

Two Cultures of Regulation?

The Production and State Control of Diphtheria Serum at the End of the Nineteenth Century in France and Germany

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At the end of the nineteenth century, diphtheria was one of the principal causes of mortality in children. The search for a remedy for the disease represented an important challenge for bacteriologists and microbiologists, and was perceived as an urgent social task. In the late 1880s two groups of scientists simultaneously started searching for a cure for diphtheria: Émile Roux (1853–1933) at the newly founded Pasteur Institute in Paris, and Emil Behring (1854–1917) in Berlin. Following Behring's successful animal experiments initiated in 1890, a serum against diphtheria was available in pharmacies starting in August 1894. Indeed, diphtheria serum represented a major therapeutic innovation in modern medicine, offering an effective curative approach first against diphtheria and subsequently against other diseases. A medicine of biological origin, the new serum therapy also attracted intense state attention in the hope of minimizing any associated public health risks.

In this article, I compare the two cultures of regulation of serum production and distribution in France and Germany at the end of the nineteenth century. In Germany, several pharmaceutical companies produced the serum and its sale was regulated by the state, which delegated the oversight of this industry to different institutions: the Imperial Health Office and the Institute for Serological Research and Serological Survey (hereafter – the Serological Institute). The collaboration and connections between the state-run institutes and the private chemical-pharmaceutical industry was particularly important, while for France the story turns around the Pasteur Institute. In France, there was no direct state control over serum production. After an initial approval of the serum producers, the quality control of the serum remained in the hands of the producers themselves. Based on an examination of the differences and similarities of

serum production and regulation in the two neighbouring countries, this article aims to characterize the different cultures of control and the different forms of governmental oversight. In this context, culture refers, on the one hand, to everyday (laboratory) life, the culture of production, the procedures and the specific ways of behaving in each case. On the other hand, culture is not understood as something natural but rather is taken to be socially constructed. Regulation includes all kinds of legislation, (state) control, instructions, adjustments, governance, and also the influence of the state and the state-run or semi-public institutions. Regulation also refers to price regulation or the regulation of industrial processes in terms of state intervention. The state itself is not viewed as a monolithic institution: the term state is used to refer to a set of actors including politicians, government, governmental institutions or semi-public organisations acting in the public sphere or simply the associated bureaucracy. The article asks about how these different actors cooperated in the two national cultures to regulate serum production, because diphtheria serum offered on the one hand the possibility of enhancing public health but on the other hand, as an unknown biological drug, the serum also represented a public health risk that had to be dealt with and minimized. In both cases we need to illuminate the nature of the collaboration between politicians, science and industry and we have to locate the different actors in the triangle “state – science – industry”. Furthermore, the article will treat the effect of these different styles of governmental influence on matters concerning public health.

I will, therefore, give a short overview of the process of serum production, which was more or less similar in the two countries. Then, I will present the regulation of the serum therapy in the two countries in two different sections. Afterwards, as a detailed case study, I will examine the financial aspects of serum production and scrutinize the interactions between the different actors. Finally, I will summarise and conclude the results of this analysis and show the differences in administering and regulating serum production and the different cultures of governmentality.

Sources

In order to talk about two cultures of organisation and regulation, we first have to consider two different cultures of archiving. With respect to this issue, the two cultures are difficult to compare. In Germany we have a large quantity of continuous sources that provide a wide range of information. In the archives of the pharmaceutical companies, there are calculations and information about serum production and regulation. Moreover, in the Prussian Archive, the Archive of the Paul Ehrlich Institute and in the Federal Archive we find several

folders on diphtheria serum concerning the related state-run institutes, their budgets and personnel.¹ In France, apart from some regional archives with scattered information there is the Archive of the Pasteur Institute.² In practical terms this means that, for example, we have several folders containing files on the budget of the Serological Institute. The sources available in Germany include information about the planned budgets with annual plans, folders for the accounting office and the income and expenses of the institute.³ At the Pasteur Institute we have a few sheets of notes, with rough calculations of the receipts and the expenses for this period.⁴ Thus, when comparing the financial aspects of serum production we have a detailed record available for Germany, documented in numerous sources while for France we have approximate information based on sporadic sources.

The differences we have just noted concerning the sources available reflect an important difference in the structure of serum production in France and Germany. All the participants in Germany were answerable to some higher institution: the state institutions were answerable to the ministry, while some of the commercial companies were answerable as a stock corporation or directly to the shareholders, to whom they had to give reports. In France, it is not clear if the Pasteur Institute was answerable to any higher institution. The only institution to which they may have reported was the supervisory board of the institute, but apparently not with any detailed reports.⁵ Moreover, the lack of sources reflects the central position of the Pasteur Institute in the process of serum production and regulation. While in Germany several actors had to

1 Regarding the research into and the state control of diphtheria serum for example: in the Federal Archive (Bundesarchiv, Berlin – hereafter BA Berlin) the collection of the Imperial Health Office R 86, folder 1179–1184, 1646, 2710–2712, 2886; in the Prussian Archive (Geheimes Staatsarchiv – Preussischer Kulturbesitz, Berlin – hereafter GStA PK) the collection of the Prussian Ministry for Cultural Affairs the folders HA 1, Rep. 76 VIII B, No. 3747–3755; in the archive of the Paul Ehrlich Institute (Paul-Ehrlich-Institut, Langen – hereafter APEI) the folder of the department V.

2 In the archive of the Pasteur Institute, Paris (hereafter AIP), there are for example the assets of the Head Office (DR-COR, DR-DOS) and the collection of Émile Roux.

3 Cf. GStA PK, HA 1, Rep. 76 Vc, Sect. 1, Tit. XI, part II, No. 19; GStA PK, HA 1, Rep. 76 Vc, Sect. 1, Tit. XI, part II, No. 21, vol. 1 and 2; APEI, Boxes reg. staff, administration, budget, accountancy – each box with several files.

4 For example concerning the calculation of the “service de la séro-thérapie” AIP, DR-DOS 2, fol. 9265, 9268–9279, 9285, 9288, 9296, 9371, 9376; concerning the calculation of staff AIP, DR-DOS 1, fol. 18474, 18476–18477, 18479, 18482; see also the Séances du Conseil d’Administration de l’Institut Pasteur, AIP.

5 It was only after the financial crises of the institute in the 1930s that some detailed information about the annual budget started to become available, cf. the correspondence in AIP, DR-COR4.

communicate over long distances and between different hierarchies; in France all the relevant actors were gathered together at the Pasteur Institute.

Production and Distribution of Diphtheria Serum in France and Germany

If we compare the different cultures of regulation of serum production in France and Germany, we can see in detail several differences but overall they present many similarities.⁶ A first similarity is that the relevant research took place in non-university research institutions – the Prussian Institute for Infectious Diseases in Berlin and the Pasteur Institute in Paris. The development of the diphtheria serum took place in a public context within the scientific community. The research results were published in France, for example, in the *Annales de l'Institut Pasteur* and in Germany in the *Deutsche Medizinische Wochenschrift* or in the *Zeitschrift für Hygiene*. Summaries of research results were published very rapidly in weekly journals with detailed accounts following later in widely read medical journal. This policy of prompt publication was used to establish priority for the relevant scientific innovations with the side effect that everybody could, in principle, reconstruct the published experiments. This immediate publication also enabled a constant exchange of information about current research. This indirect exchange of knowledge was probably one of the reasons that the process of serum production showed many similarities in both countries. In Germany as well as in France there were several actors producing serum. While in Germany there were several competing pharmaceutical companies, in France the Pasteur Institute was the main actor, and the only one producing the serum “industrially”. “Industrially”, here, means the production of large quantities of serum – thousands of litres – for national or international supply, even though the stables for the horses and the associated laboratories looked more like a farm than a factory (see fig. 1). In France, besides the Pasteur Institute there were some regional institutes in cities like Bordeaux, Montpellier,

6 For the problems, difficulties and opportunities presented by historical comparison see Hartmut Kaelble, *Der historische Vergleich. Eine Einführung zum 19. und 20. Jahrhundert* (Frankfurt, 1999); and Christian Bonah, *Instruire, Guérir, Servir. Formation et Pratique Médicales en France et en Allemagne pendant la deuxième moitié du XIXe siècle* (Strasbourg, 2000), pp. 5–7, 27–69. For a direct comparison between the Prussian Institute for Infectious Diseases and the Pasteur Institute see Paul J. Weindling, “Scientific Elites and Laboratory Organisation in fin de siècle Paris and Berlin. The Pasteur Institute and Robert Koch’s Institute for Infectious Diseases compared”, in Andrew Cunningham and Perry Williams, eds., *The Laboratory Revolution in Medicine* (Cambridge, 1992), pp. 170–188; and J. Andrew Mendelsohn, *Cultures of Bacteriology. Formation and Transformation of a Science in France and Germany, 1870–1914*, Phil. Diss. (Princeton, 1996).

Figure 1. Serum Production at Merck around 1909, Darmstadt



Source: Merck Archive (Y 1/00280), Darmstadt.

Lyon, Nancy, Grenoble and elsewhere that produced serum only in small quantities for their local region and were generally attached to the Faculty of Medicine, the local municipality or both.

The process of serum production starts with the fabrication of the diphtheria toxin. The toxin is extracted from pure bacteria cultures sown on an appropriate culture medium, and killed after a few days of breeding, using a disinfectant. This was not a simple process, with the amount of toxin produced depending on the strain of bacteria used and the handling of the culture medium, among other factors, and the details of toxin production differed from company to company. Increasing doses of the toxin were then inoculated into horses over the course of several evenly spaced injections (see fig. 2). Test-bleedings indicated when the antitoxin content of the serum was at its maximum level, at which time the horse could be bled regularly. After bleeding, the blood was left to stand so that the serum separated out. Again the different companies had different techniques involving filtration and centrifugation to ensure the purity of the serum. After the serum's quality and effectiveness had been checked,⁷ it was poured into a phial at an appropriate dose (5 or 10 millilitres), labelled with the immunisation power and date of preparation, packed and was then ready for distribution.⁸

7 The process of evaluation is too complicated to explain here, for the German procedure see Axel C. Huentelmann, "Evaluation and standardisation as a practical technique of administration. The example diphtheria-serum", in Christoph Gradmann, ed., *Evaluations. Standardising Pharmaceutical Agents 1890–1960* (in Print, app. 2008).

8 For a detailed description, see the outline for the founding of a state-run control station in the archive of the Paul Ehrlich Institute in Langen (hereafter APEI), Dept. Va, No. 1, Vol. 1. A general account is given in Carola Throm, *Das Diphtherieserum. Ein neues Therapieprinzip, seine Entwicklung und Markteinführung* (Stuttgart, 1995); see also Arnold Eiermann, "Die Einrichtung zur Darstellung des Diphtherie-Heilserums in den Höchster Farbwerken", *Münchener Medizinische Wochenschrift*, 41 (1894), pp. 1038–1040.

Figure 2. Production of diphtheria serum at the Behring-Werke around 1906 On the left, the inoculation of the toxin, and on the right, the bleeding of an immunized horse.



Source: Behring Archive, Marburg.

The first phials of diphtheria serum produced by the Farbwerke Hoechst were on sale in German pharmacies in August 1894. One month later, at the Eighth International Congress of Hygiene in Budapest, the scientific world was introduced to the new therapy against diphtheria and the serum was greeted as a great breakthrough in the treatment of a terrible disease.⁹ In Germany, the Farbwerke Hoechst had a leading position on the national serum market, providing nearly three quarters of the diphtheria serum, while in France the Pasteur Institute dominated the national market. Apart from the Pasteur Institute

⁹ For example: Émile Roux to Émile Duclaux, Head of the Pasteur Institute, 15.9.1894, Museum of the Pasteur Institute, fol. 11504. A report about the congress in *La semaine médicale*, 14 (Issue 51, 8.9.1894); *Le Bulletin Médical* (1894), pp. 827–829, 844–845, the paper of Roux given on the Congress on pp. 1165–1168. For Germany see several articles of German newspapers in BA Berlin, R 86/1182; a report in the *Deutsche Medizinische Wochenschrift*, 20 (Issue 35–37, 1894), pp. 700–703, 715, 729–731; detailed and with a print of several talks given in Budapest in *Centralblatt für Bakteriologie und Parasitenkunde*, 16 (1894), pp. 737–742, 778–784, 822–826, 881–896, 908–914, 955–959, 960–965, 1013–1018, 1054–1058; and in the *Deutsche Vierteljahrsschrift für öffentliche Gesundheitspflege*, 27 (1895), pp. 209–276, 401–464.

some regional institutes produced serum to provide serum in their districts because the Pasteur Institute was incapable of delivering the requested quantities of serum in the last months of 1894. The serum phials were distributed via pharmacies, hospitals, public health and welfare institutions especially of the municipalities or the districts. Economically, the new serum represented a major market. Thus, for example, in the first year of production, Farbwerke Hoechst made around 707,000 Marks of profit on the serum.¹⁰ The large quantities of serum on the market made the question of regulating its sale particularly urgent. Despite the similarities in the production process, the regulation of the serum production was different in the two countries – configurations that depended on the national cultures and traditions.

State Regulation of Serum Production in Germany

As mentioned above, the research results about the new serum therapy were published in several medical periodicals. The articles were freely available and so in August 1894 it was in principle possible for a well-informed microbiologist to reconstruct the production process and to produce the serum. Moreover, there was no patent covering the production and use of serum therapy and there was no protection of any particular trademark. In general, in Germany the patent legislation that applied to chemicals was transferred in 1891 onto pharmaceuticals, meaning that only processes and not products could be protected.¹¹ Thus anybody could copy the serum (as a product), and would just need to vary the production procedure to be sure to avoid encountering legal problems. Only a few years earlier tuberculin, the unsuccessful treatment for tuberculosis launched by Koch in Berlin in 1890, had triggered a public health scandal that continued to echo around the public health administration. In the tuberculin case, an initial optimistic mood had quickly turned to one of deception, while the administration watched ineffectively from the sidelines not knowing how or whether to intervene.¹² The novelty of serum therapy and a lack of information concerning its long-term effects, as well as the prospect of high

10 Cf. Throm, *Diphtherieserum*, pp. 54–55 and Tab. IV.

11 Cf. Wolfgang Wimmer, “*Wir haben fast immer was Neues*”. *Gesundheitswesen und Innovation der Pharma-Industrie in Deutschland, 1880–1935* (Berlin, 1994), pp. 85–101; Erika Hickel, *Arzneimittel-Standardisierung im 19. Jahrhundert in den Pharmakopöen Deutschlands, Frankreichs, Großbritanniens und der Vereinigten Staaten von Amerika* (Darmstadt, 1973).

12 Christoph Gradmann, “Ein Fehlschlag und seine Folgen. Robert Kochs Tuberkulin und die Gründung des Instituts für Infektionskrankheiten in Berlin 1891”, in idem and Thomas Schlich, eds., *Strategien der Kausalität. Konzepte der Krankheitsverursachung im 19. und 20. Jahrhundert* (Pfaffenweiler, 1999), pp. 29–52, in particular pp. 36–38.

profits in the serum industry pushed high-ranking government officials down the road of legislation. Nevertheless, the principle aim was probably to avoid any scandal concerning ineffective or impure serum sold by unscrupulous firms.

A conference was organized in early November 1894 by the Imperial Health Office – the highest medical authority in the German Empire – bringing together medical officials from the Prussian Ministry for Cultural Affairs, representatives of the Federal states, the Imperial Health Office and scientists from the Prussian Institute for Infectious Diseases, like Paul Ehrlich (1854–1915), Robert Koch (1843–1910) and Emil Behring. Later on, representatives of the pharmaceutical industry were also included in the discussion.¹³ The participants at this conference discussed the regulation of the new serum therapy and the need to protect the public against impure or ineffective serum.¹⁴

Interestingly, the initial German proposals for state regulation took the Pasteur Institute as their model, proposing an Imperial institute to produce and distribute the serum.¹⁵ Later on, however, this idea of a state-run institute was only raised by government medical officials as a threat to the serum producers.¹⁶ Furthermore, there was also a call for donations in the name of the Empress to found such a state-run institute for serum production,¹⁷ along with several other appeals, especially in the early months, for funds to pay for free serum for the poor.¹⁸

13 The minutes of the meeting from 3rd and 5th of November 1894 in BA Berlin, R 86/1646. Furthermore background information regarding the importance of the conference in Heinz Zeiss and Richard Bieling, *Emil von Behring. Gestalt und Werk* (Berlin, 1941), pp. 153–157; Axel C. Huentelmann, *Gesundheitspolitik im Kaiserreich und in der Weimarer Republik. Das Reichsgesundheitsamt von 1876–1933*, Diss. Phil. (University of Bremen, 2006).

14 Cf. the minutes of the meeting from 3rd and 5th of November 1894 in BA Berlin, R 86/1646.

15 Cf. the discussions on a meeting on October 19th 1894 in the Imperial Health Office, BA Berlin, R 86/1646; and the minutes of a meeting at the Prussian Ministry for Cultural Affairs on October 24th 1894, GStA PK, HA 1, Rep. 76 VIII B, No. 3747; furthermore an undated report from B. Fraenkel about the distribution of diphtheria serum in France, *ibid*; see also Throm, *Diphtherieserum*, p. 71.

16 Cf. Althoff an Behring, 15.11.1894, Behring-Archiv Marburg, folder 8–01: Correspondence Althoff, Doc. 1; the head of the Imperial Health Office, Carl Koehler, about Althoff's idea in a letter to Josef von Kerschensteiner, extraordinary member of the Imperial Health Office and privy council in the Bavarian Ministry of the Interior, 27.11.1894, BA Berlin, R 86/1646; about the plans to found a state-run institute of serum production reports a newspaper article in the *Berliner Tageblatt*, 26.2.1908.

17 Cf. the appeal for funds in the name of the Empress for a German Institute for serum production, BA Berlin, R 86/1646.

18 The Kaiserin-Friedrich Hospital in Berlin received 30,000 Marks for this cause, and a call for donations from the *Lokal-Anzeiger* in Berlin also raised some money, cf. the donation of 30,000 Marks the letter of Rudolf Virchow to an unnamed privy council, 17.10.1894,

Between November 1894 and February 1895 a series of meetings gave rise to draft legislation covering serum production. In accordance with an imperial decree from January 1890 the diphtheria serum could only be sold in pharmacies, ensuring that the distribution of diphtheria serum was limited to medical specialists. Secondly, in accordance with a Federal resolution of July 1891, a prescription was required for the diphtheria serum and the serum was inscribed in the *Pharmacopoeia germanica* as *serum antidiphthericum*.¹⁹ In the absence of empirical knowledge about the action of the serum it was decided to accompany its introduction onto the market by the compilation of medical statistics to prove the effectiveness of the new serum therapy.²⁰

The most important point in the German scheme was the state control of the production and distribution of the serum. Until the 1880s, the quality control of the ingredients and the preparation of the pharmaceuticals were entirely in the hands of the pharmacists. With the rising pharmaceutical industry, it became difficult for the apothecary to analyse the ingredients, meaning that he could no longer guarantee the quality of the tablets or pills that he sold in his shop.²¹ Indeed, only a trained expert could determine the potency of the serum, and the mass production of the serum only reinforced this state of affairs, with the industry increasingly becoming the site of both production and quality control instead of the pharmacies.²²

The surveillance of serum production combined centralized and local elements involving not only the monitoring of the production process but also the use of a state institute for serum control. In every production plant the process was permanently monitored by a medical officer, paid by the producer but answerable to the state in the form of the Prussian Ministry for Cultural Affairs or the district president. In addition, the serum was tested for purity as well as being evaluated and certified centrally at the Serological Institute founded in February 1895. There were also strict regulations concerning the

GStA PK, HA 1, Rep. 76 VIII B, No. 3747. The “Appeal to all philanthropists” for funds to buy serum for the poor by the newspaper owner August Scherl in October 1894, *ibid.*

19 Reichsgesetzblatt 1895, p. 1.

20 Cf. the minutes of the meeting from 3rd and 5th of November 1894 in BA Berlin, R 86/1646. The results of the statistics had been published as “Ergebnisse der Sammelforschung über das Diphtherieheilserum für die Zeit vom April 1895 bis März 1896” and sent to every library in the German Empire and to several institutions, cf. BA Berlin, R 86/1646; and a summary had been published in *Arbeiten aus dem Kaiserlichen Gesundheitsamt*, 13 (1897), pp. 254–292.

21 The aim of the control was the reduction of sources of error. With the industrialisation process it was easier to control a few producer than to control thousands of pharmacies.

22 Cf. Jürgen Holsten, *Das Kaiserliche Gesundheitsamt und die Pharmazie. Dargestellt an der Entstehung des Deutschen Arzneibuches, fünfte Ausgabe*, Diss. med. Free University (Berlin, 1977); Hickel, *Arzneimittel-Standardisierung*; Wimmer, *Gesundheitswesen*.

handling and packaging of the prior to distribution, and the sale price was regulated, with special tariffs for social security insurance, welfare institutions and hospitals. Finally, the producers guaranteed the withdrawal of phials from pharmacies after two years or in the case of ineffective or impure serum. The legislation was implemented within a few months, and the state institute for serum control set up.²³ Thus, after April 1st 1895, only state-certified serum could be sold in Germany.

Regulation and Serum Production in France

In France, the Pasteur Institute produced, distributed and monitored the quality of the vast majority of diphtheria serum.²⁴ There was enormous public enthusiasm for the new serum therapy. In September 1894, *Le Figaro* launched a public subscription, which raised over one million Francs in a few months.²⁵ Just as in Germany, there was discussion in France about regulating the preparation, distribution and sale of diphtheria serum to protect the public against impure, harmful or ineffective serum. As with the German legislation, the French pharmacists traditionally bore the responsibility for the purity and quality of the ingredients and their prescribable combinations as defined by the official pharmacopoeia. Thus, the French pharmacist was accountable for anything that he sold, whether he had prepared it in his pharmacy or not.²⁶ After the development of the diphtheria serum in 1894, a bill was introduced in March 1895 and debated in the *Chambre des Députés* and the *Sénat* before finally being proclaimed law by the French President on the 25th of April 1895.²⁷ The law cov-

23 See the minutes of the meeting from the 17.12.1894, 17.1.1895 and 1.2.1895 and the correspondence between the participants of the meetings in BA Berlin, R 86/1646; GStA PK, HA 1, Rep. 76 VIII B, No. 3747; about the foundation of the Serological Institute see GStA PK, HA 1, Rep. 76 Vc, Sekt. 1, Tit. XI, part II, No. 18, vol. 1.

24 For detailed information about the Pasteur Institute see *L'Institut Pasteur et ses Annexes. Organisation et Fonctionnement et ses divers Services* (Paris, undated – after 1900); Albert Delaunay, *L'Institut Pasteur. Des Origins a Aujourd'hui* (Paris, 1962); Michel Morange, ed., *L'Institut Pasteur. Contributions à son histoire* (Paris, 1991); and Ilana Löwy, “On Hybridizations, Networks and New Disciplines The Pasteur Institute and the Development of Microbiology in France”, *Studies in History and Philosophy of Science*, 25 (1994), pp. 655–688; Anne Marie Moulin, “The Pasteur Institute’s International Network: Scientific Innovations and French Tropisms”, in: Christophe Charle et al., eds., *Transnational Intellectual Networks. Forms of Academic Knowledge and the Search for Cultural Identities* (Frankfurt, 2004), pp. 135–164.

25 Cf. the subscriptions the press clipping in the AIP, DR-DOS2.

26 Hickel, *Arzneimittelstandardisierung*.

27 LOI relative à la préparation, à la vente et à la distribution des sérums thérapeutiques et autre produits analogue, cf. Ministère de l’Intérieur, *Sérums Thérapeutiques et*

ered more than just “therapeutic serums”, including “attenuated viruses,” “modified toxins” and other similar products including the whole range of “injectable substances of organic origin not chemically defined”.²⁸ Concerning serum, the law was similar to the German legislation on several points, such as stating that the diphtheria serum could only be distributed through pharmacies and required a prescription.²⁹ As the distributor of the diphtheria serum, however, the pharmacist was now exonerated from his official responsibility with respect to any approved serum, with responsibility for quality control transferred from the site of distribution to that of production. Anyone who wanted to be a producer first had to prove that he had the ability to prepare effective and sterile diphtheria serum, and only authorized institutions would be allowed to produce and distribute the serum. The audits and authorization were overseen by a committee that was set up under the auspices of the Academy of Medicine and answerable to Ministry of Interior.³⁰ This committee, the serum commission, was constituted in May 1895 and consisted of 16 members: civil servants from the Ministry of Interior, members of the Academy of Medicine and of the Consultative Committee for Public Health in France. Some of them were also members of or related to the Pasteur Institute, such as Édmond Nocard (1850–1903), Professor at the veterinary school in Alfort and associated member of the Pasteur Institute, or Émile Duclaux (1840–1904), Pasteur’s successor as the Director of the Pasteur Institute.³¹ Thus, the serum commission was dominated by members of the Pasteur Institute. Indeed, in the state’s delegation of authority to the Serum commission of the Academy for Medicine, they were relying heavily on members of the Pasteur Institute, who, within the academy, were the only ones to have the technical competence to audit potential serum producers. Furthermore, most of the French microbiologists were educated at the Pasteur Institute or had attended the “Grand cours”, a course in bacteriology taught by Émile Roux. Indeed, anyone who wanted to produce the serum had to learn or had already learnt the technique of serum production at the Pasteur Institute.

Thus, we have seen that in Germany as in France, a number of different actors were involved in the process of serum production and regulation. The following section consists of a financial analysis of serum production in the two countries,

autres Produits Analogues. Législation et Réglementation 1895 (Extract from Recueil des Travaux du Comité Consultatif d’Hygiène Publique de France et des Actes Officiels de l’Administration Sanitaire, vol. 25), Paris 1896.

28 Ibid., art. 1.

29 Ibid., art. 2.

30 Ibid., art. 1–2.

31 See the Décret du 15 mai 1895, in: Ministère de l’Intérieur, Sérums Thérapeutiques; see also *L’Institut Pasteur et ses Annexes*, p. 26–31.

with the aim of illuminating the interaction between the different actors and the impact of the state regulation.

Financial Aspects of Serum Production and Regulation – a Comparative Case Study

Financing is one of the key elements of production, with investors generally expecting a return on their investment. Nevertheless, profit does not have to be interpreted in financial terms, but can be realised in prestige, power or other expected advantages. Thus, an analysis of the financial aspects of serum production illuminates the direct and indirect connections between the different actors in the spheres of science, state and industry. Due to the separation of the functions of production and regulation of the serum in Germany we have to consider the financial aspects from both a local and a national perspective. Overall, we can suppose that the costs of production in France and Germany were comparable, although due to unequal sources, no detailed comparison is possible.

Initial Costs and Investments

Even prior to production in Germany, the Farbwerke Hoechst had invested in Behring's research and Schering in Hans Aronson's (1865–1919).³² After the experimental phase turned into an industrial one, and large-scale production started, the German companies involved invested in horses to try and maximize their profit, as well as introducing their own bacteriological departments,³³ often

32 In 1892 the Farbwerke Hoechst signed a contract with Emil Behring concerning the sponsorship of Behring's experiments, cf. August Laubenheimer, *Zur Geschichte der Serumdarstellung in den Farbwerken* (The History of the Serum Therapy at the Farbwerke Hoechst), June 1904, Behring Archive, University of Marburg, 8–01, Correspondence with the Farbwerke Hoechst, doc. 678 (hereafter Laubenheimer, *Geschichte*), p. 10. August Laubenheimer was a member of the supervisory board at the Farbwerke Hoechst. The details of Schering's payments to Hans Aronson are not known, but they were probably less than Behring had received, cf. also Throm, *Diphtherieserum*, pp. 48–49.

33 The Farbwerke Hoechst installed an own laboratory at the same time they supported Behring. After it became apparent, that the experiments of Behring would be successful and also cure human, the Farbwerke Hoechst decided to enlarge the bacteriological laboratory to an own bacteriological department, see Laubenheimer, *Geschichte*. As the head of the bacteriological laboratory Arnold Libbertz was recruited, a friend of Robert Koch, cf. Throm, *Diphtherieserum*, pp. 48–49. Between 1892 and 1894 also Schering had built up an own laboratory. Merck started to build up an own bacteriological department in 1894/1895.

building new stables and laboratories.³⁴ In France, the research on the serum was funded by the Pasteur Institute, and after September 1894 they started to produce the serum in Garches, a suburb of Paris. For this, they used a large former military stable that had been made available to Louis Pasteur for his rabies research. Part of the money from the *Le Figaro* subscription was invested in new stables and other building work at Garches,³⁵ as well as paying for the horses to produce the serum. Between autumn 1894 and the end of 1895 the Pasteur Institute bought between 79 and one hundred horses for around 26,000 Francs.³⁶ Thus, this public subscription provided the start-up financing necessary for large-scale production in France, and also provided the Pasteur Institute with long-term income through the interest on investments. In Germany, the competing companies were exposed to a significant financial risk, having to invest their own money based on prospective sales of the serum, while in France, following the unexpected success of the public subscription campaign, the Pasteur Institute had made money on the venture even before production had started. Nevertheless, the risks taken by the German investors paid off, because they were able to deliver serum far earlier than the French.

Running Costs

The running costs for the production process included the cost of feeding the horses and test-animals (mice and guinea pigs), as well as the test procedures and the maintenance of the buildings and laboratories. In addition to the material costs there were personnel costs: stable boys, laboratory assistants, the scientists and laboratory director.³⁷ While, detailed running costs no doubt differed

34 The price for one horse was 300 Marks for each in Germany, price out of the calculation from Schering, cited after Throm, *Diphtherieserum*, p. 83.

35 The construction of the new laboratories cost 180,000 Francs, cf. the draft for a report of the “Service gratuits” to competent minister, see AIP, DR-DOS2, doc. 9286.

36 Based on an article in *Le Figaro* of January 1st 1895. Jonathan Simon differentiated the quoted sum of 136 horses: 79 horses in Garches, 42 in the stables of Grenelles and 15 in Alfort, see Jonathan Simon, Jonathan Simon “Monitoring the Stable at the Pasteur Institute”, *Science in Context*, 2008 (forthcoming). We can hypothesis that the 79 horses were bought from the donated money, because there were no more capacities on the terrain of the Pasteur Institute. But it is likely that much more from the 136 horses were bought after October 1894 and taken shelter in Grenelle. In a German newspaper article that based on a statement of the Pasteur Institute a figure of 100 horses is cited, cf. *Neue Preußische Zeitung* No. 76, 14.2.1895. – The amount of 26,011.10 Francs is cited in a draft for a report of the “Service gratuits” to the competent minister, see AIP, DR-DOS2, doc. 9286.

37 Some members of the Pasteur Institute received additional income from the Ministère de l’Instruction publique, but otherwise the cost for personnel were similar, cf. for France the lists in AIP, DR-DOS1; for Germany the file with documents concerning accountancy of the Serological Institute GStA PK, HA 1, Rep. 76 Vc, Sekt 1, Tit. XI, part II, No. 21, vol. 1–3.

between France and Germany (the Pasteur Institute, for example, bought unfit military horses, and Farbwerke Hoechst bought them on the regular market), overall the cost for serum production was roughly comparable.³⁸

Expenses Due to State Regulation

Under German regulations, the serum producers nevertheless bore extra expenses, having to pay the salary of the on-site government inspector.³⁹ Furthermore, every producer who wanted to sell serum had to pay a fixed “entrance” fee of 1,000 Marks to the state institute. In addition, after the first of April 1895 every producer had to pay fees to the Serological Institute, which charged a minimum of about fifty Marks for any amount up to five litres of serum plus ten Marks for every subsequent litre.⁴⁰ The test fees were a constant topic for debate in Germany, with the industry arguing that they hindered German competitiveness, and, as a consequence, the fees were waived for any serum sold abroad. In France, the serum producer did not have to pay any fees to any outside agent, as they were themselves responsible for quality control. On the other hand, the Pasteur Institute did have to deliver serum to the “assistance publique” in and around the city of Paris for free. Between October 1894 and February 1895 the Pasteur Institute distributed 50,000 doses free of charge.⁴¹ While in France, the Pasteur Institute had a quasi monopoly over serum production, the German market was limited to the companies who could afford the ‘entrance fee’ associated with testing, making it difficult for newcomers to enter the market.

38 For subsistence (food, rent for the stable, staff) of the horses the Pasteur Institute calculated 1,000 Francs per year for every horse, cf. *Neue Preußische Zeitung* No. 76, 14.2.1895. For Germany Throm, *Diphtherieserum*, pp. 83–91, 105–110, is quoting an amount of 600 Marks for subsistence and 600 Mark for the test procedure.

39 For detailed information see Throm, *Diphtherieserum*, pp. 83–91, 105–110. The Farbwerke Hoechst for example paid 2,000 Mark each year for the medical official.

40 In short Throm, *Diphtherieserum*, pp. 148–151. See also the again and again blazing discussion about the fees in BA Berlin, R 86/1182, R 86/1646, R86/2711; GStA PK, HA 1, Rep. 76 VIII B, No. 3747–3753; and the box about fees in the APEI.

41 Cf. the report “Service gratuits – Année 1894” in the Museum of the Pasteur Institute, doc. 9269. The money for the provision of the “Service gratuit” amounting to 55,000 Francs. Cf. the draft for a report of the “Service gratuits” to competent minister, see AIP, DR-DOS2, doc. 9286.

Income Situation

In Germany the phials of diphtheria serum were sold in pharmacies. In 1894 a five centilitre, 500 Immunisation Unit phial cost five Marks, although later the price was reduced. Furthermore, the price was halved for health insurance funds, poor relief and municipal institutions as well as hospitals. Government intervention was another subject of disagreement between the serum producers and the state.⁴² Nevertheless, despite price regulation the production of serum at the Farbwerke Hoechst, Schering and other companies was highly profitable. Indeed Hoechst paid off the cost of their new production plant in a matter of months and, as mentioned above, had made a profit of 707,000 Marks before the end of 1895.⁴³

The Serological Institute also profited from the commercial success of serum, as it was principally financed by the fees for its tests. Thus, it only took the institute a few months to reimburse an initial equipment loan from the Prussian state.⁴⁴ In addition, the municipality of Frankfurt funded new buildings and paid 10,000 Marks per year to cover the running costs when the institute moved to the city in the autumn of 1899. In return, the state-run institute had to give bacteriological courses to Frankfurt physicians, as well as giving lectures on bacteriology and serology at the *Senckenbergianum* and conducting bacteriological tests for Frankfurt's public hospitals.⁴⁵ After the turn of the century, a donation was given to the institute to pay for serological and biochemical research.⁴⁶

At the Pasteur Institute the main source of income in the first year of serum production was money raised by the public subscriptions organized by *Le Figaro* that was supposed to pay for a "service gratuit". Thus, the Pasteur Institute supplied hospitals and dispensaries in and around Paris (as well as the

42 The price for the diphtheria serum was later on permanently reduced by an official decree, the price regulation in BA Berlin, R 86/1646 and R 86/1182.

43 Laubenheimer pointed out that the production plant with the amount of 444,000 Marks was written down with the profit of the first year, cf. Laubenheimer, *Geschichte*, p. 10.

44 Robert Koch to the Prussian Ministry for Cultural Affairs, 4.7.1895, GStA PK, HA 1, Rep. 76 Vc, Sekt. 1, Tit. XI, part II, No. 21, vol. 1, fol. 12.

45 The files concerning the transfer of the institute from Berlin to Frankfurt in GStA PK, HA 1, Rep. 76 Vc, Sekt 1, Tit. XI, part II, No. 19.

46 In Frankfurt the banker Georg Speyer and later his widow gave money to scientific and municipal welfare institutions, see Althoff an Ehrlich, 12.1.1901, Rockefeller Archive Center, Paul Ehrlich Collection, 650 Eh 89, box 1, folder 46; Ehrlich an Althoff, 19.1.1901, *ibid.* Later on, Paul Ehrlich spent the money he gained from Salversan. Before the First World War the Foundation of the "Georg-Speyer-Haus" had added up to more than four Million Marks, see the Correspondence with Ludwig Darmstädter in the Rockefeller Archive Center, Paul Ehrlich Collection, 650 Eh 89, box 1, folder 8.

military) with free serum.⁴⁷ Furthermore, they received a one-off subsidy of 100,000 Francs from the state.⁴⁸ The significant excess income was invested in bonds to assure a regular income.

To cover the running costs and the “Service gratuit”, the Pasteur Institute also got a supplementary annual subsidy of about 80,000 Francs from the state, as well as an annual subsidy of 15,000 Francs from the city of Paris, and 5,000 Francs from the *Département de la Seine* to assure the delivery of serum to the community.⁴⁹ Besides the “Service gratuit”, however, there was also a “Service payant” because patients who could afford it were expected to pay for the serum. In February 1895, a German newspaper reported several complaints in Paris from people who had given donations to the Pasteur Institute assuming that they would benefit from the free “Service gratuit,” but later had to pay for the serum in the pharmacy.⁵⁰ The regular income from the sale of the serum, especially from exports, added up to an estimated total income of more than 420,000 Francs in 1895.⁵¹ In sum, it could be said that the considerable investments represented by the new buildings and horses were met by subscriptions and donations, which comprised the largest part of the income in the years around 1895. The interest from the invested donations together with different subsidies from the state, departments and the city of Paris, as well as the commercial sale of the serum (which was nearly one third of the total income) covered the running costs. This mixed income structure for serum production reflects the general income structure for the institute.⁵²

Financial Aspects and the Different Administrative Actors

At first sight, the financial aspects of serum production look quite different in France and Germany, as does the regulation. In France we see private or semi-private ‘charitable’ institutions, with the Pasteur Institute occupying a central position, and complemented by some regional serum producers. In Germany we have several competing for-profit companies operating in different federal states

47 See the draft of a report of the “Service gratuits” to competent minister, see AIP, DR-DOS2, doc. 9286.

48 See the notes in AIP, DR-DOS 2.

49 See the draft of a report of the “Service gratuits” to competent minister, see AIP, DR-DOS2, doc. 9286; and the annual report of 1895 in the museum of the Pasteur Institute, doc. 9274; see also the report about the congress in Budapest in the *Revue d’Hygiene*, 16 (1894), p. 1018; and *L’Institut Pasteur et ses Annexes*, p. 26.

50 Cf. *Neue Preußische Zeitung* No. 76, 14.2.1895.

51 See the annual report of 1895 in the museum of the Pasteur Institute, doc. 9274.

52 As an example compare the balance for 1890 in GStA PK, HA 1, Rep. 76 VIII B, No. 3592; see also Sandra Legout, *La Famille Pasteurienne. Le Personnel Scientifique Permanent de l’Institut Pasteur de Paris entre 1889–1914*, Diss. phil, Paris 1999, p. 8.

with a central state-run institute that acts on behalf of the state by policing the serum. On a more abstract level, in terms of the process of serum production, the financial situation looks much more similar. In both countries the serum producers had a similar structure of expenses: salaries for the personnel, the running costs for the horses, investments in new stables and laboratories, the cost of maintenance, feeding and performing the test procedures.

The income situation was likewise not as different as it is often suggested. The Pasteur Institute's subscription was used for one-off investments such as building a production plant in Garches and the rest was invested in bonds. The regular income of the Pasteur Institute was composed of interest, state and local subsidies, and receipts from the sale of the serum. In Germany, while companies made a profit out of the commercial sale of serum, the overall financing of serum was also mixed. The state-run institute was, after all, financed by the fees paid by the producers, which also received municipal subsidies and private donations. Another parallel can be seen in the cooperation of producers with public welfare institutions, in France, the "assistance publique" and in Germany health insurance and various charitable organisations. While in France the diphtheria serum was free of charge for the poor, in Germany, the cost for employees was largely borne by health insurance (which did not exist in France).

The mixture of numerous sources of income in both countries raises the question of the intentions of the investors and other actors. For the scientists, immediate publication of innovative research was a question of prestige and would evidently help in any priority disputes. The aim of the commercial companies was essentially to maximize profit. The Pasteur Institute as a scientific institution and as a large-scale producer of serum competing on the international market had an interest in making a profit as well, in order to finance future research. In both countries, the municipalities were involved in serum production and regulation: they took the opportunity to become more independent from the central power in the capital. Thus, while the city of Frankfurt provided the buildings of the Serological Institute for reasons of prestige, they also expected a direct payoff: members of the institute had to give bacteriological courses and lectures as well as conduct bacteriological tests and, finally following the installation of a scientific institution in the city, Frankfurt could more easily pursue its plan to build up its own university.

Despite certain similarities, however, we have to point out the significant elements that differentiated serum production and regulation in the two neighbouring countries. Thus, industry played a major role in Germany, while it was absent from the French picture. Also, the German state was much more present subsequent to legislation, with the government directing, ruling and supervising the whole process of production, although not directly paying for it.

In France, the Pasteur Institute assumed this role, although it was largely financed by charitable donations, and only secondarily by state and local government.

Two Cultures of Regulation?

Serum production and regulation in France and Germany display many similarities on different levels. In the triangle formed by state, industry, and science, the conformation of serum production and regulation in the two countries does not really represent two different or antagonistic types, as is often argued. As far as the intentions of the state are concerned, we can conclude that both states desired the provision of pure and effective diphtheria serum in the required quantities. The provision of the people with diphtheria serum was a major public health issue and the state had not only to ensure the supply of diphtheria serum but also to minimize public health risks, avoiding any repetition of the tuberculine affair of 1890 in Germany. Furthermore, neither France nor Germany had significant experience with medicines of biological origin.

In Germany, industry entered the scene and invested financially shortly after Behring presented his research results in the medical periodicals. Nevertheless, soon after the diphtheria serum came onto the market, the state took over direct control. The German Empire was a federal state and the serum producers were spread throughout the whole Empire. Although the Empire was responsible for the overall legislation, it nevertheless depended on the collaboration with the federal states, especially Prussia, for its application. Finally, the state (Empire and federal states) had to cooperate with the industry to guarantee the success of the control measures and it was certainly in the interest of the companies to cooperate with the state. Thus, we can say that the central control operated by the Serological Institute was necessary to supervise the serum throughout the empire. Nevertheless, there was also a medical official in each production plant representing another control mechanism at the federal level. The implementation of a state-run institute for quality control could also be seen as a technology of trust.⁵³ For the companies, the “state approved” stamp also had an effect on marketing, guaranteeing a high quality product, in this respect functioning like a trademark.

In France there was – apart from some small regional producers – one main centralized actor in Paris, the Pasteur Institute that produced the serum on an

⁵³ Cf. Theodore Porter, *Trust in Numbers. The Pursuit of Objectivity in Science and Public Life* (Princeton, 1995).

industrial scale. The state was satisfied with implementing a law that covered not only sera, but “injectable substances of organic origin” more generally. A serum commission carried out an initial audit of the regional manufacturers before they were allowed to produce the serum. Most of the members of the serum commission were also members of the Academy of Medicine, and most of these were connected to the Pasteur Institute. The certification of the serum producers by members of the academic community also corresponds with the picture of a dominant medical elite in nineteenth century France,⁵⁴ and is also consistent with the culture of self-regulation and self-control in the medical industry. The absence of a central institution for quality control on the model of the Serological Institute did not mean, however, that there was no state regulation in France. Regulation in France was indirect, manifesting in a less concrete legislation that left the actors more freedom. The Ministry of Interior was at least involved and integrated into the self-regulation via the ministry officials who were also part of the serum commission.

On the level of representations of serum production, there is a significant difference between the two countries. While the state-run institutes in the German Empire were confined to the background, the Pasteur Institute was much more prominent in the public sphere. In order to assure the success of any future public subscriptions, the Pasteur Institute had to build up a solid reputation based on its public relations. Thus, there was an indirect form of public control in France, with publicity keeping a spotlight on the activities of the Pasteur Institute and the fate of the donated money. The serum producers and especially the Pasteur Institute had an essential interest in producing a high quality serum otherwise they would run the risk of their resources running dry.

Comparing the different cultures of regulation in the two neighbouring countries there was an indirect type of governance. In the German Empire the serum was produced by private pharmaceutical companies, but the state regulated the price and exercised control over the production process to ensure a pure and effective serum. Nevertheless, the system of quality control was not imposed by the state: it was worked out in cooperation with the scientists involved, state-run institutes, the federal states and the pharmaceutical industry. In France a process of self-regulation was implemented, leaving the different actors a free hand. This liberal type of governance was nevertheless a type of regulation and a way of regulating. As a more complete financial analysis reveals, the state was also involved in the process of serum production and as an investor via its subsidies, paying to supply the public, and more particularly the

54 Cf. Georg Weisz, *The Medical Mandarins. The French Academy of Medicine in the Nineteenth and early Twentieth Century* (New York, 1995).

military, with serum. Moreover, several members of the Pasteur Institute were members of different state advisory boards.⁵⁵

Finally, the image of the Pasteur Institute as a state-free, purely scientific institution supported by donations that provided the public with serum free of charge is a self-constructed myth. A state-free zone was an illusion, especially when one takes into account that the state is more than just the sum of its institutions, regions or departments but also a virtual/fictional feeling of nationality.⁵⁶ The main donations in France were made by the country's elite to assure the political system, as was the case in Germany as well. The difference, however, was the elite; while in France there was a liberal elite, in Germany the elite believed in a strong and authoritarian state. What we have to take into account is that the construction of two different national cultures also involved the construction of the elites of two rival countries at the end of the nineteenth century.

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55 For example Émile Roux was also president of the “Commission supérieure consultative d'hygiène et d'Epidémiologie militaire”, see a letter from Roux to the War Ministry, 31.1.1908, AIP, DR-DOS 3.

56 See for example Bruno Latour, *The Pasteurization of France* (Cambridge, 1988).

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