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A Chemist's Community as a Forerunner in Management Change and Innovation in France during the Second Part of the Twentieth Century? The Case of the *Institut de Chimie des Substances Naturelles*, a CNRS Laboratory

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Understanding the dynamics of innovation involves local and national levels and different types of analyses. Historical perspectives stress the heterogeneity of innovation processes across time, sectors, and countries. During the twentieth century, links among science, technology, and innovation became more complex. Science, state, and industry are interconnected; science and technology constitute a continuum. What do we know about the researchers themselves and their behavior? Studying a small community of French academic natural substance chemists from the 1960s until the early twenty-first century allows us to understand how researchers interacted within the various milieus encompassing their work. These chemists seem to have assimilated both industrial norms and international academic principles early on to overcome the competition inherent in their discipline and to prepare them for globalization. Although often criticized by their peers, they serve as a model on which to pattern future French research.

Few French historians working in the twenty-first century have studied as a specific topic the relationships between the academic and the industrial worlds. Nevertheless, although methodologies and results are borrowed from French sociology, anthropology, the economics and history of science, and, of course, English and American science and technology studies, this is a historian's topic.

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In French history, there are, broadly speaking, two ways to study innovation. One is the "classical way," through business history, as exemplified by François Caron or Alfred D. Chandler, Jr.[1] The other involves innovation questions some historians of science raised when, after World War II, the boundaries between science and technology, and between science and society, became both more subtle and more complex. In France, as in the United States, the United Kingdom, Switzerland, and some other Western countries, promoting science became a state prerogative. It was a time when the state championed both "big science" and "big business." Such policies contributed to blurring the links between academic research and industrial R&D (research and development), not only with regard to biotechnology research as some historians have noted, but to research as a whole, which became a "fuzzy complex of actors and actions."[2]

Understanding the dynamics of innovation, especially in the general chemistry sector, involves examining a variety of scientific fields at both local and national levels, to reveal the interconnections among science, state, and industries. At the beginning of the twentieth century, academic research results allowed the founding of enterprises and, conversely, academic researchers increasingly used industrial products. Science and technology constitute a continuum. I have argued elsewhere that in French chemistry, university-industry links were old and well established.[3]

The study of innovation in France during the second half of the twentieth century (including science and technology history), however, remains a very risky research topic, because of the difficulty and complexity associated with access to archives, files, and information. Nevertheless, governments, as well as managers of research institutes and enterprises, consider mixed laboratories (jointly financed by the state and industry, and managed equitably by academic or industrial researchers) to be a serious path for the national economy. This new atmosphere could create broader research opportunities for business historians. Historical case studies, using appropriate archives, reveal that alternative paths were not always evident, and why some choices were made and others not. A historical case study may have a general application, "because the long

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[1] François Caron, *Les deux révolutions industrielles du XX^{e} siècle* (Paris, 1997); Alfred D. Chandler, Jr., *Shaping the Industrial Century* (Cambridge, Mass., 2005).

[2] From Arnold Thackray, ed., *Private Science. Biotechnology and the Rise of Molecular Sciences* (Philadelphia, Pa., 1998), 7, quoted by Bruno Strasser and Michael Bürgi, "L'histoire des sciences, une histoire à part entière," in *Revue Suisse d'Histoire* 55, no. 1 (2005): 3-17, 11.

[3] Muriel Le Roux, *Un siècle de recherche industrielle à Pechiney, 1850-1995* (Paris, 1998).

view reveals clear patterns of success and failure based on real experience."[4]

First, we need to consider the industrial borrowing in the management field of the directors of the *Institut de Chimie des Substances Naturelles* (ICSN).[5] Part of the French National Center for Scientific Research (CNRS), the Institute is one of the main laboratories where researchers have always worked with several firms. A majority of public and academic CNRS laboratories have had industrial contracts for a long time. Although, given the ratio of French government annual budget funding to wages, it is obvious that industrial cooperation is necessary to fund new research programs, the CNRS has hidden industry cooperation, and studying it remains taboo. Contrary to the practice at the other CNRS laboratories, however, the public has always known about the ICSN's industry "exchanges."

Thus, I focus on "science in action," studying the chemists' movements after their research at the ICSN.[6] Who were they, what did they study, and where did they work when they left the ICSN? Conjugating their original management (for a public lab) with an extensive international network (academic as well as industrial), the researchers successfully patented their discoveries (two anti-cancer drugs, Navelbine and Taxotère). This work style created a fluid environment that still surrounds the ICSN, making its story so inspiring.

The Institute of Natural Substance Chemistry, 1960s-2000s

Although French organic chemistry was brilliant during the nineteenth and early twentieth century, it was declining after World War II. Most of the few French natural substance chemists went abroad to complete their training and research.

The first two co-directors of the ICSN, Maurice-Marie Janot (1903-1978) and Edgar Lederer (1908-1988), were cases in point. Janot visited the Nobel Prize–winner Leopold Ruzicka's laboratory in Switzerland for his doctorate. Lederer, married to a French woman, was Austrian, Jewish, and, at that time, communist. Because he was not French, the CNRS, founded in 1939, offered him only a part-time position.[7] He took on work contracts with different firms to survive. Thus, he worked for a Swiss

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[4] Chandler, *Shaping the Industrial Century*, 312.

[5] The Institute of the Chemistry of Natural Substances; the CNRS is the main academic body in France.

[6] Inspired by Bruno Latour's title, *Science in Action: How to Follow Scientists and Engineers through Society* (Cambridge, Mass., 1987), translated from *La science en action* (Paris, 1989).

[7] Files "Edgar Lederer," ICSN Archives.

perfume company Firmenich under the supervision of the Nobel laureate Ruzicka, who was a scientific adviser to the firm.

After World War II, French researchers' work on natural products could not compete with that of Great Britain, Switzerland, or the United States. Janot and Lederer were nevertheless striving to do research in this field. At the time of Janot's nomination to the galenical pharmacology chair at the Medical Faculty of Paris in 1941, he had a research team working on natural substances. Although Lederer was *directeur de recherche* at the CNRS (a full-time position), he worked as head of the natural substances service of the IBPC (*Institut de biologie physico-chimique de Paris*), because there was no suitable place at CNRS to accommodate his team. He received the title of professor, but with no chair or even a lecture hall to use.[8]

In 1955, in agreement with the French government, the directors-general of the CNRS founded a laboratory for the study of natural substances: "The aim was that France should send chemists to Stockholm."[9] The measures undertaken by the Mendès France and De Gaulle governments to develop French research benefited the CNRS. With universities in a difficult situation, the CNRS was the only research organization able to create such a laboratory. For political and scientific reasons (competition between Janot and Lederer's teams, increased by rivalries between universities and research centers), and certainly because of Lederer's connections to the industrial world, the directors-general decided to nominate Janot and Lederer as co-directors of the new institute.[10] Until 1989, the ICSN had two co-directors. Pierre Potier (1933-2006) succeeded his master, Janot, and Sir Derek Barton (1918-1998), who received the Nobel Prize in Chemistry in 1969, succeeded Lederer. After that, Pierre Potier and Guy Ourisson (1926-2006, professor at Strasbourg University in eastern France, and later president of the French Academy of Science) were co-directors. From 1989 until 2009, there has been a single director: first Pierre Potier, then Jean-Yves Lallemand (1943-) after Potier's retirement, followed by David Crich.[11]

The choice of co-directors may be surprising, but it was pragmatic. Creating an alliance between the two most renowned natural substance chemists was probably the best way for France to regain a place in the

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[8] The chair in natural substances chemistry was not created until 1958.
[9] Pierre Potier, interview with Muriel Le Roux, Paris, 13 March 2001.
[10] Edgar Lederer speech delivered when he received the Gold Medal of the CNRS in 1974, ICSN Archives; Edgar Lederer, "La chimie des substances naturelles," in *Cahiers pour l'histoire du CNRS* 2 (1989): 43-54.
[11] Crich completed his doctoral dissertation at the ICSN under the supervision of Sir Derek Barton, and he did postdoctoral research under the supervision of both Potier and Barton.

international competition. Janot, and especially, Lederer, were open to the international scientific and industrial world. From the beginning of the ICSN, all the researchers had connections to British or Swiss foreign teams; the doctoral students and the researchers regularly went abroad. Janot instituted the principle of real teamwork, following the Swiss model; this was far from common practice in France. As for Lederer, he collaborated with chemical firms to secure funds, raw materials, help for development, and so forth. Both patented some results. The ICSN scientific committee included famous foreign chemists, and the ICSN quickly developed international distinction. Sir Derek Barton increased the ICSN's international connections, especially with the United Kingdom and the United States, but he had to leave the CNRS because of French retirement laws. In 1986 he moved to Texas A&M University to pursue his research.

During the 1960s, the CNRS's general director did not view industrial contracts in the positive way that the ICSN co-directors did; therefore, Edgar Lederer was worried, even though the ICSN's researchers were always in accordance with the law and the researchers' statute. The co-directors did their best to encourage researchers' cooperation with industry and to protect them from the National Research Committee. Then, the top managers changed their minds without making a formal decision: the CNRS general director let the ICSN researchers do as they wished in managing their relationships with chemical firms.

In 1975, the CNRS's directors-general concluded an agreement with the chemical firm Rhône-Poulenc Rorer (R-PR) to synergize public research with industrial R&D. Trade union opposition was very strong; unionists argued that the French government wanted "to sell the main French research body to a major capitalist firm." Although this type of contract received a more favorable reaction in the 1980s, Barton did not understand why the majority of his French colleagues were suspicious when he talked about industrial collaboration. For him, it was obvious that natural substance chemistry could not progress without the help of industrial research, which had greater means for research development than the CNRS. Like Lederer before him, Barton was used to working with chemical firms. He was open-minded because this type of collaboration was more common in Britain than in France. Potier, too, did his best to pursue and increase the international ICSN network: "Lecture tours, in many different and strategic countries allow me to reinforce the ICSN world scientific and business network built by E. Lederer and developed by S. Derek Barton."[12]

The evolution was less evident for the National Research Committee in charge of academic researchers' assessment and promotion. Publishing

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[12] Pierre Potier, Additional Scientific Report, 1982-1990, p. 4, ICSN Archives.

remained the sole criterion, and patenting was not especially favored. From the 1930s until the early twenty-first century, it has been uncommon to meet "public-sector scientists" who readily admit long-time contracts between academic research and industry, even though the French government supports these connections. It is still difficult to promote the career of a researcher who has links with industrial R&D, and even worse if the researcher collaborates with enterprises.[13] However, the independence of the laboratories' management and the researchers' autonomy, both of which were highly developed at the CNRS, allowed expression of a daring idea.

Science in Action

In 2002, French president Jacques Chirac (possibly echoing U.S. president Richard M. Nixon) declared that curing cancer was a national cause. Before this program, France did not have a central, government-funded body or a central agency for coordinating funded cancer research equivalent to the National Cancer Institute, which the United States has generously funded since the 1970s. The main funding body for public-sector (academic) research in the area on medicine and health was the Inserm (*Institut National de la Santé et de la recherche médicale*, set up in the mid-1960s).[14]

Although the CNRS does not fund cancer research, strictly speaking, in practice it is very much involved. It funds a variety of basic research projects in the life sciences and chemistry, and a number of interdisciplinary research projects (for example, new technologies in imagery for application to diagnostics), and it contributes to funding a number of mixed laboratories jointly with Inserm or with industrial firms or other organizations.

To understand what has happened at the ICSN, consider Pierre Potier's ways and means of discovering new drugs. Potier's team discovered two major molecules, patented them, and dealt with two firms' laboratories, Pierre Fabre and Rhône-Poulenc Rorer (today Sanofi-

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[13] Jacqueline Belloni's account, Paris, 27 May 2005. She is director of research, emeritus, at the CNRS in the laboratory of chemistry and physics at Orsay-University. She regularly worked with Kodak and Fuji because of her discoveries. Just before her retirement, a CNRS manager told her that she had not had the academic career that she could have expected because of her industrial relationships. See Eric Chol, "Le naufrage de la recherche," *L'Express*, 20 April 2000; Jean-Marie Laborde from Grenoble, who with his team patented geometry software that gave a return of 4 million FF in 2000 to the CNRS, was portrayed as a traitor during a scientific meeting because of his research contracts with Texas Instrument.

[14] Caron, *Les deux révolutions industrielles du XX^e siècle*; Chandler, *Shaping the Industrial Century*.

Aventis), to turn the molecules into the drugs Navelbine and Taxotère. The two drugs generated roughly 90 percent of the royalties that firms paid to the CNRS until 2007, and created revenues exceeding a billion Euros per year for each company. The revenue for Taxotère in 2004 was 1.43 billion Euros.

Recruited in 1957, Pierre Potier worked all his professional life, more than forty years, at the ICSN. However, he negotiated the means to take on other responsibilities: founding and managing one of the first mixed laboratories at the CNRS, run in conjunction with the pharmaceutical firm Roussel-Uclaf (1984-1989), and being in charge of the General Head Office for Research and Technology at the Ministry of Education, Universities, and Research (1994-1996).[15] He received the most important research prize in France, the gold medal of the CNRS, in 1998, and he was amply rewarded for his discoveries in France and abroad. He was, until his death in 2006, the only Frenchman who had sold two drugs to the American market.

He had dual training, receiving his certificate in pharmacy in 1957 (which gave him good contacts at Rhône-Poulenc Rorer, the firm where he did his pharmacist certificate courses), and a doctorate in organic chemistry in 1962. One of his main precepts was a collective approach to his work, a belief shared with his master, Janot. He never published alone; he included all his team members in article credits and in drug patents, precisely quoting his colleagues. He never practiced the "lift-signature."[16]

Potier and his team always had the same work pattern. Potier cleared the way for a new research subject, creating an exhaustive bibliography, and then began his research. The team repeated colleagues' experiments to confirm their hypotheses and then defined a new research field. During this fundamental research period, Potier allowed no one in the team to communicate or speak about the work in progress. Potier managed his team as an industrial manager would have done, releasing no information outside the ICSN without his written permission.[17] When the fundamental research phases were completed, he himself contacted pharmaceutical firms that might be interested in the results of his team's research. He entered into negotiations only when he was sure of the drug's feasibility. No industrial manager was ever associated with the team at the outset of a research project. This strategy allowed Potier to keep complete control of

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[15] Directeur général de la Recherche et de la Technologie.

[16] The individual in charge of a research project might include an author even if the person had not worked with the team for strategic reasons not linked to the research. Pierre Potier did not suffer from narcissism and thought that if he wanted something, he had to achieve it himself.

[17] Muriel Le Roux, "Genèse des textes de Pierre Potier, chimiste des substances naturelles," *Genesis* 20 (2003): 91-127.

the intellectual property and guaranteed him industrial property in successful research cases. The ICSN researchers, especially Potier, used industrial R&D as a complementary service provider for academic research.

In the late 1960s, he started looking for compounds that might have anti-tumor properties, because doctors had told him that they needed to know how active chemotherapy compounds were. Already internationally recognized as an alkaloid chemist, he had patented some of his results. Potier and his team started their search for anticancer drugs by looking more closely at the vinca alkaloids, previously studied at the ICSN. For eighteen months they re-worked many published extractions as an exercise in "learning by doing," until they were able to isolate the active compounds easily. At that stage, no one had made synthetic vinca alkaloids. Potier's team was also working on alkaloids from *Thuja* and *Cinchona*, and one of their discoveries led Potier to propose a synthetic route for the vinca alkaloids.

One of Potier's colleagues, the biologist Dominique Pantaloni, told him that mescalin affected the protein tubulin. So Potier, who had worked on tubulin before, arranged for one of his young researchers, Daniel Guénard, to work with Pantaloni. After that, Potier and Guénard worked together to develop the "Tubulin test," which became a tool to determine whether chemicals could act to stop cancerous activity. The French were the only ones with this capability, thanks to the Tubulin test. It was an excellent means to test molecules and evaluate their efficacy.

In 1976, Potier's team discovered that the Tubulin test proved a semi-synthesis of one vinca alkaloid compound to be active, showing promise as an anticancer drug. They called it Navelbine. Potier offered his discovery to the head of Eli Lilly, which was already marketing naturally occurring vinca alkaloids, but he was not interested. Rhône-Poulenc, the firm where Potier had longstanding, strong partnerships and that had given him access to some of their analytical equipment and sent him compounds since his arrival at the ICSN, had broken off its external investments a few months before because of a major crisis and refused to undertake development research into Navelbine.[18]

Because none of the pharmaceutical firms involved in drug production were interested in Navelbine, Potier collaborated directly with doctors during the development phase. After three more years of negotiations came to nothing, he met Pierre Fabre, the head of a small French pharmaceutical firm, the Laboratoires Pierre Fabre, and persuaded him to produce the Navelbine drug, even though Fabre did not belong to the

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[18] Rhône-Poulenc was nationalized in 1982. Development research accounts for 75% of the global manufacturing cost for a drug. A firm can spend between $100 and $800 million over ten to twelve years.

major group controlling the production of anticancer drugs. Pierre Fabre, Anvar (*Agence nationale de valorisation de la recherche*), Pierre Potier, his team, and the CNRS obtained three main patents.[19] The French administration approved Navelbine for use in France in 1989, and the U.S. Food and Drug Administration (FDA) approved it in 1994. The discovery of Taxotère followed.

The American National Cancer Institute had funded research on Taxol for more than a decade without clear results. Since 1971, researchers had known that Taxol was an active agent, but it was one among others. In 1979, biologist Susan Band Horwitz and her team reported that Taxol's activity was caused by its ability to stop cell division, and published their results. U.S. Taxol is produced from the bark of *Taxus brevifolia*, a wild species of yew, which grows very slowly (it takes more than a century to mature fully).[20]

In France, in the meantime, using the same research method as employed in developing Navelbine, Potier's team studied *Thuja* and other alkaloids, realizing after Horwitz's publication that it was a real opportunity for them because her conclusions were close to those of their study of *Thuja* evergreens. Potier was one of the people who saw Taxol as perhaps the first in a new family of anticancer drugs. The ICSN is located in a park planted with *Taxus baccata*, a European cultivated yew. At the same time, and by chance for Potier, the yews were cut down to build a road. Potier took all the raw material that his team needed without any objection from the CNRS administration.[21]

Potier ordered to his team to study precisely all the *Taxus baccata* compounds from roots to needles. The Tubulin test, performed on all extracts to determine if a compound is active, measures the level of activity. First, they discovered that they could obtain some 0.5-1.0 grams of Taxol from a kilogram of fresh needles, while the Americans managed to get only 100-150 mg of Taxol from a kilogram of dried bark. Second, two steps before producing Taxol, they discovered another chemical, ten times more active than Taxol. They named it Taxotère. Finally, they also found a semi-synthetic route to the production of Taxol. Potier informed François Level, one of his Rhône-Poulenc Rorer colleagues, that this discovery would change the way to cure cancer. Potier knew he could expect huge royalties; he knew very well that the CNRS, a public body, would not be able to afford the development research. The clinical trials began immediately, in 1990, but this time paid for by R-PR, which regretted its

[19] Anvar is the national agency for commercialization of public-sector research.
[20] Jordan Goodman and Vivien Walsh, *The Story of Taxol: Nature and Politics in the Pursuit of an Anti-Cancer Drug* (Cambridge, England, 2001), 282.
[21] American researchers had to negotiate with the FDA, as well as with the environmentalists, to obtain raw material.

lost opportunity with Navelbine. The economic stakes involved were too high for the CNRS, so Potier drafted the contract among ICSN researchers, the CNRS, and R-PR. The firm received marketing approval for France in 1996 and, two years later, for the U.S. market. At the beginning of 2005, R-PR (then Sanofi-Aventis) received marketing approval from the U.S. FDA for the use of Taxotère for the most common cancers (breast, lung, prostate).[22] This case study shows the efficiency of the complementary nature of different structures.

In one way, Potier's team overcame the competition from the American scientists, despite the huge resources available to the National Cancer Institute program.[23] If we compare the scale of the NCI program with that of the ICSN, the United States was doing what only a country with its resources could do. Without the U.S. research system producing a huge volume of knowledge, the French would not have succeeded so quickly. In fact, Potier likened his team to a commando group, in contrast with America's massive army.[24]

Potier's work method was essential to explaining his success. He organized a scientific network and monitored academic research as well as industrial R&D; he maintained secrecy, an association with industry, and control of intellectual and industrial properties. Potier inherited his former co-directors' network and had always supported it. He also had a very active personal network of academic and industrial researchers and a thorough understanding of the global knowledge and practices in his field. He considered regular bibliographic updating an obligation to monitor scientific research and technological development. Another essential obligation was training all team members to master producing compounds as an exercise in learning by doing.[25] It was essential that the team be secretive about research in progress. This secrecy allowed Potier to patent the discoveries and to negotiate effectively with pharmaceutical managers.

Potier also developed a publication process that protected the heart of his work.[26] He published, or allowed his colleagues to do so, only after

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[22] *Wall Street Journal Europe*, 25 Jan. 2005.

[23] Vivien Walsh and Muriel Le Roux, "Contingency in Innovation and the Role of National Systems: Taxol and Taxotère in the U.S.A and France," *Research Policy* 33 (Nov. 2004): 1307-28, special issue in honor of Keith Pavitt.

[24] Pierre Potier, interview with Muriel Le Roux, Paris, 15 Sept. 2003.

[25] Ibid. Potier was convinced that practice was as important as theory, especially for young post-docs; he said that in chemistry each trial could be a route for another discovery. This manner of work is not far from what is described by Malcom Gladwell in *Outliers: The Story of Success* (London, 2009); he argues that the main heroic inventors succeed not only because of their network, knowledge, abilities, etc., but also because of the time spent on working on the same topic.

[26] Le Roux, " Genèse des textes de Pierre Potiers."

taking out a patent, never before. Potier always chose when to associate with industrial R&D, and no one ever imposed a research topic or particular schedule on him. Thus, Potier had a precise, personal method of managing his team and, subsequently, the ICSN that was closer to a business style of management than an academic one, especially for France.

Potier's ability to manage the contracts with the Laboratoires Pierre Fabre for the Navelbine and Rhône-Poulenc/Sanofi-Aventis for Taxotère is noteworthy, because he had chosen an unfashionable topic. Oncology drugs were not at first seen as the most desirable area for firm competition; for the firms, it became a strategic economic stake during the 1990s. Second, although the CNRS technically did not fund cancer research, many researchers were working on this subject, crossing borders as they needed to. Potier knew that and used it to his advantage.

One important aspect of this story was the high degree of autonomy and freedom of action the French researchers enjoyed at the CNRS. The heart of Potier's management strategy was to preserve both the public science interest and the researchers' interest by controlling the intellectual and industrial properties produced by their discoveries. He never wanted to create a start-up company, because he thought collaborative academic and industrial research was necessary because of the complementary nature of the two venues.[27]

As long as industry collaboration provided the public sector with investment returns (the license fees paid by the two firms were huge, and for a long period the patents provided most of the CNRS's income), Potier never thought of leaving, even though he had to fight to obtain his due or to make the central administration respect the law. He believed that his position was a good compromise, allowing him to work the way he wanted and with whom he wanted. He knew how to manipulate the French research system, making an apparently strict system flexible.

From the outset, there was a company training period for all researchers during their university studies; the carefully chosen students created or reinforced links with pharmaceutical companies. Research rules were very strict, with no autonomy, no publication without the director's permission, and so forth, but material conditions (salary, equipment) were good. In addition, because ICSN's directors always did their best to find employment for their young doctors, many students wanted to come.

A Worldwide Community Linked by a Common Culture

This final section is a work in progress, needing verification and further analysis. Nevertheless, the first results of our statistical enquiry reveal important trends to understand why the ICSN has such an original

[27] Pierre Potier, "Pourquoi nos labos prennent du retard," *L'expansion*, 21 Oct. 1993.

management for an academic laboratory. For this study, I used a list of all the candidates who received their doctoral degrees at the ICSN from 1960 to 2002. Since 1960, as a CNRS laboratory supervision of the Institute has been the responsibility of a *directeur de recherche* (a reader, who is a permanent full-time researcher, at the same level as a chaired professor at a university) in cooperation with a professor who previously completed a doctorate at the ICSN and who is doing research either at the ICSN or jointly at a university laboratory in cooperation with an ICSN team.

My research concerns only the students, not the researchers or the other scientific workers at the ICSN during those forty-two years, who represent more than 60 to 70 percent of those employed at ICSN. It is unclear if the CNRS will grant permission to read the personnel records of these workers, which is the only way to reconstruct the precise network used by the ICSN managers to lead and negotiate their research programs. As far as can be ascertained, after reading the archives, the trends shown in this first "alumni network" study appear to be the same for the other scientific workers of the ICSN, because a significant portion of alumni became researchers at the ICNS.

Unsurprisingly, because of the ICSN directors' fame, students in chemistry often joined the ICSN for doctoral research after graduation. Directors and team leaders chose their students carefully, paying special attention to their curricula; the leaders accepted students for their teams after interviews and the students agreed to respect the ICSN rules (including confidentiality). Generally, students made up approximately one-third of those working at the Institute, so the directors paid attention to their number, as well as to "the population pyramid" of researchers, keeping an eye on the student/researcher ratio. In addition, the Institute regularly welcomed overseas students, because team leaders believed that this was a good way to expand their overseas knowledge. It was possible to accept overseas students because industrial contracts that funded specific research projects and royalties received from patents gave them a way to bypass the government policy on foreigners.

From 1960 to 2002, the ICSN's directors supervised 571 doctorates (Ph.D. degrees).[28] The University of Paris-sud Orsay (which is the university closest to the ICSN) cooperates regularly with the Institute in awarding Ph.D.s and is clearly number one in the ranking of the number of degrees awarded. Next, come the Universities of Paris (Jussieu, Faculty of Pharmacy), other French universities, and some international universities in Madagascar, India, Latin America, Malaysia, North America, and China.

After graduates received their doctorates, as alumni they sought different types of jobs, including academic scientist (researching and/or

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[28] I hope to account for the years from 2002 to 2009 in the future. I will publish the detailed list of subjects in a book in progress.

teaching), jobs in pharmaceutical companies, and so on. Of the 571 doctorates, I have data on all but 85 of them. Three hundred and seven alumni have become academic scientists, 241 in France (at universities, the CNRS, Inserm, CEA, Ifremer, and so forth) and 66 elsewhere in the world (European, African, Asian, Latin and North American universities).

One hundred-sixty applied for industry positions, 113 in France, and 47 elsewhere. French multinational companies such as L'Oreal, Aventis, Pierre Fabre, Sanofi, Servier, and Saint-Gobain employed the majority of those working for French companies. Other well-represented companies in disparate locations include Ciba, Nestlé, Glaxo, Novartis, and Procter & Gamble. After specialized ICSN training, the young Ph.D.s were ready to apply for industrial positions. At least nineteen became scientific journalists, consultants, or worked for UNESCO (the United Nations Educational, Scientific and Cultural Organization), the European Office for Patents, or food security agencies. This short survey illustrates how a small organization developed an employment strategy that was first useful for the students and, after a while, for the ICSN.

If Paris-sud is overrepresented in the list of universities, this was, of course, not only because of its close proximity, but also because some senior researchers became Paris-sud University professors early in ICNS history, while others stayed at the ICSN as *directeurs de recherche*. Once the competition of applying for an academic position was over, the links between former ICSN members stayed strong enough to develop scientific cooperation beneficial to the university and the Institute. The same process built the industrial network. Companies traditionally linked with the laboratory such as Aventis/Rhône-Poulenc, Pierre Fabre, and Synthélabo received bonuses.

When a foreign student came to Gif-sur-Yvette to complete a Ph.D., overseas universities and companies also joined the *Gif connection* soon after developing relationships.[29] The international connections were very important, not only in bringing together people working for universities and industries, but also in sharing the feeling of belonging. Why did this spirit exist? Was it because of management, the directors' personalities, or the small size of the international community of natural substance chemists?

If attention to networks is an important aspect of doing research in the academic world, the ICSN's managers transformed this common practice into strategy. They built this strategy on both a shared economic interest and a very strong common culture. Each year, for more than twenty-five years, they have organized an ICSN workshop or conference to present the ICSN's scientific results, as well as to promote their doctoral and post-

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[29] Named after the location of the ICSN in Gif-sur-Yvette in the south of Paris.

doctoral researchers and help them find jobs. These events are also a real time of sharing and reunion.

My intention is not to generalize what happened at the ICSN to the entire French research system, but to show the community structure of the natural substance chemists based in Gif-sur-Yvette. Historians might rethink the importance of the interaction between everyday research life and community to the innovation process. This cosmopolitan community had excellent connections to others around the world. The ICSN's renown in France and abroad was due to this strong network building over the years, as well as to its discoveries. This network allowed ICSN members with few means, before the age of the Internet, to connect to all those involved in the quest for new natural substances, including botanists, ethno-botanists, biologists, chemists, and physicists all over the world, and to industries able to sustain, cooperate in, or fund research programs. The lengthy correspondence among alumni, team leaders, and directors confirms this hypothesis.

Allowing great mobility between academic labs (unusual in France compared to the United States) as well as between academic and industrial labs, this lively network was most probably one of the strategic strengths of the Institute. People (politicians included) knew the quality of the ICSN research, which helped the laboratory to obtain natural substances and to export/import them from overseas. These networks permitted dispensations for field trips, credits, funds, employment, and equipment, increasing the ways and means of information exchange.

Having considered one path to innovation in chemistry taken in France since the 1960s, we may conclude that the relationship between the individual and the collective (*l'individuel et le collectif*) is the key to success, whatever the role of the state, of structures, and of organizations. If French drugs are among the most commonly used drugs everywhere around the world for cancer therapy, it is because the ICSN managers were able to lead their teams in mixing academic and industrial practices, management and networks, by protecting, first of all, a space for creativity.

Conclusion

Alfred D. Chandler, Jr., pointed to the fact that "industry leaders have succeeded by focusing on product and process development rather than fundamental research," so we could say of ICSN history, that is why funding public/academic research is so important, why we need to collaborate with industry.[30]

If we apply Helga Nowotny, Peter Scott, and Michael Gibbons' analysis, we might conclude that the ICSN fits into their modes I and II—mode I, because the care of independent fundamental knowledge was

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[30] Chandler, *Shaping the Industrial Century*, 311.

important (Ph.D. degrees and the Institute contribution to university training); and mode II because research always involved many disciplines, and researchers tried to respond to social demands (health) with respect to economic realities (keeping the research results under control until the patent process was complete).[31]

The history of this French institute shows us that the difference between fundamental and applied research is not the researchers' wills or motivations or their search methods, but an institutional environment in which the "market" is not pressuring the researchers. Researchers may do basic research in an industrial lab in the same way that they can carry out applied research in an academic research center; the ICSN borrows from both models. The only criterion was that researchers not have to answer to specific economic or industrial objectives, but focus on understanding chemical reactions and, if possible, produce new active molecules. The directors fought against state or industrial injunctions to give their teams the best research environment possible (including time, tranquility, and autonomy). The key issue is not (as is often said in France) to know if researchers do or do not have links to industry, but, rather, how they conduct and evaluate research.

Nevertheless, peers (in charge of assessment and promotion) were very critical of the continuous links with industry and the hybrid management. The "scientific policy" of the ICSN did not conform to the general atmosphere of the academic milieu, whatever the quality of the research, and despite the fact that the methods of the ICSN's directors could provide a means to restore the French system of research and innovation.[32]

The long view of history reveals the different paths to innovation, explains successes and failures, and restores the facts, far from the official firm or university auto-hagiography. If globalization changes the pattern of innovation, it is not clear that pharmaceutical firm managers can ignore the past, which shows how much they need academic research. The history of ICSN appears to exemplify Chandler's point on this matter.

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[31] Helga Nowotny, Peter Scott, and Michael Gibbons, *Re-Thinking Science: Knowledge and the Public in an Age of Uncertainty* (London, 2001), translated as *Repenser la science* (Paris, 2003); Michael Gibbons et al., *The New Production of Knowledge: The Dynamics of Science and Research in Contemporary Society* (London, 1994).

[32] Edgar Lederer's speech delivered when he received the Gold Medal of the CNRS; Lederer, "La chimie des substances naturelles," 43-54.