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Appropriation and commercialization of the Pasteur anthrax vaccine

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7 Abstract

8 Whereas Pasteur patented the biotechnological processes that he invented between 1857 and 1873
9 in the agro-food domain, he did not file any patents on the artificial vaccine preparation processes that
10 he subsequently developed. This absence of patents can probably be explained by the 1844 patent law
11 in France that established the non-patentable status of pharmaceutical preparations and remedies,
12 including those for use in veterinary medicine. Despite the absence of patents, the commercial exploi-
13 tation of the anthrax vaccine in the 1880s and 1890s led to a technical and commercial monopoly by
14 Pasteur's laboratory as well as the founding of a commercial company to diffuse the vaccine abroad.
15 Pasteur repeatedly refused to transfer his know-how and anthrax vaccine production methods to for-
16 eign laboratories, on the grounds that he wished to control the quality of the vaccines produced.
17 Indeed, it was relatively difficult to transfer a method that was not yet perfectly stabilized in the early
18 1880s. Pasteur also wanted to maintain the monopoly of his commercial company and to increase the
19 profits from vaccine sales so that the Institut Pasteur could be financially independent. The 'Pasteur
20 anthrax vaccine' operating licences are described and analysed in detail in this article.
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22 *Keywords:* Anthrax vaccine; Know-how; Intellectual property rights; Licensing agreements

24 1. Introduction

25 In the controversy that took place between Robert Koch and Louis Pasteur in 1881 and
26 1882 over the efficacy of the anthrax vaccine, Koch criticized Pasteur's incomplete disclo-
27 sure of his process for preparing the vaccine: 'Mr. Pasteur's information on his technique

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

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

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'.

56 filed three patents to protect a new filtering process that they had invented.⁷ This absence of a
57 patent on the anthrax vaccine could be explained by the fact that their method was still not
58 completely stable in the 1880s and would therefore have been difficult to describe in sufficient
59 detail for the patent. But a more probable explanation is the fact that under the terms of the
60 1844 patent law, pharmaceutical products, including veterinary products, could not be pat-
61 ented in France, while the question of patents on pharmaceutical processes remained a dis-
62 puted area under this legislation.⁸ Nevertheless, even in the absence of patent protection,
63 Pasteur and his concessionary companies organized a monopoly on the production and dis-
64 tribution of the anthrax vaccine that combined several modes of appropriation. First, the
65 know-how accumulated by the laboratory was kept partially secret; this included not only
66 the methods and technical devices used for the attenuation of the microbe, but also the stan-
67 dards and scales for establishing the virulence of vaccines and the associated tests. Second,
68 there was an asymmetry between Pasteur's laboratory and local laboratories established
69 abroad in terms of competencies and rights. Third, there was the more formal use of con-
70 tracts to establish the right to exclusive exploitation of the vaccine, and, finally, the control
71 exercised over the commercial use of Pasteur's name, and later the trade name. Overall, we
72 can say that this system of managing the industrial and commercial interests associated with
73 the vaccine compensated for the absence of any patents.⁹

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

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

85 The production of the anthrax vaccine was started as early as 1881, even though at this
86 point the preparation method had still not been stabilized, and controversy over the effi-
87 cacy of the vaccine opposed 'practising believers' and 'resisters', as a popular book on the
88 subject published in 1886 put it. Available figures indicate a rapid diffusion of the vaccines:
89 245,000 sheep were vaccinated in 1882, and some two million animals were vaccinated be-
90 tween 1882 and 1887, despite a slight drop in 1883.¹⁰

91 To meet the growing demand, Pasteur soon set up a small laboratory for the production
92 and distribution of vaccines, near his laboratory in the Rue d'Ulm on a site made available
93 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.

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

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

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; 'Etat 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 Salomont-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.

128 studying in detail, as there is more to it than his simple statement: ‘I therefore undertake to
129 offer the state this special service of delivering the anthrax vaccine for France’. In return
130 for his invention and know-how, Pasteur asked for payment of a rent: ‘The only remunera-
131 tion he requested was that he and his family be spared from material concerns’.¹⁷ This
132 transaction aimed both at guaranteeing the recognition and reward of the inventor, Pas-
133 teur, and at putting the invention at the disposal of the state with a view to improving pub-
134 lic welfare and increasing national wealth.¹⁸ In the end, the state did not agree to
135 incorporate the production of Pasteur’s vaccines into its sphere of activity, but the Minis-
136 try of Agriculture did agree to subsidize the Pasteur laboratory both for the preparation of
137 the existing vaccines that had already been distributed, and for research into developing
138 new vaccines.¹⁹ In a document from 1888 concerning the various laboratories run by Louis
139 Pasteur, the laboratory at Rue Vauquelin for the production and dispatching of vaccines
140 was specifically associated with the subsidies from the Ministry of Agriculture.

141 The organization of the production of vaccines was set out by Pasteur in correspon-
142 dence with the prefect of the Seine et Marne district during the summer of 1881. The pre-
143 fect, who had participated in the trial of the vaccine at Pouilly-le-Fort, proposed the
144 creation of a local laboratory for the production of anthrax vaccine: ‘I was in London
145 when you came to talk to me about your wish to ask the *Conseil Général*²⁰ of the Seine
146 et Marne for a sum of money to use in setting up a small vaccine production labora-
147 tory’.²¹ Thus, in this case, we see that it was the local state authorities that offered to fi-
148 nance a laboratory for vaccine production. Pasteur refused this proposition which he
149 judged ‘premature’, primarily because the vaccine preparation method was not stable en-
150 ough to be easily transferred any distance from his laboratory and more particularly out
151 from under his direct control. Clearly, the rapid increase in production would mean the
152 storage and thus the delayed use of vaccines.²² ‘All the vaccine that has left my labora-
153 tory during the past month is from recent cultures. Factories imply stocks, and the use of
154 prepared tubes after long intervals’. Pasteur expressed his doubts concerning the preser-
155 vation of the vaccine: ‘Problems, albeit ones that are probably easy to solve, can arise in
156 the preservation of the vaccine, the shape of the flasks, etc. During the first year, it will
157 be necessary to check the state of the preserved vaccine, and the persistence of its virtues’.
158 Pasteur considered that at that stage he was the only one capable of appropriately moni-
159 toring the quality of vaccines and to overcome any difficulties that may arise: ‘Many de-
160 tails are still to be sorted out, and only I can do so . . . a production laboratory in the

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.

161 provinces would take up just as much of my time as the laboratory that I am going to
162 have here'. The monitoring of the production and preservation of vaccines, the 'details'
163 that he needed to sort out personally, allowed Pasteur and his direct collaborators in
164 the preparation of the vaccines to establish a *de facto* technical monopoly over this oper-
165 ation. In the short term this state of affairs precluded any technology transfer to other
166 preparation units, and facilitated Pasteur's control over the system of diffusion. Hence,
167 the comments made by the editor of *La Semaine Médicale*, who used the journal to ex-
168 press his indignation at Pasteur's use of his power and accused him of infringing the law
169 on secret remedies:²³ 'As long as Mr. Pasteur has not divulged his processes for culturing
170 the vaccines to the scientific community, we will continue to inform the competent
171 authorities that they are taking on a serious responsibility by allowing the sale of such
172 poisons'.²⁴

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

the production of vaccines is going to become a highly important service. In the lab-
oratory in Rue Vauquelin, anthrax, rouget and chicken cholera vaccines are pro-
duced 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, represent-
ing prophylaxis against anthrax for 100,000 head of livestock (sheep, cattle and
horses).²⁶

193 An inventory from 1888 mentioned that four assistants were employed at the Rue Vauqu-
194 elin laboratory.²⁷

195 The creation of this laboratory was accompanied by the establishment of a special
196 accounting system for the vaccines. This accounting system was justified with reference
197 to several objectives. First, it was necessary to justify the use of the subsidy granted by

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 Étrangère* 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 Étrangère* 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.

198 the agriculture ministry.²⁸ Second, it was necessary to calculate the production cost of a
199 vaccine in order to determine its sale price for breeders. A list of expenditures for the year
200 1882 set the cost price of a tube of vaccine at two francs, 13 centimes. An analysis of the
201 pricing structure shows that the culture of the vaccine represented only a very small por-
202 tion of this sale price.²⁹ The highest proportion was for packaging and postage (30% of
203 costs), correspondence and administrative costs (25%), and commercial management
204 (30% of the budget). The third reason for the accounting system was to assess the profits
205 generated by this activity in order to allocate them to the inventors and the laboratory and
206 later to the Institut Pasteur itself. The distribution of profit was as follows: 'The balance
207 left over constitutes a profit which is divided into five parts: Mr. Pasteur keeps two and
208 allocates two, that is, one equal part to each of his assistants; the fifth part constitutes a
209 legal reserve'.³⁰ This use of earnings thus constituted a form of profit-sharing for the inven-
210 tors Pasteur, Roux, and Chamberland. In 1887, during the creation of the Institut Pasteur,
211 the three inventors renounced their share of the profits for the benefit of the institute.³¹
212 The profits of the vaccination service, henceforth incorporated into the services of the
213 institute, were to play a crucial part in balancing its budget.³²

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

217 The first problem, related to standardization, was particularly complicated in so far as
218 anthrax vaccination involved the use of two vaccines of increasing virulence administered
219 consecutively with an interval of a few days between them: 'All the difficulty with anthrax
220 vaccines lies in the choice of these two viruses and in the maintenance of their virulence in
221 an unchanging ratio'.³³ In a letter to Duclaux dated 30 June 1882, Pasteur noted that the
222 laboratory director was exercising insufficient surveillance over these aspects of the vac-
223 cine: 'Our production will improve with time, I hope. In November and December the vac-
224 cines were too weak. We had to strengthen them. They weren't strengthened enough
225 though, because they induced a shorter period of immunity. The ratio of virulence between
226 the first and the second doesn't satisfy me. In a sense it would be necessary to achieve noth-
227 ing else but that. That is what I expect from Chamberland, but sometimes his enthusiasm
228 wanes'.³⁴ To test the quality of the vaccine strains obtained, the production laboratory
229 introduced testing on laboratory animals and established scales of virulence. In cases
230 where the virulence weakened, it selected a new 'origin' for the vaccine production, tested
231 it, and adjusted the relation of virulence between the first and second vaccines. Test

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

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.

232 notebooks record this constant work of adjustment of vaccines as well as the selection of
233 ‘new origins’.³⁵

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

248 3. The construction of a commercial and technical monopoly

249 Pasteur had to deal with requests to transfer his technology and know-how concerning
250 the preparation of the anthrax vaccine as early as 1881, while the process was still in the
251 first stages of development. He had several options. He could choose to disclose his
252 method and to place it in the public domain so that any outside user could reproduce
253 it. Alternatively, he could choose to transfer his technique in the form of licenses covering
254 the appropriate know-how, thereby maintaining his property rights and guaranteeing the
255 royalties for his laboratory. Finally, he could choose to exploit his invention exclusively in
256 his own laboratory establishing a monopoly over the production of all the vaccines, which
257 the laboratory could then sell throughout the world. Because the process was still in its
258 early stages and quality control was still a problem, transfer of the relevant technology
259 and the exporting of production away from the original laboratory were highly complex
260 matters. Moreover, neither the reputation of the vaccine nor even the principle of the preventive
261 inoculation were soundly established. The question of the vaccines’ stability was
262 also essential. If they were stable and their efficacy did not alter over time, it would be possible
263 to transport them over long distances and to store them for long periods of time. In
264 this case, one could conceive of their production at a single site. On the other hand, if their
265 stability was uncertain or poor, it would be necessary to diversify the sites of production
266 and to negotiate licenses with ‘local laboratories’. These alternatives were discussed in the

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).

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.

267 early 1880s, and no single one of them was selected as the exclusive policy to be pursued by
268 Pasteur and his institute. The combination of solutions that was chosen evolved through-
269 out the development of the large-scale use of the vaccine.

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

277 First, Pasteur emphasized the importance of the laboratory know-how necessary for the
278 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 par-
asite 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.

286 Apart from knowledge concerning the principle of attenuation, Pasteur revealed the impor-
287 tance of the system for measuring and verifying virulence, which made it possible to estab-
288 lish a scale of virulence for the different cultures and to determine the appropriate virulence
289 ratio between the first and the second vaccines needed to produce immunity. Roux’s note-
290 books on the preparation and culture of the anthrax vaccine,⁴¹ as well as the test notebooks
291 of the vaccine service, confirm the importance of measurement and control, with the insti-
292 tute investing heavily in the animals on which the vaccines were tested.⁴² The time required
293 for the attenuation of microbes and the setting up of such measurement procedures would,
294 according to Pasteur, exceed his assistant’s mission: ‘Mr. Thuillier will absolutely not have
295 the time to carry out this study’.⁴³ Since the vaccine preparation method was still not per-
296 fectly stable, it had to remain under the inventors’ control so that they could perfect the pro-
297 cedure: ‘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.

298 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
299 point out the fact that out of caution and so as not to compromise the success of a method
300 which is tricky, to say the least, I wish very much that, for at least a year, any vaccine used
301 by sheep or livestock breeders be prepared by me or under my immediate supervision'. Bad
302 preparations could ruin the career of the anthrax vaccine since the principle of vaccination
303 was still a highly controversial issue. Before considering diversifying the sites of vaccine
304 production, it was first necessary to consolidate and extend the network that was promoting
305 the use of the vaccine: 'For the moment, it is necessary to persuade farmers and large
306 landowners of the advantages of the method'.
307

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

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

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

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

350 In 1884 and 1885 the Indian government and Pasteur negotiated the most appropri-
351 ate model for diffusion of the vaccine in that country.⁴⁷ Initially, Mills, an inspector of
352 diseased livestock in Madras, performed a series of tests of Pasteur’s anthrax vaccine on
353 several types of animal. These tests proved to be conclusive and the inspector ‘recom-
354 mended the importation here of anthraxine [the vaccine] coming from Mr. Pasteur, in
355 France, and its methodical use throughout the presidency of Madras’. This recommen-
356 dation was contested by another veterinary inspector, Evans, who based his arguments
357 on several negative reports drawn up in England and who doubted ‘that the liquid in
358 question is still effective in India . . . Although Mr. Pasteur always succeeded for him-
359 self, it was not rare for the liquid sold by his approved agents to be not only ineffective
360 but sometimes even harmful’. Evans advised the continuation of the tests before defin-
361 itively adopting the vaccine, for he suspected a possible alteration of imported vaccines.
362 New experiments on elephants proved to be conclusive and the chief superintendent of
363 the stud farms of India, Hallen, went to the Pasteur laboratory ‘in order to learn not
364 only the method followed for the vaccination but also the way of preparing the vaccine’.
365 On his return he did not recommend importing vaccines from Paris but instead sug-
366 gested setting up laboratories in India, in stations where the vaccine would be produced
367 and distributed. Considering the risk of failure related to the use of imported vaccines,
368 India opted for the establishment of local laboratories. On 19 March 1884 Pasteur re-
369 plied to a letter from the British ambassador on the appropriate mode of organization:
370 ‘Can one transport the vaccination practice to India and expect the same effects as in
371 France? Without any doubt’. Yet it is essential to use ‘good vaccines that have been well
372 tested and freshly prepared’, as the ‘mistakes’ associated with vaccinations performed in
373 France had shown. To assure this result, Pasteur considered two types of organization.
374 The first option, which he preferred, consisted in setting up a vaccine production labo-
375 ratory in India, with the mission of culturing the spores or ‘seeds’ sent out by the Paris
376 laboratory: ‘the vaccines in question change with time, and lose some of their effective-
377 ness if one uses them after a long period; however, it is easy to regenerate them and to
378 give them back their value in India, even after the necessary time period for travelling
379 from Paris to that distant country’. Pasteur envisioned the movement of spores from
380 France to India to supply the local laboratory, and the training of laboratory agents
381 in Paris: ‘An intelligent young man, somewhat familiar with chemical research, could
382 come and familiarize himself with vaccine cultures by first spending two or three weeks,
383 a month at the most, in my laboratory in Paris, before going to India’. Pasteur wanted

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).

384 to use the capacity to culture anthrax spores, which had first been attenuated in his
385 Paris laboratory, in order to retain control over the chain of vaccine preparation.
386 The Indian laboratory would remain linked to Paris through the ‘vaccine spores’ ‘fixed’
387 in Paris and ‘sown’ in India, and the training of laboratory agents, also dispensed in
388 Paris.

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

409 Several ‘special’ laboratories were set up abroad, based on the organizational model fa-
410 voured by Pasteur himself, that is, they received vaccine spores, culture fluids, and exper-
411 tise from Paris and then prepared the fresh vaccines and distributed them to veterinarians
412 and breeders. Laboratories of this sort were created in Budapest for Austria–Hungary,
413 Bosnia–Herzegovina, Serbia, Bulgaria, and Romania, in Buenos-Aires for Argentina,
414 Uruguay, and Paraguay, and in Madrid for Spain. The Laboratoire Pasteur–Chamber-
415 land, Vaccins Contre le Charbon et le Rouget was founded in Budapest under ‘the patron-
416 age of the Hungarian ministry for agriculture’.⁴⁸

417 In 1886, the Pasteur laboratory was instrumental in the creation of a commercial
418 enterprise, La Compagnie de Vulgarisation du Vaccin Charbonneux Pasteur, to exploit
419 the anthrax vaccine abroad. The inventors had noted that there was insufficient diffu-
420 sion of the vaccine abroad, due to the absence of any commercial network and ‘because
421 of the total lack of publicity’, as well as problems related to the instability of the vaccine
422 and to ‘dispatching it to various countries’.⁴⁹ To get round these problems, the company
423 was to set up a network of agencies and local laboratories: ‘it has been acknowledged

⁴⁸ Letter to Chamberland dated 11 June 1886, 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.

424 that its diffusion would be possible only with the establishment of laboratories abroad'.
425 The preamble of the contract between the inventors—Chamberland, Pasteur, and
426 Roux—and the director of the company, Mr. De Sainte Marie, a former inspector gen-
427 eral of agriculture, clearly established the division of work between the Pasteur labora-
428 tory and local laboratories, based on the model described by Pasteur in his letter to the
429 British ambassador in March 1884: 'Mr. De Sainte Marie proposed to Mr. Chamber-
430 land to take care of this creation provided that the assistants of the said laboratories
431 are trained by him and remain under his technical supervision, and that the spores
432 and fluid for preparing the vaccine are supplied by Mr. Pasteur's laboratory in Paris'.

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

438 This agreement gave legal recognition to the monopoly over the exploitation of Pas-
439 teur's vaccine: 'Mr. Chamberland grants Mr. De Sainte Marie the exclusive monopoly
440 to create laboratories abroad (with the exception of France and its colonies) for the dif-
441 fusion and exploitation of the anthrax vaccine under the name of "Laboratoire du vac-
442 cin charbonneux Pasteur."' The territorial scope of the license excluded those areas for
443 which treaties had already been signed: 'the said monopoly excludes the countries of the
444 Republic of Argentina, Paraguay, Uruguay, and Austria-Hungary, already granted in
445 prior agreements'.⁵⁰ The contract did, however, provide for 'special conventions' be-
446 tween the new company and laboratory in Austria-Hungary. In case of termination
447 of the contract with the concessionary laboratory in South America, the concession
448 would be transferred to Mr. De Sainte Marie's monopoly. The sharing of markets
449 was carefully defined, although the concession granted to the new company excluded
450 France and the colonies, which were reserved for Pasteur and Chamberland's labora-
451 tory. The contract stipulated that 'as from this day, Mr. Chamberland will no longer
452 be able to sell the anthrax vaccine for his own profit in the countries in which the
453 monopoly has been granted to Mr. De Sainte Marie'. Chamberland was also required
454 to transmit the relevant information needed to facilitate the establishment of new lab-
455 oratories, and to participate in the writing of documents to help the diffusion of the vac-
456 cine, helping with 'all information and brochures to be published in the different
457 countries'.

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

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

466 Second, the directors of those laboratories would be subject to commercial and techni-
467 cal 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.

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

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

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

501 We have collected several contracts signed between 1886 and 1896 between the com-
502 pany set up to diffuse the anthrax vaccine and concessionary companies abroad.

503 In June 1887 the Compagnie de Vulgarisation and the Pasteur laboratory drew up a con-
504 tract granting Russia a monopoly on the anthrax vaccine.⁵¹ This agreement between 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).

505 two partners was, however, only the first level of a more elaborate contract. The Compagnie de Vulgarisation subsequently negotiated a licence with the local laboratory, in terms of
506 which a monopoly was granted in exchange for the payment of a set sum—150,000 French
507 francs—shared between the Pasteur laboratory and the company, and a set charge per vac-
508 cination—5 centimes for small animals and 10 centimes for large ones. A part of that fee—1
509 centime per head for small animals and 2 centimes per head for large ones—was shared be-
510 tween the Pasteur laboratory and the Compagnie de Vulgarisation. The money received by
511 the Pasteur laboratory was used to remunerate the owner for his invention and the produc-
512 tion services provided by Paris (the provision of spores and culture fluids). It is important
513 here to note the inventors' direct involvement in the negotiation of this contract: 'to facil-
514 itate any negotiation and convention, Mr. Pasteur and yourselves should deal directly with
515 Prince Olienbourg and the imperial government. To this effect, I have the honour, in the
516 name of the Compagnie de Vulgarisation, to grant you full powers'. The commercial com-
517 pany was unable to bypass the inventors in setting up a new company due to the technical
518 expertise required to conclude the negotiation successfully and the close link between the
519 vaccine and the names of Pasteur, Chamberland, and Roux.

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

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

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.

546 stock of instruments, plans and equipment now belonging to and existing on the premises
547 occupied by the selling company in Sydney'. The contract provided for prosecution of
548 counterfeiters in case of 'violations of the said anthrax vaccine or secret process of Pasteur
549 anthrax vaccination'. The financial arrangement provided for the payment of a fixed sum at
550 the signing of the contract as well as the seller owning capital in the Australian company.⁵⁴
551 Note here that the contract renewed the system of vaccine production fixed by Pasteur in
552 1884: the Compagnie de Vulgarisation was to provide the colonies necessary for culturing
553 the vaccine and to train laboratory assistants for the Australian concessionary company.
554 The Compagnie de Vulgarisation was also to transmit improvements in the method to
555 the Australian company, as well as the material necessary to implement them.

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

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

584 4. Tools for appropriating the anthrax vaccine: know-how, operating licences and industrial 585 property rights

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

611 Nevertheless, there was not simply a *de facto* monopoly over vaccine production.
612 The secrecy of the necessary know-how was protected and its diffusion controlled in
613 the form of contracts or restricted access to knowledge that preserved the commercial
614 monopoly of the Compagnie de Vulgarisation over the anthrax vaccine. Pasteur was
615 very cautious when answering requests to train biologists who wanted to learn how
616 to produce the vaccine. In 1889, a Canadian biologist requested a stay in the Pasteur
617 laboratory ‘to learn everything necessary for the production of the anthrax vaccine. Do
618 you issue a certificate to certify the competence of persons who have received such
619 training?’⁵⁸ Pasteur’s reply differentiates between two contexts of acquiring knowledge:
620 on the one hand, training in an academic context, on the other, the learning of tech-
621 nical know-how in a professional and commercial context. If he wished to remain in
622 the sphere of the first, Dr. Murray could receive academic training at the Institut Pas-
623 teur: ‘If a young man who already has some training in biology wishes to learn, from a

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.

624 scientific point of view, about attenuation of the anthrax bacterium and the different
625 questions concerning it, he can be admitted to the Institut Pasteur in the technical
626 *microbie* laboratory under the direction of Dr. Roux. This subject is studied, along
627 with many other matters of pathological *microbie*. In the second case, the learning
628 of laboratory know-how for production of the vaccine, access to this knowledge was
629 subject to agreement from the holder of the commercialization rights: 'If this young
630 man wishes not to limit his studies to the scientific aspect and wishes to acquire more
631 in-depth knowledge of the technical and practical side of anthrax vaccinations, you are
632 requested to contact Mr. De Sainte Marie, former inspector of agriculture, resident at
633 47 rue Laffite. Since anthrax vaccines have become a matter of practice, I have been
634 looking for a person to teach this technique abroad. Mr. De Sainte Marie has accepted
635 this mission. It is therefore him that you should approach if you wish to use our vac-
636 cines'. If the training was authorized by the owner of the foreign rights over diffusion
637 of the vaccine, it would then be given by the head of the technical *microbie* service ap-
638 plied to health, Mr. Chamberland, who supervised the preparation of vaccines. This
639 exchange reveals several fundamental points in the appropriation of vaccines. First,
640 while it was possible to have free access to classes on the principles of microbe atten-
641 uation, access to laboratory expertise and to the service producing the vaccines was re-
642 stricted. In making this distinction, Pasteur differentiated between two types of
643 knowledge: theoretical knowledge, which was freely available, and practical knowledge,
644 inscribed in semi-industrial devices, which was protected. Second, Pasteur thus had to
645 manage two systems of knowledge appropriation: the academic system, and the com-
646 mercial system which he had helped to put in place. Whereas he had the authority
647 to grant access rights to classes at the Institut Pasteur, it was the licensee exploiting
648 the vaccine who decided on access rights to the production laboratory.⁵⁹

649 The third means of appropriation of the anthrax vaccine, apart from the specific
650 nature of the technical know-how and secrecy, was the exclusive right to produce
651 and distribute the vaccine, defined by a system of contracts and operating licenses.
652 These licenses acted as a kind of patent, except that their scope was limited to the net-
653 work of licensees.⁶⁰ They effectively delimited operating monopolies for geographic
654 areas. The extension of these areas had to be renegotiated between the commercial
655 company and the Compagnie de Vulgarisation, which also wanted to gain access to
656 France and those colonies directly supplied by the Institut Pasteur.⁶¹ These licenses
657 were not limited to a simple transfer of operating rights, however. As the vaccines were
658 products that were still largely unstable, and the central laboratory in Paris continued
659 to play an essential part in their production, licenses ensured that the concessionary
660 companies would receive a transfer not only of technical know-how—via the training
661 of technicians from the local labs who would cultivate the vaccines—but also of

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.

662 material—seeds and culture fluids needed in the final phase of vaccine preparation.
663 They were therefore not simple commercial licences but contracts that organized the
664 transfer of technical know-how and products between the contracting parties. Finally,
665 these contracts established and reinforced the asymmetry of competencies and power
666 between the central laboratory and peripheral local laboratories.

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

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

683 The anthrax vaccine technique, as with Pasteur's other vaccines for veterinary or hu-
684 man medicine, was not patented. In this respect there was an asymmetry between the pro-
685 tection of his vaccine production techniques, which were not patented, and the protection
686 of the biotechnology processes invented by Pasteur in the agro-food domain, which were
687 protected by several patents and supplementary certificates covering improvements. Pas-
688 teur had thus found a way of using patents to prevent any attempt at usurping his inven-
689 tions and to control their industrial diffusion.⁶⁴ The absence of patents on the vaccines that
690 he invented cannot be put down to a lack of knowledge on Pasteur's part concerning intel-
691 lectual property. The primary explanation is that starting in 1844 France no longer permit-
692 ted patents on 'pharmaceutical compositions and remedies of all kinds'. This amendment
693 excluding remedies was not initially planned by the government, but French members of
694 parliament introduced it in order to avoid the emergence of a monopoly in the field of
695 health products: 'According to the law and simple common sense there is an incompatibil-
696 ity between a pharmaceutical composition useful to humanity and the exclusive exploita-
697 tion for a single person's profit . . .'.⁶⁵ After a debate over whether this exclusion ought to
698 be extended to veterinary products, parliament decided not to differentiate them from hu-
699 man medical products. Note, however, that the question of the patentability of vaccine

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*).

700 production processes was raised in the inter-war period,⁶⁶ when industrial leaders and jur-
701 ists pleaded for patents on pharmaceutical processes to compensate for the absence of pat-
702 ents on the pharmaceutical products themselves.⁶⁷

703 Despite the lack of patents, Pasteur nevertheless succeeded in gradually building up a
704 technical and commercial monopoly over the production and distribution of the anthrax
705 vaccine. He deliberately avoided putting his vaccine preparation technique into the public
706 domain, which would have made it freely accessible to any other bacteriology laboratory.
707 This position was clearly set out in the letter to Baron Kemeny in September 1881. In
708 1882, he offered his invention to the state in exchange for a salary that would have pro-
709 vided for himself and his family, and he proposed that the state set up a production plant
710 under his direction. This solution resembled the system of buying back pharmaceutical
711 inventions that the French state had instituted in 1810. Because of the absence of any
712 engagement by the state in the production of the vaccine, it was directly produced and
713 commercialized by Pasteur's laboratory, and then produced and distributed worldwide
714 by the concession of know-how and operating licences. The construction and defence of
715 this monopoly can be explained in terms of a combination of several factors. First, due
716 to problems of quality control concerning the anthrax vaccine—the efficacy of which
717 was still being questioned—and the need for control over the technical details of its prep-
718 aration, Pasteur felt it was necessary to control its production and diffusion. Second, the
719 creation of a commercial company devoted to the exploitation of the vaccine reinforced
720 and extended the monopoly held by the Institut Pasteur as the company set out to conquer
721 new territory for the vaccine, but always needed to rely on the institute to provide the
722 essential technical know-how the company lacked. Third, from 1888 the Institut Pasteur's
723 self-financing rationale had the same effect of strengthening the monopoly since vaccines
724 accounted for a large portion of the foundation's income.

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

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).

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).

735 6. Uncited references

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