leadership from the center mitigates problems of contract incompleteness and conflict of interest with the extended range of partners to whom core R&D is outsourced. We explain in some detail what each of these elements involve both conceptually and empirically.

Our study deepens existing knowledge and reaches well beyond past studies that have been based on cross sectional data and perceptual measures (e.g. Fey and Birkinshaw, 2005; Jansen et al., 2005; Cassiman and Veugelers, 2006), and have failed to capture the different ways in which organization practices are used as knowledge integration capabilities. The study also highlights important implications for commercializing technology from academic and public research labs which will often need particular integration capabilities to actually make them work.

The remainder of this paper is organized as follows: Section 2 presents a literature review, and Section 3 describes our methods. Section 4 presents the case description and in Section 5, we explain how and why both product systems succeed; with conclusions presented in Section 6.

2. Literature review

When a product system integrator develops cutting edge products in networks of specialized firms, it acts as the knowledge integrator, bringing together relevant partners and choosing where and how to collaborate (e.g. Prencipe et al., 2003; Hobday et al., 2005). As noted in the introduction, hitherto the product systems integration literature has focused on modular products in which functions can be associated clearly with particular product components and the interfaces between components are stable and fully specified (e.g. Sanchez and Mahoney, 1996). Modularity thus ensures cost effective outsourcing and coordination of outsourced components to partners. In addition, the literature notes that the role of product system integrator extends beyond mere direction, it has to sense and understand how and whether changes across components have a negative or positive impact on knowledge integration during product development. This requires a well-developed diverse knowledge base that comprehends the development of individual components, as well as knowledge underpinning the development of the product architecture (e.g. Henderson and Clark, 1990; Brusoni and Prencipe, 2011).

There is, however, a gap in our understanding for the non-modular context. Although non-modular high technology products may be developed in distinct development stages, the underlying knowledge does not have fully specified interfaces and so requires a different outsourcing approach. The challenge is amplified when there are differences in technology development rates between developmental stages (e.g. Prencipe, 1997); uncertainty in knowledge-product linkages, and underspecified interdependences between product development stages. Therefore the product system integrator has to frame its learning approach in its alliances carefully, so as to manage dense knowledge dependencies across components and domains (e.g. Grant and Baden-Fuller, 2004).

For an internally focused strategy, the density of interdependencies *between* domains or components and *within* domains or components is high. Hence the internally focused product system

employs hierarchical control to economize on coordination costs and to reduce risks of expropriation and opportunism (e.g. Cohen and Levinthal, 1990; Grant, 1996; Rothaermel and Deeds, 2006).

The externally focused product system integrator accesses partners' R&D expertise on an on-going basis, without necessarily having a primary desire to internalize that knowledge (e.g. Grant and Baden-Fuller, 2004); and this is underexplored in literature. The extant literature gives strong clues about an externally focused product system integrator's role – i.e. it has to avoid high coordination costs and high risks of expropriation and opportunism (e.g. Chesbrough and Teece, 1996; Grant, 1996). This means that it has to consider (1) the number and type of partnerships in the firm's network (e.g. Lane and Lubatkin, 1998; Baum et al., 2000; Rothaermel and Deeds, 2004; Hobday et al., 2005) and (2) the coordination mechanisms required for managing on-going partner interdependencies and the conveying of knowledge across firm boundaries (Rothaermel and Deeds, 2006). And in making these decisions, the integrator's role is to assemble an alliance portfolio where: (1) the partnerships are mutually compatible with the focal firm and with each other and that they are all supportive of the mission, and (2) there are appropriate firm level monitoring mechanisms to coordinate activities and knowledge flows across individual partnerships (e.g. Hoffmann, 2007). Because these differences are likely to be greater in upstream (early stage – explorative) activities than in mid-stream (mid-stage) activities, and because downstream (late stage – exploitative – close to market) activities are likely to be undertaken by partners that have well developed systems to deal with partner interactions, we can anticipate the coordination efforts required for product system integration roles will be greater in activities involving upstream than mid- and downstream partners (Rothaermel and Deeds, 2006).

All of the above points explain what the product system integration role involves, but do not tell us how the system integrator solves the coordination and monitoring challenge. Solving this problem requires understanding two different but interrelated organizational design decisions concerning role allocation and delegation of decision rights (Jansen et al., 2005; Schreiner et al., 2009; Foss et al., 2011). Role allocation is specifying the part that an alliance partner or the focal firm plays in task execution. Delegation of decision rights is the assignment of accountability or responsibility for task completion and the empowering of the assigned party with the authority to make particular decisions. For example, the decisions necessary for execution of the task as agreed between the contracting parties or concerning changes or priorities involving the process or project (e.g. Schreiner et al., 2009; Foss et al., 2011).

Unclear roles and responsibilities impede the firm from effectively managing inter-dependencies between partners through on-going coordination and from dealing with inevitable unforeseen contingencies (e.g. Van de Ven and Polley, 1992; Arino and De la Torre, 1998; Madhok and Tallman, 1998; Poppo and Zenger, 2002; Luo, 2006). The clarity of role allocation and delegation of decision rights depends on the extent to which dependencies between product components or knowledge domains are stable and predictable.

When managing on-going partner interdependencies, relevant information and knowledge needs to be communicated with partners effectively, credibly and at minimal cost (e.g. Mohr and Spekman, 1994; Ring and Van de Ven, 1994; Das and Teng, 1998; Dyer and Singh, 1998; Park and Ungson, 2001). Effective communication – defined as the 'formal as well as informal sharing of timely and meaningful information between firms' (Anderson and Narus, 1990: 44) – occurs when it assists in building a shared understanding of obligations and engagement rules between partners that enables effective cooperation (e.g. Klimoski and Mohammed, 1994). Communication may also reduce the negative effects of information asymmetry in alliances (e.g. Schreiner et al., 2009). A key communication mode is formal communication, such as scheduled project review meetings which are specified contractually in the formal governance structure of collaborations or alliances. Formal meetings provide essential assessment and feedback points for R&D managers (e.g. Uzzi, 1997; Jansen et al., 2005; Schreiner et al., 2009; Foss et al., 2011). However, previous research has also found that informal communication – often conducted in social settings between diverse R&D teams – to be critical, as contracts are necessarily incomplete (e.g. Grossman and Hart, 1986) and cannot specify in advance all the communication content that may be required in a collaboration.

Conducive social settings and relations underpin any kind of commercial and contractually-based relationship (e.g. Padgett and Powell, 2003) and are developed through social bonding (e.g. Schreiner et al., 2009) – mutual attraction and psychological linkages between individuals and firms. Social bonding is embedded in professional relations and friendships based on reciprocity involving exchanges of different types depending on social and cultural contexts to create and maintain relations (e.g. Padgett and Powell, 2003). Social bonding can be used as a conduit for creating and maintaining expectations of mutual cooperation, sharing of knowledge for mutual benefit in alliances or for conflict resolution and to help firms in an alliance to adapt as required in the face of changes (e.g. Klimoski and Mohammed, 1994). Social bonds are created and maintained when individuals or firms expect to derive (1) some instrumental value from their partners, such as getting access to resources that help further one's own interests (e.g. Schreiner et al., 2009), and/or (2) expressive benefits, for example, to establish and maintain reputation (within and between organizations), or getting recognition as a legitimate member of a subgroup or firm (e.g. Brusoni and Prencipe, 2011). Examples of activities that build social bonds 'include providing reliable and timely responses to a partner's work-related needs, being proactively responsive to its concerns, spending time on *connecting* with a partner and remaining in frequent contact, as well as attending seriously to their views, ideas, and circumstances so as to signal respect and appreciation for the other' (e.g. Schreiner et al., 2009: 1402). Often the social bonding process involves going beyond the call of duty and foregoing doing things for only short term gains (e.g. Schreiner et al., 2009). When social bonding is built through socialization processes, individuals (and firms) become psychologically linked together in pursuit of a common goal and evoke in each other norms of reciprocity that facilitate their work.

So, taken together, although the literature has identified (a) the steps that the product system integrator has to undertake in forming its alliance structure, and (b) the considerations it has to make regarding the three constituent parts of the coordination mechanisms required – role allocation and delegation of decision rights, communication and social bonding – it has not clearly explained how these elements work differently depending on which strategy product system integrators adopt with regard to knowledge development. In particular, it has not explained how the coordination mechanisms of product system integrators that externalize their core R&D knowledge solve the huge anticipated coordination issues involved on an on-going basis.

Put another way, the above knowledge tells us what matters, but it does not really answer the question "Will it work in reducing transactions costs and solving coordination difficulties?". So, this study explores how and why product system integrators that build knowledge using different R&D outsourcing strategies develop knowledge bases that support successful knowledge integration. We also explore how product system integrators adopting such different strategies develop their partner networks differently and utilize different but appropriate coordination mechanisms to support their knowledge integration capabilities while minimizing coordination costs. Fig. 1 depicts this conceptual

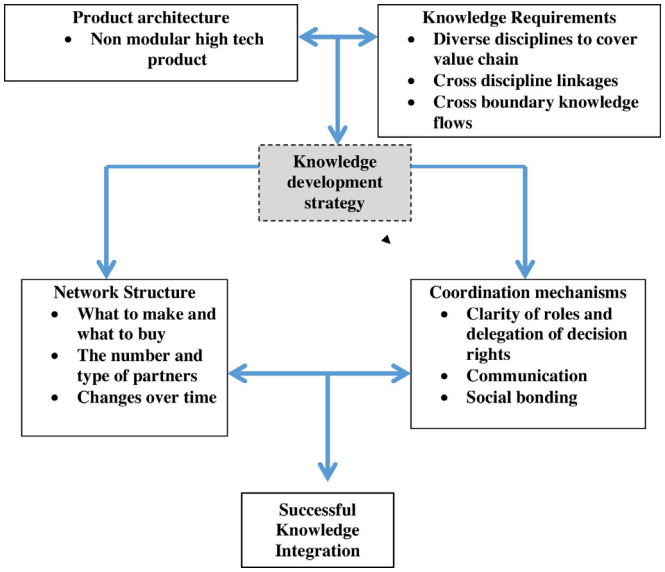

Fig. 1. Conceptual framework for successful knowledge integration in biotechnology.

framing, and shows the factors product system integrators take into account in successfully integrating knowledge in non-modular contexts.

We use case studies to illustrate these different development patterns and have chosen the biotechnology sector as our setting. We operationalize the concepts highlighted above and measure (a) the extent to which each firm develops their knowledge – diversity, amount and quality of knowledge and how each firm facilitates relevant knowledge flows across boundaries (b) the trajectory of the development of the firm's partner network – the number and type of its partners and what knowledge is accessed from each; and the direction of that trajectory – how the variables change over time, (c) the coordinating mechanisms each firm employs (e.g., allocation of roles and delegation of decision rights and how each firm communicates and develops and uses social bonds to facilitate communication and minimize its coordination efforts and costs).

3. Methods

3.1. The case study – basis of sampling

Past research looking at small firms' product development strategies generally (e.g. Ebben and Johnson, 2005) and at biotechnology's drug development sector in particular (e.g. Haagen et al., 2007) suggests that there is a bipolar distribution of firms' knowledge building strategies. In the first strategy, firms build internally organized R&D as their core capabilities (e.g. Powell et al., 1996; Rothaermel and Deeds, 2004); in the second strategy, firms design their R&D efforts internally, but outsource the specific work to their external partners (e.g. Cavalla et al., 1997; Haagen et al., 2007; Chakma et al., 2009; Sabatier et al., 2010). Our own detailed evidence on the UK sector reveals that, of a sample of 68 drug discovery firms in the UK (which between them account for over 80% of products under development), almost two thirds adopted the first strategy (i.e. the internally focused R&D approach) and the others adopted the second. We found no examples of firms following hybrid strategies i.e. mixing the two knowledge building approaches for different projects within the same firm. This bipolar distribution has been observed not only in the UK, but also in France (e.g. Sabatier et al., 2010), Germany (e.g. Haagen et al., 2007) and the USA (e.g. Chakma et al., 2009). Therefore, the externally focused strategy for organizing R&D is not an outlier but is quite prevalent and becoming increasingly so.

Given the two contrasting pools of firm types, we followed a theoretical sampling approach and identified two firms which were exemplars of each of these two knowledge development strategies (Miles and Huberman, 1994; Siggelkow, 2007). As is explained in more detail below, we then investigated and tracked the two firms using interviews, internal documents and other external sources to identify their organizational processes, mechanisms and logics. To limit bias and retrospective sense making, our interviews involved numerous highly knowledgeable informants, as well as managers from different hierarchical levels and functional areas (e.g. Eisenhardt and Graebner, 2007).

Our sample case companies – anonymized as Avertical and Ehub – are UK based dedicated biotechnology firms, both founded in 1998. Avertical's product development approach involved building an extensive R&D laboratory and hiring in-house scientists (over eighty full time employees by 2005) to cover the range of value chain activities required for its product development efforts, as well as accessing specific knowledge elements externally through alliances and contracting (see Table 1). Ehub, on the other hand, hired comparatively few staff, all highly experienced executives (nine by 2005) who designed its R&D studies – in collaboration with carefully selected partners – and then outsourced all relevant R&D activities, firstly on a local and then, progressively, on a global basis (see Table 2). The progress of both firms was highlighted by outside commentators as they successfully negotiated the pre and post-millennium 'boom and bust' periods.

3.2. Data collection

We collected data through 27 interviews and secondary sources (see Table 3 for a detailed breakdown of the data sources, types and their use in analysis). The interviews were with management team members in the two case firms, industry experts and managers at other related companies such as service firms and venture capitalists. The interviews included seven follow up interviews as well as visits to the company premises and (often iterative) telephone and email contact over a three-year period.[1] All key interviews with the two subject companies were transcribed: in other cases we usually used recordings, but sometimes only took detailed notes.

We supplemented the primary and secondary interviews with data from company documents, including detailed financial reports of the companies (filed for each year of each firm's existence), some internally produced product profile reports, archived press releases, a history of all of each company's deals as recorded internally and checked with Bio Century Database, websites of the companies and via other web searches. We searched the US patent office database for all their patent applications (whether granted or not) and studied the patent reports and applications to retrieve content, inventors, technology classes, citations, etc. We also searched for all research articles published by the companies' scientists and by those linked to the companies through sponsorship and other formal collaborations, which allowed us to trace publications about their research collaboration exhaustively, and yielded additional information about their research collaborators and patterns of engagement.

[1] We conducted 6 interviews at Ehub with all senior managers, plus 3 follow up interviews with three of them after about a year. We conducted 5 interviews with the top managers at Avertical, plus 4 follow up interviews with four of them about a year later. We interviewed 4 managers at service companies that dealt with the companies, 2 biotech industry consultants and 3 biotech venture capitalists.

Table 1
Avertical summary company description.

Time period	1998–2000	2001–2003	2004–2005
Number of employees			
Admin	1	13	13
R&D and operations	9	66	70
Total operating exp/year	£1.2m	£9m	£12m
Funds raised	£1.5m	£18m	£20m
Patents granted (13 applications: all patent inventors were company employees)		2	
Knowledge stocks	Intellectual property (IP) from founding university; technology platform and data; experienced founders: six prominent scientists	Hired 2 experienced R&D managers including new CFO; acquired genetic company	Hired 2 experienced R&D managers
Product pipeline	2 main projects: antivirals and antibacterial at discovery stage	Lead candidate in preclinical stage and 3 others in lead optimization stages	Lead candidate in clinical Phase I; one candidate in preclinical stage and 2 others in earlier stages
External partnering			
Alliances	7	2	1
Contracting			5
Publications total		6	7
Internal research effort		1	1
Co-authored – univ/rl		1	3
Co-authored – company		1	
Sponsored research – univ/rl		3	3

Table 2
Ehub summary company description.

Time period	1998–2000	2001–2003	2004–2005
Number of employees			
Admin	1	4	6
R&D and operations	1	1	3
Total operating exp/year	£1.2m	£1.2m	£4m
Funds raised	£2m	£12m	£20m
Patents granted (14 applications – all patent inventors were NOT firm employees but employees of partner firms)		2	4
Knowledge stocks	IP from NERC; hired experienced managers	Hired experienced managers including new CEO	Hired experienced managers including new CFO
Product pipeline	4 possible projects at discovery stage	Lead candidate in preclinical stage and 3 candidates in earlier stages	Lead in Phase I; 2 other candidates in preclinical stage and one in earlier stages
External partnering			
Alliances			
Contracting	5	9	14
Publications total	2	7	5
Internal research effort			
Co-authored – univ/rl			1
Co-authored – company			
Sponsored research – univ/rl	2	7	4

Table 3
Data sources and their use.

Data sources	Type of data	Use in the analysis
Semi-structured interviews (27 interviews in total)	*Interviews at Ehub*: 6 interviews at Ehub with all 6 senior managers, plus 3 follow up interviews with three of them after about a year *Interviews at Avertical*: 5 interviews with the top managers at Avertical, plus 4 follow up interviews with four of them about a year later *Interviews with other relevant actors*: 4 managers at service companies that dealt with the companies, 2 biotech industry consultants and 3 biotech venture capitalists	*Reconstruct* how R&D was organized *Reconstruct* the historical, organizational and institutional context within which R&D organization decisions were taken and implemented *Integrate and cross check* accounts from managers with those from partners or other industry experts
Secondary sources	*Company documents*: detailed financial reports of the companies (filed for each year of each firm's existence), product brochures *Press releases for each firm*: for the years 1998–2005 and all company deals from BioCentury Database *Patents:* applications and granted for the years 1998–2005 in the US patents office *Scientific publications:* company affiliated and sponsored research for the years 1998–2005	*Support, integrate and cross check accounts* from semi-structured interviews *Gather information* on partners, knowledge metrics *Track media* coverage of the development of each firm and its partnerships and deals

Table 4
Internal and external knowledge sources by value chain stage in Company-Avertical and Company-Ehub.

Value chain stage	Avertical with examples	Ehub with examples
Drug discovery: (1) target ID and validation; (2) lead screening; (3) lead optimization	Hired scientists and developed a well-equipped laboratory, but also developed alliances with 4 universities and 7 service and biotech companies. "*In biology terms, we have a strong cell biology group, strong virology group, molecular biology support*" "*Our early collaborations with Inpharmatica, Tripos and Replizyme provided us with small areas of expertise that we later on filled in-house*"	Hired a highly experienced R&D executive who designed studies and outsourced R&D work to 5 universities. "*At our peak in the early phases we had access to six scientists at Oxford University. We also worked with four or five academic researchers around the world*"
Preclinical trials (medicinal/pharmaceutical chemistry, toxicology, animal model studies, etc.)	Hired scientists in relevant disciplines and developed laboratory further. Hired senior R&D managers. Made three alliances with biotechnology firms. "*We can do combinatorial chemistry, we can do medicinal chemistry, we can do scale up chemistry, so we can supply material for preclinical development, so we can take it to a certain stage. We have the ability to do chemically almost anything*"	Hired executive with R&D experience. Continued development of lead candidate drugs with external partners – specialist service companies and public research laboratories. "*We worked with companies that specialized in manufacturing materials and companies that specialized in analyzing and all these kind of things we did externally*"
Clinical trials	Hired two experienced R&D managers to manage the outsourcing of work to major contract research organizations. "*We actually manage our outsourcing very actively, we design the studies, manage them very closely, and influence very much what's being done. CROs are always, however much you talk to them, more distant from a company's requirements*"	Hired two experienced R&D executives to manage the outsourcing of work to contract research organizations and public research laboratories. "*Initially we went to one of the big contract research companies, Quintiles*"

3.3. Case analysis approach

Our analysis was based on a systematic investigation of sample cases (e.g. Chandler, 1962), with the overall aim of trying to understand how R&D was organized in the case firms. Data to support underlying variables under investigation was based on both quantitative and qualitative evidence obtained and triangulated from multiple sources (Jick, 1979) in a process designed to add an extra layer of respondent validation (Silverman, 1993). Information obtained from each contact or secondary source was summarized against target questions and constructs: these summaries were used to identify gaps in information that could be filled by further on-going interviews or other pertinent secondary sources (e.g. Miles and Huberman, 1994). The analysis across the two cases broadly compared their knowledge building approaches based on the biotechnology product development stages defined by Rothaermel and Deeds (2004).

We noted which R&D product development stages were developed in-house and which were outsourced. We longitudinally tracked each firm's R&D product development systems and used tabular data displays to understand each firm's R&D organization as a stand-alone entity. As we were comparing two case firms that integrated knowledge successfully, cross case comparison also identified and verified *which* knowledge was integrated in each case. So we constructed tables that compared several product development stages using their value chain categories across the two cases, and also noted similarities and differences between the cases, juxtaposing qualitative and quantitative evidence to ensure that our conclusions were stronger and better grounded.

In the next sections we present our detailed case descriptions and findings. Section 4.1 is a brief comparison of the two firms' product system strategies and presents the differences in their internal and external knowledge sources at each value chain stage through which new products are developed. Sections 4.2 and 4.3 present in detail each firm's knowledge development pattern. In Section 5 we discuss how and why product system integrators as typified by our findings in the case studies integrate knowledge through R&D outsourcing successfully.

4. Case description

4.1. Comparing the two firms' knowledge development patterns by analyzing value chain stages

We employ the standard (pharmaceutical) industry value chain classification to analyze the extent of each firm's investment in particular product development stages,[2] and follow Rothaermel and Deeds (2004) classification of the biotechnology product development value chain, and we report the results of our analysis in Table 4, and discuss them in detail below.

4.2. Avertical's knowledge development system

At its founding in 1998, Avertical's target markets within the class of anti-infective medicines were the sub-segments of anti-viral and anti-bacterial drugs.[3] By 2003 Avertical had developed a portfolio up to 8 projects with a 50–50 focus on the two main therapeutic sub-segments as shown in Fig. 2. After 2003, Avertical refocused its portfolio to only anti-viral products, and shelved its anti-bacterial programs altogether, because the anti-viral programs

[2] We used the standard industry classifications – e.g. Giovannetti and Morrison (2000): 46–47 – that consists of the following distinct stages: (1) drug discovery; (2) pre-clinical trials; (3) three sets of clinical trials; (4) FDA review and approval; (5) Launch – post-marketing testing, manufacturing, distribution. We also noted that the discovery stage has three sub stages: (1) target ID and validation; (2) lead screening; (3) lead optimization. The preclinical stages require capabilities in testing drug candidates but also areas of specialized medicinal/pharmaceutical chemistry, toxicology, etc.

[3] Anti-infective drugs are those that kill an infectious agent or inhibit it from spreading. Anti-viral and anti-bacterial drugs are sub-classes of medication designed to treat viral or bacterial infections respectively.

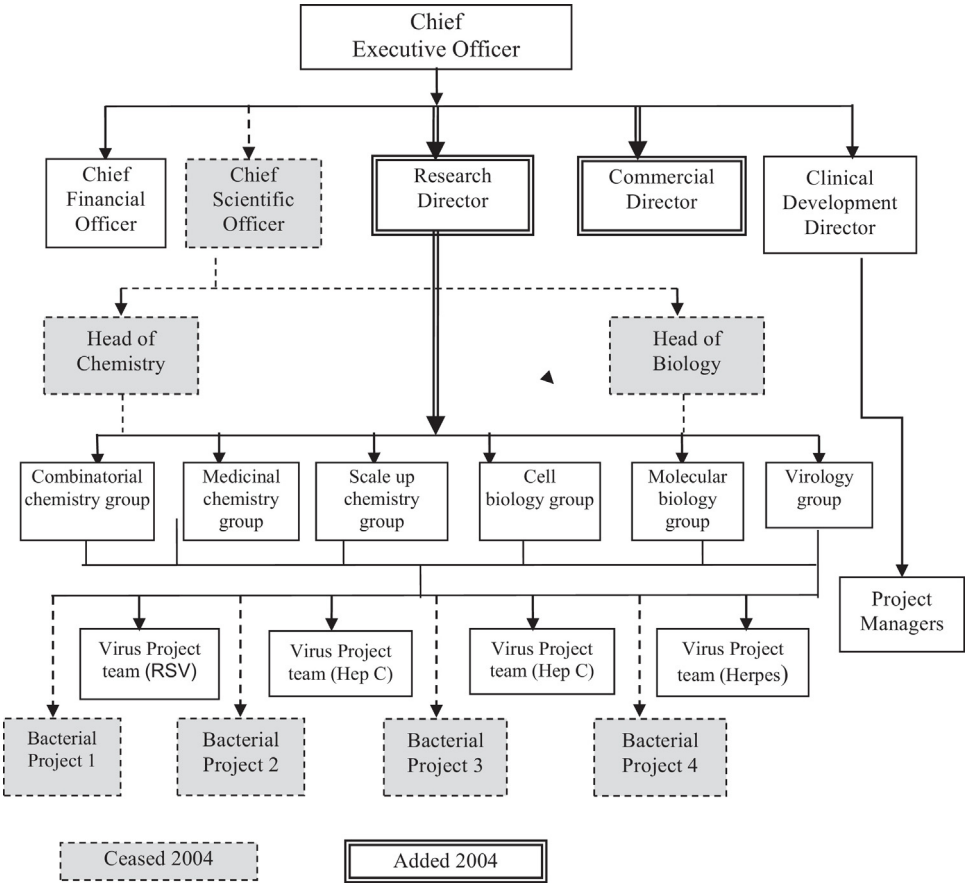

Fig. 2. Organization chart showing key capability areas of Avertical.

were making faster scientific progress. This shift meant reorganizing the company, downsizing R&D staff numbers from a peak of 70 in early 2004 to about 50 by late 2005, and adopting a flatter organizational structure by removing a whole layer of management (see Fig. 2). After this move, according to senior managers, Avertical's R&D capabilities were '*at the cutting edge of science*' and targeted '*novel markets*' and its lead therapeutic 'RSV'[4] was a novel 'first in class' drug candidate. Assessing Avertical's situation suggests it was developing high technology (using the Hobday et al., 2005, classification) and that the knowledge that underpinned the development of its products was complex and ambiguous (e.g. Rothaermel and Deeds, 2006).

Table 4 shows, Avertical initially (i.e. 1998–2000) depended on seven external partners for its upstream activities and (after 2000) progressively developed core in-house R&D capabilities. Its upstream R&D partners were three small companies: Inpharmatica (a specialist provider of bioinformatics data), Tripos (Avertical's supplier of chemistry in its early days) and Replizyme (a specialist assaying service provider); and four universities that provided specialist services, including chemistry and assaying. As its CEO explained, these early collaborations '*provided us with small areas of expertise that we later on filled in-house*'.

Within a few years of its founding (i.e. 2000), Avertical had developed a wide range of in-house R&D capabilities to tackle both upstream and mid-stream activities: as its Research Director explained:

> '. . .we are not limited to a specific functionality like some companies. . .we have the ability to do chemically almost anything. In biology terms, we have a strong cell biology group, strong virology group, molecular biology support. . .'

Avertical also had three mid-stage collaborations – with Virogen Inc., Triangle Pharmaceuticals and Acambis – exchanging intellectual property rights (IPR) and sharing development costs – a stance that was in line with its predominant learning approach in alliances i.e. engaging with partners with knowledge transfer as the goal. Avertical's learning approach in alliances, role allocation and delegation of decision rights was also evident in the terms of agreements to exchange IPRs, where each firm would pledge to use their internal capabilities to incorporate the other's IPRs, and to choose – independently – promising technology that they would jointly fund going forward.

Avertical's managers believed that having in-house upstream core R&D capabilities allowed the firm to make changes quickly in response to new evidence, communicate findings easily, and build an environment where the co-located scientists from multiple disciplines can exchange ideas easily – often informally but overall in keeping with its predominant learning strategy where the focus was to spur internal knowledge development. As one of Avertical's managers said:

> '. . .we need to have chemists and biologists to be working in the same building, having coffee together and talking. And that's how we get good research on-going.'

Avertical took a different approach to managing its downstream activities; all of which were outsourced and managed by senior project managers. The CEO explained that the UK funding

[4] Respiratory syncytial virus (RSV) causes infection of the lungs and breathing passages, and is a major cause of respiratory illness in young children.

environment made it impossible for a small venture to finance late stage development capabilities in-house – i.e. to conduct clinical trials, manufacture and market their products. However, since large pharmaceutical companies have very sophisticated organizations for late stage clinical development, manufacturing and marketing, but relatively poor research productivity, Avertical saw itself as a good strategic complement to such companies: as the CEO explained:

> 'I see us as a company providing that expertise in the early stage research. And the large Pharmaceutical companies providing us with expertise in late stage development and the marketing expertise so that we don't have to. . .which is the major expense in drug development.'

Avertical had a consistent policy toward managing its partnerships. Each major external partnership had an oversight board with overall strategic responsibility for the deliverables in the agreement and there would be regular oversight meetings at which key stakeholders would present progress reports. These structures allowed team members to meet and socialize, a process that led to further informal contacts through the phone or other media. In fact, one of the directors said that any real knowledge transfer arising from alliances depended on how their researchers took advantage of social contacts (just as described by Liebeskind, 1996).

4.3. Ehub's knowledge development system

From the time of founding in 1998, Ehub's focus was innovative anti-inflammation therapeutics. Its technology came from a prominent national public research laboratory in Oxford, where the company's scientific founder was director in charge of work on vector[5] saliva and its role in the transmission of pathogens.[6] The globally acclaimed technology was pioneering and complex because it involved extracting tick saliva molecules for use as potential anti-inflammatory drugs using emerging recombinant technology. Working with scientists from different laboratories, Ehub's key challenges included how to isolate saliva molecules from a tick – which is obviously a pretty tiny beast – and to accumulate first grams and then kilos of such materials for discovery research. Further research carried out by key collaborators involved recombinant technology, and it included identifying pharmacological activities, and understanding how disease and infection are controlled at the molecular level.

The knowledge-product linkage ambiguity was high and like most biotechnology firms, Ehub sought to resolve this risk by commissioning its technology in many different application areas with research groups around the world.

Ehub also paid particular attention to its patenting strategy, as its CEO explained:

> '[Essentially] the strategy is to try to patent the biology source, to patent the means of discovery of the agents and then to patent the agents themselves. And then when the activity in human beings is observed for the first time, to patent that mode of treatment again. So you have actual substance of matter patents through to use patents. And the whole purpose of this was to try to get a reasonable lifetime for the overall patent.'

Organizationally, in keeping with its learning approach in alliances of primarily accessing rather than seeking to transfer knowledge from partners, Ehub allocated R&D roles through a broad range of research agreements targeting different therapeutic applications in the anti-inflammation domain (see Fig. 3 for project portfolio range).

As said earlier, in contrast to Avertical's management and staff structure, Ehub employed only a small number of experienced managers, who outsourced all of Ehub's R&D by working collaboratively with carefully selected partners to design studies and commission external development for each and every stage in the drug development value chain (as shown in Table 4). The approach was knowledge access rather than knowledge transfer, which meant that Ehub's partners were fully empowered to undertake core R&D work and provided specialized product development work, each typically focusing on a particular value chain stage. We stress, Ehub had no in-house laboratories and employed no bench scientists.

Upstream – Ehub set up its first upstream research agreement to outsource basic R&D with the founding national research laboratory from where it sourced its primary IP. The terms of the agreement required the founding public research laboratory to carry on basic R&D on specified applications and sign over to Ehub any IP resulting from the research, in return for R&D funding, a promise of a single digit royalty stream if the resulting technology came to market, and an equity consideration in Ehub. Ehub signed similar agreements with other academic units both in the UK, and around the world in areas such as Slovakia and Brazil (all involving scientists who had previous co-working experience with the founding scientist). Ehub managers reported that these non-UK agreements were much cheaper than its original UK research agreement – as they did not involve giving up equity, the royalty stream being much smaller (about 2%) and the scientist were funded at about a tenth of the equivalent UK cost.

Mid-stream – Ehub's midstream work involved testing one of the recombinant molecules with an animal model. Initially, Ehub approached major contract research organizations (CROs) such as Quintiles, but later it moved to working with Centre Nationale pour Reserche Scientifique (CNRS) in Orleans, France, and later on at the Ophthalmic Research Associates Inc., North Andover, MA, USA. The Development Director explained these academic units and smaller companies were considered more responsive:

> 'What you got [from large CROs] was what came straight out of the shelf, they weren't interested in sitting down with you and trying to deliver exactly what it was you were looking for or to modify the way they did things or something like that. . . and it's usually quite expensive and in many cases it just didn't work or it wasn't quite what you wanted. And so [after a while] we started going much [more] generally to smaller companies, not [necessarily] paying [them], and also to academic units.'

Downstream – In a similar pattern to Avertical – Ehub relied on contract research organizations to outsource late stage development and employed a couple of senior managers as project managers to oversee their activities. As with Avertical, Ehub's selection process for engaging late stage development (clinical trials) partners was formalized into a very structured tendering process that was typically geared to drive down costs. As the Development Director explained:

> '. . . all contractors sign a confidential agreement and a technical agreement on the back of a commercial contract describing what they should perform. This is backed by a rigorous selection process based on capability, quality, experience and track record and availability. In addition, our ability to outsource on a global basis gives us competitive prices.'

We obtained evidence in our field work that Ehub created 'firm type intimacy' by building relational capital with employees of development partners and that they exploited factors such as similarity in size of firms and orientation to reinforce the intimacy. For

[5] An organism, typically a biting insect or tick that transmits a disease or parasite from one animal or plant to another.

[6] Anything that can transmit disease such as a virus or bacteria.

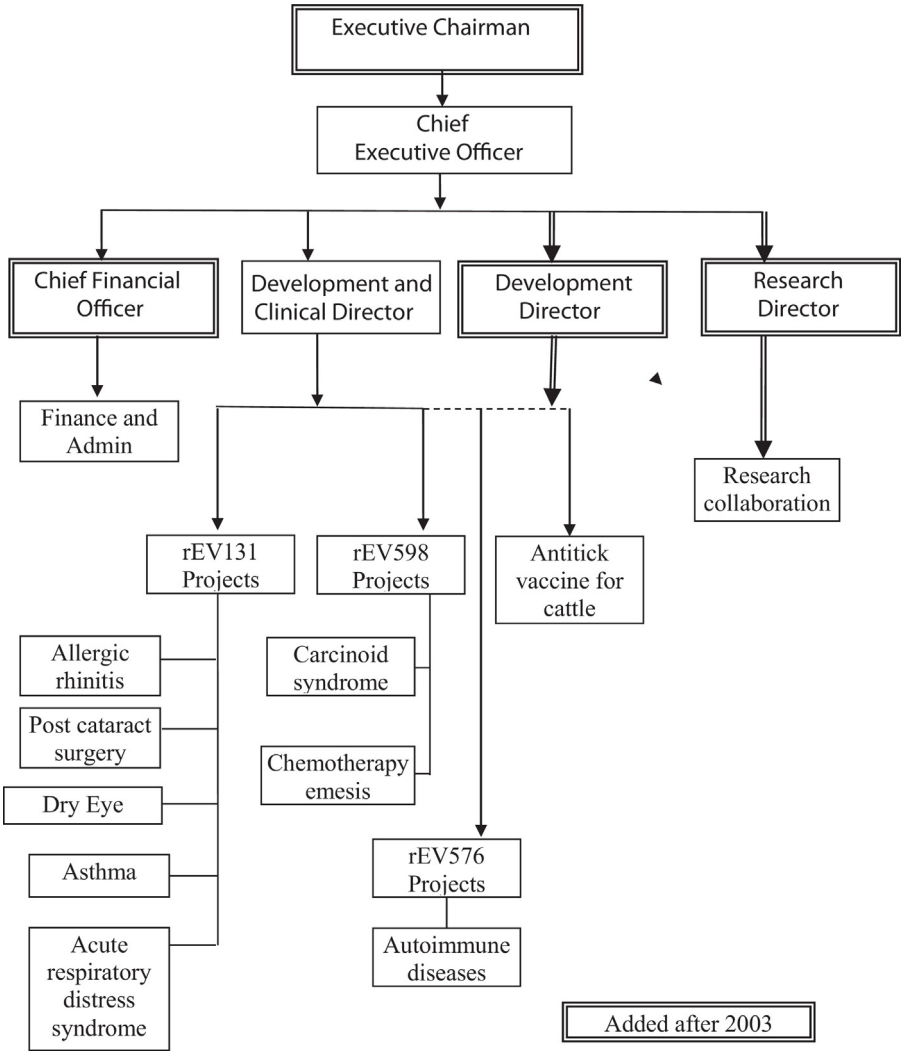

Fig. 3. Organization chart showing key capability areas of Ehub.

example, one of Ehub's managers stated that '*relations with individual employees of development partners are more important than with the firm itself*'. Building relations involved making frequent visits to partner premises that were not necessarily scheduled formally, helping the partners with equipment purchases possibly needed in the course of research, facilitating attendance at scientific conferences and funding research activities. It seems that Ehub understood the importance of project management skills in terms of engaging and communicating to partners formally as well as holding them to account, as one R&D executive said:

> 'And there was a lot of interest in these proteins so some people were prepared to do things for nothing. So [over time] we tried to find people that were good but would be doing things for interest rather than for money. And we formed some good long lasting relationships that way.'

5. Findings concerning knowledge integration strategies in non-modular contexts

Pavitt (1998), Padgett and Powell (2003) and Brusoni and Prencipe (2011) explain that successful knowledge integration is based on the firm's ability to own or access diverse scientific and technological disciplines – that is bodies of knowledge or understanding and practice – that underpin the firm's product design and manufacturing. This involves facilitating dense knowledge flows and cross domain linkages that aid innovation and knowledge building (e.g. Padgett and Powell, 2003; Brusoni and Prencipe, 2011) and also aid in sensing, absorbing and integrating external knowledge (e.g. Cohen and Levinthal, 1990).

As the Avertical case indicates (please refer to Fig. 4), for the internally focused product system integrator, core in-house multi-discipline R&D knowledge consisting of diverse scientific and technological disciplines, underpins product development for the upstream and mid-stage value chains. The co-location of in-house multi-discipline R&D enables the product system integrator to facilitate dense transactional knowledge flows and cross discipline linkages necessary for innovative activity within and across these early product development stages – an approach that is consistent with its predominant learning framing of transfer of knowledge. Hierarchical control is employed to cost effectively manage coordination of in-house cross boundary knowledge flows.

For external partners, consistent with its predominant framing of transfer of knowledge, Avertical's approach as revealed in Table 1 mentioned earlier, shows its capacity to transfer dense external knowledge flows by the extensive co-authorships and citations in scientific publications and patents between the firm's scientists and other organizations (measures explained to be important by Liebeskind, 1996). Additionally, Avertical's alliances leveraged its

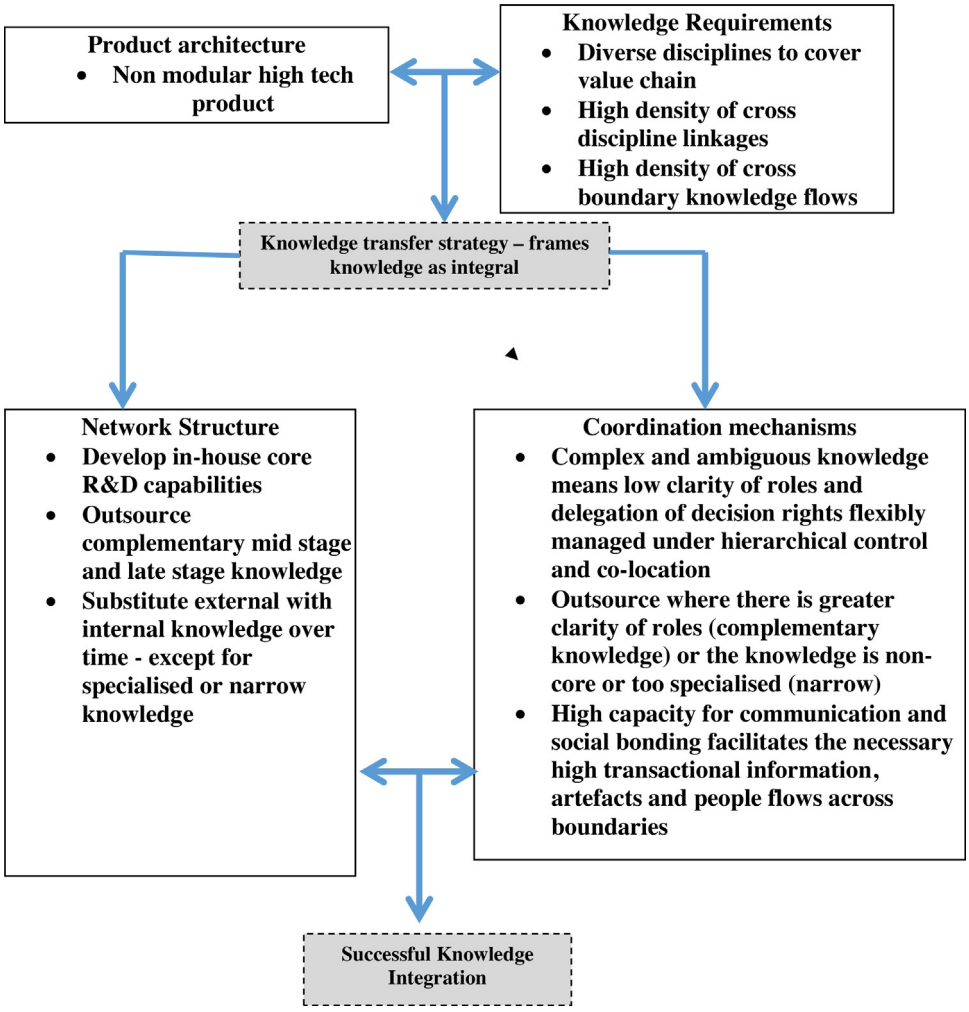

Fig. 4. Summary of key findings – conventional internally focused strategy.

internal R&D expertise to engage in exchange of IPR deals which were used to spur its internal efforts.

For the externally focused product system integrator there is a puzzle concerning how it can develop a product system with high innovation levels, with a relatively low knowledge base. Ehub had a low knowledge base because it had no laboratories and no scientific publications, however, it owned many patents because they were legally ascribed to Ehub by virtue of its scientific and technological agreements (see Table 2). And as expected, consistent with its learning approach in alliances, the affiliations of inventors on Ehub's patent list (applied for and granted) were external agents rather than employees. Traditionally, it has been assumed that an integrator needs to have deep knowledge to support cross-boundary knowledge flows (e.g. Cohen and Levinthal, 1990). To explain this paradox, we argue below that a product system integrator frames its knowledge as modular, even though it is not actually modular (see Fig. 5). This permits the accessing of knowledge rather than knowledge transfer (e.g. Grant and Baden-Fuller, 2004).

5.1. *Framing complex, seemingly non-decomposable knowledge as modular*

Although products may be complex (because they are pioneering and based on emerging technology) and ambiguous (they have uncertain knowledge-product linkages), the externally focused product system integrator can frame knowledge to support its product system as essentially modular – i.e. not in the sense that interfaces were fully specified as would be expected in multi-technology physical products, but that cross domain or cross product stage dependencies and hence knowledge flows were deemed to be not so dense as to render outsourcing too costly. And this framing relies on the concept of analogical reasoning (e.g. Gavetti and Rivkin, 2005). When firms take existing innovations from other contexts (that may have failed or succeeded) and transplant them into a different context, they may choose to use those findings as external (objective) reference points to decide on the likely trajectory of product development in the new setting (e.g. Gavetti and Rivkin, 2005). Where such external references exist, they may be used by product system integrators to justify initial hypothesis about the likelihood of the importance of cross domain or product stage dependencies and therefore whether to frame development as essentially modular or not.

The Ehub case illustrates the above points. Ehub's technology involved extracting tick saliva molecules from their natural environment where ticks are known to feed stealthily on their hosts without being detected. Ehub executives believed that the tick stealth feeding process – successful in its natural environment – could serve as a reference point to pioneer a therapeutic application

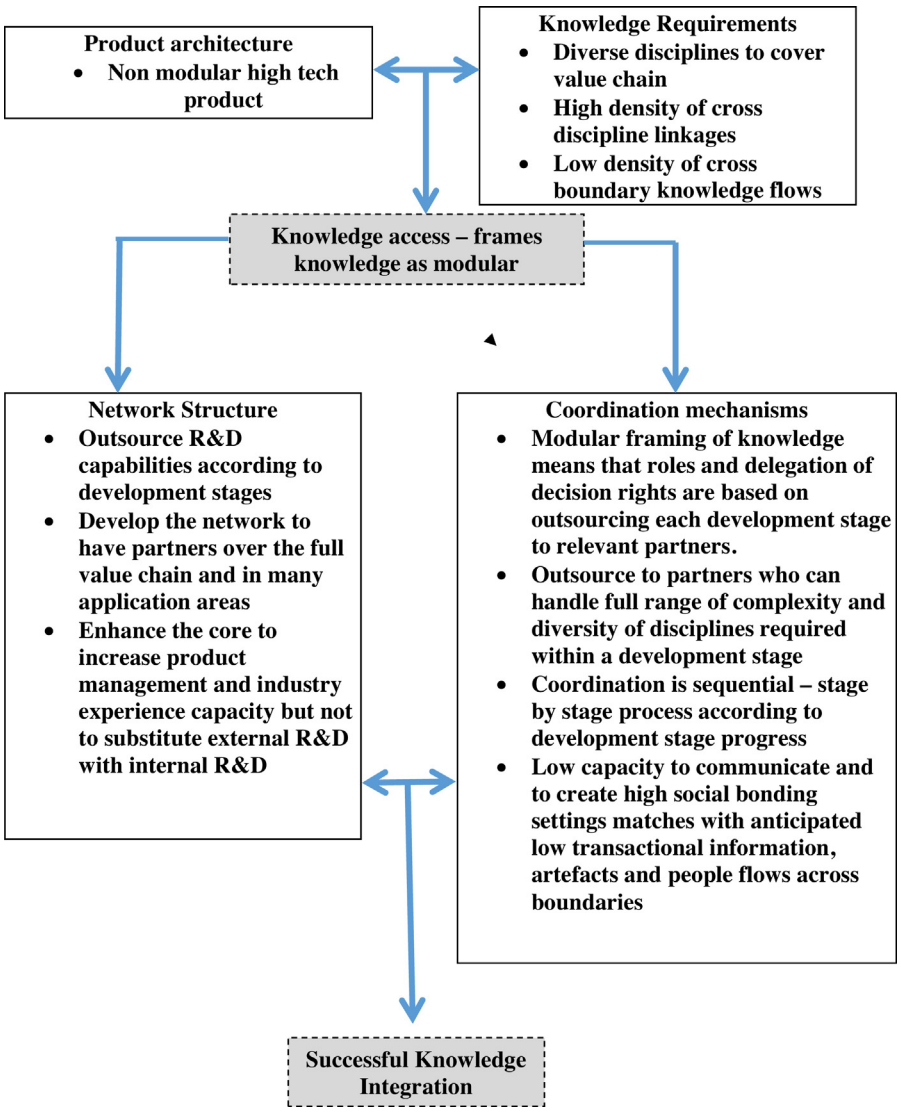

Fig. 5. Summary of key findings – externally focused strategy.

for humans. The executives – who were scientists themselves – then combined their experience and expertise to help design studies in the new setting of developing human therapeutics, as Ehub's R&D executive explained:

> 'Partly it was intuitive, in other words, if you knew that the tick wanted to stop [its] host from scratching, you knew the types of pathways that it would be trying to interfere with and one of the obvious ones was the histamine pathway. . .because histamine is one of the earlier substances released in the skin which causes itching. So it was obvious that the tick had to be able to do something to histamine. So the scientists went to look for molecules that would bind onto histamine and sure enough they were there.'

Additionally, Ehub's CEO explained how they designed the studies in collaboration with its partners by drawing from known scientific findings or existing knowledge to determine mechanisms of action in subsequent stages:

> 'Just at a simple level what we knew was that the particular pathways obviously had to be suppressed with the immune system and basically we had a procedure which enabled us to discover the mechanism of some of these drugs and some of them worked on some pharmaceutical agents that we knew to be interesting but in novel ways.'

The use of external reference points allows the development system to be streamlined by providing starting points in hypotheses development which obviate the need for dense cross stage knowledge flows but still allow the integrator to access very specialized knowledge within each development stage. The Ehub example shows how a product system integrator can frame a complex seemingly non-decomposable problem as modular – thereby allowing separation of development stages. The framing means that the anticipated knowledge flows between development stages are low even though the knowledge within each product development stage is quite complex and cutting edge.

Thus, in summary we propose that:

> A product system integrator with a relatively low knowledge base and limited capacity to support cross boundary transactional knowledge flows and cross domain linkages can still successfully produce products that require complex and ambiguous knowledge by accessing specialist partner knowledge. This strategy requires the product system integrator to frame its knowledge requirements for the product system

as modular by using compelling reference points that lessen the necessity of dense cross development stage transactional knowledge flows.

5.2. Framing the learning approach to network structure development

The internally focused product system integrator has few upstream or mid-stream external partners. In contrast, the network structure of the externally focused system integrator involves outsourcing product development stages to partners – a division of labor in which a product development stage is linked to a relevant network partner with the necessary knowledge. Our case studies also showed how the development of the network structure occurs.

Both types of product system integrators are likely to start with many external partners. Consistent with its framing of learning within alliances, the internally focused product system integrator progressively relies less on (the number of) external partners over time. The finding whereby externally accessed knowledge is progressively substituted with in-house R&D teams, echoes other biotech industry studies (Rothaermel and Deeds, 2004; Rothaermel and Deeds, 2006) or that of the literature on organizational learning (e.g. Cohen and Levinthal, 1990; Powell et al., 1996; Zahra and George, 2002; Chesbrough, 2003; Cassiman and Veugelers, 2006). Consistent with conventional firm boundary literature, hierarchical control is employed to curtail opportunism and reduce coordination costs (e.g. Grant, 1996). The consequence of this strategy is, over time to confine the firm's R&D outsourcing only to non-core or specialized and discrete complementary knowledge areas to reduce opportunism and to minimize coordination costs (e.g. Chesbrough and Teece, 1996; Cassiman et al., 2005).

In contrast, an externally focused product system integrator relies on external partners to access high value core R&D (e.g. Lubatkin et al., 2001; Grant and Baden-Fuller, 2004). The network grows as the product system integrator allocates tasks to fill the industry value chain. Rather than substituting its partners' capabilities with in-house R&D teams, the integrator's reliance on partners is on-going. The core of the externally focused product system integrator does grow, not to substitute partner R&D expertise but to increase the focal firm's capacity to manage its network: thus an externally focused system integrator doesn't grow in employee numbers as fast as in an internally focused one.

In particular, we propose that:

When high technology products can be supported by mainly modular knowledge for their development, the network structure can be developed by outsourcing each development stage to a different external partner.

5.3. Solving the coordination challenge

Following Padgett and Powell (2003) and Brusoni and Prencipe (2011), organizing the network involves linking work programs – decomposed into projects or contracts as visible elements of network tasks. This requires clarity of role allocation and delegation of decision rights so that product system integrators manage effectively on-going interdependencies and address the inevitable unforeseeable contingencies (Schreiner et al., 2009). Clear role allocations and decision rights help the product system integrator to cope with the expected dense transactional flows of information, artifacts and people across domain or organizational boundaries by lowering coordination costs. Unclear roles, procedures and responsibilities impede the ability of the product system integrator to capitalize on specialized but interdependent activities of partners (Thompson, 1967).

Our case studies show these processes at work. The internally focused product system integrator allocates core R&D internally under hierarchical control; and manages flexibly the dense dependencies between product stages or knowledge domains in upstream and mid-stream value chain stages, leveraging the benefits of internalized R&D decision rights (e.g. Chesbrough and Teece, 1996; Cassiman et al., 2005; Rothaermel and Deeds, 2006). Co-location of R&D teams improves effective communication and develops a conducive social setting. Flexibility can be enhanced further by a flatter organizational structure that allows management to act quickly and flexibly by for example reconstituting R&D teams as new evidence comes to light. Formal communication is through scheduled management, team leader and project review meetings but also unscheduled meetings that can be arranged as necessary. Additionally, socialization tactics include facilitating informal meetings and managing flexible career paths for juniors to move between departments as they are promoted.

In the externally focused product system integrator, role allocations and delegation of decision rights are allocated on the basis of outsourcing development stages to partners with the capacity to undertake core R&D in those stages. In addition, allocating core R&D work in relatively big chunks to partners with multidisciplinary teams and capabilities helps the externally focused product system integrator to confine dense interactions within a development stage to a single partner and hence save on coordination costs. Moreover, to further limit cross stage dependencies, work mostly proceeded on a stage by stage basis i.e. sequentially coordinated from upstream to mid-stream and then downstream (e.g. Lawrence and Lorsch, 1967).

Although it has only a handful of executives at its core, communication is both through formalized channels such as project review meetings and informal social channels when project managers pay often unscheduled visits to partner laboratories. Unlike in internally focused product system integrators, where communication is used primarily to facilitate transfer of knowledge, communication in externally focused system integrators is used mainly to shape product development efforts of partners. Ehub chose partners who could provide customized solutions rather than off-the shelf projects.

Communication through informal social channels was facilitated through appropriate social bonding developed by a wide range of tactics. Starting from the experience base of executives and founders, Ehub's early partnerships were with research laboratories where scientists had a past work or academic affiliation with the founders. In addition, social bonding was developed through proactively meeting the needs of their partners through making relevant investments in upgrades of partner technology or capacity improvements to create and develop mutual appreciation. By actively engaging in selling Ehub's vision of its projects, the potential of its technology, and presenting partners with a credible prospect of funding and sharing intellectual property (IP) with them, and highlighting what they could all achieve together by collaborating, the firm was able to create a climate for positive engagement by signaling respect and appreciation for each other. In addition, partners were deeply involved in project design because the commissioning firm's initial hypothesis was often initially at a very broad level. Therefore the development of projects required a lot of responsiveness from partners where development proceeded over many long visits involving sharing and responding proactively to each other's needs. The focal firm would often provide funding or purchase required equipment that would not be readily available, facilitate conference or event sponsorships or meetings or introductions required in the course of development – thus responding to their partner's development concerns but also using the time to connect socially.

Summarizing our discussion, we suggest that the two product system integrator types have different but consistent product systems whose elements of coordination: role allocation and delegation of decision rights, communication and social bonding are developed to align with its approach to learning in alliances within the network alliances. Specifically we propose that:

For the internally focused product system integrator, role allocation and delegation of decision rights of core R&D to co-located multidisciplinary R&D teams use hierarchical control to flexibly manage the anticipated dense transactional knowledge flows across boundaries and reciprocal coordination of development stages. External partners are engaged based on the complementarity of knowledge that partners bring to product development. For internally focused integrators, the goal of communication is speedy, timely and accurate information sharing within and across in-house project teams and from external partners. The goal of social bonding is to facilitate knowledge transfer as well as mitigate problems of knowledge sharing between in-house teams and external partners.

For the externally focused product system integrator, roles and decision rights are mapped to product development stages and allocated to partners with the capacity to undertake core R&D and coordination of development is a sequential stage by stage process with relatively low anticipated cross development stage/boundary knowledge flows. Communication is used for assessing project progress and exchange information that helps shape the direction of future efforts. The objective of communication by the integrator is to shape the efforts of partners by reaching a common agreement about the direction of future efforts rather than to transfer knowledge, and the main goal of social bonding is to provide leadership from the center and the necessary conditions to mitigate problems of contract incompleteness and conflicts of interests with the extended range of partners to whom core functions of R&D are outsourced.[7]

6. Conclusion

Although the literature has emphasized that successful knowledge integration is based on how product system integrators leverage external knowledge sources (e.g. Arora and Gambardella, 1994; Chesbrough, 2003; Fey and Birkinshaw, 2005; Cassiman and Veugelers, 2006), it has not spelled out how integrators can use external knowledge differently. We describe two basic choices: in the first, the product system integrator type relies on in-house core R&D upstream and mid-stream to accelerate new product development through the effective transfer of relevant external knowledge (Cohen and Levinthal, 1990). This is in contrast to the second route where the product system integrator relies on externally sourced core R&D on an on-going basis for all stages and all activities.

Our study shows that an externally focused knowledge building strategy based on heavy reliance on external partners is much more than just a transitional arrangement for the development of a firm's core capabilities in R&D (e.g. Rothaermel and Deeds, 2004). It should not be seen as risky and unwise (e.g. Chesbrough and Teece, 1996; Tether and Tajar, 2008; Grimpe and Kaiser, 2010; Zirpoli and Becker, 2011) but rather that the strategy is an exemplar of pushing the envelope of boundaries to accessible R&D outsourcing (e.g. Grimpe and Kaiser, 2010). Our study shows how and why such a product system integrator can build valuable knowledge that results in successful product innovation; how and why its organizational arrangement of relying on partners is stable enough to support growth; and how and why such a firm can indeed solve the coordination problems inherent in managing on-going partner inter-dependencies efficiently, when they involve complex and ambiguous knowledge flows. In making these claims we build on product system integration literature which views product systems as those which relate knowledge strategy choices of the firm to the pattern of development of the system i.e. the manner the focal firm integrates product components, assembles the network structure and coordinates the network to achieve innovative outcomes (Hobday et al., 2005; Brusoni and Prencipe, 2011).

We also use two longitudinal in-depth studies of "exemplar" firms to show how things work in practice. We have established that product system integrators have different ways of successfully integrating knowledge in a context where the non-modularity of the activities makes outsourcing of R&D both potentially costly to manage and risky. The two firms in our study achieved comparable product innovation outcomes, either owned or accessed diverse scientific and technological knowledge necessary to develop products. We find that though the knowledge base of the externally focused product system integrator is relatively smaller, its product system outcomes are not stunted by the greater on-going externalization of its R&D.

The externally focused product system integrator's smaller knowledge base has lower capacity to support dense cross boundary transactional knowledge flows and the cross domain linkages necessary for innovative product development (e.g. Padgett and Powell, 2003; Brusoni and Prencipe, 2011). However, such an integrator can still successfully produce products that require complex and ambiguous knowledge by accessing specialist partner knowledge in conditions where dense cross boundary knowledge flows are not crucial for product development and the firm can frame the knowledge requirements as modular.

The framing of knowledge as modular to support development of non-modular products in externally focused product systems is critical and made possible through use of external reference points or analogies. Generally speaking, other reference points used in the biotech sector include drug re-purposing i.e. the use of the results of a failed development program in another project, or the use of successful project results in a new project (e.g. Cavalla et al., 1997).

There is also a stage-by-stage process of gaining externalization experience – and of learning by doing – that is inherent in the development of the externally focused product system integrator. This study shows how this may require the product system integrator to start with less complex knowledge areas to gain confidence and legitimacy, before moving on to more complex projects. Our study findings are in line with prior work that found that accessing valuable external work is likely to require experimentation and experiential feedback – of learning by doing through trial and error (e.g. Lorenzoni and Baden-Fuller, 1995; Brown and Eisenhardt, 1997). We also found that because of the ambiguity of knowledge, the firm resolved knowledge-product linkage uncertainty by applying technology in different applications through different partnerships.

There are some key boundary conditions. The externally focused strategy relies for its success on the availability of the specialized firms in a well-organized innovation ecosystem, in sufficient quantity and range to meet the needs of systems integration (e.g. Mowery and Sampat, 2005). Typically product system integrators in the biotech sector create value by taking very early stage IP from universities and public research laboratories and forming drug discovery and development companies to develop the IP further. Other specialist biotech suppliers and service firms provide complementary capabilities. Although product system integrators may differ in their strategies to develop their partner networks, they all need quality IP inputs from willing (usually public sector sources) partners and cost effective scientific infrastructures (e.g. Owen-Smith

[7] We thank the editor and an anonymous reviewer for this insight.

et al., 2002). In addition, the increasing availability of experienced out of work pharmaceutical industry managers has also helped system integrators with experienced hires that help to build capabilities for outsourcing complex R&D (e.g. Powell and Sandholtz, 2011).

A key difference for the externally focused strategy *vis a vis* the conventional internally focused strategy is that externally focused product system integrators develop partners for a long term game. Partnerships are stable and enduring because the reliance of the product system integrator on its partners does not diminish significantly as in the first strategy approach. To engage prospective partners for the long haul, the product system integrator plays a leadership role that involves motivating prospective partners and exciting them about the technology, and building their confidence by sharing the prospects of what they can achieve together when sharing their IP and working collaboratively.

We found that both product system integrator's knowledge strategies align the coordinating elements – clarity of roles and delegation of decision rights, communication and conducive social bonding in a way that handles effectively the density of transactional knowledge flows in the system. In both cases, the product system integrator's work is decomposed into projects or contracts. However, as we explain above, the clarity of roles and delegation of decision rights is different.

Effective communication and social bonding builds relational capital that helps to curb opportunistic behavior and thus prevent leakage of critical know how between partners (e.g. Kale et al., 2000). However, there are limits to their effectiveness. Solving the problems of coordinating mechanisms does not obviate the need for the systems integrator to always take appropriate measures to protect its IP, such as adopting a strong patenting strategy. However, sharing core IP with partners should not necessarily place the firm at risk because it also depends on the nature of the sharing involved. First, the firm does not have to share all of the core knowledge at once to any one partner – this reduces the partner's ability to appropriate the value of the IP (e.g. Liebeskind, 1996). Second, the timing of sharing can also be used as a defensive mechanism: research has shown that it is better to share IP with bigger companies at later rather that earlier product development stages (e.g. Katila et al., 2008). Effective management and defense of IP also requires the right backdrop, provided by formal crafting of contracts to deliver a credible alignment of incentives (e.g. offering performance based rewards), and risk mitigation measures with acceptable deal terms that will encourage different key stakeholders to work together. All this also depends on there being a strong IP regime in place in the country.

Finally, in this study we proposed a product systems lens as superior to explain how different but competing product systems work (e.g. Prencipe et al., 2003). We argued that successful knowledge integration is a systems integration capability that is best understood in terms of how it integrates, in our case product development stages, the network structure and coordination mechanisms. Our contribution lies in conceiving each product system as a learning trajectory with different dependencies within the system related to the learning objective within its alliances. The learning objectives i.e. transfer partner knowledge (e.g. Cohen and Levinthal, 1990) or access partner knowledge (e.g. Grant and Baden-Fuller, 2004) are so predominant that they result in different but competing product systems. Our study has shown how and why the system components – the firm's knowledge and product architecture, network structure and coordination mechanisms have to align consistently with each knowledge or learning strategy to be successful. Therefore, a hybrid system – consisting of both product systems within a single firm would be untenable. Either product system represents two distinct ways in which internal and external knowledge may be used in a complementary manner for successful knowledge integration – thus representing two different hybridization strategies of how and why internal and external knowledge integration may work (e.g. Cassiman and Veugelers, 2006). In the first strategy, external knowledge is incorporated to spur internal efforts, whilst in the second strategy the focal firm uses internal knowledge to direct and shape and exploit external efforts.

Conventional knowledge theories that emphasize the primacy of core R&D or core capabilities being kept in-house (e.g. Chesbrough and Teece, 1996), under-explore and under-value the fact that firms with low knowledge bases can be competitive if they view their advantage from a system perspective (e.g. Lorenzoni and Baden-Fuller, 1995). The systems capability develops an internally consistent product system that relates the product system integrator's knowledge base to the network structure and relevant coordination mechanisms required in order to be competitive. Viewed in this way, the systems integration capability may be viewed as a higher order capability that underpins a systems integrator's competitive advantage.

The study also highlights important implications for managers and policy. The spawning of start-ups in high tech sectors in general – and biotechnologies in particular – has been driven in large part by policy measures and regulations supporting spin-outs from public laboratories and academic units, and thus easing the way for funding from the venture capital sector (e.g. Mowery and Sampat, 2005; Owen-Smith et al., 2002; Powell and Sandholtz, 2011). Our study shows that these well-meaning policy measures to commercialize technology from academic and public research labs will often demand that specific knowledge integration capabilities are deployed to develop new cutting edge products successfully – a point that has not been highlighted in prior research.

As with most studies, ours suffers from limitations, which in turn point to opportunities for future research. Our study focuses solely on the biotechnology sector, and our two case firms were involved in innovative research and the use of biotechnologies in developing drugs, using minor equity and contract alliances to access cutting-edge technology at various product development phases. Not only did these firms operate in the same sector, they were in the same jurisdiction and were of similar size and age. While these factors all serve to reduce any differential impact, this similarity decreases the generalizability of our findings to other industries, which will require identifying how similar knowledge integration processes work in other industry settings.

Acknowledgements

We are grateful for the support from the EPSRC grant EP/E037208/1 on Financial and Organizational Innovation in Biotechnology and the EPSRC grant EP/K039695/1 on Building Better Business Models. We benefited from helpful and extensive discussions with colleagues at Cass Business School and Sussex University (SPRU), as well as at AOM, SMS and EGOS conferences, and particularly Hans Frankort, Santi Furnari, Michael Hopkins, Vincent Mangematin, Paul Nightingale, Davide Ravasi, Joanne J. Zhang and the late John Pool as well as three anonymous reviewers and the editor Ed Steinmueller of this journal. The views expressed in this article, errors, and omissions are our own.

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