



Appropriation and commercialization of the Pasteur anthrax vaccine

Maurice Cassier

CERMES, INSERM-CNRS, Paris, France

Abstract

Whereas Pasteur patented the biotechnological processes that he invented between 1857 and 1873 in the agro-food domain, he did not file any patents on the artificial vaccine preparation processes that he subsequently developed. This absence of patents can probably be explained by the 1844 patent law in France that established the non-patentable status of pharmaceutical preparations and remedies, including those for use in veterinary medicine. Despite the absence of patents, the commercial exploitation of the anthrax vaccine in the 1880s and 1890s led to a technical and commercial monopoly by Pasteur's laboratory as well as the founding of a commercial company to diffuse the vaccine abroad. Pasteur repeatedly refused to transfer his know-how and anthrax vaccine production methods to foreign laboratories, on the grounds that he wished to control the quality of the vaccines produced. Indeed, it was relatively difficult to transfer a method that was not yet perfectly stabilized in the early 1880s. Pasteur also wanted to maintain the monopoly of his commercial company and to increase the profits from vaccine sales so that the Institut Pasteur could be financially independent. The 'Pasteur anthrax vaccine' operating licences are described and analysed in detail in this article.

© 2005 Published by Elsevier Ltd.

Keywords: Anthrax vaccine; Know-how; Intellectual property rights; Licensing agreements

1. Introduction

In the controversy that took place between Robert Koch and Louis Pasteur in 1881 and 1882 over the efficacy of the anthrax vaccine, Koch criticized Pasteur's incomplete disclosure of his process for preparing the vaccine: 'Mr. Pasteur's information on his technique for attenuating the anthrax bacillus is so incomplete that, in order to repeat and test it, it

E-mail address: cassier@vjf.cnrs.fr (M. Cassier).

was necessary to carry out extensive prior research'.¹ To this, Pasteur replied in 1882: 'you wish to be excused by asserting that my report of 28 February 1881 provided incomplete information on the process for attenuating the anthrax virus. What is true is that when you applied yourself to following the instructions in that report, step by step, without changing anything, you managed, like the learned Dr. Feltz and several others, to attenuate the anthrax virus'.² Yet, in a letter dated 4 October 1881 to the Austro-Hungarian minister of agriculture, trade and industry, Baron Kemeny, Pasteur noted the difference between the published method and the technical know-how required to obtain the vaccine.³ Although the secrecy concerning the 'details of production of the vaccine' complicated the task of biologists who wanted to reproduce the invention, forcing them either to learn how to do it directly from the inventors or to redo part of the investigative research work themselves, it nevertheless reinforced the technical monopoly over the production and mass diffusion of the anthrax vaccine in the 1880s and 1890s held by the Pasteur laboratory. Apart from Pasteur's secrecy concerning the details of the technique employed for the preparation of the vaccines used at the Pouilly le Fort public trial in May 1881, which was itself borrowed from one of his rivals, Toussaint,⁴ the subsequent commercial exploitation of the anthrax vaccine resulted in the construction of a dual monopoly: first, a *de facto* monopoly based on the industrial know-how needed for the production and quality control of the vaccine, and second, a monopoly defined by a system of contracts and exclusive operating licences granted to commercial enterprises and local agents.

The exclusive commercial control over the anthrax vaccine and Pasteur's other animal vaccines is remarkable in that no patent was filed for these first artificial vaccines.⁵ Indeed, Pasteur and his co-inventors, Chamberland and Roux, never applied for any patents on the production process of the anthrax vaccine that they developed in the early 1880s, even though, prior to that, Pasteur had patented several of his biotechnology processes in the agro-food domain. Between 1857 and 1873, he filed six patents on the fermentation of vinegar and beer, and on a method for preserving wine.⁶ In 1886, Pasteur and Chamberland

¹ Koch (1883), p. 69.

² Pasteur (1883), p. 74.

³ Letter dated 4 October 1881, Archives de l'Institut Pasteur.

⁴ Pasteur's laboratory notebooks studied by Cadeddu (1987); and Geison (1995) show that the vaccines used at Pouilly le Fort were prepared according to a method of attenuation of microbes by addition of a chemical compound, borrowed from Toussaint, and not the attenuation method by atmospheric oxygen that had been developed by Pasteur. It is nevertheless believed that the commercial vaccines prepared after Pouilly le Fort were produced by Pasteur's method which was gradually fine-tuned, as attested by Pasteur's correspondence, Chamberland's writings in 1883–, and Roux's notebooks from 1885 and 1889 (Archives de l'Institut Pasteur, Fonds E. Roux; ROU.4, 'Notes sur le charbon et la vaccination charbonneuse' ('Notes on anthrax and the anthrax vaccine'), document 10612, and 'Vaccins charbonneux: Semences et manipulation' ('Anthrax vaccines: Seeds and manipulation'), document 10611).

⁵ Pasteur kept the process for preparing the chicken cholera vaccine secret for months but did not patent it. The anthrax vaccine developed by Toussaint was registered in the form of a 'sealed letter' at the Académie des Sciences, but only its scientific anteriority was recognized, not industrial property rights. An OECD publication in 1985 on 'patenting biotechnologies' noted that the United States had granted the first patent for an anti-toxin serum in 1877, for a bacteria vaccine in 1904 and for a virus vaccine in 1916.

⁶ Institut National de la Propriété Industrielle, no. 30646, 'Procédé de fermentation alcoolique'; no. 50359, 'Fabrication de l'acide acétique'; no. 67006, 'Procédé relatif à la conservation des vins'; no. 91941, 'Mode nouveau de fabrication de la bière'; no. 92505, 'Nouveau mode de conservation du moût de bière et de la bière qui en provient'; no. 98476, 'Procédés de fabrication et de conservation de la bière inaltérable, appareils relatifs à cette fabrication et à cette conservation, les produits industriels obtenus par ces procédés'.

also filed three patents to protect a new filtering process that they had invented.⁷ This absence of a patent on the anthrax vaccine could be explained by the fact that their method was still not completely stable in the 1880s and would therefore have been difficult to describe in sufficient detail for the patent. But a more probable explanation is the fact that under the terms of the 1844 patent law, pharmaceutical products, including veterinary products, could not be patented in France, while the question of patents on pharmaceutical processes remained a disputed area under this legislation.⁸ Nevertheless, even in the absence of patent protection, Pasteur and his concessionary companies organized a monopoly on the production and distribution of the anthrax vaccine that combined several modes of appropriation. First, the know-how accumulated by the laboratory was kept partially secret; this included not only the methods and technical devices used for the attenuation of the microbe, but also the standards and scales for establishing the virulence of vaccines and the associated tests. Second, there was an asymmetry between Pasteur's laboratory and local laboratories established abroad in terms of competencies and rights. Third, there was the more formal use of contracts to establish the right to exclusive exploitation of the vaccine, and, finally, the control exercised over the commercial use of Pasteur's name, and later the trade name. Overall, we can say that this system of managing the industrial and commercial interests associated with the vaccine compensated for the absence of any patents.⁹

The second section of this article summarizes the rapid emergence of a bio-industry even though problems concerning the stability of vaccine preparations had not been solved. The third section analyses the construction of a technical and commercial monopoly as well as the problems generated by a concentration of production and know-how in a central laboratory. In the fourth section I briefly describe the various tools of appropriation used to construct the monopoly described in the third section, and in the conclusion we will again consider the double opposition: i) between the property status of Pasteur's inventions in the agro-food domain on the one hand and the medical domain on the other; ii) and between the property status of Pasteur's vaccines for veterinarian medicine on the one hand and human medicine on the other.

2. The birth of a bio-industry: producing and stabilizing vaccines

The production of the anthrax vaccine was started as early as 1881, even though at this point the preparation method had still not been stabilized, and controversy over the efficacy of the vaccine opposed 'practising believers' and 'resisters', as a popular book on the subject published in 1886 put it. Available figures indicate a rapid diffusion of the vaccines: 245,000 sheep were vaccinated in 1882, and some two million animals were vaccinated between 1882 and 1887, despite a slight drop in 1883.¹⁰

To meet the growing demand, Pasteur soon set up a small laboratory for the production and distribution of vaccines, near his laboratory in the Rue d'Ulm on a site made available by the ministry for public education and the municipality of Paris: 'From that day forward

⁷ *Bulletin Officiel de la Propriété Industrielle*, 1886: brevets no. 174611, 176387, 180324.

⁸ One of the jurists with the most authority on the question, Pouillet, considered at the time that even if medicines were not patentable, the same did not apply to pharmaceutical processes (Pouillet, 1872).

⁹ In the latter half of the nineteenth century, jurists wrote manuals advising inventors of pharmaceutical products to compensate for the absence of patents in this domain. See, for example, Allart (1883).

¹⁰ E. Roux, 'Les inoculations préventives', 1889, Archives Institut Pasteur, document 15720.

[the Pouilly le Fort trial], farmers in the *départements* affected by anthrax asked for the vaccine to be sent to them. I was rapidly obliged to organize a dispensary for preparing and an office for dispatching the vaccines near my laboratory'.¹¹ Pasteur entrusted the management of this small production laboratory to one of the co-inventors of the vaccine, Chamberland, and the administration of the laboratory and of the dispatching of vaccines to one of his assistants, Boutroux. From then on, orders for vaccines were processed by a specific unit, with an associated address: 'Le Vaccin charbonneux, F. Boutroux, 28 rue Vauquelin à Paris'. Manuals aimed at popularizing the vaccine and instructions intended for veterinarians and breeders would mention this particular commercial name, which was also placed on letterheads and accounting books.¹² This manufacturing subsidiary instituted by Pasteur is described in the report that Paul Bert made to the National Assembly in 1883: 'It is therefore not surprising that it was necessary to set up a small industry outside the ENS laboratory which had become inadequate. Tubes containing the two degrees of vaccines have been sent out from there every day, carriage paid, to farmers in countries throughout the world, at the price of 10 centimes per dose for sheep and 20 centimes for large animals'.¹³ The demand was so great that Pasteur not only had to expand his business to accommodate the preparation and dispatching of large quantities of vaccines, but also had to organize a small industrial laboratory and a commercial unit quite separate from his Rue d'Ulm laboratory. As he commented on the situation, 'I learned a long time ago that a research laboratory must not rest on its laurels'.¹⁴

While setting up this new organization, Pasteur conceived of the creation of a sort of state factory responsible for the production and distribution of the anthrax vaccine. In early 1882, he met Gambetta, President of the Council of Ministers, to discuss this project with him: 'Mr. Gambetta was very much in favour of my idea. But his ministry was so short-lived that it was not possible to implement the plan'.¹⁵ Pasteur did not give up, however, and sent the same proposal to the ministry of agriculture: 'Later I once again offered this service of an anthrax vaccine to Mr. Méline, then minister of agriculture, which had since been joined by other vaccines such as chicken cholera and pig *rouget*'. Pasteur proposed the creation of an anthrax vaccine production laboratory that he would manage with the assistance of the other two co-inventors, Chamberland and Roux: 'The state stands to gain in terms of credit and prestige, and the disease would recede'.¹⁶ Having founded this laboratory, the state would dispose of the tool required to implement its agricultural policy of fighting epizootic diseases. It would thereby strengthen its efforts in the service of public welfare. The terms of the arrangement proposed by Pasteur are worth studying in detail, as there is more to it than his simple statement: 'I therefore undertake

¹¹ Letter to the honorary president of the Institut Pasteur Comité de Patronage, 2 March 1887 (Pasteur, 1940–1951, Vol. 4, pp. 173–174).

¹² 'Etat des sommes dépensées en 1882 pour la fabrication et l'expédition du vaccin charbonneux' ('Expenditures in 1882 on manufacturing and consignment of the anthrax vaccine'), Paris, Archives de l'Institut Pasteur, Fonds Louis Pasteur, cote LP.G1 46, 17640; 'État des fonds du laboratoire au 23 mai 1883' ('Statement on laboratory funds on 23 May 1883'), Fonds Louis Pasteur, cote LP.G1 46, document 17641; 'Vaccination charbonneuse. Principe de la Vaccination. Pratique de l'opération' ('Anthrax vaccine. Principle of vaccination. Operation in practice'), Fonds Louis Pasteur, cote LP.G1.46, document 17993.

¹³ Cited in Salomon-Bayet (1986).

¹⁴ Letter dated 2 March 1887, cited above.

¹⁵ Ibid.

¹⁶ These were the terms of Pasteur's report, reported by Vallery Radot in Pasteur (1940–1951), Vol. 3, pp. 271–272.

to offer the state this special service of delivering the anthrax vaccine for France'. In return for his invention and know-how, Pasteur asked for payment of a rent: 'The only remuneration he requested was that he and his family be spared from material concerns'.¹⁷ This transaction aimed both at guaranteeing the recognition and reward of the inventor, Pasteur, and at putting the invention at the disposal of the state with a view to improving public welfare and increasing national wealth.¹⁸ In the end, the state did not agree to incorporate the production of Pasteur's vaccines into its sphere of activity, but the Ministry of Agriculture did agree to subsidize the Pasteur laboratory both for the preparation of the existing vaccines that had already been distributed, and for research into developing new vaccines.¹⁹ In a document from 1888 concerning the various laboratories run by Louis Pasteur, the laboratory at Rue Vauquelin for the production and dispatching of vaccines was specifically associated with the subsidies from the Ministry of Agriculture.

The organization of the production of vaccines was set out by Pasteur in correspondence with the prefect of the Seine et Marne district during the summer of 1881. The prefect, who had participated in the trial of the vaccine at Pouilly-le-Fort, proposed the creation of a local laboratory for the production of anthrax vaccine: 'I was in London when you came to talk to me about your wish to ask the *Conseil Général*²⁰ of the Seine et Marne for a sum of money to use in setting up a small vaccine production laboratory'.²¹ Thus, in this case, we see that it was the local state authorities that offered to finance a laboratory for vaccine production. Pasteur refused this proposition which he judged 'premature', primarily because the vaccine preparation method was not stable enough to be easily transferred any distance from his laboratory and more particularly out from under his direct control. Clearly, the rapid increase in production would mean the storage and thus the delayed use of vaccines:²² 'All the vaccine that has left my laboratory during the past month is from recent cultures. Factories imply stocks, and the use of prepared tubes after long intervals'. Pasteur expressed his doubts concerning the preservation of the vaccine: 'Problems, albeit ones that are probably easy to solve, can arise in the preservation of the vaccine, the shape of the flasks, etc. During the first year, it will be necessary to check the state of the preserved vaccine, and the persistence of its virtues'. Pasteur considered that at that stage he was the only one capable of appropriately monitoring the quality of vaccines and to overcome any difficulties that may arise: 'Many details are still to be sorted out, and only I can do so . . . a production laboratory in the provinces would take up just as much of my time as the laboratory that I am going to have here'. The monitoring of the production and preservation of vaccines, the 'details' that he needed to sort

¹⁷ Note to Gambetta, *ibid.*

¹⁸ This transaction is comparable to the system of purchasing of pharmaceutical inventions by the state, established in France in 1810 and completed in 1850. The state bought their preparation formulae from inventors in order to put them in the public domain. In return, the inventors were paid compensation. This system functioned very little. See Cassier (2000).

¹⁹ For several years in a row, Pasteur wrote to the agriculture minister to ask for the renewal of the 50,000 franc subsidy granted to him in 1880 to develop vaccines against animal diseases. Letter to the agriculture minister of 6 June 1882 and letter of 20 October 1882, Pasteur (1940–1951), Vol. 3, pp. 285–286, 317–318.

²⁰ The local council of the *département*.

²¹ Letter published in a supplement to *La Revue Médicale Française et Etrangère* of 1 October 1881, Archives de l'Institut Pasteur, document 17945.

²² Especially since the vaccinations were not spread uniformly throughout the year: 'Don't worry about a shortage of the precious liquid next year. Anthrax can't survive the winter'. It was therefore possible to take advantage of the winter months to prepare stocks.

out personally, allowed Pasteur and his direct collaborators in the preparation of the vaccines to establish a *de facto* technical monopoly over this operation. In the short term this state of affairs precluded any technology transfer to other preparation units, and facilitated Pasteur's control over the system of diffusion. Hence, the comments made by the editor of *La Semaine Médicale*, who used the journal to express his indignation at Pasteur's use of his power and accused him of infringing the law on secret remedies:²³ 'As long as Mr. Pasteur has not divulged his processes for culturing the vaccines to the scientific community, we will continue to inform the competent authorities that they are taking on a serious responsibility by allowing the sale of such poisons'.²⁴

Thus, initially, at least, the production of anthrax vaccines was localized exclusively at the Paris laboratory supervised by Pasteur.²⁵ The laboratory for the preparation and dispatching of vaccines was not very large. Located on temporary premises, it initially employed only two or three people: 'One intelligent person in my laboratory will have no other occupation than preparing vaccines throughout the year. That person will need to be assisted by one man, at the most. There will be a storeroom for vaccine tubes in our neighbourhood'. A third person was to receive orders and dispatch the vaccines. This fairly light structure was, nevertheless, capable of producing and distributing the required quantity of vaccines, both in France and abroad: 'I now have everything needed to produce on a large scale. After the holidays I'll have one or two hectolitres of culture already prepared, and in March or April, when the vaccination can usefully begin, there will, I hope, be enough vaccine ready for one million animals'. In 1884 a report by the Senate, drawn up with a view to allocating new facilities to Pasteur, described the production facilities at Rue Vauquelin in the following terms:

the production of vaccines is going to become a highly important service. In the laboratory in Rue Vauquelin, anthrax, rouget and chicken cholera vaccines are produced on a large scale. Records kept there show that in a single month 200,000 doses of anthrax vaccine have been dispatched [to destinations] in France, representing prophylaxis against anthrax for 100,000 head of livestock (sheep, cattle and horses).²⁶

An inventory from 1888 mentioned that four assistants were employed at the Rue Vauquelin laboratory.²⁷

The creation of this laboratory was accompanied by the establishment of a special accounting system for the vaccines. This accounting system was justified with reference to several objectives. First, it was necessary to justify the use of the subsidy granted by the agriculture ministry.²⁸ Second, it was necessary to calculate the production cost of a vaccine in order to determine its sale price for breeders. A list of expenditures for the year 1882 set the cost price of a tube of vaccine at two francs, 13 centimes. An analysis of the

²³ This law, passed in 1810, cancelled authorizations to sell drugs granted 'to inventors or owners of remedies or compositions, of which only they knew the formulae'.

²⁴ *La Revue Médicale Française et Etrangère* of 1 October 1881, cited above.

²⁵ 'When the regularity of its functioning has been proved, we will be able to consider your project', Pasteur, letter to the prefect of Seine et Marne, in *La Revue Médicale Française et Etrangère* of 1 October 1881, cited above.

²⁶ Senate, special session 1884, no. 48, report by Mr. Edouard Millaud, Archives de l'Institut Pasteur, document 18630.

²⁷ 'Récapitulation des émoluments individuels' ('Recapitulation of individual remuneration'), Archives de l'Institut Pasteur, document 18476.

²⁸ Cf. 'Statement on laboratory funds on 23 May 1883', Fonds Louis Pasteur, cote LP.G1 46, 17641.

pricing structure shows that the culture of the vaccine represented only a very small portion of this sale price.²⁹ The highest proportion was for packaging and postage (30% of costs), correspondence and administrative costs (25%), and commercial management (30% of the budget). The third reason for the accounting system was to assess the profits generated by this activity in order to allocate them to the inventors and the laboratory and later to the Institut Pasteur itself. The distribution of profit was as follows: ‘The balance left over constitutes a profit which is divided into five parts: Mr. Pasteur keeps two and allocates two, that is, one equal part to each of his assistants; the fifth part constitutes a legal reserve’.³⁰ This use of earnings thus constituted a form of profit-sharing for the inventors Pasteur, Roux, and Chamberland. In 1887, during the creation of the Institut Pasteur, the three inventors renounced their share of the profits for the benefit of the institute.³¹ The profits of the vaccination service, henceforth incorporated into the services of the institute, were to play a crucial part in balancing its budget.³²

As Pasteur suggested in his letter of 1881 to the prefect of the Seine et Marne, the production of anthrax vaccines posed problems of standardization and stability that were not entirely overcome in the following years.

The first problem, related to standardization, was particularly complicated in so far as anthrax vaccination involved the use of two vaccines of increasing virulence administered consecutively with an interval of a few days between them: ‘All the difficulty with anthrax vaccines lies in the choice of these two viruses and in the maintenance of their virulence in an unchanging ratio’.³³ In a letter to Duclaux dated 30 June 1882, Pasteur noted that the laboratory director was exercising insufficient surveillance over these aspects of the vaccine: ‘Our production will improve with time, I hope. In November and December the vaccines were too weak. We had to strengthen them. They weren’t strengthened enough though, because they induced a shorter period of immunity. The ratio of virulence between the first and the second doesn’t satisfy me. In a sense it would be necessary to achieve nothing else but that. That is what I expect from Chamberland, but sometimes his enthusiasm wanes’.³⁴ To test the quality of the vaccine strains obtained, the production laboratory introduced testing on laboratory animals and established scales of virulence. In cases where the virulence weakened, it selected a new ‘origin’ for the vaccine production, tested it, and adjusted the relation of virulence between the first and second vaccines. Test notebooks record this constant work of adjustment of vaccines as well as the selection of ‘new origins’.³⁵

²⁹ In June 1881, at the congress of agronomic station directors, in Versailles, Pasteur mentioned the negligible production cost of the anthrax vaccine: ‘As for the virus-vaccine, it costs next to nothing and it would not be difficult to vaccinate every year’ (Pasteur, 1933, p. 366).

³⁰ ‘Etats des sommes dépensés en 1882 pour la fabrication et l’expédition du vaccin charbonneux’ (‘Statement of accounts on expenditure in 1882 for production and dispatching of anthrax vaccine’), Fonds Louis Pasteur, cote LP.G1 46, document 17640.

³¹ Board of Governors, Archives de l’Institut Pasteur, 25 March 1887: ‘This large income which rightly belongs to Mr. Pasteur and his collaborators, Mr. Pasteur is prepared to give up . . . This great example of disinterestedness’.

³² During the 1890s, the anthrax vaccine accounted for most of the income. During the 1900s, it was to be the diphtheria serum. Cf. the report by the Board of the Institut Pasteur, 1896–1910, Archives de l’Institut Pasteur.

³³ Roux, ‘Les inoculations préventives’, 1889, cited above.

³⁴ ‘A. Duclaux’, Pasteur (1940–1951), Vol. 3, pp. 297–298.

³⁵ These vaccine trials can be studied from 1889 onwards. The vaccination trial notebooks of the anthrax vaccine service up to World War II show almost constant problems of adjustment as well as incidents and poorly explained oddities (Fonds du Service du Vaccin Charbonneux, cote SVC).

The second problem concerned stability. By 1881 Pasteur believed that he had vaccines whose virulence was definitively established.³⁶ Nevertheless, in 1882, while conducting a full-scale experiment in the form of a mass vaccination program started in 1881, he discovered that his vaccines had weakened: ‘Unfortunately, practice showed that the vaccines had weakened, and then accidents of various kinds occurred’.³⁷ Despite the improvement in vaccine preparation methods highlighted by Pasteur in 1883, doubts remained, especially regarding vaccines that were to be used several months after being stored in tubes: ‘we are still unable to state whether the vaccines will have exactly the same properties as if they were fresh’.³⁸ Consequently, problems of storage and transport time, and any long intervals before the vaccines were used, became crucial in the organization of their production and distribution. Instruction manuals gave instructions for the use of fresh vaccines. A great deal of attention was paid to the delivery time for vaccines. Thus, questions were raised concerning the relationship between the localization of production laboratories and the diversity of the sites where inoculation could take place.

3. The construction of a commercial and technical monopoly

Pasteur had to deal with requests to transfer his technology and know-how concerning the preparation of the anthrax vaccine as early as 1881, while the process was still in the first stages of development. He had several options. He could choose to disclose his method and to place it in the public domain so that any outside user could reproduce it. Alternatively, he could choose to transfer his technique in the form of licenses covering the appropriate know-how, thereby maintaining his property rights and guaranteeing the royalties for his laboratory. Finally, he could choose to exploit his invention exclusively in his own laboratory establishing a monopoly over the production of all the vaccines, which the laboratory could then sell throughout the world. Because the process was still in its early stages and quality control was still a problem, transfer of the relevant technology and the exporting of production away from the original laboratory were highly complex matters. Moreover, neither the reputation of the vaccine nor even the principle of the preventive inoculation were soundly established. The question of the vaccines’ stability was also essential. If they were stable and their efficacy did not alter over time, it would be possible to transport them over long distances and to store them for long periods of time. In this case, one could conceive of their production at a single site. On the other hand, if their stability was uncertain or poor, it would be necessary to diversify the sites of production and to negotiate licenses with ‘local laboratories’. These alternatives were discussed in the early 1880s, and no single one of them was selected as the exclusive policy to be pursued by Pasteur and his institute. The combination of solutions that was chosen evolved throughout the development of the large-scale use of the vaccine.

³⁶ ‘Apart from the subsequent study of the detailed problems that we encounter in the implementation of a vast anthrax prophylaxis, the fact remains that we have at our disposal not only filamentous bacillus that could serve as virus vaccines for anthrax, but also virus vaccines fixed in their germ with all their own qualities, transportable without any possible alteration’ (Pasteur, 1881, p. 668).

³⁷ Pasteur’s lectures at the Société Centrale de Médecine Vétérinaire, 8 June 1882 session, in Chamberland (1883), pp. 284–296.

³⁸ Chamberland (1883), Ch. 30.

In 1881, anthrax vaccine trials were performed on the livestock of two major land-owners in Hungary. In this case, Pasteur sent his assistant Thuillier to vaccinate the animals.³⁹ Baron Kemeny, the Austro-Hungarian minister for agriculture, trade, and industry asked Pasteur to authorize his assistant to ‘perform the full preparation of the vaccine in front of the commission set up to witness the experiments’, but Pasteur refused.⁴⁰ The arguments Pasteur offered to support his refusal justified his laboratory’s technical monopoly over the preparation of the vaccine, at least during the initial phase of development.

First, Pasteur emphasized the importance of the laboratory know-how necessary for the preparation of the vaccine, as well as the time and cost involved in developing it:

This preparation is fairly simple in theory. I published it in the report of the Académie des Sciences de Paris. Its application takes a lot of time and is very expensive if one is to attain absolute certainty. But to ensure its full value, a lot of time and even expense are required. One has daily to test, so to speak, the state of the virulent anthrax parasite as it progressively changes, and this testing can be achieved only by means of inoculations practised on animals, and finally on a large enough number of sheep.

Apart from knowledge concerning the principle of attenuation, Pasteur revealed the importance of the system for measuring and verifying virulence, which made it possible to establish a scale of virulence for the different cultures and to determine the appropriate virulence ratio between the first and the second vaccines needed to produce immunity. Roux’s notebooks on the preparation and culture of the anthrax vaccine,⁴¹ as well as the test notebooks of the vaccine service, confirm the importance of measurement and control, with the institute investing heavily in the animals on which the vaccines were tested.⁴² The time required for the attenuation of microbes and the setting up of such measurement procedures would, according to Pasteur, exceed his assistant’s mission: ‘Mr. Thuillier will absolutely not have the time to carry out this study’.⁴³ Since the vaccine preparation method was still not perfectly stable, it had to remain under the inventors’ control so that they could perfect the procedure: ‘there are still some details to study, that at this stage only I can illuminate’.⁴⁴

³⁹ During the first vaccination campaigns in 1881, Pasteur was careful to ensure that the inoculations were performed by those of his assistants who had mastered the technique: ‘but for this campaign I do not wish to entrust these vaccine inoculations to anyone but Chamberland, Roux, Thuillier and Eugène Viala, who also vaccinates very well’ (letter dated 9 July 1881, *Pasteur (1940–1951)*, Vol. 3, pp. 221–222).

⁴⁰ Letter dated 4 October 1881, Archives de l’Institut Pasteur, cited above.

⁴¹ Notebook from 1885: ‘We are made aware of the excess or deficiency of virulence by inoculating sheep or cattle, or even rabbits or guinea pigs’ (Fonds E. Roux, document 10612).

⁴² The animals accounted for a substantial proportion of the vaccine service’s expenditure.

⁴³ In a notebook from 1885, Roux wrote that it took fifteen to twenty days to obtain a series of increasingly attenuated cultures. The first vaccine, the less virulent one, was taken between the eleventh and the twelfth day, while the second was taken between the seventh and the eighth day (Fonds E. Roux, cited above).

⁴⁴ The contrary could be deduced: the dissemination of the technique, even incomplete, would facilitate rapid development through the additions and improvements of other users. This alternative—monopolization or dissemination of the invention to ensure its development—is classic in the economics of innovation and of intellectual property rights.

Pasteur also justified his refusal to transfer the production of the vaccine out of a concern for the quality and reputation of the anthrax vaccine: 'Furthermore, allow me to point out the fact that out of caution and so as not to compromise the success of a method which is tricky, to say the least, I wish very much that, for at least a year, any vaccine used by sheep or livestock breeders be prepared by me or under my immediate supervision'. Bad preparations could ruin the career of the anthrax vaccine since the principle of vaccination was still a highly controversial issue. Before considering diversifying the sites of vaccine production, it was first necessary to consolidate and extend the network that was promoting the use of the vaccine: 'For the moment, it is necessary to persuade farmers and large landowners of the advantages of the method'.

Pasteur had definite ideas for the industrial and commercial organization of vaccine production. Thus, he described the launching of his small industrial laboratory in these terms: 'Moreover, I am presently setting up a sort of factory. I already have no less than two hectolitres of liquid ready to be transformed into vaccine. Next spring I will be able to send tubes filled with vaccine liquid far away, at the very modest cost price, or more or less'. His Paris laboratory was to mass produce the vaccines that were to be sent out to other countries. He proposed a trade agreement: 'After France, Hungary will be the preferred nation'. He then considered setting up a production laboratory in Hungary to cater for the expanding market. 'If the practice of vaccination spreads more and more as I hope it will, I will be able to deliver all the vaccine requested only little by little. A factory could be created in Hungary and I would be the first to guarantee its success by giving the most precise instructions'. This last sentence confirms both the importance of the know-how that would be transferred in such a case, and Pasteur's refusal at that moment in time to share this know-how with the Hungarians.

This monopoly was supposed to be temporary, and Pasteur justified it with reference to the problems and risks involved in diffusing an emergent invention. In 1994, M. Callon, while considering the public or private status of science, put forward the idea that any emergent innovation is necessarily of a 'private' nature if it does not have a socio-technical network able to receive and reproduce it. This line of reasoning fits with Pasteur's argument. Yet the explanation based on the state of the network—emergent or stabilized—is not enough to explain Pasteur's policy. He clearly intended limiting and controlling the extent of the network itself, despite pressing demands made on him to expand it. He was wary of counterfeiters and on several occasions reacted with suspicion when asked to give precise descriptions of his production methods, not only for the anthrax vaccine but for other preparations as well (Cadeddu, 1985). Although his goal was not financial profit—he specified that the price of the vaccine would be close to the cost price—he was determined to maintain total control over the use and diffusion of his invention. Furthermore, the diffusion of this vaccine benefited from France's influence in Central and Eastern Europe. We know that Pasteur deliberately put several of his inventions at the service of France's economy and its expansionist agenda.⁴⁵ However, if he agreed to divulge the production method of his vaccine to the Hungarians, he would lose his control over the diffusion of his invention in the region and would thus hand the exploitation of that particular market over to the Hungarian producer.

⁴⁵ This explains his decisions to patent his fermentation processes, notably the fabrication of beer, and his use of those patents.

This mode of exploitation of the anthrax vaccine—a single laboratory producing the vaccines and distributing them throughout France and abroad—was called into question in 1882 and 1883 when it became apparent that the vaccines lost their strength over time. In his book on anthrax and the anthrax vaccine (*Le charbon et le vaccin charbonneux*) published in 1883, Chamberland made the following recommendation: ‘I therefore think that, for distant countries, for all those requiring more than fifteen or twenty days before the vaccine arrives at its destination, it would be extremely advantageous, indispensable even, to set up small laboratories for producing fresh vaccines that would be sent, fresh, throughout the surrounding areas’.⁴⁶

In 1884 and 1885 the Indian government and Pasteur negotiated the most appropriate model for diffusion of the vaccine in that country.⁴⁷ Initially, Mills, an inspector of diseased livestock in Madras, performed a series of tests of Pasteur’s anthrax vaccine on several types of animal. These tests proved to be conclusive and the inspector ‘recommended the importation here of anthraxine [the vaccine] coming from Mr. Pasteur, in France, and its methodical use throughout the presidency of Madras’. This recommendation was contested by another veterinary inspector, Evans, who based his arguments on several negative reports drawn up in England and who doubted ‘that the liquid in question is still effective in India . . . Although Mr. Pasteur always succeeded for himself, it was not rare for the liquid sold by his approved agents to be not only ineffective but sometimes even harmful’. Evans advised the continuation of the tests before definitively adopting the vaccine, for he suspected a possible alteration of imported vaccines. New experiments on elephants proved to be conclusive and the chief superintendent of the stud farms of India, Hallen, went to the Pasteur laboratory ‘in order to learn not only the method followed for the vaccination but also the way of preparing the vaccine’. On his return he did not recommend importing vaccines from Paris but instead suggested setting up laboratories in India, in stations where the vaccine would be produced and distributed. Considering the risk of failure related to the use of imported vaccines, India opted for the establishment of local laboratories. On 19 March 1884 Pasteur replied to a letter from the British ambassador on the appropriate mode of organization: ‘Can one transport the vaccination practice to India and expect the same effects as in France? Without any doubt’. Yet it is essential to use ‘good vaccines that have been well tested and freshly prepared’, as the ‘mistakes’ associated with vaccinations performed in France had shown. To assure this result, Pasteur considered two types of organization. The first option, which he preferred, consisted in setting up a vaccine production laboratory in India, with the mission of culturing the spores or ‘seeds’ sent out by the Paris laboratory: ‘the vaccines in question change with time, and lose some of their effectiveness if one uses them after a long period; however, it is easy to regenerate them and to give them back their value in India, even after the necessary time period for travelling from Paris to that distant country’. Pasteur envisioned the movement of spores from France to India to supply the local laboratory, and the training of laboratory agents in Paris: ‘An intelligent young man, somewhat familiar with chemical research, could come and familiarize himself with vaccine cul-

⁴⁶ Chamberland (1883), p 296.

⁴⁷ This negotiation is reported in *M. Pasteur, la rage, le vaccin charbonneux*, Bernard Tigniol Editeur, 1886, Ch. 12, ‘Le charbon dans les pays étrangers’, pp. 107–119 (Fonds Louis Pasteur, cote LP.G1 46, document 17987).

tures by first spending two or three weeks, a month at the most, in my laboratory in Paris, before going to India'. Pasteur wanted to use the capacity to culture anthrax spores, which had first been attenuated in his Paris laboratory, in order to retain control over the chain of vaccine preparation. The Indian laboratory would remain linked to Paris through the 'vaccine spores' 'fixed' in Paris and 'sown' in India, and the training of laboratory agents, also dispensed in Paris.

The second option for transferring the vaccine to India was more radical: 'There is another way of proceeding: it would consist in reproducing in India, *ab ovo*, all the manipulations and tests that are indispensable to the production and preservation of the two vaccines'—in other words, duplicate the Paris laboratory. Pasteur was against this: 'I believe that this way of proceeding would result in immense difficulties'. He stressed the time and costs involved in testing the virulence of vaccines on animals, 'tests that are indispensable for establishing the state of virulence of the two vaccines'. He also highlighted an economic justification: it would be unnecessarily expensive and time-consuming to reproduce a system of measurement and control along with all the other know-how that already existed at the laboratory in Paris and could simply be used: 'All that has already been done for my laboratory, and does not have to be repeated for France'. It would furthermore be expensive to create new vaccine colonies when they could simply be put in culture: 'We always use the same vaccines, constantly regenerated by culture, for the needs of French breeders. I undertake to use the same starting point, that is, these same French vaccines, for the Indies'. Pasteur justified his laboratory's monopoly, as opposed to the creation of laboratories abroad, by the high cost of reproducing know-how concerning attenuation and other vaccine tests, and by the low cost of the cultured vaccine colonies themselves. We shall see that this monopoly also had a cost, in that it impeded invention of new vaccines, especially ones adapted to local breeds and, more generally, to local breeding conditions.

Several 'special' laboratories were set up abroad, based on the organizational model favoured by Pasteur himself, that is, they received vaccine spores, culture fluids, and expertise from Paris and then prepared the fresh vaccines and distributed them to veterinarians and breeders. Laboratories of this sort were created in Budapest for Austria–Hungary, Bosnia–Herzegovina, Serbia, Bulgaria, and Romania, in Buenos-Aires for Argentina, Uruguay, and Paraguay, and in Madrid for Spain. The Laboratoire Pasteur–Chamberland, Vaccins Contre le Charbon et le Rouget was founded in Budapest under 'the patronage of the Hungarian ministry for agriculture'.⁴⁸

In 1886, the Pasteur laboratory was instrumental in the creation of a commercial enterprise, La Compagnie de Vulgarisation du Vaccin Charbonneux Pasteur, to exploit the anthrax vaccine abroad (Liebenau & Robson, 1991). The inventors had noted that there was insufficient diffusion of the vaccine abroad, due to the absence of any commercial network and 'because of the total lack of publicity', as well as problems related to the instability of the vaccine and to 'dispatching it to various countries'.⁴⁹ To get

⁴⁸ Letter to Chamberland dated 11 June 1896, Fonds Louis Pasteur, document 10602.

⁴⁹ 'Traité entre M. Chamberland et M. de Sainte Marie en vue de la réalisation de laboratoires du Vaccin Charbonneux Pasteur à l'étranger' ('Treaty between Mr. Chamberland and Mr. De Sainte Marie with a view to setting up Pasteur anthrax vaccine laboratories abroad'), 19 April 1886, Paris, Archives de l'Institut Pasteur, Fonds IP Direction, document 10587.

round these problems, the company was to set up a network of agencies and local laboratories: 'it has been acknowledged that its diffusion would be possible only with the establishment of laboratories abroad'. The preamble of the contract between the inventors—Chamberland, Pasteur, and Roux—and the director of the company, Mr. De Sainte Marie, a former inspector general of agriculture, clearly established the division of work between the Pasteur laboratory and local laboratories, based on the model described by Pasteur in his letter to the British ambassador in March 1884: 'Mr. De Sainte Marie proposed to Mr. Chamberland to take care of this creation provided that the assistants of the said laboratories are trained by him and remain under his technical supervision, and that the spores and fluid for preparing the vaccine are supplied by Mr. Pasteur's laboratory in Paris'.

This contract specified the scope of the concession granted to the company set up to diffuse the anthrax vaccine, determined the circulation of products and transfers of knowledge between the Pasteur laboratory and the company, confirmed the Paris laboratory's technical supremacy, fixed prices, and set the sum of royalties that the company was to pay to the inventors.

This agreement gave legal recognition to the monopoly over the exploitation of Pasteur's vaccine: '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."' The territorial scope of the license excluded those areas for which treaties had already been signed: 'the said monopoly excludes the countries of the Republic of Argentina, Paraguay, Uruguay, and Austria-Hungary, already granted in prior agreements'.⁵⁰ The contract did, however, provide for 'special conventions' between the new company and laboratory in Austria-Hungary. In case of termination of the contract with the concessionary laboratory in South America, the concession would be transferred to Mr. De Sainte Marie's monopoly. The sharing of markets was carefully defined, although the concession granted to the new company excluded France and the colonies, which were reserved for Pasteur and Chamberland's laboratory. The contract stipulated that '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'. Chamberland was also required to transmit the relevant information needed to facilitate the establishment of new laboratories, and to participate in the writing of documents to help the diffusion of the vaccine, helping with 'all information and brochures to be published in the different countries'.

Apart from delimiting the monopoly on exploitation of the invention and the transfer of property rights, the contract stipulated the respective rights of the laboratory and the company to set up and run new laboratories. While Mr. De Sainte Marie's company received an exclusive right to exploit the vaccines abroad, that right was strongly dependent on the technical rights of Pasteur and Chamberland's laboratory. These rights were exercised at every step in the creation and functioning of other laboratories. First, Article 3 stipulated that laboratories created by the new company would be created 'according to the instructions provided by Mr. Chamber-

⁵⁰ Other licences to exploit the anthrax vaccine had already been granted for Argentina, Paraguay, Uruguay, and Austria-Hungary.

land'. Second, the directors of those laboratories would be subject to commercial and technical authority:

the head technician of each laboratory is to be chosen by Mr. De Sainte Marie but trained and taught by Mr. Chamberland. He is to be under Mr. De Sainte Marie's management, but for all technical questions he will remain subject to the instructions of Mr. Chamberland who will have the permanent right to demand his replacement if he fails to comply with the said technical instructions. Likewise, he will have to answer any technical question put to him by Mr. Chamberland.

Thus, the concessionary company's exploitation rights were subject to the authority and technical expertise of the central laboratory. To that technical power was added a right to audit the concessionary company's accounts, for licence fees were based on the number of tubes of vaccine sold: 'In order to check the number of doses sold, Mr. Chamberland reserves the right to audit Mr. de Sainte Marie's accounts' (Article 4).

Far from being limited to a mere transfer of rights, this contract determined multiple technical exchanges between the two parties, including: instructions from the central laboratory to the concessionary company concerning any decisions on the establishment of a new laboratory; knowledge transfer between inventors and local laboratories for the training of laboratory assistants, and the communication of any improvements to the invention: 'Any new improvement relative to the cure for anthrax and any improvements by Messrs. Pasteur, Chamberland and Roux, will benefit Mr. de Sainte Marie fully and at no cost, for the entire duration of the contract'. In return, laboratory assistants would have to answer requests for technical information from the central laboratory. Finally, the contract determined the circulation of products and material between Paris and the local laboratories, especially spores and culture fluids.

The legitimate use of the inventors' names was clearly defined by the contract. The monopoly over the exploitation of the vaccine was based on the exclusive use of Pasteur's name. The laboratories set up abroad were called 'Laboratoire du Vaccin Charbonneux Pasteur', and the contract stipulated that the origin of the vaccines would be guaranteed by the central laboratory: 'Mr. Chamberland undertakes to guarantee the origin and high quality of the vaccine sold under the name of Pasteur anthrax vaccine by means of the stamp indicating its origin'. The new company would be able to use the inventors' names to mobilize capital, subject to the inventors' prior approval: 'There is to be no financial advertising foreselling stocks bearing the names of Messrs. Pasteur, Chamberland and Roux without prior submittal to and approval by Mr. Chamberland' (Article 14).

We have collected several contracts signed between 1886 and 1896 between the company set up to diffuse the anthrax vaccine and concessionary companies abroad.

In June 1887 the *Compagnie de Vulgarisation* and the Pasteur laboratory drew up a contract granting Russia a monopoly on the anthrax vaccine.⁵¹ This agreement between the two partners was, however, only the first level of a more elaborate contract. The

⁵¹ Letter from the *Cie de Vulgarisation du Vaccin Charbonneux Pasteur* to Chamberland, 26 June 1887, Fonds IP Direction, 1887–1940, document 10577. In June 1883 Pasteur had an exchange of correspondence with the governor of the province of Central Russia. He proposed the establishment of local laboratories: 'Nevertheless we have recognized that the vaccines, in order to be fully effective, must be used when they are as fresh and recent as possible. That is why my colleagues and myself wish to encourage the establishment of small production laboratories, close to the areas infected by anthrax, so that the vaccine does not take more than five to eight days to arrive from the factory to the place where it is used on animals' (Pasteur (1940–1951), Vol. 3, pp. 361–362).

Compagnie de Vulgarisation subsequently negotiated a licence with the local laboratory, in terms of which a monopoly was granted in exchange for the payment of a set sum—150,000 French francs—shared between the Pasteur laboratory and the company, and a set charge per vaccination—5 centimes for small animals and 10 centimes for large ones. A part of that fee—1 centime per head for small animals and 2 centimes per head for large ones—was shared between the Pasteur laboratory and the Compagnie de Vulgarisation. The money received by the Pasteur laboratory was used to remunerate the owner for his invention and the production services provided by Paris (the provision of spores and culture fluids). It is important here to note the inventors' direct involvement in the negotiation of this contract: 'to facilitate any negotiation and convention, Mr. Pasteur and yourselves should deal directly with Prince Olienbourg and the imperial government. To this effect, I have the honour, in the name of the Compagnie de Vulgarisation, to grant you full powers'. The commercial company was unable to bypass the inventors in setting up a new company due to the technical expertise required to conclude the negotiation successfully and the close link between the vaccine and the names of Pasteur, Chamberland, and Roux.

On 10 June 1890, a contract was signed with a private concessionary company in the Kingdom of Siam granting an 'authorization to produce the vaccine'.⁵² The licensee—the Check & Durando company—was authorized to set up a local laboratory which would receive spores and culture fluid from Paris. The concession was for a period of twenty-five years. The contract provided for the payment of a set amount of 1,500 French francs for the first year and a variable rate for the following years starting at 3,000 French francs if fewer than 3,000 elephants were vaccinated, and otherwise 1 franc per elephant, 'this sum representing the excess of spores and fluids over and above 3,000 animals'. The contract provided for a change in the system for supplying the vaccine: if the concessionary company chose not to prepare the vaccine locally, the anthrax vaccine service of the Institut Pasteur would supply a vaccine ready for use: 'Mr. Chamberland, director of the vaccine service at the Institut Pasteur, would be able to supply a ready-made vaccine that is sufficiently resistant to be sent to the Kingdom of Siam'. In the latter configuration, the price of each vaccination would be 5 francs, with a minimum annual demand of 600 vaccinations of elephants.

In 1890 the Compagnie de Vulgarisation du Vaccin Charbonneux set up an agency in Australia, that operated with a laboratory financed by the government (Todd, 1990). The agent sent by Pasteur produced local cultures of vaccine spores received from Paris. In 1896, a new licence was granted to an Australian company, covering 'the right to produce, prepare, use, negotiate and sell the vaccine liquid known under the name of Pasteur anthrax vaccine' in Australia, New Zealand, and Tasmania.⁵³ The property rights laid out in the contract were relatively broad in scope, for they protected both the production method and the use of the vaccine, specifying 'a certain secret process or vaccination method' as well as re-affirming that the product was covered by the commercial name of Pasteur and by a brand name. The Australian company bought out the existing laboratory, that is, 'the entire stock of instruments, plans and equipment now belonging to and

⁵² 'Traité avec le Dr Durand pour la vulgarisation du vaccin charbonneux dans le royaume de Siam' ('Treaty with Dr. Durand for popularising the anthrax vaccine in the Kingdom of Siam'), 27 May 1888, Fonds IP Direction (1870–1940), DR.DOS.1, document 10593.

⁵³ Proposed contract between the Société du Vaccin Charbonneux Pasteur and the purchasing company, Fonds IP Direction (1887–1940), DR.DOS.1, document 10597.

existing on the premises occupied by the selling company in Sydney'. The contract provided for prosecution of counterfeiters in case of 'violations of the said anthrax vaccine or secret process of Pasteur anthrax vaccination'. The financial arrangement provided for the payment of a fixed sum at the signing of the contract as well as the seller owning capital in the Australian company.⁵⁴ Note here that the contract renewed the system of vaccine production fixed by Pasteur in 1884: the *Compagnie de Vulgarisation* was to provide the colonies necessary for culturing the vaccine and to train laboratory assistants for the Australian concessionary company. The *Compagnie de Vulgarisation* was also to transmit improvements in the method to the Australian company, as well as the material necessary to implement them.

In these negotiations and contracts we can see three different models for the production and distribution of the Pasteur vaccine. The first model, set out in a letter from Pasteur to Baron Kemeny in 1881, was based on the creation of a single laboratory for production of the vaccine to be distributed and sold throughout the world. This represented a maximum concentration of production and know-how at one central location. By contrast, the second model, described in a letter to the British ambassador in 1884, was based on the spinning-off of multiple laboratories, all reproductions of the Paris laboratory. Each laboratory would have the know-how and material needed for the complete implementation of vaccine preparation, including the attenuation and fixation processes as well as the operations to test virulence. This solution corresponded to a maximal distribution of the laboratory's production and know-how. This second model was rejected by Pasteur, and was never implemented. The third model, described by Pasteur in 1884 and subsequently adopted by the *Compagnie de Vulgarisation du Vaccin Charbonneux*, was based on the creation of local laboratories that in turn depended on the know-how and basic products of the central laboratory.

The sharing of surplus value and the transfer of technology are very different in these three configurations. In the first model, the central laboratory generates and concentrates the entire surplus value associated with production of the vaccine, and technology transfer is minimal. In the second model, technology transfer is maximal and the surplus value is shared between the different laboratories, with the Pasteur laboratory receiving royalties to compensate for the exploitation of its invention. In the third model, technology transfer exists but is limited, and the central laboratory, apart from remuneration for its invention, receives a payment to pay the cost of its production of spores and culture fluids. The degree of control of ownership is clearly different in each configuration: the monopoly is complete in the first model, where know-how is not shared; in the second model, where the laboratory's know-how is disseminated, ownership is essentially guaranteed by legal means (contracts and industrial property rights); lastly, in the third model, protection is guaranteed both by control over the technique and by the preparation of vaccines upstream, as well as by licence contracts and property rights.⁵⁵

⁵⁴ The *Compagnie de Vulgarisation du Vaccin Charbonneux* also owned shares in the British vaccination company *Animal Vaccination*.

⁵⁵ We can today observe a comparable debate and even conflict between the different models of production and distribution of genetic testing. For example, the company *Myriad Genetics* claims the right to perform most *BRCA* gene tests in its Salt Lake City laboratory, based on arguments relative to the quality of tests, and refuses to allow other laboratories the complete sequencing of genes. The other genetic laboratories refuse such asymmetrical licences and demand the right to carry out tests themselves, if necessary by paying royalties to *Myriad* for use of its patents.

4. Tools for appropriating the anthrax vaccine: know-how, operating licences and industrial property rights

Appropriation of the anthrax vaccine was initially based on specific technical know-how involved in producing large quantities of relatively standardized vaccine, which was exclusively held by the Pasteur laboratory. As Pasteur explained in a letter to Baron Kemeny in 1881, there is a considerable gap between the published principles and the multiple operations that need to be mastered by the technicians. It was precisely by exploiting this gap that Pasteur was able to retain a monopoly over the vaccine. Pasteur often referred to the ‘technical details’ that only he, or a limited group around him, could understand. The exclusive licences to produce the vaccine mentioned the ‘instruction’ that laboratory technicians would receive when they were sent to Paris for several weeks. This period of apprenticeship in vaccine culture, considered by Pasteur to require three to four weeks, also gives an indication of the knowledge acquired by the visiting laboratory agents. Roux’s notebooks on the preparation of the anthrax vaccine are filled with precise details, some added in the margins, for example on how to culture vaccines prepared for foreign use or the need to mix vaccines of two different ages. Roux added drawings of the equipment to his notes on ‘the means of cultivating vaccines’.⁵⁶ Not all these instructions were published, nor were all the observations made on the animals—for example oedema—used to measure the degree of virulence of vaccines and the ratio of virulence between the two vaccines. On several occasions Pasteur highlighted the cost of developing these scales of virulence. The different tests as well as the different laboratory notebooks on vaccine preparation recorded this know-how, the specific nature of which was particularly noteworthy in so far as few bacteriology laboratories existed that would be able to reproduce the method, itself still unstable and largely tacit. In this context, the exclusive appropriation of vaccine production and distribution by Pasteur’s laboratory seems easier to defend.⁵⁷

Nevertheless, there was not simply a *de facto* monopoly over vaccine production. The secrecy of the necessary know-how was protected and its diffusion controlled in the form of contracts or restricted access to knowledge that preserved the commercial monopoly of the Compagnie de Vulgarisation over the anthrax vaccine. Pasteur was very cautious when answering requests to train biologists who wanted to learn how to produce the vaccine. In 1889, a Canadian biologist requested a stay in the Pasteur laboratory ‘to learn everything necessary for the production of the anthrax vaccine. Do you issue a certificate to certify the competence of persons who have received such training?’⁵⁸ Pasteur’s reply differentiates between two contexts of acquiring knowledge: on the one hand, training in an academic context, on the other, the learning of technical know-how in a professional and commercial context. If he wished to remain in the sphere of the first, Dr. Murray could receive academic training at the Institut Pasteur: ‘If a young man who already has some training in biology wishes to learn, from a scientific point of view, about attenuation of the anthrax bacterium and the different questions concerning it, he can be admitted to the Institut Pasteur in the technical *microbie* laboratory under the direction of Dr. Roux. This subject is studied, along with many other matters of pathological *microbie*’. In the

⁵⁶ The inventors also developed specific equipment for vaccine culture. For example, Roux’s notebook from 1889 presents ‘the Pasteur sterilizer used abroad for anthrax vaccine culture’.

⁵⁷ Cf. Callon (1994).

⁵⁸ Letter by Dr. Murray dated 3 April 1889, Fonds IP Direction (1887-1940), DR COR 1, document 27795-6. Reply by Louis Pasteur, letter dated 10 April 1889, document 27797.

second case, the learning of laboratory know-how for production of the vaccine, access to this knowledge was subject to agreement from the holder of the commercialization rights: ‘If this young man wishes not to limit his studies to the scientific aspect and wishes to acquire more in-depth knowledge of the technical and practical side of anthrax vaccinations, you are requested to contact Mr. De Sainte Marie, former inspector of agriculture, resident at 47 rue Laffite. Since anthrax vaccines have become a matter of practice, I have been looking for a person to teach this technique abroad. Mr. De Sainte Marie has accepted this mission. It is therefore him that you should approach if you wish to use our vaccines’. If the training was authorized by the owner of the foreign rights over diffusion of the vaccine, it would then be given by the head of the technical *microbie* service applied to health, Mr. Chamberland, who supervised the preparation of vaccines. This exchange reveals several fundamental points in the appropriation of vaccines. First, while it was possible to have free access to classes on the principles of microbe attenuation, access to laboratory expertise and to the service producing the vaccines was restricted. In making this distinction, Pasteur differentiated between two types of knowledge: theoretical knowledge, which was freely available, and practical knowledge, inscribed in semi-industrial devices, which was protected. Second, Pasteur thus had to manage two systems of knowledge appropriation: the academic system, and the commercial system which he had helped to put in place. Whereas he had the authority to grant access rights to classes at the Institut Pasteur, it was the licensee exploiting the vaccine who decided on access rights to the production laboratory.⁵⁹

The third means of appropriation of the anthrax vaccine, apart from the specific nature of the technical know-how and secrecy, was the exclusive right to produce and distribute the vaccine, defined by a system of contracts and operating licenses. These licenses acted as a kind of patent, except that their scope was limited to the network of licensees.⁶⁰ They effectively delimited operating monopolies for geographic areas. The extension of these areas had to be renegotiated between the commercial company and the Compagnie de Vulgarisation, which also wanted to gain access to France and those colonies directly supplied by the Institut Pasteur.⁶¹ These licenses were not limited to a simple transfer of operating rights, however. As the vaccines were products that were still largely unstable, and the central laboratory in Paris continued to play an essential part in their production, licenses ensured that the concessionary companies would receive a transfer not only of technical know-how—via the training of technicians from the local labs who would cultivate the vaccines—but also of material—seeds and culture fluids needed in the final phase of vaccine preparation. They were therefore not simple commercial licences but contracts that organized the transfer of technical know-how and products between the contracting parties. Finally, these contracts established and reinforced the asymmetry of competencies and power between the central laboratory and peripheral local laboratories.

⁵⁹ Likewise, laboratory directors who currently have research contracts with industry generally have to submit their publications to the industry before divulging information. They also manage two types of knowledge: that reserved for the industry and that which is accessible for scientific exchange.

⁶⁰ Property defined by contract applies to the contracting parties only, for instance in this case the concessionary companies exploiting the vaccine. Third parties have the possibility of freely reproducing the invention of the anthrax vaccine, provided that their knowledge is not obtained through a leak or illicit borrowing, even though the patent monopoly covers all potential users, at least on the territory of the states in which it is issued.

⁶¹ Letter from M. de Sainte Marie to Chamberland, 27 May 1888, Fonds IP Direction, 1887–1940, DR DOS.1, 10599.

The last means of protection was the promotion of the commercial use of Pasteur's own name and, eventually, the registration of a trade name. Exploitation of the commercial name of a product, in this case the *Vaccin Charbonneux Pasteur*, and registration of a trade name, were industrial property rights commonly used at the time to protect pharmaceutical products which, as we have seen, could not be patented in France.⁶² The commercial name *Laboratoire du Vaccin Charbonneux Pasteur* protected the laboratory's business at home, and this protection was extended to its business abroad starting with the 1883 Paris agreement. The brand name was a distinctive sign of the product. Unlike the patent, it protected neither the composition of the product nor its production process, but only a commercial name: *Vaccin Charbonneux Pasteur*. Note that licences granted for exploitation of the anthrax vaccine abroad protected three elements: first, the trade name and the brand of the vaccine, second, the product as such—the vaccine liquid—and third, the production process. Their scope was, therefore, particularly broad.⁶³ Finally, all contracts signed for the anthrax vaccine were exclusive for a particular geographic area. These contracts made it possible to create rights that could partly offset the absence of patents.

5. Conclusion: defining an economic and legal status for health products

The anthrax vaccine technique, as with Pasteur's other vaccines for veterinary or human medicine, was not patented. In this respect there was an asymmetry between the protection of his vaccine production techniques, which were not patented, and the protection of the biotechnology processes invented by Pasteur in the agro-food domain, which were protected by several patents and supplementary certificates covering improvements. Pasteur had thus found a way of using patents to prevent any attempt at usurping his inventions and to control their industrial diffusion.⁶⁴ The absence of patents on the vaccines that he invented cannot be put down to a lack of knowledge on Pasteur's part concerning intellectual property. The primary explanation is that starting in 1844 France no longer permitted patents on 'pharmaceutical compositions and remedies of all kinds'. This amendment excluding remedies was not initially planned by the government, but French members of parliament introduced it in order to avoid the emergence of a monopoly in the field of health products: 'According to the law and simple common sense there is an incompatibility between a pharmaceutical composition useful to humanity and the exclusive exploitation for a single person's profit . . .'.⁶⁵ After a debate over whether this exclusion ought to be extended to veterinary products, parliament decided not to differentiate them from human medical products. Note, however, that the question of the patentability of vaccine production processes was raised in the inter-war period,⁶⁶ when industrial lead-

⁶² Cassier (2000).

⁶³ The contract negotiated with the Australian company in 1896 was the most complete in terms of protection, including an indication of the origin of vaccine spores—the Paris laboratory (Fonds IP Direction, 1887-1940, DR.DOS.1, 10597).

⁶⁴ Cassier (2002).

⁶⁵ Félix Barthe (*Chambre des Pairs: Séance des samedi 25 mars, 1843*, p. 559).

⁶⁶ In a report dated 1938, Professor Delaby of the Faculty of Pharmacy distinguished between 'identifiable vaccines' such as the diphtheria, TB, and anthrax vaccines, of which the components could be characterized and 'the procedures for obtaining these products seems patentable', and 'killed vaccines' that 'contain diverse products which are impossible to identify' and whose processes do not seem to be patentable. In Senac (1943).

ers and jurists pleaded for patents on pharmaceutical processes to compensate for the absence of patents on the pharmaceutical products themselves.⁶⁷

Despite the lack of patents, Pasteur nevertheless succeeded in gradually building up a technical and commercial monopoly over the production and distribution of the anthrax vaccine. He deliberately avoided putting his vaccine preparation technique into the public domain, which would have made it freely accessible to any other bacteriology laboratory. This position was clearly set out in the letter to Baron Kemeny in September 1881. In 1882, he offered his invention to the state in exchange for a salary that would have provided for himself and his family, and he proposed that the state set up a production plant under his direction. This solution resembled the system of buying back pharmaceutical inventions that the French state had instituted in 1810. Because of the absence of any engagement by the state in the production of the vaccine, it was directly produced and commercialized by Pasteur's laboratory, and then produced and distributed worldwide by the concession of know-how and operating licences. The construction and defence of this monopoly can be explained in terms of a combination of several factors. First, due to problems of quality control concerning the anthrax vaccine—the efficacy of which was still being questioned—and the need for control over the technical details of its preparation, Pasteur felt it was necessary to control its production and diffusion. Second, the creation of a commercial company devoted to the exploitation of the vaccine reinforced and extended the monopoly held by the Institut Pasteur as the company set out to conquer new territory for the vaccine, but always needed to rely on the institute to provide the essential technical know-how the company lacked. Third, from 1888 the Institut Pasteur's self-financing rationale had the same effect of strengthening the monopoly since vaccines accounted for a large portion of the foundation's income (Löwy, 1994; Moulin, 1993).

Finally, we can note that there was another asymmetry in respect to the protection of Pasteur's inventions, this time between the vaccines for veterinary use, over which there were clear monopolies, and the vaccines for human medicine, where the production methods were more broadly and more actively disseminated. In 1886, for example, the British commission of inquiry sent to Paris to study the rabies vaccine praised 'the speed with which the French scientist informed the commission of the slightest details of his method'.⁶⁸ In the case of human medicine, the question of accessibility to vaccines is a quite different ethical issue, as current debate on intellectual property rights in the field of health products attests.⁶⁹ Nevertheless, we need to conduct further research in order to verify this hypothesis for Pasteur's medicines intended for use in human health.

⁶⁷ The issue of the patentability of the germs themselves was not addressed. In the case of the anthrax bacillus this was no simple matter, for it had been in the public domain for several years. It is often said that Pasteur filed the first patent on a living organism by claiming to have 'purified yeast' in a patent on beer production (e.g. Beier, Creispi, & Straus, 1985). In fact, Pasteur's patents on beer do not cover a natural yeast strain but a yeast that is an intermediary product in a particular process.

⁶⁸ *M. Pasteur, la rage, le vaccin charbonneux*, Bernard Tignol Editeur, Paris, 1886, (Fonds Louis Pasteur, cote LP.G1 46, document 17987).

⁶⁹ Cassier (2000). On this topic, see also Swann (1984); Apple (1989); Weiner (1987); Rasmussen (2004).

References

- Allart, H. (1883). *De la pharmacie du point de vue de la propriété industrielle*. Paris: Marchal, Billard et Cie.
- Apple, R. D. (1989). Patenting university research. *Isis*, 80, 375–394.
- Beier, F. K., Crespi, R. S., & Straus, J. (1985). *Biotechnologie et protection par brevet*. Paris: OCDE.
- Cadeddu, A. (1985). Pasteur et le choléra des poules: Révision critique d'un récit historique. *History and Philosophy of the Life Sciences*, 7, 87–104.
- Cadeddu, A. (1987). Pasteur et la vaccination contre le charbon: Une analyse historique et critique. *History and Philosophy of the Life Sciences*, 9, 255–276.
- Callon, M. (1994). Is science a public good? *Science, Technology and Human Values*, 19, 395–424.
- Cassier, M. (2000). Patent and public health: Genome patents nowadays and pharmaceutical patents in the 19th century: A parallel. International Conference, *Technological policy and innovation: Economical and historical perspectives*, Paris, 20–22 November.
- Cassier, M. (2002). L'engagement des chercheurs vis-à-vis de l'industrie et du marché: Normes et pratiques de recherche dans les biotechnologies. In N. Alter (Ed.), *Les logiques de l'innovation. Approche pluridisciplinaire* (pp. 155–182). Paris: La Découverte.
- Chamberland, C. (1883). *Le charbon et la vaccination charbonneuse*. Paris: Bernard Tignol.
- Chambre des pairs: Séance du samedi 25 mars. (1843). *Le Moniteur universel*, 85 (26 mars), 557–563.
- Geison, G. L. (1995). *The private science of Louis Pasteur*. Princeton, NJ: Princeton University Press.
- Koch, R. (1883). La vaccination charbonneuse. *Revue Scientifique de la France et de l'Étranger*, 3rd series, 5, 65–74.
- Liebenau, J., & Robson, M. (1991). L'Institut Pasteur et l'industrie pharmaceutique. In M. Morange (Ed.), *L'Institut Pasteur, contributions à son histoire* (pp. 52–61). Paris: La Découverte.
- Löwy, I. (1994). On hybridizations, networks, and new disciplines: Pasteur Institute and the development of microbiology in France. *Studies in History and Philosophy of Science*, 25, 655–688.
- Moulin, A.M. (1993). Une maison de commerce scientifique. Naissance de l'industrie de la santé. Colloque international, 'Les biologistes entre l'état et l'industrie: Des usages à la production du vivant', Centre de Recherche en Histoire des Sciences et des Techniques, Editions de la Cité des Sciences et de l'Industrie. Paris: La Villette.
- Pasteur, L. (1881). Le vaccin du charbon (with the collaboration of C. Chamberland & E. Roux). *Comptes Rendus Hebdomadaires des Séances de l'Académie des Sciences*, 92 (21 March), 666–668.
- Pasteur, L. (1883). Réponse au docteur Koch par M. Pasteur. *Revue Scientifique de la France et de l'Étranger*, 3rd series, 5, 74–84.
- Pasteur, L. (1933). *Oeuvres de Pasteur, Vol. 6*. Paris: Masson.
- Pasteur, L. (1940–1951). *Pasteur correspondence* (P. Vallery Radot, Ed.) (4 vols.). Paris: Flammarion.
- Pouillet, E. (1872). *Traité théorique et pratique des brevets d'invention*. Paris: Cosse, Marchal et Billard.
- Rasmussen, N. (2004). The moral economy of the drug company–medical scientist collaboration in interwar America. *Social Studies of Science*, 34, 161–185.
- Salomon-Bayet, C. (1986). Penser la révolution pastoriennne. In idem, *Pasteur et la révolution pastoriennne* (pp. 17–62). Paris: Payot.
- Senac, D. (1943). *De la brevetabilité du produit pharmaceutique. Etude de législation comparée*. Paris: Montchrestien.
- Swann, J. P. (1984). *Academic scientists and the pharmaceutical industry*. Baltimore, MD: Johns Hopkins University Press.
- Todd, J. (1990). The Pasteur Institute in Australia, success and failure. In J. Chaussivert, & M. Blackman (Eds.), *Louis Pasteur and the Pasteur Institute in Australia* (pp. 25–37). Kensington: University of New South Wales Press.
- Weiner, C. (1987). Patenting and academic research: Historical case studies. *Science, Technology and Human Values*, 12, 50–62.