

**ISRICH Working Paper Series**

ISRICH Working Paper No. 04

**Care Supply for Rare Diseases: Some Stakes for an  
Organizational Innovation within the French Healthcare System**

by

**Alexandra Le Chaffotec  
Isabelle Hirtzlin  
Carine Staropoli  
Claude Ménard**

**International Society for Research on  
Innovation and Change in Health Care Systems  
(ISRICH)**

ISSN 1789-6517

**ISRICH Working Paper Series**

ISRICH Working Paper No. 04

**Care Supply for Rare Diseases: Some Stakes for an  
Organizational Innovation within the French Healthcare System**

by

**Alexandra Le Chaffotec  
Isabelle Hirtzlin  
Carine Staropoli  
Claude Ménard**

**International Society for Research on  
Innovation and Change in Health Care Systems  
(ISRICH)**

2008

*Editorial Policy:*

*The purpose of the ISRICH working paper series is to promote the circulation of working papers prepared by economists and other social scientists working on the evolution of health care systems and their interaction with the wider environment in society, politics and culture with the aim of stimulating comments and suggestions. The views expressed in the articles are those of the authors.*

For more information on the **International Society for Research on Innovation and Change in Health Care Systems** see <http://www.isrich.eu>

*Review Process:*

The editors screen manuscripts submitted to the ISRICH Working Paper Series. Papers thought suitable are then passed to a referee. Based on the referee report papers are (1) accepted, (2) accepted subject to revision or (3) rejected. Authorship of papers under consideration as well as identity of the referee is anonymous.

*Managing Editors:* Martina Eckardt, Stefan Okruch

Mail questions to: Martina Eckardt ([martina.eckardt@andrassyuni.hu](mailto:martina.eckardt@andrassyuni.hu)) or to Stefan Okruch ([stefan.okruch@andrassyuni.hu](mailto:stefan.okruch@andrassyuni.hu)), Andrassy University Budapest, Hungary, H-1088 Budapest, Pollack Mihály tér 3

*Board of Editors:*

*Rajat Acharyya*, Jadavpur University, Calcutta, India; *Davide Consoli*, University of Manchester, Manchester, United Kingdom; *Martina Eckardt*, Andrassy University Budapest, Hungary; *Thomas Grebel*, Friedrich Schiller University, Jena, Germany; *Corinne Grenier*, Euromed Marseille Ecole de Management, Marseille, France; *Carsten Herrmann-Pillath*, Frankfurt School of Finance and Management, Frankfurt/Main, Germany; *Stefan Okruch*, Andrassy University Budapest, Hungary; *Bertrand Pauget*, Groupe ESC Troyes, Troyes, France; *Magdalena Radulescu*, University of Pitesti, Romania

© Andrassy University Budapest, Hungary, H-1088 Budapest, Pollack Mihály tér 3

Electronic copy available at: <http://ssrn.com/abstract> .

# **Care Supply for Rare Diseases: Some Stakes for an Organizational Innovation within the French Healthcare System**

**Alexandra Le Chaffotec** a

**Isabelle Hirtzlin** b

**Carine Staropoli** a

**Claude Ménard** a

a Maison des Sciences Economiques  
ATOM, University of Paris 1  
106-112 Bd de l'Hôpital, 75647 Paris Cedex 13, France  
Email: [alechaffotec@gmail.com](mailto:alechaffotec@gmail.com)  
b University of Paris

**Revised Draft: December 2007**

## **ABSTRACT**

This paper deals with the organizational change in the provision of care for rare diseases, and the creation of a new structure: the centre of reference for rare diseases (CRMR). It aims to show that this new organization of care introduces a new “authority” within the healthcare organizational structure, by referring of the Transaction costs paradigm and its recognition of hybrid forms. It tackles then several conditions this authority has to fulfill in order to complete CRMR missions and awaited results.

This work is supported by grants from Région Ile-de-France.

## 1. Introduction

This article aims to characterize the “centre of reference for rare diseases” (CRMR) and to analyse the undergone stakes in improving care for patients with a rare disease. We identify the CRMR as an organizational innovation and a hybrid form, involving concomitantly the settlement of a label<sup>1</sup> by the French health authorities and the development of networks committing hospitals and outpatient services.

A CRMR is framed by a small group of very specialized practitioners of distinct organs, joined in a multidisciplinary medical consultation, inter-hospital departments, and dedicated to a rare disease or a group of closely related rare diseases.

We focus on this new structure within the French healthcare system since rare diseases display specificities and thereupon high difficulties in the provision of care. CRMR moreover not only reshaped a section of the French healthcare system, but also introduced a new authority within the French healthcare system. Additionally, the label is an unprecedented organisational solution in the field of healthcare in France, since neither ranking in the quality of provided care, nor orientation (an “arrowing”) in the medical trajectory<sup>2</sup> existed previously. We explain the choices for these institutional arrangements governing the cooperation between specialized practitioners for rare diseases.

Facing the richness of the object CRMR, we intend in this paper to focus on the notion of authority which springs from the set up of CRMR, among the healthcare system. We question whether the introduction of a new authority is better than the initial organization of provision of care: is the new organisation of care through the creation of networks is a good method? To what conditions this organizational device would bring about costs savings and more generally more efficiency, which means also better quality in the provision of care for rare diseases? What mechanisms could help to achieve these targets? Could it be seen as a solution to recommend for the organization of care for all kind of diseases, including non rare diseases?

---

<sup>1</sup> The concept of “label” refers in France to quality certification by public authorities, and is as well quite similar to collective trademark. We intend to use this definition over the analysis.

<sup>2</sup> Medical trajectory corresponds to the itinerary followed by the patient inside the different structures of care. It is “an arranged sequence of pathological episodes and related interactions with healthcare system”(Grémy, 1997). Medical path corresponds to the “consolidation of several frequent or typical individual medical trajectories and which may be susceptible of a model” (ibid).

We show first that rare diseases specificities sharply influence the set up of respective organizational devices facing the traditional French healthcare system structure, and particularly the creation of a direction in the medical trajectory followed by patients, and of innovative institutional arrangements between practitioners. Next, we resort to the definition and features of hybrid forms provided by Transaction costs economics, notably the importance of the governance tools within hybrids such as authority. Last we discuss the concept of authority, encapsulated in this new governance mode and the condition of its efficiency in providing care for rare diseases, and we suggest that CRMR may embody a model through its network design, which can be apply to the whole French healthcare system, including for non rare diseases.

### **1. The adoption of an organisational change in the provision of care for rare diseases**

Because of the specificities of rare diseases, French healthcare system, in its traditional scheme, proved to be inefficient in the provision of care for them. A public health policy in 2004 has created the CRMR, as a structure within the healthcare system aiming to support this specific provision of care.

What is a rare disease?

As indicated by the generic term qualifying them, rare diseases are obviously defined by their low prevalence. Those diseases attain few people comparing to the overall population, i.e. a prevalence of less than 1 per 2 000 persons according to the European norms, corresponding to less than 30 000 persons concomitantly affected by a given rare disease in France (5% of the French population). Further, the rarity degree isn't the same for each disease: in France, about fifty rare diseases affect a few thousand of people each, about five hundred other diseases affect a few hundred of people, and thousands of rare diseases concern only ten or so people. Although the occurrence of those diseases is weak, they however are very numerous and very heterogeneous. Nowadays, more than 7 000 rare diseases have been described around the world, and between 200 and 300 new rare diseases are newly identified each year. Because of their rarity, most of physicians don't even know those diseases.

At the same time, they affect various organs, and each disease shows its own symptoms, and there is also a great variety of clinical expressions for each disease; which means that they each call for several competencies inherent to each affected organ, and that a practitioner may be a specialist of one rare disease or of a group of closely-related diseases. Diagnosis is declared

through several clinical and symptomatic additional signs and it is often based on a multidisciplinary advice.

Rare diseases are also defined by their seriousness: they are life-threatening or chronically debilitating diseases<sup>3</sup>: Patients then need a provision of continuous care, and adapted treatment at each step of the disease.

Finally, as they are complex and have usually a genetic cause<sup>4</sup>, rare diseases require in-depth competences, owned by few specialists, to establish the diagnosis and the follow-up. In the case of gene mutation, for which no clinical case could have been observed up to then, knowledge has still to be acquired. For most of those diseases, there is no therapeutic solution, and obviously no curative therapy.

These features of rare diseases generate problems notably in the institutional context of the French healthcare system.

### **Organizational context and resulting problems concerning care for rare diseases**

French healthcare system's paragon remains encapsulated by i) a highly compartmentalized exercise of medicine according to specialities and structures that frame practitioners' activities (division of role between inpatient and outpatient services for example), ii) no gate-keeping for choosing specialists iii) organs medicine.

The second characteristic of the healthcare system may have dramatic consequences for patients in the case of rare diseases in connection with lack of information about those diseases: patients are free to choose a practitioner inside or outside hospital, when expressing their primary demand for diagnosis. This freedom is also valid for visited practitioners when expressing a secondary demand, in order to have deeper investigations (Béjean 1994). Yet, those diseases remain relatively unknown among the medical world, both in hospital and outpatient services, partly because of the low frequency of clinical cases observations. Thus, the traditional care framework in France isn't able to answer efficiently to care demand for rare diseases because patients are im-

---

<sup>3</sup> Sources: European Commission, General Direction for Health, and French Minister for Health and Solidarities: [http://ec.europa.eu/health/ph\\_threats/non\\_com/rare\\_diseases\\_fr.htm](http://ec.europa.eu/health/ph_threats/non_com/rare_diseases_fr.htm), [http://www.sante.gouv.fr/htm/dossiers/maladies\\_rares/sommaire.htm](http://www.sante.gouv.fr/htm/dossiers/maladies_rares/sommaire.htm)

<sup>4</sup> They result from gene alteration that may run in the family (even when they occurs belatedly in patient life); or they may be provoked by a new gene mutation. Source: French Minister for Health (ibid).

plicitly considered as experts of their own medical trajectory. GPs or specialists are often chosen by the patient on a geographical proximity criterion. They probably can't provide care for rare diseases: seeking information about an unusual symptom displayed by a patient might take a long time and be subjected to shuttle back and forth between practitioners before its characterization. Meeting the right specialist, in the right place and at the right moment (before the medical complications appear) is thus a lottery.

De facto, rare diseases are behind a great difficulty in orientation at the start of medical trajectory, in diagnosis, in settlement of adequate follow-up. The majority of practitioners often ignore not only how to proceed to establish the diagnosis, but also to which practitioner they have to address the patient, since competences required for rare diseases remain owned by a small number of specialists respectively for each of them. The Eurordiscare 2<sup>5</sup> survey, about the delay before a diagnosis can be made for eight rare diseases in Europe (including France), showed that 25% of patients had to wait between 5 and 30 years from early symptoms to confirmatory diagnosis of their disease. We call it on this account, "diagnostic nomadism"<sup>6</sup>. Two studies led in France (Godet, Hirtzlin, Costet 2001; Hirtzlin et al. 2004) revealed that the number of medical contacts, before the diagnosis may be found out, vary from a patient to another, and the length of the medical trajectories followed by patients is often influenced by the first doctor met on the patient's initiative. For instance, patients affected by Marfan syndrome had in average 8 contacts before being diagnosed (the median being 2 or 3). Above-mentioned Eurordiscare 2 survey highlighted as well that before receiving a confirmatory diagnosis, 40% of patients first were misdiagnosed, which has given rise to medical interventions that were useless, or even inadequate.

When none of the practitioners are able to produce a diagnosis and the ad hoc care (which is most often the case), the succession of consultations generates wastes in terms of time consuming and medical acts, in addition to human costs: the lengthening of the delay preceding the follow-up may have severe consequences on the patient living prognosis or be responsible for the disease's progression. To date, there isn't any figure about an estimation of extra costs, either for the pa-

---

<sup>5</sup> Survey published in 2005. EURORDIS is a European federation of ill persons and active persons associations in the field of rare diseases.

<sup>6</sup> B. Barataud defines "diagnosis nomadism" as "belated diagnostics" as well as "wrong diagnostics", Barataud B. « Cinq mille maladies rares, le choc de la génétique : constat, perspectives et possibilités d'évolution », Paris: Conseil Economique et Social; 2001.



tients or for community, relative to diagnosis nomadism; but those medical expenses are under the Social Security charge<sup>7</sup>.

The first and third characteristics of the French healthcare system stated above entail other outcomes to the provision of care for rare diseases according to multiple competences they require. In the context of a fragmented medical practise, patients affected by a rare disease are cut into pieces according to their symptoms and could have false diagnosis. For instance, a patient suffering respectively from eye trouble, heart disease and orthopaedic problems, will be led to consult separately the different physicians specialized in each of these organs, as it is the case for non rare diseases. Unfortunately this combination evokes a Marfan syndrome, which could be recognized only through a multidisciplinary advice by a college of specialists of each concerned organ and of the concerned rare disease<sup>8</sup>.

Besides the diagnosis phase by “super specialists”, patients often need a multidisciplinary follow-up performed by other types of medical or medico-social professionals (for example, general medicine, physiotherapy, psychiatry, orthopaedics or else social assistance), that also requires a specific knowledge in comparison with “classical patients”, for their practicing by themselves without knowledge about rare diseases could be hazardous and even harmful for patients<sup>9</sup>. Though, inpatient and outpatient services work separately, whereas rare diseases specialists are often taken into hospitals, and although follow-up needs to be achieved near patients home. Though, in the course of medicine studies rare diseases are not broached. Doctors have to specialize in a medical discipline, which often corresponds to an organ or a system (heart, eye, skin, for instance), but as some of them grant it, with respect to rare diseases they are “like non-specialized because patients rarely come with specificity”<sup>10</sup>. Knowledge for each rare disease is hold by few specialists (whose speciality refers to an organ too) since this knowledge is untitled to specific investments, like observing a high critical number of patients, or carrying out clinical trials and researches.

---

<sup>7</sup> Source : « Prise en charge des maladies rares dans le cadre du dispositif ALD : avis », rapport annexe, Haute autorité de la santé, 2005. To our knowledge, there is no further available study dealing with diagnosis nomadim costs that would have been carried out ever since.

<sup>8</sup> This information has been collected through an interview with the coordinator of the Centre of reference for the Marfan Syndrome, Hôpital Ambroise Paré, APHP Boulogne.

<sup>9</sup> A patient affected by myasthenia is reported to have been staying 8 years in psychiatric hospital. “This mistake is not uncommon, and so is abusive usage of psychiatric domain”. (Ibid)

<sup>10</sup> Ibid. For most of their “classical” patients, needs are identified and codified.

Knowledge for rare diseases comes as a human specific asset in the sense of Williamson (1991)<sup>11</sup>: it is non-redeployable asset, since competencies for a rare disease are hardly valuable for frequent diseases since they are particular cases of a general knowledge<sup>12</sup>.

Health care provision for rare diseases requires to create a more anchored and legible marking-off of specialists to reduce the information problem, and to discard speciality and structural fragmentation, in order to favour a tight coordination between various complementary competences, for the establishment of diagnosis and the medical and social follow-up, in order to mitigate the specific assets complementarity problem.

### **Public policy advocated organizational solution**

Facing this two main identified problems, French health authorities adopted the National Plan For Rare Diseases in 2004, which instituted the CRMR. CRMR are selected through annual competitive calls for proposals<sup>13</sup>. Applications are exclusively opened to physicians practicing in public teaching hospitals<sup>14</sup>, and are reviewed by the National Consultative Comity for Labellization (CNCL)<sup>15</sup> according to objective criteria based on medical data (such as the prevalence of the disease, the state of the art in the knowledge of the concerned rare disease). Nevertheless criteria are obviously based on applicant team of practitioners characteristics, which enable to appreciate their scientific excellence and their ability to become the main correspondent for patient affected by the rare disease they will be labelled for (i.e. observation of critical numbers of patients, results from carried-out program researches, participation to clinical trials and publication of scientific works on the concerned rare disease). The selected teams of practitioners are awarded with the label, embodied by the name “CRMR”, for one rare disease or a group of closely-related rare

---

<sup>11</sup> As Williamson (1991) describes them, human specific assets refer to experience effects hold by some actors.

<sup>12</sup> The knowledge dealing with human genes may help to better understand some frequent diseases and some drugs dedicated to a rare disease may be used for a non rare disease as well, but this obviously refers to pharmaceutical sector and fundamental research rather than to applications or consultations. For example, knowledge about Neurofibromatosis in the field of dermatology isn't valuable for acne, rash, sclerosis or squama.

<sup>13</sup> Calls for proposals are ruled by decrees, cf.: DHOS/DGS/2004 no245 du 27 mai 2004 relative à l'appel à projets auprès des centres hospitaliers universitaires en vue de l'obtention du label de « centre de référence pour la prise en charge de maladies rares ».

<sup>14</sup> “Centres hospitaliers universitaires” (CHU) in France are mandated to provide care services for patients but also to train future doctors and to proceed to research programs. They are publicly funded.

<sup>15</sup> The CNCL (Comité National Consultatif de Labellisation des centres de reference de maladies rares)] is composed of experts, patients' representatives, and members of learned societies and relevant authorities.

diseases, for an initial 5 years duration, which period is sanctioned by an evaluation. Specific funds are allocated to each CRMR over this period. To date, 132 CRMR have been labelled respectively in 2004, 2005 2006 and 2007. Those CRMR are entrusted with five missions<sup>16</sup>:

To improve diagnosis access and define medical and social follow-up of patients, through links of care<sup>17</sup>, and clinical pathways between them and other health services;

To improve care and follow-up of patients near their home by identifying geographical medical correspondents scattered over the national territory<sup>18</sup>: CRMR especially coordinates its actions with the other centres dealing with the same pathology(ies), organises links of care, care paths or implements networks of care, it trains and informs health professionals non specialized in rare diseases; CRMR has then to develop tools to disseminate information about the rare disease(s) it deals with;

To involve in the improvement of knowledge and practices dealing with rare diseases: CRMR disseminates follow-up protocols (in relation with the national health service for the reimbursements of care costs), sets and diffuse good professional practices in connection with other national and international teams dealing with the same disease(s), and has to guide and coordinate non-specialist professionals, who may be medical or social actors, or else proximity hospital; CRMR has to carry out research programs and epidemiologic observation, it has to support research and clinical trials;

To develop coordination tools tying the various actors and structures dealing with same disease or group of diseases;

To give health authorities the means to manage health policy concerning rare diseases, and to work with patients associations in order to implement social follow-up.

---

<sup>16</sup> Source: National Plan for rare diseases, 2004; decree with reference DHOS/DGS/2004 no245 du 27 mai (ibid) ; « Référentiel pour l'évaluation des centres de référence maladies rares », HAS, 2007 (the guide for CRMR evaluation).

<sup>17</sup> By analogy with the definition given to the supply chain in Raynaud, Sauvée, Valceschini (2005), within the framework of the agro-food sector, as the set of successive stages through which a product is passed around before being sold, "links of care" may be seen as the set of successive and related provision of care by multiple physicians (or more generally health professionals) treating the same patient, from the first visit of patient to its possible recovery, and through technical, clinical, surgery acts.

<sup>18</sup> A ministerial act of April 2007 officially institutes the nomination of these correspondents, who will be designated by CRMR and acknowledged by Health regional agencies (ARH). They will be called "competency centres". Links between these structures and CRMR should be more formal then.

CRMR will be assessed through two devices respectively after three and five years. The first one is an auto-evaluation led by CRMR thanks to a guide elaborated by the Health regulator including 12 criteria to assess the degree of achievement of the above-mentioned five missions. The second one is an external audit led by health authorities: label might then be taken away from its holder, when the concerned team wouldn't achieve the missions they are entrusted with.

This French public health policy also inscribes in the framework of a European public health program for rare diseases. To date, except France, five other European countries “have officially adopted the concept of centres of reference for rare diseases within the context of a national policy regarding rare diseases: Bulgaria, Denmark, Italy, Spain and Sweden”<sup>19</sup>. As noticed by the DG Sanco of the European Commission<sup>20</sup>, there are discrepancies between EU countries in the definition of rare diseases (in connection with the prevalence), in the process for selecting and designating centres of reference (“Some countries take a national approach to the concept, while others take a more regional one”<sup>21</sup>), and in the geographical distribution of centres per country.

The more recent concept of European network for rare diseases developed by the DG Sanco Task Force for rare diseases<sup>22</sup> intends to homogenize the definition of centre of reference for rare diseases within the EU members. It aims besides to encourage national centres of reference in working together rather than remaining isolated, for that patients could benefit from the latest results of research including those springing from another member country, and that “expertise should travel rather than patients themselves”<sup>23</sup>.

---

<sup>19</sup> Source: “Centres of Reference for rare diseases in Europe: State-of-the-art in 2006 and recommendations of the Rare Diseases Task Force”, December 2006.

<sup>20</sup> DG Sanco is the Health and Consumer Protection Directorate General: [http://ec.europa.eu/health/ph\\_threats/non\\_com/rare\\_8\\_en.htm](http://ec.europa.eu/health/ph_threats/non_com/rare_8_en.htm)

<sup>21</sup> Idem

<sup>22</sup> SANCO Rare Diseases Task Force (RDTF) was set up in January 2004 by the European Commission's Public Health Directorate and aims notably to advise and assist the European Commission Public Health Directorate in promoting the optimal prevention, diagnosis and treatment of rare diseases in Europe, in recognition of the unique added value to be gained for rare diseases through European co-ordination (source: <http://www.rdtf.org/testor/cgi-bin/OTmain.php>). It is mandated to provide and develop a general concept for a European system of centres of reference, and furthermore not limited to the area of rare diseases.

<sup>23</sup> Source: “Centres of Reference for rare diseases in Europe: State-of-the-art in 2006 and recommendations of the Rare Diseases Task Force”, December 2006.

To better analyse CRMR, better understand the stakes for care provision and organizational outcomes in the healthcare system and to assess the economic results that may be expected from this new device, we call on the organizational teaching from the Transactions costs theory.

## **2. The resort to transaction costs economics contributions to tackle CRMR**

Transaction costs economics (TCE) recognises hybrid forms, as a class of governance mode supporting exchanges between agents (Williamson 1991; Ménard 1997, 2004a, 2004b, 2005), and to which we identify CRMR. TCE paradigm is also helpful for its focussing on the need for a tight coordination between agents when transacting –and in this specific case transactions would refer to the various stages in the provision of care and links between them, for example the transfer of patients between practitioners. This coordination appears to be governed by an authority which may be more or less strong and implies governance costs. The principle of “discreet alignment” advocates that governance should be aligned on the transaction characteristics so that costs could be minimized.

### **The “Economics of hybrid forms”**

CRMR appears like a hybrid, in its designation as a label and a network by health authorities and in its functioning. Hybrids are defined by a comparison to the two polar governance modes, firm and market; hybrids “govern transactions involving a significant dependency between assets that are hold by autonomous entities, without justifying integration within a firm” (Ménard 1997)<sup>24</sup>. Although this definition rather fits to business-related or industrial sector (i.e. for profit area, whereas in France hospitals are non-for profit entities), some features of hybrids exist in CRMR, notably the fact that hybrids include multilateral arrangements between two or more partners remaining independent, such as doctors or hospitals. In the case of CRMR, those arrangements coincide with the coordination tools they are supposed to implement, to tie relations with other necessary professionals involving in the follow-up of patients. Those arrangements are expected to favour information transfers between actors and to allow coordination between complementary – and here, human– assets, as these properties are acknowledged to hybrid forms (Ménard 2004a). Hybrids features are encapsulated both in the label and in the network aspect of the CRMR.

---

<sup>24</sup> Hybrid forms may take on different kind of designations, such as network, collective trademark, alliance, subcontracting, franchise, and so on (Ménard 2004a).

Since label is likely the privilege of the agro-food domain (Ménard 1996; Raynaud, Sauvée, Valceschini 2005), it is a reputation mechanism signalling a quality level or characteristics of a good or service. By attributing a label to teams of practitioners, health authorities wanted to clearly identify specialists for each rare disease, and moreover to identify specialists who may be considered as the best ones. It means that they target a level of quality of care, which we may suppose to be at a higher level than it is expected from the provision of care for non rare diseases, since labelling procedure selection and assessment is unprecedented and more demanding than previous quality procedure in the healthcare system. Quality is specified through norms in the provision of care, over the medical trajectory, and norms coincide with the achievement of the five missions CRMR are mandated with. Norms are collectively (i.e. for all CRMR and consequently for rare diseases that benefit from the labellization) implemented and enforced like for the agro-food label. Like for agro-food label, the label CRMR involves a third party (*ibid*) which in the present case is entirely public, embodied by the health authorities, and which monitor the labelled team activities (as would be the farmer). Like the producers making specific investments inherent to the respect of norms and specifications of the good they provide, CRMR have made such specific investments prior to the labellization (the above-mentioned specific assets, and what made their reputation vis-à-vis health authorities) and will do it further to the labelling in sharpening their knowledge about rare diseases and in settling coordination tools between the various professionals dealing with the same diseases and patients.

The network is often the special governance mode chosen for R&D cooperations, in various sectors of activity based on knowledge, like biotechnologies (Powel, Koput, Smith-Doerr 1996; Staropoli 1998). Actually, the required knowledge for these activities is diverse and scattered between different actors, as it is true for the provision of care for rare diseases. Confronting these knowledge demands to create an interface which is able to coordinate them.

Like the network, CRMR will be shaped by institutional arrangements involving repeated and stable contractual links between remaining autonomous entities (Ménard 2004a). The contractual aspect is encapsulated by the application proposals the labelled team has made, each member inscribing his name in it: contract is concluded between the team and health authorities, but implicitly, and above all, between the team members either. Those entities, alluded in the aforesaid missions of CRMR, may be identified and likely framing the CRMR network:

- A first interface of the network is the CRMR itself (namely, the labelled team) which appears as the core of a “great” and loose network (framed by other health professionals and which will be tackled thereafter), as well as a small and tight network (in the sense of Thorelli analysis, 1986; see also Staropoli 1998a, 1998b). This first interface is constituted by different super-specialists who are organized in a multidisciplinary consultation<sup>25</sup> to enable them to deliver a collegial advice on diagnosis and follow-up schedule; or who share their practice (and practice time) and pool their acquired knowledge<sup>26</sup>. Though, those specialists are taken in different services –with respect to their respective speciality–, or even different hospitals.

- A second interface includes several types of members in the “greater” network, including: 1) the competency centres for rare diseases (which have been instituted by a decree and will soon be nominated by CRMR) are the local correspondents of CRMR, framed by inpatient specialists identified by the CRMR as holding capabilities to deal with the concerned rare disease within local hospitals, notably because of their experience. Those competency centres for rare diseases (CCRM) will be able to provide patients with multidisciplinary consultation so that patients spare time and travel costs they would have to bear when CRMR would be the only one competent to be consulted for the concerned rare disease<sup>27</sup>, and it is better for patients’ satisfaction that they can benefit from a follow-up near home. Moreover consultation services capacity (in term of patients number) of a unique labelled team isn’t sufficient, in a context of chronically diseases.

---

<sup>25</sup> According to the experience of centres of reference for Marfan syndrome and for Neurofibromatosis, practitioners of CRMR (often prior to the labellization) have agreed to consult patients together one or several days per week. This consultation concerns the rare disease they have been labelled for, in which each practitioner of all necessary specialties plays a part, and aims to make a diagnosis or to follow up previously-diagnosed patients. Although these practitioners are taken into distinct hospitals or at least distinct hospital departments, for this consultation they are often induced to practice clinical examination in unity of time and place, in order to avoid that patients have to come out several times, and to allow a better efficiency of an only consultation where practitioners may corroborate their results. After the consultation, practitioners deliberate about diagnosis and recommendations for treatment. CRMR coordinator takes decision about diagnosis and helps the other specialists of the multidisciplinary consultation to formulate recommendations.

<sup>26</sup> For example the observation of a further patient by one of these specialists may enrich the knowledge of the whole labelled team thanks to information transfer, since the patient would display new clinical signs or reaction, or since the observation of a further clinical case would increase the statistics of a sign, allowing to establish it as redundant among patients suffering from the same disease. This organizational solution advantage is to mutualize acquired knowledge, which may be entered in a database, as it is the case in the centre of reference for “Embryonic development abnormality” of Robert Debré hospital in Paris. Other coordination tools have been considered such as shared medical file making a n easier medical trajectory for the patient, like in the centre of reference for Marfan syndrome in Boulogne.

<sup>27</sup> Travel costs may also be borne by community since reimbursements are integrated in the social security program for rare diseases.

They also may take part in research programs and clinical trials led by CRMR: the more specialists available to observe patients affected by a rare disease, the more knowledge about it to be acquired. 2) Other health or medico-social professionals frame the care paths or links of care, such as general practitioners, specialists of outpatient services, but also physiotherapists, psychologists, orthopaedists, social workers, for example. These professionals hold complementary competencies towards those hold by the CRMR and the CCMR, and are necessary for the follow-up of patients, for treatments, adapted education or social welfare. 3) European or even international specialists of a concerned rare disease are also entitled to be correspondents for CRMR, to transfer mutually their knowledge and to carry out research programs or clinical trials.

In both of the interfaces of the CRMR network, members remain also autonomous but share human assets and make common investments for coordination tools and a growing mutual knowledge. Such network echoes to Kogut (2000) definition of network as the capacity to promote variety, of goods and specialities, and to coordinate specific activities. In a sociological meaning, network is defined as “a collection of specific relations (for instance collaboration, help, advice, monitoring or else influence) among a finite set of actors” (Lazega 1998). This underlines the multiple possibilities of transfers or exchanges that each member may have with another, depending on his position and role within the network. Thorelli (1986) argues on this purpose that network may be tight or loose, according to the number of participants, to the intensity of relations between actors, to the role of members in the whole activity of the network (whether it is a core role or not) and of the type of interactions between the different positions of the members in the network. Position in the network is also linked to the power hold by a member.

### **Authority and coordination**

TCE lays emphasis on the notion of coordination which we mentioned several times above. Coordination is “a set of processes by which initially distinct plans are brought to a condition of compatibility” (Ménard 1994), as it would be the case for care provided by several doctors dealing with same patients and diseases. Ménard (2004b) stresses the role of information and communication for a good coordination: hybrids are chosen notably to permit a better circulation of information (with arrangements such as devices that plan for partners how to share information, with which communication feature, to which frequency, and how to stock it, etc.). What allows coordination between actors actions is then the implementation of institutional arrangements which rule the conditions of partners for cooperating (Staropoli 1998b). In hybrid forms, rules are



implemented by an authority which may be compared to health authorities implementing the missions and specifications of CRMR. Relying on the definition of authority, we identify either the labelled team as holding authority within the network of practitioners acting along the medical trajectory.

Speaking about hybrids, authority is the “means to alleviate the lack of hierarchy which would have influenced actions of each agent within an integrated form, and would have decided in last resort” (Ménard 1997). Authority within hybrids manages resources, takes decisions about actions to lead, rules the conditions of transacting between members (as the aforesaid conditions to share information), and monitors member activities. Health authorities carry out this last activity of monitoring through the evaluation of CRMR and the possibility to remove the label to a team. The CRMR (embodied by the labeled team) rules the actions of other professionals acting in the provision of care for rare diseases through the missions that it is mandated to: namely, i) the provision of protocols of care and the good practices for the rare disease CRMR has been labeled for, which will be spread among health professional and social workers; ii) the division of task and distribution of roles CRMR has to implement between health professionals; iii) the identification of health professionals who work with CRMR through a network, like the nomination of CCMR. It isn't uncommon to hybrid forms that authority be delegated to a member of the agreement (Ménard 1995) and it may be held to the actors displaying one of these three characteristics: influence, trust and leadership (Ménard 1997). Besides, Lazega (1998) underlines that actors concentrating a lot of resources are in a better position within a network to influence the setting of rules. Resources here may be considered as the knowledge held by CRMR teams.

The view of authority suits to practitioners since it supposes symmetry of agents (Ménard 1995a), notably with respect of decision making power, and since there's no hierarchy between practitioners of inpatient and outpatient services.

### **Alignment principle and costs comparison**

TCE conjectures that the choice of a mode of governance supporting transactions –and a fortiori provision– is guided by agents' purpose of minimizing costs (Williamson 1985). It emphasises that specificity of assets and uncertainty involved in the transaction strongly influence the level of

these costs and, by the way, the choice for a governance mode. Uncertainty<sup>28</sup> may be evoked by a lack of information (it isn't widely spread among people), complex or opaque information, or else the difficulty to obtain information as it is the case for rare diseases. Typically, this kind of undergone problem with information or assets specificity gives rise to important transaction costs. In that sense, TCE advocates that governance choice is "aligned" with the transaction attributes which may arouse high governance costs: TCE aims to show how to minimize those costs (Williamson, 1991).

Common tool to allow assessing the advantage of a governance mode is to compare governance costs of each organisational solution relatively to the benefits they bring about (Ménard 2005b). Governance costs may be defined as costs undergone when transacting: they may be for example information costs, partner-seeking costs, activity-planning costs (i.e. how to forecast every situations and the actions to lead when facing each situation), monitoring and incentive costs (Williamson, Riordan 1985), which costs are increasing, but may increase less quickly when transactions are governed by hybrids<sup>29</sup> facing with specific assets.

Referring to TCE, we could admit that CRMR are aligned, organizing care provision through a hybrid governance mode when facing information issues and asset specificity. Nevertheless, that doesn't mean that CRMR are efficient to provide care for rare disease. Efficiency depends on how incentives to cooperate are implemented, surrounding transactions between practitioners who are used to providing care individually. In that way, it depends on the degree of authority, and credibility and acceptance thereof, that rules the governance mode. Finally, it is linked to costs of implementing these new structures, label and networks –the governance costs– relatively to the ability of CRMR to lessen diagnosis nomadism problem and to improve quality of care for rare disease.

---

<sup>28</sup> Uncertainty is often assimilated as environmental uncertainty, dealing with institutions, market design, for example, and as behavioural uncertainty, dealing with opportunistic nature of agents, as it is postulated in the TCE paradigm. Such uncertainty isn't relevant in the case of provision of care and notably when practicing within public hospital, since appropriability hazards and opportunism are mitigated by the medical deontology of practitioners'

<sup>29</sup> This assertion is usually done to compare hybrids relatively to market and hierarchy, as alternative governance modes. This comparison isn't relevant in these terms for the provision of care within the French healthcare system, since we can't qualify it as a market: notably, there is no price system since a reimbursement of care costs exists through the Social security. Comparison is more relevant between a centralised or decentralized organisation of care.

### **3. The introduction of a new authority within the healthcare system: conditions of a success**

We qualify authority of CRMR within the healthcare system as a new one since the introduction of labeling reshapes the French healthcare organization. On the one hand, the selection of teams of practitioners of excellence breaks with the traditional principles of recognition of the right to practice medicine. The granting of for a quality certification with the label is a hitherto original approach from the regulator in the field of health. It brings about numerous outcomes on medicine practice conception. CRMR label is based on the acknowledgement of a medical excellence to a small number of practitioners. Theoretically, the right for practice of medicine is granted through university education and based on the success in a specialization chosen by the future doctor. On the other hand, labeling short-circuits the principle for allocation of resources in the framework of public health policy. CRMR is included in a hospital department, though it doesn't meet any hospital compartmentalization definition. This lack of "legal" definition of CRMR is due to decompartmentalization involved by care provision for rare diseases, but also to resources allocation. By awarding a label, health authorities allocate to CRMR human, financial, and material resources (such as scanner, electrocardiogram, for instance). This allocating method breaks with the "Healthcare Regional Map" (SROS)<sup>30</sup> that allows a hospital to acquire technical equipment and to create jobs, in connection with needs of the patient attraction area (i.e. regarding demographic and geographic data).

Besides, CRMR, and obviously its coordinator, has full discretion for the use of CRMR resources. He also has full decision rights on CRMR activity. This introduces interference in hospital hierarchy in which department chief traditionally decides of the use of resources of its department. Although CRMR is included in a department it has its own resources, without the department chief having any decision right on CRMR resources<sup>31</sup>. This new allocation principle releases CRMR from the decision right of hospital director. In the traditional hospital organization sketch, practitioners are constrained by hospital administration objectives that plan resources allocation by department. Administration is also constrained by health authorities budgeting, and it

---

<sup>30</sup> SROS (Schémas régionaux d'organisation sanitaire) are defining health territories and graduate levels for health care which are based on proximity and specialisation. It is conceived as planning device which is a base for creation, extension or cancellation of a hospital.

<sup>31</sup> This analyse isn't of interest when CRMR coordinator is also hospital department chief; but CRMR coordinator may also be a hospital practitioner.

may be reluctant to provide certain services or it may command restrictions of medical activity (Harris 1977)<sup>32</sup>.

Finally, decompartmentalization of specialities and hospital structures, which is entailed by CRMR, is equivalent to a lending of practitioners between hospitals or departments, since they give medical time to CRMR to the “detriment” of the hospital or department they are appointed to. This breaks with traditional hospital organization too. A survey carried out by Binst and Schweyer (1995) reveals that staff reshuffle and loan between services are really difficult, even when they would be rational in regard to activity constraints.

This new way to tackle the organization of care may constitute a model, but it must achieve at first some conditions of legitimacy of the new perception of a ranking among practitioners and practice, and prove to be efficient.

### **Legitimacy of CRMR authority**

One of the main conditions for a label to play its role of signaling a quality level is the credibility of the label (Crespi, Marette 2005; Raynaud, Sauvée, Valceschini 2005). Credibility can be considered through the evaluation procedure by authorities. But is it sufficient in the case of CRMR?

The labelling procedure intends to promote a new competition between practitioners to take selection process as credible: some professionals haven't been granted by the label, since they were not considered as qualifying for the settled excellence criteria. As far as knowledge inherent to each disease is held by few practitioners, we may question whether a competition for each disease actually exists. Moreover, since several CRMR have been labeled for a same group of closely-related rare diseases<sup>33</sup>, did any competition principle preside over the labellization of those centres? Finally, will there be still other specialists who will be able to apply to the labellization and challenge the team in position: notably will those potential challengers be able to improve their competencies and ability to deal with a rare disease, since they won't benefit from resources in that purpose? Then will health authorities be able to find replacement solution?

---

<sup>32</sup> About conflict between administrators and practitioners, see Harris, 1977: hospital is seen has a double firm, the first one deals with medical staff provision, the second with administration offer; each has its own managers, objectives, price strategy and constraint.

<sup>33</sup> For instance, 7 centres of reference for “Embryonic development abnormality” have been labelled.

The leadership of CRMR should also be acknowledged by other practitioners: they have to agree to follow recommendations expressed by CRMR, and to comply with the role they will be attributed by CRMR. This aspect would be made credible for example by the reimbursement regime that health authorities could set up (and they have actually planned to implement such a system), since care could be reimbursed only when they inscribe in the CRMR sketch. Though, the ranking of quality of care implied by the labelling livens up “corporatism”. Other practitioners, and in particular other specialists of rare diseases, need to be motivated to participate in the results of this public policy, and to allow performance. CRMR should then implement organizational motivations (Ménard 2004) involving necessary professionals in the medical and social path. At the same time, CRMR authority is the means to manage resources and reallocate them within the network and to take decisions. The question is which decisions will be taken –and will have to be taken, in order to permit performance–: this question also raises the issue of a centralization or decentralization of decision-making within the network of practitioners. French authorities seem rather to advocate centralization by attributing resources only to CRMR.

## **Performance**

Performance in healthcare targets both the minimization of care provision costs and the maximization of quality of care (which is called “technical efficiency”, Hirtlzin 1999). Indicators for quality have been developed for health sector, and focussing on inpatient services, they deal in part with the improvement of patients satisfaction, the accessibility to services in terms of delays, the respect of good practices.

CRMR will be assessed on these criterions, and particularly access to care for patients is one of the main goals to achieve in order to avoid the pitfall of diagnosis nomadism. The label intends to make the competencies of practitioners for rare diseases more legible and to have medical trajectories of patients be more homogeneous. However this is again challenging, since we may suggest that GP or outpatient specialists, in such a device, won’t be able to know better where to address patients, when facing to an unusual clinical sign, if they don’t know the disease and the sign. Orientation at the beginning of the medical trajectory might remain problematic. CRMR being may be more efficient after the diagnosis than before, because CRMR might be unable to have patients with a rare disease be systematically followed up by adequate structures.

Centralization of decisions and resources by CRMR may appear to be inefficient with respect to the medical actions before the diagnosis. Decentralization, like regionalization (i.e. a multi-competencies platform enabled to take in patients with all kind of rare diseases, and to reorient them to the competent more specialized centre) would then be a solution to be compared to the organization with CRMR.

According to economic performance of CRMR, costs will be arisen: the costs of implementing CRMR (40 million euros have been allocated to the settlement of CRMR over the four labellization periods), the costs of building networks and of implementing coordination tools (which also may be time consuming and time which isn't devoted to medical activities). At the same time, care provision costs should be reduced, notably by avoiding redundancy or uselessness or else conterproductivity in medical acts. Authority should reduce information costs and accelerates decision-making (Ménard 1994, 2004b). Network should bring increasing informational yields. These costs (and the former may be assimilated to internal governance costs) will be compared to costs undergone through the previous sketch of care provision, as TCE method suggests it, that is to say for instance, cost of seeking adequate health professionals, costs of diagnosis nomadism (this latter costs could be assess regarding the difference in length of medical trajectory and in number of medical contacts before the diagnosis).

### **The CRMR as a model of organization?**

If the device settled by this public health policy achieves performance in quality and costs, it will prove to be efficient for the provision of care for rare diseases. As this device appears like a reform in the provision of care and in a context of debate about how to decrease health costs, we may ask whether CRMR would represent a model of organization of care for non rare diseases, particularly on purpose to rationalize health costs, and then to improve technical efficiency as well.

Indeed, a speech<sup>34</sup> addressed by the French Health Secretary in 2005 revealed that the costs of medical acts redundancy raise 1,5 M€ –corresponding to 15% of medical acts and representing 13,6% or so of the French health budget–, which may be considered as wastes for community and

---

<sup>34</sup> This speech aimed to provide about “personal medical file”, which device has been set up in order to diminish redundant acts costs.

is linked to all kind of diseases, including non rare diseases. Those costs may notably be due to the lack of coordination between practitioners' actions with a same patient for example or concerning the knowledge sharing: this is particularly true for aged patients who are followed-up by several practitioners, or more generally for patients suffering from chronic diseases calling for a multidisciplinary follow-up, or else for very complex diseases.

Additionally, in a costs rationalization and quality outlook, previous studies, dealing with non rare diseases, have already shown evidence that a better coordination between healthcare system actors would be necessary to allow important sparing. They have underlined the need for care provision within the framework of a structured and coordinated network emphasizing the importance of practitioners tasks complementarity when treating a same patient (Binst, Schweyer 1995).

A report<sup>35</sup> states that “care supply suffers from important lasting compartmentalizations, particularly regarding relationship between outpatient services and hospital”, and highlights the need for a better repartition of tasks between hospitals and between different structures of care, including outpatient services (GP, nurses, etc.) either. This hyphenation bothers the global and coherent approach of the patient. But it is also a source of extra costs, since there is a bad using of the healthcare system: hospital does acts which could be done by the GP to less expensive costs, GP does paramedical acts which could be done by other professionals, or else nurse does acts which could be done by auxiliary nurse. A better distribution of tasks, resources and follow-up could save money and improve quality of care, which could be possible by the implementation of networks of care of outpatient and inpatient services. Similarly, another fact of healthcare overusing revealed in the same report is convincing: “when more than a thousand hospitals of any size and without coordination provide emergency services, involving each night ten persons on duty in each entity, whereas we count less than four hundred urgent surgery acts a night in France, we measure the waste of medical staff who could be employed in another way with a better efficiency. In addition to financial aspect, this situation raises also a health security issue, since under a number of annual surgery acts it is proved that a surgeon loses his technical capacities and may be able of less performance or even become harmful”. This implies a differentiation of hospitals and a sharing of technical equipment and of night guard.

---

<sup>35</sup> Conseil économique et social : « L'Hôpital Public en France : Bilan et Perspectives », Éric Molinié, 2005

It is mainly the organization of CRMR in a network design which enables to develop coordination between practitioners involved over the medical trajectory and that could create a paragon, for other non rare diseases either. One of the originality –in comparison with other design of network of care– of CRMR lies in the obligation for practitioners to form networks and to shape it with strong coordination tools (that we may imagine as being rules for information and knowledge transmission, meetings, consultations, etc.): those obligations are inscribed by the health regulator in the five-year duration contract granting the label and CRMR will be evaluated to know if and to what extent these missions have been completed. The completion of those obligations conditions also CRMR funding.

Networks in the healthcare sector have already been experienced before CRMR in France, as being introduced in the legal framework: for instance Hospital Laws in 1991 and a decree in 1996 incite hospitals and practitioners to contract with each other and build networks of care (Hirtzlin 1999; de Pourville 2003). Nevertheless these legal devices are left totally to the discretion and initiative of practitioners, which explain that few of them got involved in such designs. In 2001, five years after the introduction of the law dealing with hospitals “targets and means contracts”, and providing hospitals with devices to conclude arrangements with other health entities (hospitals or outpatient services), only 33% of hospitals engaged in such “targets and means contracts”, of which only 40% involved in outside cooperation mechanisms (Gottsmann 2001).

Some networks have been constituted notably to answer to the needs formulated by HIV patients, cancer patients or aged patients, who typically needn't a punctual curative intervention, but a set of medical acts in continuity. However a report from health authorities<sup>36</sup> stressed that coordination (and we assume it as “authority”, in the sense we have defined above for CRMR, or else as a more formal coordination) in those networks isn't sufficient: “in numerous cases coordination is reduced to the only follow-up and data collection, leaving each member in a relative isolation for lack of interactions and links”; “for numerous networks, coordination and management features are often badly defined and under-estimated when preparing the project of network, which give then rise to functioning difficulties”. This explain that they can't plainly benefit from the network features: notably, gathering of individual competencies in a collective competence, and closer

---

<sup>36</sup> ANAES (Agence nationale de l'accréditation et d'évaluation en santé), today named HAS (Haute autorité de la santé): « Evaluation des réseaux de soins, bilan de l'existant et cadre méthodologique », D. LE BOEUF, Pr Y. MATILLON, et C. LACHENAYE-LLANAS, 2001.



and more extensive cooperation. Moreover, these networks have generally a regional characteristic when a national logic would be more relevant since medical guidelines and expertise could be expressed by specialists of a disease and circulated to doctors, and since allocation of resources and tasks should be organized over the national territory, to guaranty to the patient the same quality of care and of coordination in every region. An added value carried by the concept of CRMIR is that they haven't got the choice whether or not to implement networks and strong devices of coordination: it is their task specified in a contract and they are created in that purpose and monitored directly by central health authorities.

In that viewpoint, the European Commission's Rare disease Task force, mandated to provide and develop a general concept for a European system of centres of reference, is not limited to the area of rare diseases. The working group chose rare diseases "as a starting point" but also aimed to "develop a general concept for European system of centres of reference"<sup>37</sup>. Such networks could be recommended specially for diseases involving a specific knowledge, complications, chronic characteristic or several specialists.

#### **4. Conclusions**

These first thoughts about what could be conditions of success for CRMIR governance for the provision of care for rare diseases draw up a research agenda. Next step will be to analyse individually CRMIR, and to set a typology of network designs, in connection with notably centralization or decentralization of decision-making, for which we have here assumed that strong authority within the network design should bring more efficiency (in costs and quality). The analysis of patients viewpoint with respect to the criterion of improving their satisfaction, their follow-up and their delay to be diagnosed should be carried out, in order to balance this aspect of the performance of CRMIR, with the type of organization adopted by CRMIR. Finally centralization of resources and decision-making allocation need to be compared with other European (among others) health policies for rare diseases.

---

<sup>37</sup> European Commission, High level group on health services and medical care, Executive summary, November 2005

## References

- Aoki M., (1991) *Economie japonaise*, Economica, translation H. P. Bernard.
- Barzel Y., (1982) "Measurement Costs and the Organization of Markets", *Journal of Law and Economics*, Vol. 25, No 1, pp.27-48
- Bejean S., (1994) "Economie du système de santé, du marché à l'organisation", *Economica*.
- Binst M., Schweyer F. X., (1995) *La santé otage de son système*, InterEditions.
- Brousseau E., (1995) "Contracts as Modular Mechanisms: Some Propositions for the Study of 'Hybrid Forms' ", *International Journal of the Economics of Business*, Vol. 2, No 3, November, pp. 409-439.
- Brousseau E., Codron J. M., (1998) "La complémentarité entre formes de gouvernance le cas de l'approvisionnement des grandes surfaces en fruits de contre-saison", *Economie Rurale*, No 245-246, mai-août.
- Carrere M. O., (1987) "Le médecin ambulatoire et la réalité économique", *Journal d'Economie Médicale*, Vol. 5, No 4.
- Chandler A., (1977) *La main visible des managers*, Economica, 1988.
- Crespi J. M., Marette S., (2005) "Some Economic Implication of Public Labelling", Working Paper.
- Cueille S., (2002), "L'engagement des hôpitaux publics dans des stratégies d'alliance : construction et test d'un modèle d'analyse", *Finance, Contrôle, Stratégie*, Vol. 5, No 2, 5-31.
- De Pourville G. (2003), « Contractualisation interne dans les établissements publics hospitaliers », *Revue Française de Gestion*, Vol. 29, No 146.
- Godet V, Hirtzlin I, Costet N, (2001) "Prise en charge diagnostique des patients atteints de maladies génétiques rares: exemple de cinq pathologies", *Revue d'Epidémiologie et de Santé Publique*, No 49, pp.357-366.
- Gottsmann J. (2001) « Contrats d'objectifs et de moyens : où en sommes-nous cinq ans après l'ordonnance de 1996? » *Gestions Hospitalières*, Août/Septembre 2001
- Grémy F., (1997) "Filières et réseaux Vers l'organisation et la coordination du système de soins", *Gestions Hospitalières*, Juin-Juillet, pp. 433-438
- Harris J. E., (1977) "The Internal Organization of Hospitals: Some Economics Implications" *The Bell Journal of Economics*, Vol. 8, No 2, 467-482.
- Hirtzlin I, (1999) "La coopération entre organisations comme indicateur de la performance publique: exemple du secteur de la santé », *Politique et management public*, Vol. 17, No 3, septembre, pp. 108.
- Hirtzlin I, Kieyila-Loubaki F., Jondeau G., (2001) "Les trajectoires médicales des personnes atteintes par le Syndrome de Marfan", *Archives des Maladies du Coeur et des Vaisseaux*, Tome 97, No 9, 855-860.

- Kogut B., (2000) "The Network as Knowledge: Generative Rules and Emergence of Structure", *Strategic Management Journal*, Vol. 21, No. 3, Special Issue: Strategic Networks (Mar), 405-425.
- Lazega E., (1998) Réseaux sociaux et structures relationnelles, Que sais-je, Puf.
- Maze A., (2005) "Economie de la qualité : économie des conventions versus théorie des coûts de transaction ? ", *Economie Appliquée*, Tome LVIII, No 2, 71-98.
- Menard C., (1994a) "Organization as coordinating devices", *Metroeconomica*, 45 (3), pp. 224-247
- Menard C., (1994b) "La nature de l'innovation organisationnelle, Eléments de réflexion", *Revue d'Economie Industrielle*, Hors Série, 173-192.
- Menard C., (1995) "Inside the black box: the variety of hierarchical forms", in John Groenewegen (ed), *Transaction Costs Economics and Beyond*, Dordrecht: Kluwer Academic Press, pp 149-170.
- Menard C., (1996) "On clusters, hybrids, and other strange forms: the case of the French poultry industry", *Journal of Institutional and theoretical Economics*
- Menard C., (1997) "Le Pilotage des formes organisationnelles hybrides", *Revue Economique*, 48, 741-751.
- Menard C., (2004a) "The Economic of Hybrid Organizations", *Journal of Institutional and Theoretical Economics*, 160 (3), 345-376.
- Menard C., (2004b) *L'économie des organisations*, Repères, La Découverte.
- Menard C., (2005a) "A new institutional approach to organization", in C. Ménard and M. Shirley (eds) *Handbook of new institutional economics*, Kluwer Academic Press, chap. 12.
- Menard c., (2005b) "Cooperative: hierarchies or hybrids?" in J. Nilsson and K. Karantininis (eds), *Vertical Markets and Hierarchical Cooperative*, Berlin-Boston-Dordrecht-New York: Springer
- Oxley J., (1997) "Appropriability Hazards and Governance in Strategic Alliance: A Transaction Cost. Approach", *Journal of Law, Economics & Organization*, Vol. 13, No. 2., (Oct., 1997), pp. 387-409.
- Powell W., Koput K., Smith-doerr l., (1996) "Interorganizational Collaboration and the Locus of Innovation: Networks of Learning in Biotechnology", *Administrative Science Quarterly*, Vol. 41, No. 1, March, pp 116-145.
- Quelin B., (2002) *Les frontières de la firme*, *Economica*.
- Raynaud E., Sauvée l., Valceschini e., (2005) "Marques et organisation des filières agroalimentaires: une analyse par la gouvernance", *Economies et Sociétés*, Série « Systèmes agroalimentaires », No 27 (5), 837-854.
- Schumpeter J., (1912) *Théorie de l'évolution économique*, édition française, Dalloz, 1935.
- Simon H., (1957) *Model of a man, Social and Rational*, New-York, John Willey & Sons.

- Staropoli C., (1998a) "Cooperation in R&D in the Pharmaceutical Industry – The Network as an Organisational Innovation Governing Technological Innovation" *Technovation*, 1998, 18 (1) 13-23.
- Staropoli C. (1998b) "Cooperation in R&D Through a Network, an 'Organizational Gamble?' An Empirical Analysis of Rhône Poulenc Rorer-Gencell", *Technology Analysis & Strategic Management*, 1998, Vol. 10, No 4, 511-527.
- Thorelli H. B. (1986), "Networks: Between Markets and Hierarchies", *Strategic Management Journal* Vol. 7, No.1, Jan.-Feb., 37-51.
- Williamson O. E., (1965) "Innovation and Market Structure", *Journal of Political Economy*, Vol. 73 No 1, 67-73.
- Williamson O. E., (1971) "The Vertical Integration of Production: Market Failure Considerations", *American Economic Review*, May, 61, 112-23.
- Williamson O. E., (1973) "Markets and Hierarchies: Some Elementary Considerations", *American Economic Review*, May, 63, 316-25.
- Williamson O. E., (1975) *Markets and Hierarchies*, New-York: the Free Press.
- Williamson O. E., (1985) *The Economic Institution of Capitalism: Firms, Market, Relational Contracting*, Free Press, Collier Macmillan Publishers.
- Williamson O. E., (1991) "Comparative Economic Organization: The Analysis of Discrete Structural Alternatives", *Administrative Science Quarterly*, June, 36, 269-296.
- Williamson O. E., (1996) *The Mechanisms of Governance*, Oxford University Press.
- Williamson O. E., (1999) "Public and Private Bureaucracies: A Transaction Costs Economics Perspective", *The Journal of Law, Economics, & Organization*, 306-342.