STUDYING THE IMPACT OF CONVERGING TECHNOLOGIES ON THE PRODUCT DEVELOPMENT PROCESS: A CASE STUDY OF A START-UP COMPANY AT THE DRUG DEVICE INTERFACE

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Abstract

This paper presents early results from a qualitative study of the drivers of the convergence of the pharmaceutical and medical device sectors by exploring the impact of converging technologies on firms' product development process. The first of three intended case studies of firms developing products at the drug-device interface, describes how a biotechnology start-up company managed to survive and grow by successfully aligning the required knowledge and capabilities to leverage the regulatory, financing and knowledge management issues. Through semi-structured interviews of four key stakeholders of the firm and archival data analysis, the evolution of the company's product development process and overall strategy is set against the constraints it faced, to identify how converging technologies were managed and how they leveraged or hampered efficiency of the product development process. Though further investigation is needed, the key success factors that seem to emerge are the internalisation of regulatory management, manufacturing process management and partnering management capabilities, a strong opportunistic mindset, and a positioning of the firm as a technology provider. These preliminary results suggest that contrary to practitioners' main belief, drug-device convergence can positively impact a firm's product development, at least at the start-up stage.

Key words: Convergence, Product Development Process, Pharmaceutical industry, Medical device industry

JEL Code: O31, O32

Introduction

Drug-device convergence (DDC) is an emerging trend in the healthcare industry. It stems from the technological opportunity to design combination products, *i.e.* medical treatments which draw on the advantages of both a drug and a medical device. Drug and medical devices

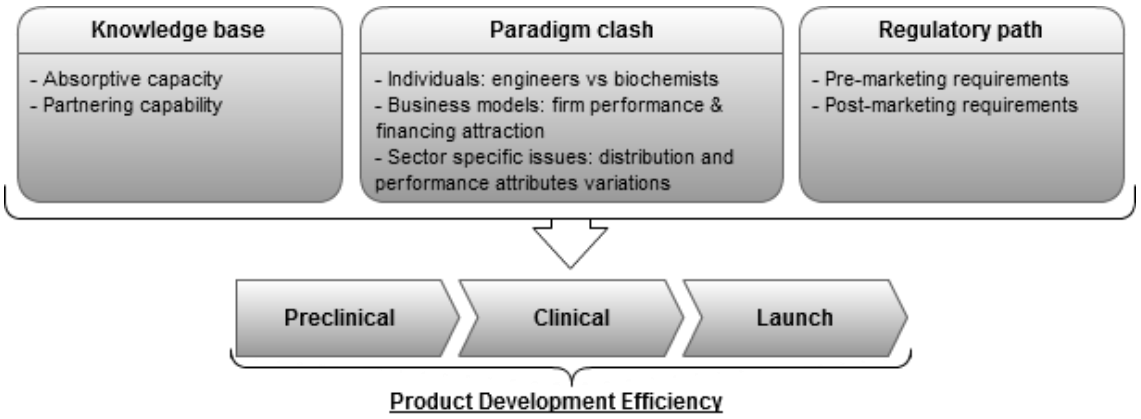
rely on very different scientific and technological knowledge bases for their development: the former is based on life sciences (biotechnology, chemistry) whereas the latter uses engineering sciences. This confrontation of paradigms on the shared aim to provide solutions to treat or improve patient's condition characterises drug-device convergence as an example of converging technologies (CTs) (Nordmann, 2004; Roco & Bainbridge, 2003). From a business viewpoint, CTs are an opportunity, as was biotechnology for the pharmaceutical industry, but also raise concerns. Drug and device firms use very different business models, capturing the value created by leveraging the different performance attributes of their respective value network (Christensen & Rosenbloom, 1995; Westergren & Holmström, 2012). Combination product development then sums the risk of developing a drug with that of a medical device, possibly not in par with expected returns on investment. Likewise, the evolving but sill rather fuzzy regulatory framework, which is a driving force in the establishment of new technology-based innovations, is as much an opportunity as a threat.

As part of a doctoral work that will proceed with three case studies, this paper presents the first one, which purpose is to understand how the process of developing a product at the interface of a drug and a medical device is managed inside Hemarina, a biotechnology start-up company. Specifically, the case study aims to answer the following research questions:

1- How did the company happen to develop a product at the drug-device interface?
2- How did it impact the product development process?
3- What key issues impacted the strategy?
4- What key responses enable the effective management of these issues?

This study proposes to analyse firm-, sector- and industry-specific factors that impact firms that develop products at the drug-device interface. It draws on evolutionary economics and organisational learning theory to understand innovation and the paradigmatic nature of technical change, and to accordingly develop the analysis model of drug-device convergence presented in fig.1. The structure and management of the focal firm's knowledge base should determine its ability to deal with very diverse knowledge and partners. The paradigm clash refers to sectoral differences in terms of value network, from scientific to marketing and financing issues. Finally, the regulatory environment is a primary constraint on the product development strategy. Using this analysis model, this paper seeks to understand how these factors impact the focal start-up firm, at the preclinical, clinical and launch stages of its product development process. The case study method was used to elicit the interpretation of the DDC phenomenon by key members of the company and eventually identify the key factors (table 1).

Fig. 1: Theoretical model of analysis



Tab. 1: List of interviewees

Franck Zal	CEO and CSO, founder of Hemarina
Morgane Rousselot	CTO, co-founder of Hemarina
Gilles Avenard	Board's chairman
Alain Naccache	Qualified Person[1] – Management of regulatory issues: R&D, manufacturing, AMM

1 Company overview

Like several French biotechnology companies, Hemarina emerged from the academic research environment. While still a PhD student, Franck Zal studied the properties of particular Haemoglobins extracted from a marine invertebrate named Arenicola Marina. His work suggested to several physicians that the hypothesis of using the molecule as a potential blood substitute could be valid. After a few years of experimentation and positive results, Franck created the company in 2007 to develop and market this product. Unfortunately, the company failed to attract investors with its biotech business model, especially after the FDA (American Food and Drug Administration) announced in 2008 that it would be more cautious before granting marketing authorization of new blood substitutes given the previous experiences from companies that tried to bring to market synthetic blood.

Understanding that the product value and mechanism of action is based on its unique oxygen universal carriage properties, blood substitute applications would be just one field among other development that could be envisaged by Hemarina. The company strategy scope is then extended to technology and expertise related deals beyond mere product related deals.

[1] A qualified person is responsible for securing "that each batch of medicinal products has been manufactured and checked […] in accordance with the requirements of the marketing authorization"(European Commission, 2009). The QP is typically a licensed pharmacist, biologist or chemist with extended experience working in manufacturing operations.

Since traditional venture capital funds (VCs) of the biotech sector stepped back following the FDA announcement, Hemarina has then chosen to target business angels (BAs) – local BAs Finistère Angels being first to invest – after securing investment from Institutional Funding Programs such as INSERM Transfert Initiative[2], which confirmed the scientific credibility and industrial value of the project.

Tab. 2: Applications developed by Hemarina, as of December 2011

Commercial name	Application	Regulation	Targeted market	Market size
HEMOXYCarrier®	Universal oxygen carrier	Drug/Device (long term)	Blood substitute	$72 Billions in 2009 worldwide
HEMO$_2$ling®	Active dressing for wound healing	Device/Drug (medium term)	Wound healing	$962 Millions in 2005 for Europe
HEMO$_2$life®	Organ preservation	Device (short, medium term)	Organ preservation solution	$50 Millions in 2009 worldwide
HEMOXCell®, HEMUpstream®	Cell culture media	Lab reagents (short term)	Cell culture media and reagents	$1 billion in 2006 worldwide

Source: Company data

In parallel, based on regulatory requirements, and thanks to astute hiring, the company puts in place a multi-stage strategy, based on a unified manufacturing process of one active pharmaceutical ingredient (API) extracted from Hemarina's proprietary molecule, that can be developed into multiple applications that would target various markets with various regulatory complexities, so that a product could generate early revenues to finance long-term projects (table 2). From this point, Hemarina is at the interface of the drug and medical device sectors, developing applications for both sectors, as well as combination products. It uses its technology and expertise to develop the proof of concept (PoC) of an application and then license them to a partner that will further develop the product and market it. Moreover, Hemarina has the ability to entirely develop an application and then market it through distribution agreements (table 3).

Tab. 3: Examples of collaborations, by application

Application	Partner(s)	Collaboration's purpose	Type of collaboration
Universal oxygen carrier	Various partners according to clinical case	PoC: demonstrating molecule efficacy in various pathologies (e.g. Brain ischemia)	Research, demonstrating PoC, expanding scientific knowledge
Active wound dressing	Plasters industry	Attaching molecule to partner's dressing	Demonstrating feasibility, out-licensing technology to partner, Discovering new market
Organ preservation	Distributors	Distributing Hemarina's product, Sales force	Regional distribution

[2] the national venture fund from the French institute for medical research

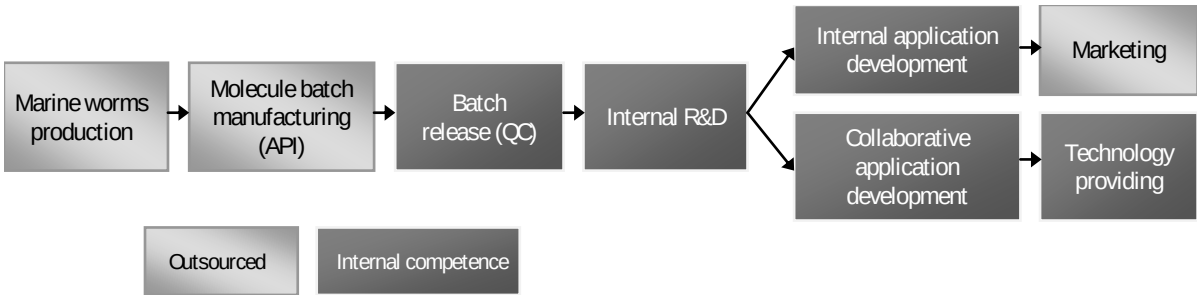
Biomanufacturing active ingredients	Large pharmaceutical company	Enhancing and optimising a biomanufacturing process	Developing then out-licensing the technology, Acquiring knowledge from partner

Source: Compiled by author from company data and interviews

Figure 2 displays Hemarina's current organization, opposing outsourced and internal activities. Upstream outsourced functions remain under Hemarina's control, in particular via regulatory and quality control. For instance, the manufacturing process is outsourced but results from an internal expertise, adapted to regulatory constraints, and materialized in internally controlled batch release. Downstream, commercialization agreements including the distribution of products with the Hemarina trademark, remain based on scientific communication and consequently on the firm's knowledge of the molecules properties. The other branch concerns partnered application development in which case Hemarina holds technology and expertise by developing the PoC and can envisage a broad spectrum of deals from license deal to co-development.

The new application development process is grounded in a stable and commonly manufactured API. They are the basic material that Hemarina's team studies, analyses and fashions to develop the PoC that lead to new healthcare as well as industrial applications. This process and the firm built themselves concomitantly according to constraints that lead to the current positioning.

Fig. 2: Hemarina's product development process



Source: Compiled by author from company data and interviews

2 Results

Gathered from interviews (table 1), table 4 groups together the main themes that impacted the definition and the organizational implementation of the firm's strategy, as well as related issues and how they were solved. It displays the factors that enabled Hemarina to manage the hurdles of implementing its product development process and to position itself at the drug-device interface to stimulate its development.

2.1 Core competences internalisation

Tab. 4: Factors impacting the firm's strategy and key lessons

Themes	Issues	Solutions	Key lessons/caveats
Regulation	• Multiple regulations • Identifying best-suited path	• Very early definition of regulatory strategy • Internalized quality control (QC) • Firm strategy draws from it • Skills internalization	• Cost/time optimization (one API manufacturing process) • Key capability
Investment	• Trouble finding investors • Need early revenue generation	• Unusual investors ○ Time ○ Trust • Multi-applications strategy	• Strategic independence
Manufacturing process industrialization	• Process compliant with each application's regulation • Process industrialization	• Early solving of regulatory issues • Board composition: experience+++ • Hiring experts • Developing one API for all applications	• Key capability • Cost/time optimization (one API manufacturing process)
Collaborations	• Partners identification and selection	• Technology attracts partners • Intent to learn	• Need to organize business development
	• Setting collaboration's details, managing collaboration	• Clear technological contribution (one API), Precise definition of scientific goals and milestones	• Key capability
	• Teams' scientific and technologic diversity =>bad molecule usage, time loss	• On-site training, protocol sharing when not confidential	• Little sharing and retention of tacit knowledge
	• Diversity of partners' objectives (business, time, size)	• Technology providing	• Little learning from partner
Performance attributes identification	• Contacts with clinicians	• Early contact at the R&D phase • Keep contact via sales force • High impact of scientific discourse on sales	•
	• Identifying partners' performance attributes	• Common problematic : oxygen carriage	• Effective collaboration management required
	• Identifying performance attributes of partner's target market	• Collaboration allows for a first understanding of those attributes through partner's eyes • Hemarina only provides technology, partner defines performance attributes by itself	• Little knowledge acquisition and retention for future projects

Source: Compiled and analysed by author from company data and interviews

Early recognition of regulatory constraints has been a key factor. After a first filing that failed granting authorities approval, the management of regulatory requirements has been internalized in order to avoid such episodes by outsourcing an important strategic lever when seeking for such indication in new products. This was influential in the design of the manufacturing process, stabilizing the "one API/multiple applications" strategy. Generally

speaking, regulation management is critical for the firm's strategy since it impacts the balance between implementation cost and time, according to available financial resources.

Getting G. Avenard in the board of administrators, with his large experience of biotech development, was obviously crucial. Moreover he also brought his skills for industrialising blood-related processes and helped hiring blood fractionation experts. This shows how critical the manufacturing process is, and is symptomatic of the passage from start-up to a more advanced industrialized stage.

Finally, identifying and managing collaborations has been from the beginning a specific strength for the firm (Jiang & Li, 2009), thanks to its founders' ability to setup and manage scientific collaborations. These scientific partnerships are a way for Hemarina to develop its technological expertise and new applications. The sharing and retention of knowledge occur at the scientific level. Regarding commercial collaborations, the terms of the license agreements are stated with precise milestones based on scientific key performance indicators. However, except for some collaborations in project mode, the confidentiality of partner's experimental protocols often limits the depth of shared knowledge.

2.2 Seizing opportunities

The ability to seize opportunities is a recurrent theme in all interviews. It conveys the firm's propensity to adapt to constraints of its environment, regulatory issues and potential partners requests.

First, in response to the hurdles Hemarina faced to find VCs willing to invest in its initially classic biotech start-up model to develop a drug from a molecule, the firm has been able to redesign its business model to offer a less risky project that would generate early revenues. Along with scientific credibility and the local dimension of the venture, this has raised several BAs interest and commitment to invest in the long term which is quite unusual in the biotech sector. Second, the company has been able to leverage regulatory issues by positioning itself at the interface of the drug and medical device sectors and by implementing a "multi-stage" strategy based on a unified API manufacturing process. Finally, Hemarina seized the various opportunities to engage in various markets when potential partners suggested applications that had not been previously envisioned.

In Hemarina's context, opportunism has three dimensions. First is the intent to learn (Hamel, 1991; Inkpen, 2008; Simonin, 2004) from partners, from investors and board members regarding company management, and the intent to acquire the needed knowledge to manage regulation and industrialization issues. Such a level of intent to learn led to broaden considerably Hemarina's knowledge base since its launch.

Second, organizational flexibility enables the implementation of the objectives that were designed thanks to newly-acquired knowledge. As a consequence of its youth, the firm's initial lack of processes and pre-established routines enabled it to shape these goals according to the needs that emerged with the evolution of the company (Nelson & Winter, 1982, 2002).

Strategic independence is the third dimension. Since BA investors were not drug or medical device experts, they chose to not interfere and gave the management team much more autonomy than biotech-specialized VCs would have by setting precise milestones and by expecting very early and high return on investment. The extent of Hemarina's diversification would have probably been impossible with such VCs. Consequently, the team cultivated trust with its investors by putting in place reporting procedures and therefore was given enough latitude to apply its strategy and get correctly structured.

2.3 Upcoming challenges and future development of the company

In 2012, Hemarina is at the shifting point that will drive the future being of the company based on the strategic pillars choice to some extent and to staffing and management for the rest. As of today, Hemarina does not have the resources to merely process all the requests from potential partners and *a fortiori* to give them complete answers. Though its ability to seize opportunities to develop, internally or externally, very diversified applications has been a key strength, the firm must now keep focused on most efficient business model.

It emphasizes the risk of decreasing the efficiency of the product development process as a consequence of too much scientific and technological heterogeneity, which is required at the preclinical stage but becomes an issue when reaching clinical and marketing stages. With such diversity, hiring new resources becomes as problematic as "finding a white elephant" or duplicating each function to get the needed skills, which is costly. It also limits the acquisition of new knowledge from projects. Seizing opportunity has its limits, and despite a strong intent to learn, identifying each market's performance attributes becomes more and more troublesome and consequently requires more and more resources.

The firm's industrialization then raises the issue of specialisation, although diversity was initially a key factor of its development. Selling out one or two applications is an option worth considering, in order to focus on one high-potential application, by acquiring other technologies. Will the company be able to sustain its position at the drug-device interface?

3 Conclusion

Hemarina positioned itself at the drug-device interface thanks to its ability to develop several types of applications from a unique API. Early in its development, it also decided to be a

provider, as opposed to a drug or medical device developer. It gives the freedom to develop internally or externally each potential application based on its technology. With such a model, the risk related to one approach is mitigated by the other, and it leaves the opportunity to focus at some point on a more specific model once the potential success of one or more applications will be better assessed.

With a positioning as a technology provider and its unconventional financing structure, Hemarina avoids the usual pressures of the drug and medical device sectors ecosystem, and avoids suffering from their respective value networks' discrepancies. It allows enough flexibility to learn the required performance attributes and then adapt to most promising application. The company should then be able to adapt its structure and align the key capabilities whether internally or via alliances (Teece, 2007), which it learned to master, though mostly through out-licensing deals.

The firm turned regulatory issues into opportunities and took advantage of the various pathways to optimize the ratio between development time and cost and try to generate early revenues. However, when setting this balance, the team took care of analyzing future developments to implement a manufacturing process that would suit each application.

As a conclusion, this case exemplifies how a company can leverage DDC to develop a successful technological start-up business model (García-Muiña & Navas-López, 2007). The key factors are very much related to its entrepreneurial nature. The next step will be to analyse how middle- and mature-stage firms deal with these factors, and determine specific factors.

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