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LOUIS PASTEUR'S PATENTS: AGRI-FOOD BIOTECHNOLOGIES, INDUSTRY AND PUBLIC GOOD

MAURICE CASSIER

In January 2001, in response to comments that genes were not patentable since they were discoveries and products of nature, the US Patent Office (USPTO) justified the patentability of genes isolated from their natural environment by citing a patent on purified yeast granted to Louis Pasteur in 1873.¹ Pasteur's patent covered a new process for manufacturing beer that included not only new fermentation methods but also the equipment used and "pure yeast" as an "industrial product obtained by means of these processes" (French patent)² or "yeast, free from organic germs of disease, as an article of manufacture" (US patent)³. The question of a patent on purified yeast had already been an issue in the US in the 1930s, when patents issued to scientists and the patentability of "products of nature" were called into question.⁴ Jurists specialized in industrial property consider the patent granted to Pasteur in 1873 to be "the first known patent covering a micro-organism."⁵ In this paper we examine the conditions in which Louis Pasteur patented biotechnological inventions pertaining to the fermentation and conservation of food products (vinegar, wine, beer), whereas his vaccines invented in the 1880s were not patented.⁶ We analyse in detail the structure and scope of his patents, particularly those on beer, which covered purified yeast as an industrial product. While the content of these patents seemed new, so were the uses to which Pasteur put them, to keep control over his inventions and make them freely available to manufacturers. Finally, Pasteur was rewarded for his scientific work and his industrial applications by two National Reward laws passed in 1874 and 1883. National rewards, granted by the state to inventors, were an alternative form of recompense and encouragement.⁷ Pasteur's biotechnological inventions were thus set in a context of tension between industrial property and the public good.

Little attention is given to these patents in the historical literature. In *The Private Science of Louis Pasteur*, G. Geison does mention several patents taken out by Pasteur, but devotes only a single paragraph (p. 41) to them, and no more than two lines to the patents granted in the United States (p. 266). He notes that most of these patents "were deliberately allowed to fall into the public domain or were unexploited for other reasons."⁸ Geison's book excludes Louis Pasteur's patents because the focus is not on his work in the agri-food biotechnology field, where these patents were applied: "...the only major topics of Pasteur's research that receive no focused attention here are his conceptually undistinguished studies on the manufacture and preservation of vinegar, wine and beer." Geison also focused his study on secrecy and disclosure in science, and on the ethics of biomedical research more than on Pasteur's industrial work of which these patents were part.

¹ "Utility Examination Guidelines", Federal Register, vol 66, n° 4, 5 January 2001.

² Patent 98476, issued on 9 March 1873 in Paris.

³ US Patent 141 072, filed on 9 May 1873. The title of this patent covered the production of both beer and yeast: "Improvement in the manufacture of beer and yeast."

⁴ Federico, "Louis Pasteur's Patents", *Science*, October 8, 1937, p. 327.

⁵ Beier, Crespi and Straus, *Biotechnology and Patent Protection*, OECD, 1985, p. 26.

⁶ Cassier, M., 2005, "Appropriation and Commercialization of the Pasteur Anthrax Vaccine", *Studies in History and Philosophy of Biological and Biomedical Sciences*, 36: 722-742.

⁷ This alternative is contained and discussed in the first law on the "authors of useful discoveries" of December 1790 – January 1791.

⁸ He nevertheless mentions that the patents on a bacterial filter – the Chamberland-Pasteur system – issued in 1886 were exploited "and probably yield significant revenues", in *The Private Science of Louis Pasteur*, Princeton University Press, 1995.

Patents and the domestication of micro-organisms in laboratory and industry

Pasteur applied for at least six patents in the period from 1857 to 1873, covering a “new alcohol fermentation process” (3 February 1857), “a manufacturing process for acetic acid” (9 July 1861), “a process relative to the conservation of wine” (11 April 1865), and three patents covering methods for manufacturing beer.⁹ Apart from these six patents issued in France, which were completed by certifications of additions recording the specifications and improvements of new processes, patents on beer were also taken out in the United States, in the UK and in Italy.¹⁰ Three patents on a bacterial filter were furthermore taken out in 1886 by Chamberland, Pasteur's colleague, and then by the Société du Filtre Chamberland Système Pasteur.¹¹ These patents were extended to the United States. In this article we study the first six patents on biotechnological processes – and where relevant the resulting products – in the agri-food industry.

The patents under consideration were all landmarks in the constitution of the microbiological science of Louis Pasteur, who produced both basic knowledge and industrial applications. In an article published in early 1871, Pasteur set out the theory of this mode of production of science and techniques applied to industry, by challenging the notion of “applied sciences” which he believed impeded the progress of science and its industrial applications.¹² Apart from the fact that it was both academic and industrial, Pasteur's microbiological research was produced in close interaction with industrial practices, sometimes both in the factory and in the laboratory. For instance, after being involved since November 1856 in studies on fermentation accidents at the Bigo sugar refinery in Lille, Pasteur filed his first patent, on a “new alcohol fermentation process”, on 3 February 1857. The patent cites sugar beet juice as an example and mentions “the many experiments” that Pasteur had undertaken in the preceding months on “the action of alcohol ferment.”¹³ Studies and patents on beer are other examples of this mode of production of science and technology. Pasteur's laboratory notebook for the months of May, June and July 1871 when he was hosted by his colleague Duclaux in his laboratory at the Clermont-Ferrand Science Faculty, as well as in the chemistry laboratory of the Clermont-Ferrand Medical School¹⁴, started with a detailed description of the method used to manufacture beer at the Kuhn breweries, that Pasteur used for his experiments.¹⁵ These took place both in the laboratory and in the brewery, where 25-litre barrels and experimental apparatus were set up in May 1871. At the end of May comparative tests on Pasteur's new beer and the brewery's usual beer were undertaken. On 24 June, four days before the first patent application was filed, in Clermont-Ferrand, Pasteur proposed to Mr Kuhn a plan “for larger equipment.” His patent applications then followed him from Clermont-

⁹ “Nouveau mode de fabrication de la bière” (“New method for manufacturing beer”) (Patent n° 91941, 28 June 1871), “nouveau mode de conservation du moût de bière et de la bière qui en provient” (New method for conserving beer wort and the beer derived from it) (92505, 21 August 1871) and, finally, a patent on “1- procédés de fabrication et de conservation de la bière inaltérable; 2- appareils relatifs à cette fabrication; 3- produits industriels obtenus par ces procédés” (1- processes of manufacturing and conserving stable beer; 2- equipment relative to this production; 3- industrial products obtained by means of these processes) (98 476; 13 March 1873).

¹⁰ US n° 135 245, filed on 8 December 1871 and issued on 28 January 1873: “Brewing Beer and Ale”; US n° 141 072 filed on 9 May 1873 and issued on 28 July 1873: “Improvement in the manufacture of beer and yeast”; in the UK, Letters Patent n° 2225 “Improvements in brewing”, 24th August 1871; Letters Patents n° 1106, “Improvements in the Manufacture and Preservation of Beer, and in the Treatment of Yeast and Wort, together with the apparatus for the same”, 25th March 1873. Pasteur also took out two patents in Italy.

¹¹ Patent 174611 of 8 March 1886; patent 176 387 of 27 May 1886; patent 180324 of 17 December 1886.

¹² “Quelques réflexions sur la science en France”, excerpt from the *Salut Public* of 20 March 1871, Laboratory notebook NAF 17984 : March-April 1871.

¹³ Patent 30646 for “an alcohol fermentation process”, Lille, 3 February 1857.

¹⁴ Duclaux, *Pasteur, l'histoire d'un esprit*, 1896, p. 235.

¹⁵ NAF 17984 “Laboratoires de l'Hôtel Dieu à Clermont Ferrand mai, juin, juillet 1871.”

Ferrand to Paris, where the additions were filed while the Pasteur laboratory was developing new industrial partnerships with breweries, first in Paris and then in Lorraine. When Pasteur returned to the Rue d'Ulm laboratory, the Clermont-Ferrand brewer, Mr Kuhn, sent him reports on the fermentation process in the new equipment.

Pasteur's patents were direct translations of the domestication of micro-organisms¹⁶ that he undertook in his laboratory. This domestication, described by his colleagues Duclaux¹⁷ and later Fernbach¹⁸, and analysed by R. Dubos in 1950¹⁹, was based on the characterization and isolation of micro-organisms, the discovery of their specificity, the practice of "pure cultures" in vitro, and control of the conditions of their use. Each patent described the industrial use of a specific micro-organism (mycoderma aceti for the production of vinegar; yeast for beer) or processes of sterilization of products obtained through fermentation (wine, beer). Once the special agent of a fermentation process was identified, it became possible to separate the useful microbe from those that were harmful to the industrial operation and, where relevant, to appropriate the purified micro-organism which was distinguished from the "mixtures" used until then (for example commercial yeasts that circulated between breweries). The patents extended the principles and methods of the domestication of microbes to industrial processes and products, and changed the conditions in which micro-organisms were used in various industries to reduce losses, increase productivity and enhance product quality. Consider the example of the patent on a new vinegar manufacturing process, which used "mucors and especially mycoderma vini and mycoderma aceti."²⁰ The patent directly transposed Pasteur's discoveries to the properties of the mycodermes in order to optimize their culture in industry: "I realized that these plants were the cause of acetic fermentation. The process consisted in developing them on a large surface, by feeding them with organic liquids containing mainly phosphates and nitrogen, and then putting them in contact with the alcoholic liquid that one wishes to acidify, in contact with the air."²¹ The patent summed up the principles and methods of the domestication of micro-organisms: discovery of their specific characteristics, isolation, and cultivation in an appropriate medium to avoid contamination and improve the yield from their industrial use. Patents on the manufacture of beer were based on the same principles: specificity of micro-organisms²²; methods of sterilized cultivation²³; and prevention of contamination by undesirable micro-organisms, through the use of purified micro-organisms, heating and fermentation in isolation: "I hereby declare that I am taking out a fifteen-year patent on a new method of manufacturing beer which consists essentially of fermentation isolated from any contact with the air ... This process is based on new scientific data which I will disclose elsewhere and which shows that contact with the air causes serious damage in the manufacturing of beer"²⁴. Pasteur's patents contained passages concerning the scientific controversies over fermentation. For instance, the patent on vinegar referred to the debate with Liebig, without actually citing him: "The fermentation processes using beech wood chips are based on completely erroneous theories"²⁵. While codifying Pasteur's biotechnological inventions, these patents fuelled scientific debate.

¹⁶ This is the title of a chapter in René Dobos' book: "La domestication de la vie microbienne", in *Louis Pasteur, Franc Tireur de la Science*, 1950.

¹⁷ Duclaux, *Pasteur, histoire d'un esprit*, Charaire, Sceaux, 1896.

¹⁸ A. Fernbach, *Pasteur et l'industrie des fermentations*, Musée Pasteur.

¹⁹ R. Dubos, *Pasteur, franc tireur de la science*, French edition, La Découverte, 1995.

²⁰ Patent 50359 of 9 July 1861.

²¹ Patent 50359 of 9 July 1861

²² Although with regard to specificity, a definition was more difficult. An addition to the 1871 patent stated that "the mycoderma vini can become the germ of the bottom yeast" (3rd addition, dated 22 January 1872).

²³ "Obtention du levain pur par l'éloignement des germes organisés étrangers à la levure de bîre" ("Obtaining pure pitching yeast by removing organized germs foreign to beer yeast") (Patent 98476 of 13 March 1873 issued in Paris).

²⁴ Patent 91941 on a process for manufacturing beer, issued on 28 June 1871 in Clermont-Ferrand.

²⁵ Patent N°50359. Addition certificate of 12 December 1861.

The patents justified the new biological processes in terms of product quality and productivity of industrial fermentation. For example, in the case of vinegar: “simplicity and rapid execution, quality of products, and very easy application, even to alcohol diluted with water, are advantages that seem to be guaranteed in the use of this manufacturing technique ... this process will make it possible to deliver at the price of ten centimes per litre, acetic acids with seven to eight per cent of acid; its application is unlimited.” (Patent 50359 of 9 July 1861)

The economic advantages of the new beer manufacturing process were summed up as follows: “with this process and the equipment used to apply it, the beer wort can be transported over longer distances, and the beer has better qualities of taste and conservation than those of existing beers, without it being necessary to apply the strict temperature conditions required by the processes in use today.” (Patent 92505, 21 August 1871) All these patents attested to in-depth knowledge of the processes and know-how in use in industry at the time. It was therefore possible to envisage their partial or gradual replacement by new biotechnologies so that manufacturers would not be required to make heavy investments.²⁶

Patents on green biotechnologies

Whereas Pasteur took out many patents on biotechnological processes applied to agriculture or to agri-food industries, he patented none of his vaccine preparation methods, contrary to some of his contemporaries' claims (Lutaud, 1887).²⁷ Biotechnological processes and microbiological products isolated, purified and modified in vitro, “by artificial culture” (Pasteur) had differing statuses, depending on whether they were applied to agriculture or medicine. This difference of status between food biotechnologies and health technologies stemmed from the exceptional status of medicines, which were not patentable in terms of the law of July 1844. This exclusion concerned remedies used in human medicine (e.g. rabies vaccine) as well as veterinary medicine (anthrax, chicken cholera, and swine fever vaccines).

Veterinary vaccines were not however put into the public domain.²⁸ Pasteur had a technical monopoly on them, based on secret know-how in manufacturing processes and on the Pasteur laboratory's possession of the vaccine virulence standards, as well as a legal monopoly based on contracts and exclusive licences granted to a commercial company and local agents. The contract between Chamberland's production laboratory and the Société de Vulgarisation du Vaccin Charbonneux Pasteur legally concretized Pasteur's monopoly on the exploitation of the vaccine invention: “Mr Chamberland grants Mr De Sainte Marie the exclusive monopoly to create laboratories abroad (with the exception of France and its colonies) for the diffusion and exploitation of the anthrax vaccine under the name of *Laboratoire du Vaccin Charbonneux Pasteur*.”²⁹ The various contracts signed between the Société de Vulgarisation du Vaccin Charbonneux and local laboratories in Russia, Australia, Cambodia and India furthermore delimited exclusive territorial concessions for the sale of the vaccine: “as from this day, Mr Chamberland will no longer be able to sell the anthrax vaccine for his own profit in the countries in which the monopoly has been granted to Mr De Sainte Marie.” (Article 8) Use of the inventors' names was clearly defined by the contract; the monopoly on the exploitation of the vaccine was based on the exclusive use of Pasteur's name. The monopoly on veterinary vaccines had two objectives: first, Pasteur wanted to retain control over technologies and preparations that were not yet stable or standardized, at a time when the

²⁶ “We see that the current processes and the new process could function simultaneously, which would enable breweries to change their equipment gradually” (Patent 98476 issued on 13 March 1873, Paris).

²⁷ *M Pasteur et la rage*, Publications du Journal de Médecine de Paris, 1887.

²⁸ Cassier M, 2005, *op.cit.*

²⁹ “Traité entre M. Chamberland et M de Sainte Marie en vue de la création de laboratoires du Vaccin Charbonneux Pasteur à l'étranger” (“Agreement between Mr Chamberland and Mr de Sainte Marie with a view to setting up Pasteur anthrax vaccine laboratories abroad”), IP Direction DR DOS 1, Document 10 587.

principle of artificial immunity was still being challenged; and, second, he used the commercial rent earned from these vaccines to finance the creation and functioning of the Pasteur Institute.

The monopoly on veterinary vaccines contrasted with the sharing of knowledge on the rabies vaccine and its technology.³⁰ This sharing of the rabies vaccine technology was motivated by the sanitary emergency consisting of the need to treat people who had been bitten, as vaccine preparations were not easily transportable and anti-rabies centres had to be as close to patients as possible. Pasteur therefore actively undertook the transfer of his technology by hosting and training foreign laboratory assistants. When they left to set up a rabies centre in their country, he gave them rabbits inoculated with the rabies virus, from which they could extract spinal cord to produce the liquid vaccine. The modes of appropriation of Pasteur's biotechnologies, by patent or contract, and their status as reserved or common goods, were therefore diverse, whether they concerned the food industry, veterinary medicine or human medicine.

The first biotechnology patents

In their book *Biotechnology and Patent Protection*, jurists Beier, Crespi and Straus attribute the first patent on a living organism to Louis Pasteur. They also note that patents were granted at the beginning of the twentieth century in the United States on processes using living organisms³¹.³² At the same time, Pasteur's contemporaries strongly challenged his patent on the heating of wines³², from the point of view of priority of an invention. In 1869, four years after the patent had been filed, the controversy broke out at the General Council of the Côte d'Or – a major wine-producing region in France – and then in 1872 at the Science Academy. In 1869 Mr Thénard claimed that it was not Louis Pasteur who had invented the method for heating wine, but a Mr Appert, before 1810, and a wine producer in the Côte d'Or, Mr de Vergnette-Lamotte, who had continued Appert's experiments. Thénard's argument was based on the anteriority of Appert's method, and he confined Pasteur to the status of discoverer of the germ theory, thus refusing him the status of inventor: “As for Mr Pasteur ... he gave only a rational theory, but was no more the inventor of the method than someone who developed a new theory of the plough would be the inventor of ploughing, irrespective of how ingenious it may be.”³³

Pasteur qualified his answer. On the one hand, he emphasized the originality, utility and priority of his process compared to Mr Vergnette-Lamotte's heating method; on the other, he recognized Appert's anteriority: “When I published the first results of my experiments on the possible conservation of wine by means of heating, it was obvious that I was simply applying the Appert method in a new way, but I was totally unaware that Appert had thought of the same application long before me.” (*Études sur le vin*, second edition, p. 133) Pasteur noted however that Appert's observations on his wine conservation process were “clearly insufficient.” He also mentioned the work of a Mr Gervais who had continued Appert's experiments. Gervais took out a patent in 1827³⁴ and published two brochures on the heating of wine. Considering this anteriority of the wine heating method, Pasteur granted himself the merit of having provided a scientific explanation: “For me, the merit that I lay claim to is the fact of having proved the very real virtue of Appert's method applied to wine, through rigorous experimental demonstrations and scientifically inferred principles.” (*Études sur le vin*, second edition) He noted that Appert's experiments had not mentioned wine diseases. This quarrel over

³⁰ Cassier, M., 2008, “Producing, Controlling and Stabilizing Pasteur's Anthrax Vaccine: Creating a New Industry and a Health Market”, *Science in Context*, Vol. 21, No. 2.

³¹ “A patent was granted and declared valid in 1908 for 'a process and an apparatus for recycling water' using bacteria for purifying the water”, in Beier, Crespi and Straus, p. 26.

³² Patent 67006 of 11 April 1865 on “a process relative to the conservation of wines.”

³³ Note by Mr. Thénard, cited in *Études sur le vin* by Pasteur, 2nd edition, Paris, 1873, p. 143.

³⁴ “Amélioration des vins, des eaux de vie et autres liqueurs vineuses, en les faisant passer dans des tuyaux aplatis qui sont en contact avec l'eau chaude” (“Improvement of wines, eaux de vie and other wine liqueurs, by pumping them through flattened tubes in contact with hot water”), Patent issued on 16 August 1827.

priority clearly shows that manufacturers and inventors endeavoured to improve their control over the production and conservation of biological products by means of the processes that they invented. This represented a form of domestication of microbial life, before the isolation and culture of micro-organisms *in vitro*. Pasteur moreover recognized the inventive work “of a few enlightened practitioners” (*Etude sur le vin*, p. 133) and of “this skilled manufacturer” (referring to Appert).³⁵

Patents on “living beings”?

The six patents taken out by Pasteur covered all the new processes of use or control of micro-organisms in industry. The last patent on beer, extended to various countries, also included pure yeast as an industrial product.

Consider the format of these different patents. While the first patent on “a new process of alcoholic fermentation”, issued in 1857, concerned the addition of carbonates to alter the fermentation medium, the second patent, on vinegar, issued in July 1861, referred precisely to the use of two mycodermes: *mycoderma vini* and *mycoderma aceti*. The certificate of addition applied for a few months later, in December 1861, included only *mycoderma aceti*.³⁶ The patent therefore contained the identification of the micro-organism used in the production of vinegar: “I recognized that these plants were the cause of acetic fermentation”, but no explicit claim to these “plants” *per se*.³⁷ Pasteur then described the cultivation process that he had developed: “the process consists in cultivating these plants on a large surface, feeding them with organic liquids containing mainly phosphates and nitrogen substances, and then putting them into contact with the alcoholic liquid that one wants to acidify, in contact with the air.” (Patent 50359 of 9 July 1861) The plants were used in the new manufacturing process, but the patent did not specify that they were the products of a human industry. Pasteur specified that “the process consists” in defining the appropriate cultivation conditions.

The patent on the conservation of wines was clearly a process patent. It also started with the announcement of new microbiological knowledge: “I realized that diseases or spontaneous alteration in wines are produced by microscopic beings whose germs exist in the wine before it becomes diseased.” The patent set out “a simple and practical means to kill these germs” by heating the wine to between 60° and 100°C. Pasteur explicitly laid claim to the process: “I hereby state that I am taking out a patent on the application of this process.” (Patent 67006 of 11 April 1865).

Two types of patent were filed on beer. The first two, filed in 1871 and completed in 1872, laid claim to “a manufacturing process” or “improvements” in the manufacturing and conservation of beer. After setting out the principle of the process – “fermentation out of any contact with air” – these patents detailed the equipment that Pasteur had designed and tested to implement it. These patents contained very detailed drawings and legends, with comprehensive instructions for application of the process. An addition to the first patent nevertheless informs us that Pasteur worked on obtaining a pure yeast: “soon, I’ll indicate the means for obtaining the two low and high ferments at will, in all seasons and places, so as to prepare them in a pure state without having to use those of the breweries.” (2nd addition to the first patent, n°, 91941 24 november 1871)

The last patent, which was in a sense a sort of culmination of this work on beer, was more soundly structured than the preceding ones. The title immediately indicates the nature of the claims:

³⁵ Appert chose not to patent his inventions, but to publish them. He received a national reward from the state.

³⁶ “Alors que je l’ai annoncé dans le brevet que j’ai pris à la date du 9 juillet 1861, l’acétification des liquides alcooliques est produite par les espèces végétales du genre *mycoderma*, notamment par le *mycoderma aceti*.” (certificat du 12 décembre 1861) “As announced in my patent filed on 9 July 1861, the fermentation of alcoholic liquids is produced by plant species of the *mycoderma* type, especially by the *mycoderma aceti*” (Certificate of 12 December 1861).

³⁷ René Dubos informs us that Persoon had an idea of the existence of “the vinegar plant” in 1822 and called it *mycoderma* was 1852; Thompson came to the same conclusion in 1852; Louis Pasteur, *franc tireur de la science*, La Découverte, Edition française, 1995.

"1) processes for the manufacturing and conservation of stable beer; 2) equipment relative to this manufacturing and conservation; 3) industrial products obtained by means of these processes."³⁸ The novelty lay in the formal claim to pure yeast as an industrial product: "new industrial products obtained by means of these processes: stable beer, pure yeast, pure wort, are all products that can be transported over long distances without any alterations." (Patent 98476, 13 March 1873, Paris) This claim is also found in the US patent of 1873: "I claim : 1) the method of obtaining pure yeast by eliminating the organic germs of disease from brewer's yeasts, in the manner described ; 2) yeast, free from organic germs of disease, as an article of manufacture." (US Patent 141 072) The British patent was a translation of the French one: "The obtention by these processes and means of the improved products herein specified, viz., beer unalterable in character, pure yeast, or pure wort, substantially as described ; all three products being capable of transport to any distance without alteration or deterioration." (AD.1873, 25th March, n° 1106)

What was the scope of this patent? Apart from the process, it covered products: beer, wort and a pure yeast.³⁹ The meaning and scope of this claim on products nevertheless needs to be specified. Pure yeast clearly did not include beer yeast as a natural species or a particular strain of that yeast. Nor did the patent cover cultivated yeasts that brewers traded freely on the basis of reciprocity, as analysed by Pasteur, and that they could therefore carry on exchanging freely.⁴⁰ Pasteur considered these commercial yeasts as impure mixtures. He noted in his patent that the invention of pure and stable yeast enabled brewers to break out of this economy of reciprocity which they practised, and to procure new yeasts in cases of contamination of their own: "this is considerable progress in the art of brewing, since it frees the brewer of the necessity to obtain yeast from distant breweries when their own yeast has deteriorated, and makes a pure and stable yeast available to them" (Patent 98476).

Hence, this patent did not cover natural yeast strains or industrial strains, but only pure yeasts obtained by means of the appropriate purification methods. Did it cover all the purification methods imaginable or simply the one described in the patent? The patent specified that purification could be obtained in various ways. It did not however supply an exhaustive list: "the source of this new product that I call pure yeast or yeasts free of foreign germs can be obtained in various ways; I will limit myself to indicating the following here" (Patent 98476). The US patent seemed to limit the scope of the claim to the purification method as described in the patent: "I claim: 1. the method of obtaining pure yeast by eliminating the organic germs of disease from brewers' yeast, in the manner described." (Patent 141 072)

The product patent was therefore limited to a particular industry that used means to control and to domesticate yeasts. The yeast in question was embedded in those means and in that particular type of industry: the "stable beer" industry. Newly collected yeasts or the industrial yeasts that circulated outside of this specific process could be used freely. The patent covered "a living being" if it was treated – purified, separated and isolated – by means of these processes.

Note that this pure yeast was patented as an "industrial product"⁴¹ or "an article of manufacture." Purified yeast was described as the result of the invention of specific cultivation methods, that is, of a process of human industry. The operator used laboratory instruments and manipulations to ensure that the yeast obtained was pure: "to guarantee the purity of the yeast, it is possible to observe it under a microscope, as this will easily show up the presence of disease ferments, and then to try to establish whether the yeast can produce stable beer at any temperature." The patent contained a diagram (Figure 1), on which the left side represented a pure alcoholic yeast, and the right side an alcoholic yeast associated with filiform disease ferments. (Patent 98476) The microscope served

³⁸ Patent 98476, Paris, 13 March 1873.

³⁹ In his comparative study of patents on biological innovations (*La Protection des innovations biologiques. Une étude de droit comparé*), Bernhard Bergmans points out the novelty of this patent: "In the USA, Pasteur obtained a product patent for a yeast as early as 1873" (p. 78).

⁴⁰ *Études sur la bière*, page 24.

⁴¹ In his studies on beer, Pasteur distinguished "spontaneous yeasts" that appeared without having been sown, for example in wine fermentation, and yeasts that were "industrial products", "manipulated and used" by humans, such as brewers' yeasts. *Études sur la bière*, 1876, p. 152.

to isolate the pure yeast from mixtures of all kinds, and the purity of that yeast could be tested by pitching it and then by controlling the purity of the beer obtained: "If this beer examined under the microscope shows no disease ferments at all after several weeks in an stove at 20 or 25°C, it is because the small quantity of yeast that one sowed in the flask was also perfectly free of these ferments." (Patent 98476)

The patent described pure yeast as an economic object that could be produced in large quantities and transported over long distances at no risk of deterioration: "with the yeast thus obtained, one is able to prepare large quantities as the yeast is regenerated during the manufacturing of the beer." This pure yeast was an input or an entrant for the brewing industry; the brewer could obtain it during the brewing process itself. It could also be an output for biological industries to commercialize the yeast and sell it to breweries. When he started his research on beer in early 1871, Pasteur had collected economic data on the beer trade. He showed that France had a deficit, as it consumed more than it produced, and that it imported large quantities of beer from the UK, Belgium, Switzerland and Germany.⁴² At the beginning of the 1890s, after the creation of the Pasteur Institute, Duclaux, who had hosted Pasteur's first studies on beer, proposed that the Pasteur Institute produce and sell pure yeast to breweries. Pasteur however refused the idea of mass production and trade: "Mr Pasteur agreed with Mr Duclaux on the possibility of producing and selling small quantities of pure yeasts to brewers ... but he was against the idea of the mass production and sale of beer yeast by the kilo."⁴³

Patents for what purpose?

Pasteur described how he intended to use his patents. He justified a patent on a new vinegar manufacturing process in the following terms: "As scientific principles, publicized by their authors, are often patented by others who make insignificant alterations or add to the equipment, I took out a patent prior to my February paper, on the advice of authorized persons. This patent will take precedence over all the others that have resulted from my work. And I wish to add that I am determined to put this patent into the public domain" (Pasteur, *Oeuvres complètes*). Pasteur used the patent here for defensive purposes, to preclude the appropriation of his invention by opportunistic actors and to preserve the accessibility of his process. By placing his invention in the public domain, he facilitated its diffusion in industry. The patent thus enabled him to maintain control over his invention, but he did not use the monopoly on exploitation that it granted him.

Pasteur also used this strategy with his patent on the heating of wine. His approach was explained by Balard at the Science Academy, in 1872: "This patent was taken out by Mr. Pasteur when his ideas on the conservation of wine were established, to protect himself from the sharks in industry. He deliberately put it into the public domain, and those who talk with contempt about this way of appropriating an industrial discovery will be able to use it freely."⁴⁴ Although Pasteur had hesitated with regard to exploitation of his patent on the heating of wine – in 1865 he had mentioned a partnership with the wine producer Vergnette-Lamotte⁴⁵ –, he finally decided to put it into the public domain in order to facilitate the wide diffusion of his process: "Propagate the heating process as much as possible. I am now determined not to sell my patent and therefore my only ambition is to see this process used to completely revolutionize the art of wine making."⁴⁶ This strategy was justified by the public interest, if not the national interest (the preamble to the patent mentions "the beers of national revenge"), and by the wish not to limit his action to the industrialization of his processes: "Had I wanted to follow-up on my practical results relative to the production of vinegar, I am convinced that I

⁴² Laboratory notebook NAF 17984: March-April 1871, p. 73.

⁴³ Minutes of the Pasteur Institute Board Meeting, 19 February 1891.

⁴⁴ Balard's report to the Science Academy, 1872.

⁴⁵ Pasteur's letter to Mr Vergnette-Lamotte dated 11 July 1865, *Correspondance Générale*, Vol. 2, p 561-562.

⁴⁶ Letter to Duclaux dated 2 September 1865, *Correspondance Générale*, Vol. 2, p 203-204.

would still be doing so, and if I attempted to manage all the aspects of total industrial success of those that I have just obtained for wines, I am sure that I would not be able to do so for a long time.” (letter to Emperor Napoleon III's aide-de-camp dated 19 December 1865, *Correspondance Générale*, Vol. 2, p. 236-238) By putting his patents into the public domain, Pasteur hoped for a form of recognition by the nation or the state: “And if things are like this [i.e. successful transformation of the wine industry in France thanks to his process] in a few years' time, I am hopeful that the country or else the state will recognize the benefit. That is why I have decided not to act in the individual interest of exploitation for the benefit of one person or a small number of persons.” (letter to Duclaux dated 2 September 1872)

It seems that patents on beer were not either exploited or sold. The jurist Federico found no trace of their exploitation in the United States. (*Science*, 1937) In France, programmes for the transfer of his process and experimentation on it at the Tourtel breweries in Tantonville⁴⁷ or at the Velten breweries in Marseille, contained very complete lists of the equipment to install and of the pure yeast to procure. However, on closer inspection one finds no mention of patents or licences. In fact work on beer had been motivated after the 1871 defeat by the wish to strengthen the national industry: “The idea of this research was inspired by our misfortune. I undertook it immediately after the 1870 war and have pursued it consistently since then, with the resolution to take it far enough to make sustainable progress in an industry in which Germany is superior to us.” (*Œuvres Complètes*, Etudes sur la bière, p. 314)

Unlike these public patents, the patents that were taken out by Pasteur's colleague Chamberland in 1886 on a bacterial filter and its improvements were both exploited by a private company created in 1886 for that purpose – the Societe du Filtre Chamberland Système Pasteur – and protected (there was a lawsuit in the US over this patent).⁴⁸

Patents and laws on national rewards

We have seen that in September 1865 Pasteur associated the fact of relinquishing the sale of his patent on the heating of wines, with a possible recognition by the state of the benefits of these inventions for the national wealth. This transaction – renunciation of industrial property in exchange for a public reward – underlay the national reward laws passed by the National Assembly in 1874 and 1883 in Pasteur's favour. In 1874 Paul Bert, rapporteur at the National Assembly, argued that the state's payment of an allowance to Pasteur and his family was justified by the scientist and inventor's disinterestedness: “Regarding the nature of the work that should justify them, it seems that these rewards should apply to those who directly generate a source of new wealth for the nation, when the creator of that source has refused the immediate advantages” (National Assembly, Annex n° 2468, 12 June 1874 session). Paul Bert did not fail to mention Pasteur's attitude regarding his patent on the heating of wines: “It is to ensure these millions for his country without keeping for himself the slightest part, that Mr Pasteur took out a patent in 1865, which he immediately put into the public domain.” The report submitted to the National Assembly, proposing a national reward, described in detail the economic impact of Pasteur's inventions. For example, in respect of the heating of wine, it presented a series of reports on the application of this process and the invention of heating equipment. In 1874, in spite of a short controversy over the anteriority of Appert's invention of the heating process, a resounding majority in the National Assembly approved the granting of the national reward (532 votes against 24). In 1883 a new law on national rewards was justified *inter alia* by the invention of the anthrax vaccine and the creation of a “small factory.” (Annex 2091, 2 July 1883 session) The controversy was far more intense when it came to the question of commercializing the anthrax vaccine. The National Assembly nevertheless approved an increase in the allowance paid to Pasteur and his family.

Pasteur was entirely familiar with the national reward system. In 1882 he was seeking a solution for the industrial production of the anthrax vaccine. After considering the sale of his

⁴⁷ NF 17996: “4 mai 1874: Programme d'expériences à faire à Tantonville”.

⁴⁸ Blount v. Société Anonyme du Filtre Chamberland Système Pasteur, 1892.

invention to a company in the form of shares – something that certain members of the National Assembly reproached him for in 1883 – he envisaged handing over his invention to the government so that it could establish a public vaccine factory: “I have therefore decided to do the state this special service of giving it the anthrax vaccine for France.” In return for the offer of his invention and know-how, Pasteur requested the payment of an allowance: “In return, all he requested was that he and his family be spared any financial concerns.”⁴⁹ The principle of negotiation between inventors and the state, in exchange for them putting their invention into the public domain, was enshrined in the 1791 patent law. This law comprised two options to encourage inventions: the first was of course the patent; the second was the purchase of the invention by the state. The latter option was applied in the pharmaceutical field in France between 1810 and 1850.⁵⁰ Another example is the purchase of the daguerreotype by the government in 1839, following Arago's proposal, and which was cited as a precedent to justify Pasteur's national reward. As soon as Pasteur relinquished any benefits from his patents, his biotechnological inventions were rewarded by the state and considered as public goods – even though the commercial monopoly on veterinary vaccines posed some problems.

Conclusion

In this paper we witness a shift in the subject of controversies over Pasteur's patents on new biotechnological processes and products. The controversies raised by his contemporaries concerned the priority of his inventions relative to that of Appert, in particular; his disinterestedness, which he contradicted by taking out a patent – Lutaud, 1887 –; and the mixture of patriotism with commercialization, and academism with industrial property: “And it was the ENS laboratory in the Rue d'Ulm in Paris that served as his experimental brewery ... We fail to understand this marriage of speculation and patriotism ... principles are not patentable. Only applications are.”⁵¹ We find no trace of questions as to the patenting of what Pasteur called “a living being” with regard to yeast.⁵² The fact that he did not withhold his patent from those who applied his method may help to explain the absence of conflict over the product patent. The absence of a prior examination of patents in France is another reason for the lack of debate on the patentability of his claims.⁵³

Federico's article “Louis Pasteur's Patents”, published in *Science* in October 1937, shifted the debate substantially. Federico noted that there were two types of question. The first pertained to

⁴⁹ Report to Gambetta, *Correspondance Générale*, Vallery-Radot, Vol. 3, p. 271-272.

⁵⁰ Cassier, M., 2004, “Brevets pharmaceutiques et santé publique en France entre 1791 et 2004: opposition et dispositions spécifiques d'appropriation des médicaments”, journal *Entreprise et Histoire*, p.29-47.

⁵¹ *La semaine politique*, 8 April 1873, cited by Salomon-Bayet, *Pasteur et la Révolution pastoriennne*, Payot, 1986.

⁵² Beieir, Crespi and Straus, in *Biotechnology and patent protection* (OECD, 1986) note with regard to Germany that patents were delivered without any difficulty for inventions relative to yeast culture and to the manufacture of bread, beer and vinegar: “These patents were issued with due regard to the existing industries that used fermentation processes, without any real relationship being established with the specific problem of the use of living matter in the course of the chemical process. Moreover, this did not concern inventions that claimed to be innovations or improvements of the micro-organisms used. These remained unchanged: they were cultivated by the industries themselves and were generally available.” But the methods for cultivating pure yeast, proposed by Pasteur, did propose a product innovation concerning brewers' yeast. The idea was to stop using commercial yeasts, which were “mixtures”, and to produce and use a new purified yeast. The brewing industry could still produce its own yeast; each brewery would even be less dependent on the others since yeast contaminations would become rare. However, this new pure yeast economy would fall under Pasteur's product patent if he chose to lay claim to his rights.

⁵³ The first jurisprudence mentioned for France with regard to the refusal of patents on micro-organisms produced naturally was the Sine Court ruling in 1921 pertaining to a fungus used in industry; Bergmans, *La protection des innovations biologiques*, p. 76.

academics' patenting of their own inventions:⁵⁴ "That Louis Pasteur actually patented several of his discoveries is a fact little known. Attention is directed to these patents in view of the current interest in the question of whether research workers should obtain patents for any industrial and commercial utilization of their discoveries." The second question related to the patent "directed to the production of pure yeast free from 'organic germs of disease.'" Federico expressed his surprise concerning the product patent which covered pure yeast: "the second claim, which reads, 'Yeast, free from organic germs of disease as an article of manufacture' is unique in patents in respect to its subject matter." The products-of-nature doctrine underlay this surprise: "A claim of this type would now probably be refused by the examiner, since it may be doubted that the subject matter is capable of being patented." To support his questions on the patentable nature of this type of matter, he cited a Supreme Court ruling from 1931, in the *American Fruit Growers v. Brodgetex* case. The court ruled that a fruit treated to prevent its alteration by a fungus could not be covered by a product patent, as the term "article of manufacture" could not apply to a natural article. According to Federico, the process whereby yeast was purified did not change its status as a product of nature.

In January 2001 the USPTO refused the products-of-nature doctrine by referring to Pasteur's product patent on "pure yeast." The debate on the patentability of pure yeast, relative to the product-of-nature doctrine in the 1930s, has been forgotten. Pasteur's patent, far from being questioned, now serves as a landmark. Micro-organisms have in the meantime become patentable.⁵⁵ Yet the scope of the patent on pure yeast, dependent on the cultivation process and limited to the manufacture of stable beer, is not as absolute as the scope of a gene patent, claimed *per se*, which generally covers all forms of existence of the gene, both natural and artificial, as well as the biological entities in which it is expressed and all the uses derived from it. The monopoly of these two product patents is not the same. In the case of the gene patent, the product, claimed *per se*, outside of any obtention process, is the base of the entire range of claims – on proteins, host cells, transgenic animals – and all possible industrial and medical applications of the gene. In the case of Pasteur's patent, the claim on yeast as a product was the culmination of a particular cultivation process.⁵⁶ Yeasts traditionally cultivated by brewers and traded between them, or "accidentally pure yeasts" – as Pasteur put it (*Etudes sur la bière*, p. 23) – did not fall under this patent.

While the patent produced by Pasteur was mobilized to extend patentability to genes, and exclusive rights to biological entities, Pasteur's strategy in the use of patents to control and maintain the accessibility of his inventions in industry can serve as a basis for reflection on the use of "public patents" on life forms. A system in which the state buys inventions, in exchange for national rewards or various transactions between the inventor and public institutions, of interest to economists in the pharmaceutical field⁵⁷, also offers some ideas of how to reconcile encouragement of invention with public interest.

⁵⁴ This controversy has been studied with regard to patents taken in north America by Weiner, Charles, 'Patenting and Academic Research: Historical Case Studies', *Science, Technology and Human Values*, 12 (1987) : 50-62 ; Swann, John Paul, *Academic Scientists and the Pharmaceutical Industry: Cooperative Research in twentieth-century America*, Baltimore: Johns Hopkins University Press, 1988 ; Rasmussen, Nicolas, 'The moral economy of the drug company medical scientist collaboration in interwar America', *Social Studies of Science*, 34 (2004): 161-185 ; Metlay, 2006, "Reconsidering Renormalization: Stability and Change in 20th Century Views on University patents", *Social Studies on Science*, p 565-597; Cassier, Sinding, 2008, 'Patenting for the Public Interest': Administration of Insulin Patents by the University of Toronto, *History and Technology*, vol 24 (2) p 153-171.

⁵⁵ Bergmans, *La protection des innovations biologiques. Une Etude de droit comparé*, Larciat, 1986.

⁵⁶ On the difference between these two types of product patent, by a process and *per se*, see Beir, Crespi and Straus, *op. cit.*

⁵⁷ Kremer M, 1998, "Patent buyouts: A mechanism for encouraging innovation". *Quarterly Journal of Economics*, 1137-1167.