Priority, Property, and Trust

Patent law and pharmaceuticals in the German Empire[1]

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In February 1913 an article in the *Vossische Zeitung* reported on a new remedy that was supposed to cure tuberculosis. An effective cure for tuberculosis would have meant a breakthrough in the control of a widespread disease. Apart from the promising announcement, little was known about the remedy that was allegedly based on a substance of biological origin. It had been developed by the physician Friedrich Franz Friedmann and was presented to the public for the first time in November 1912. Since then it had triggered a controversial debate (Werner 2002; Hüntelmann 2008) that is outlined exemplarily in the newspaper article mentioned above. After reporting about facts of the remedy, the journalist complained that no further information about its composition was available. He suspected that Friedmann »wishes to secure the money he is entitled to as the inventor,« and for this reason Friedmann »has applied for a patent for a method of producing protective substances against tuberculosis.« An expert on tuberculosis, cited in the article, identified attenuated tuberculosis bacteria originating from turtles as the

1 I would like to thank the editors for inviting me to participate in this volume and for their helpful comments on this paper. Moreover I want to thank two anonymous reviewers for their stimulating suggestions. The *Paul Ehrlich Institute* and the *Rockefeller Archive Center* supported me in my archival research. Finally, I want to thank the *European Science Foundation* and the *Steering Committee of the ESF Network Group Drug History* for supporting my research in this field and allowing me to finish this article. Special thanks also go to Christoph Gradmann, Volker Hess, Carsten Timmermann, and Michael Worboys.

active ingredient. However, the expert doubted that the remedy was »patent-ready,« as it was unclear what kind of a patent Friedmann had applied for. Turtles generally fall ill from tuberculosis and any bacteriologically trained person would be able to breed these bacterial cultures. »Claiming a patent on a living bacterial culture is something new, and we may look forward with interest to the way in which it will be dealt with« (Lennhoff 1913).

Several times the newspaper article referred to patents and the patenting of drugs, discussed the application's prospects of success and the economic motives that led to the patent application. However, the medical community and the public condemned claiming profits for therapeutic agents and considered it unethical.

Beyond economic interest, patent law is related to claims of priority. There is no doubt that the development of a new remedy to cure tuberculosis would have significantly increased the scientific reputation and social prestige of the inventing researcher. In a certain sense, the patent became an institutionalized procedure to ensure property rights on the invention as well as to secure legal priority status. Furthermore, the newspaper article invokes the aspect of trust when asking for further information about the composition of the remedy. If neither the ingredients nor the composition were known, the remedy might cause unintended effects and entail a severe public health risk, bringing up the regulatory role of the state.

In the following article I explain in more detail how these aspects—property, priority, and trust—and the actors mentioned—scientists, the industry, and the state—were linked together and how this affected the patenting of pharmaceuticals. Moreover, I analyze the interaction between different actors and possible conflicts resulting from this interaction. Finally, I investigate the role of patents within, and their influence on, the research process. I thus emphasize in particular the importance of law and legal aspects in the history of science and pharmaceuticals. After a more general introduction and review of the literature on law and legal aspects in the history of pharmaceuticals, I sketch the state regulation of pharmaceuticals and the impact of patent law on pharmaceuticals

in historical perspective. Furthermore, I explore the nexus of priority, prestige, and originality to explain why applications for patents became attractive to scientists. I then demonstrate the influence of patents on and the entanglement between legal, economic, and scientific aspects within the research process, using the example of the *Institute for Experimental Therapy* (*IET*) and the *Georg Speyer House* (*GSH*) in Frankfurt in the first decade in the 20th century. I emphasize the aspect of scientific research, patent law, economic interest, and public trust by returning to Friedrich Franz Friedmann's patent application for his tuberculosis remedy. Finally, I summarize the relation between patents, priority, property, and trust as well as the entanglement of law and science in the history of pharmaceuticals.

Law in the history of science. Legal aspects and patent law in the history of pharmaceuticals

Only a few decades ago, the history of medicine and of pharmaceuticals was written as a story of great discoveries, focusing on altruistic experts searching for ›magic bullets‹ to save mankind from suffering. More recent publications on the history of pharmaceuticals trace the epistemological process of drug development, which is linked to knowledge production. They locate the experiment and the experimental setting in the specific space of the laboratory and emphasize the importance of social factors in science. Outside the laboratory, historical studies delineate the socio-cultural and biopolitical background against which the development of new therapeutics took place. Furthermore, they analyze the negotiation processes between different actors such as politicians, patients, scientists, clinicians, the pharmaceutical industry, and other pressure groups who are all involved in the development of new pharmaceuticals.[2]

2 This describes only a tendency in the historiography of pharmaceuticals and is not intended as a comprehensive historical account. For the newer approach see Gaudillière and Löwy 1998; Gijswijt-Hostra et al. 2002; the volume on Drug Trajectories edited by Jean Paul Gaudillière in *Studies in the History and Philosophie of Biological and Biomedical Sciences* (4/36, 2005); the articles on the history, production and regulation of diphtheria serotherapy in *Dynamis. Acta Hispanica ad Medicinae Scientarumque Historiam*

Recent publications on the history of pharmaceuticals emphasize the close entanglement between science, industry, and politics. There is now little doubt that science is driven by economic interests. Pharmaceuticals are developed and produced less for the benefit of mankind than for the benefit of pharmaceutical companies. This is not a modern or post-modern phenomenon of a genetic or biotechnological era, but a historic process that started at least at the end of the 19th century (Gaudillière 2005: 609). The pharmaceutical industry and the sciences formed an interdependent interest community for two reasons. First, the increasing complexity of the production of chemical compounds or preparations of biological origin required technological know-how. Natural scientists became involved in the production process and formed the core staff of the new research and development departments. Some scientists, like Emil Behring or Emil Fischer, became entrepreneurs themselves. Second, the chemical and pharmaceutical industry sponsored scientists in (university) laboratories either directly by providing funding or indirectly by contributing working facilities, material, or manpower. Although the basis of economic activities in a free market system is legal certainty and protection of property (rights), only few studies have as yet analyzed legal aspects and the importance of law as an issue in the history of pharmaceuticals. In what ways did law and legal issues influence the pharmaceutical industry—the research, production and distribution of therapeutics—and vice versa?

One junction where history and law, science and industry intersect is the historical relation of patent law and pharmaceuticals (Fleischer 1984; Wimmer 1994; Seckelmann 2006). Most publications focus on the socio-economic and legal aspects of patent law. They see companies as black

Illustrandam (27) in 2007; and, in the same journal, on the circulation of antibiotics (ed. by Christoph Gradmann and María Jesús Santesmases, 2011, 2/31); the volume on locating therapeutic vaccines in the 19th and early 20th century in *Science in Context* (21, 2008); Prüll et al. 2008; Bonah et al. 2009; Eschenbruch et al. 2009; and Gaudillière and Hess 2013; studies such as those by Bud 2007; Greene 2007; Quirke 2008; Bächi 2009; or Ratmoko 2010.

boxes and do not touch on the consequences of the production of knowledge for the companies. In contrary, Jean-Paul Gaudillière has recently edited a special issue on the patenting of pharmaceuticals (2008a) and of living organisms (2009). The articles in this issue address the question of how therapeutic agents—not considered commodities until the end of the 19th century—were transformed into large-scale manufactured commercial products during the early 20th century. The patenting of pharmaceuticals played an important role during this transition process and the articles investigate the local practices concerning scientific, industrial and legal aspects that altered the meaning of drug patents (Gaudillière 2008b). In this article I attempt a similar analysis of the entanglement between patent law and the development of new drugs in the history of science.

The state regulation of pharmaceuticals

Until the end of the 1880s, remedies and pharmaceuticals were made and distributed almost exclusively by pharmacists. The production of pharmaceuticals was mostly restricted to the local or regional level. Pharmacies were provided with a fixed catalogue of organic and inorganic substances which were said to have a healing effect. The pharmacist guaranteed and was personally responsible for the purity and harmlessness of the pharmaceuticals he produced and distributed. Thus, pharmaceutical law aimed at pharmacists and regulated their education and the distribution of pharmaceuticals (Schmitz 2005: 1015–1019).

Similar to other European states and to North America, in the German Empire, the *Pharmacopoea Germanica* prescribed the degree of purity of the raw materials used as of 1872.[3] Erika Hickel (1973 and 1977) and Jürgen

3 A published ›book,‹ the *pharmacopoeia* contains detailed definitions of pharmaceutical compounds; their composition, the degree of purity of individual substances, and instructions for their preparation. The *pharmacopoeia* is a reference work on drug specifications and is legally binding for all drug producers on the city, district, and national level. Today, on the supranational level, there is also a European *pharmacopoeia* and an international *pharmacopoeia*.

Holsten (1977) have elaborated on the design of the *Pharmacopoea Germanica*. Its revision was coordinated by a permanent pharmaceutical commission comprised of public health officials, pharmacologists, and life scientists as well as representatives of the chemical-pharmaceutical industry. The 1910 revision of the pharmacopoiea has been described as a negotiation process, influenced by economic and political interests and driven by professional and industrial pressure groups (Holsten 1977).

At the end of the 1880s, the organizational principle—which was based on professionalism and trust—began to totter. With the industrial production of pharmaceuticals by the chemical industry, distributed to pharmacists as packaged sales units in the form of powders and pills, the latter were no longer able to guarantee purity and harmlessness. Thus standardized norms, such as the Ordinance on Pharmaceutical Trafficking (*Verordnung betreffend den Verkehr mit Arzneimittel*, later the *Medical Products Act AMG*) enacted in 1890, were supposed to regulate the composition of freely available remedies. A further regulation was passed in 1891, stipulating that highly effective medications could be only sold to the consumer after he or she had presented a medical prescription.

A second difficulty for pharmacists resulted from the development of remedies of biological origin, such as sera and vaccines. Their harmlessness and effectiveness could only be proven by complex procedures which required extensive bacteriological and serological knowledge, something pharmacists did not have. With the establishment of an institute for serum control that tested, evaluated, and approved the quality and potency of the serum produced, state control of sera shifted from distribution to production as it was easier to test a few producers than thousands of pharmacies (Wimmer 1994: 85–101; Hüntelmann 2007; Gradmann 2010).

(Pre-)history of patent law and pharmaceuticals

In the 1880s, the chemical industry started to establish research departments or to cooperate with chemists, pharmacologists, and physicians. This resulted in the launch of new, mass-produced, and ready-made pharmaceuticals. The German patent law of 1877 ruled out any protec-

tion for pharmaceuticals. Likewise, chemical substances could not be registered, only chemical procedures. This regulation suited the German chemical industry, whose main source of revenue at the time stemmed from imitating new products developed in Great Britain. In the course of the 1880s however, the chemical industry in Germany changed its strategy and supported an extension of patent law in order to protect their own innovations. But in the 1891 revision of the patent law, pharmaceuticals remained excluded from patent protection. This was defended by pointing to the significance of pharmaceuticals for public health. On the one hand, inventors promised that their new remedies would be able to prevent or cure threatening diseases, but on the other hand, the new remedies might involve the risk of unintended side effects, and in so far the composition should become known to the public. Furthermore, it was doubted that medical activity could be considered trade (Fleischer 1984; Wimmer 1994; Seckelmann 2006, Gaudillière 2008a and 2009). Beyond this, concern was raised that consumers might mistakenly see patents as a form of state approval for drugs (Gaudillière 2008a: 101). The chemical industry responded with varying attempts to circumvent this exception. First, companies defined the process to be patented as broadly as possible, also including potential alterations of the process, so that competitors could not vary the process and market and patent it as a their own (Schmitz 2005: 1017). A second way of bypassing the exception for product patents was to protect newly developed remedies as registered trademarks.[4] After the revision of German patent law in 1891, a third possibility was to obtain patent protection for chemical components or sub-components that provided the basis for a remedy. Finally, if

4 In reference to the contemporary discussion on patents in the United States at the end of the 19th century, Joseph Gabriel (2009: 155–156) clearly distinguishes between patents and trademarks. The latter do not include the aspect of information exchange and registered trademarks do not expire.

the chemical companies marketed their therapeutics abroad, they could apply for patents for these products in the respective foreign countries.[5]

Patent protection was supposed to secure the commercial exploitation of an invention for a certain period of time. The patent should legally guarantee the amortization of research and development expenses (Fleischer 1984: 9). In return, the patent holder disclosed his method. The guaranteed right to exploitation of an invention via patent protection and the rule of transparency was supposed to ensure further research and thereby support technological development. According to Margit Seckelmann, the introduction of patent law was nothing less than a catalyst for the Second Industrial Revolution (Seckelmann 2006: 11). Openness and accountability regarding the composition of remedies also served to counter the image of so-called secret remedies and nostrums. As the latter term indicates, the formula of remedies had previously been kept as a trade secret by the inventor, who exploited the nostrum commercially (Ramsey 1987: 79). This secrecy was understood as a form of temporary monopoly that restricted the circulation of information about the drug. Because nothing was known about their composition and active principles, secret remedies were considered a public health hazard and the owners of the property rights were vilified as unethical and unscrupulous quacks (Gabriel 2009: 142; see also the contributions in Bynum 1987). The legal protection of inventions was meant to create an atmosphere of trust and create advantages for the inventor as well as for the public. The inventor could present (and market) himself as an ethical manufacturer who circulated all information about his invention which in turn might generate further research and thereby promote progress (Wimmer 1994; Ripperger 1998; Seckelmann 2006: 14). The public benefited from the free circulation of information about the new remedy, because it was now possible to evaluate positive effects and balance them against possible health risks. »Patents,« as Joseph M. Gabriel summarized the American discussion on patents for remedies in the 1880s,

5 Joseph Gabriel (2009: 157) remarks that German remedies were often protected by patents and trademarks.

should »simultaneously protect a firm's financial investment in the development of a new remedy and provide the openness necessary to promote the advancement of science and the public welfare« (Gabriel 2009: 154). In accordance with Theodore M. Porter, one could interpret the institutionalized protection of inventions and the rise of patent law as a technology to generate trust in a social environment.[6] Juridification by way of patent law, the bureaucratization of registering processes and institutionalization in the form of the patent office worked as elements of constituting trust by way of protection for inventors (Seckelmann 2006: 27).

In contrast to Seckelmann,[7] who points out that patent law reduces the variety and complexity of contractual relationships, Martin Hartmann (2011: 9–15) emphasizes that trust does not reduce the complexity of relationships between contract partners, but that the establishment and practice of trust itself is a complex communicative and social set of regulations. In the following sections I will describe this complex interplay between the different actors involved in patent applications for remedies with an eye toward the various levels of trust in this process.

Before there were patents: Quarrels about priority and originality

Before there were patents, medical science was understood as the accumulation of empirical data and knowledge about therapeutic cures and methods. The free circulation of this knowledge among a community of honorable practitioners was assumed. These men saw themselves as conducting medical research as part of a larger collaborative project to improve the common good. Research results were reviewed by the medical community, discussed in medical journals, and either rejected or,

6 Porter describes how trust in numbers, considered an objective value, is generated in a bureaucratic and legally formalized setting (Porter 1995). The implementation of a system of serum regulation and evaluation, or in general of remedies of biological origin, can also be understood as a technology to generate public trust; see Hüntelmann 2006; Gradmann 2010.

7 See Seckelmann 2006: 16, in accordance with Luhmann 2000.

when verified, accepted as part of a larger body of knowledge that was accessible to all. This ethical concept of medicine was divorced from any commercial interest or private gain (Gabriel 2009: 138–140). As Joseph M. Gabriel illustrates, this ideal changed in the United States in the second half of the 19th century. But between the ideal of interest-free, ethical medicine and mercantile quackery corrupted by the selfish pursuit of profit, lies a broad field of interpretation and negotiation of the moral economy[8] of medical science. In this field of discussion about medical ethics and drug innovation prior to and in the early years of patent law, two aspects are directly related to the idea of patents: priority and resources.

In the last third of the 19th century there were countless quarrels between life scientists on the issue of priority. When in 1890 Emil von Behring postulated the principle that immunity against a certain disease could be transferred by blood serum, scientific colleagues raised objections and claimed that they themselves had discovered this principle, known as passive immunization (Zeiss and Bieling 1941; Linton 2005; Throm 1995: 45–46).

Behring was involved in many debates about the priority of his invention of serum therapy. A publication entitled *The History of Diphtheria* (Behring 1893), or a similar publication by Paul Ehrlich on the *History of Granula*

8 Nicolas Rasmussen (2004) uses this term to describe the ambivalent cooperation between scientists and the pharmaceutical industry. Originally, the term »moral economy« was characterized by E. P. Thompson (1971) as the ethical foundation of economy; and modified by Lorraine Daston (1995) as a set of values—an organized system of balanced emotional forces. In a certain socio-cultural context, these values elucidate why the scientific community considered some arguments for and methods of explaining scientific facts to be more convincing and plausible than others. The ethical arguments of 19th century physicians against secret remedies refer in a similar way to the moral economy as »thinking about the values and practices grounding the system of reciprocal gifts that dominates the world of open knowledge« as elaborated in Daston (Gaudillière 2008: 100). This becomes important in the further discussion on priority and originality.

(Ehrlich 1891), dealt less with the history of a topic and more with the history of an epistemic process. Behring presented his view on the development of the diphtheria serum, while Ehrlich claimed that he had been the first who had colored and identified cell nuclei.[9]

The claim to having been first with a development, a discovery or an invention[10] can be seen as the institutional anchoring of originality. Great significance was attributed to this value,[11] which was considered a contribution to the further development of science and linked to progress and modernity. The claim to priority is connected with the prospect of public recognition. In terms of reciprocal give and take, the scientist making the claim expects that his own (life-time) achievements will in return be rewarded by society.[12] With his claim to priority the inventor also indirectly

9 The system of literary references and the exchange of information and knowledge was (and is) linked to the idea of science as a collaborative project as mentioned above. Beyond this idealized imagination, the production of knowledge is a collaborative process involving many people, as illustrated by theories such Ludwik Fleck's thought collectives and by current social science studies. But after a certain point, usually when the success of a project becomes obvious, the scientists involved claim their intellectual property rights on the development. This tracing of the individual part of collaborative work provide the background for the histories of certain epistemic processes cited above, which often ended in claims to priority of invention or discovery. The history of the diphtheria serum could serve as an example for this shift from a collaborative we/our to an individual me/my.

10 In her discussion of the discourse on and legal disputes over the patenting of adrenaline, Mercedes Bunz distinguishes between »discovery« and »invention.« If a substance—such as plant extracts or other organic substances like adrenaline—already existed and only its therapeutic use was developed, this process was seen as a »discovery.« The development of a new substance was considered an invention and only the latter was supposed to be patentable (Gaudilliere 2009; Bud 2009; Bunz 2009).

11 The *German Patent Office* for instance tested the patent application only on its originality; see Fleischer 1984; Seckelmann 2006: 19.

12 From a sociological perspective Merton 1985: *Prioritätsstreitigkeiten in der Wissenschaft* (priority conflicts in scicence): 258–300.

called for the right to benefit from his invention. In this way the claim to priority was a substitute for patent protection unless it was not possible to patent remedies. One could not have expected any material reward as »compensation« for the originality of an achievement, but—as an alternative—social recognition, which is expressed by status symbols such as decorations or by promotion. The significance of priority in the context of exploitation rights can be illustrated by the example of the diphtheria serum. After the development of a remedy for diphtheria, celebrated by the scientific community as a milestone in medicine, Emil von Behring became Professor of Hygienics (Zeiss and Bieling 1941: 198–210; Linton 2005). The claim to priority of invention was less about economic compensation for research and development expenses, but about prestige and recognition. With the onset of patent law, patent applications became the institutionalized process for claiming priority. However, patent law and the claims derived from it reduced the aspect of recognition solely to material rewards. This was however necessary; the inclusion of scientific actors in industrial processes (and vice versa) meant that actors from outside the scientific community were also becoming involved and the industry was rooted in a value system which was different from that of the sciences.

The example of the diphtheria serum combines a number of aspects that appear within patent protection: priority, prestige, trust, and economic interests. In their publication on a promising serum to combat diphtheria, Emil Behring and his co-worker Erich Wernicke concluded that they had to terminate their research because they ran out of money (Behring and Wernicke 1892). After the director of *Farbwerke Höchst* read the article, he contacted Behring and offered his cooperation. They made a contractual agreement that *Farbwerke Höchst* would fund future experiments and would in return, should a successful therapeutic be developed, be entitled to market and exploit the prospective remedy.[13] The funding

13 August Laubenheimer: *Zur Geschichte der Serumdarstellung in den Farbwerken* (The History of the Serum Therapy at Farbwerke Hoechst). June 1904. *Behring Archive*, University of Marburg, 8-01, Correspondence with

of Behring's research by *Farbwerke Höchst* makes clear that they trusted in his capabilities to develop an diphtheria serum. For his part, Behring trusted that the investor would finance his research.[14] In contrast, the community of orthodox physicians and practitioners, as characterized in Joseph Gabriel's work (2009), mistrusted the industry. The cooperation of a scientist with the industry could compromise his scientific reputation.

For life scientists, the exchange relationship with the chemical industry offered the advantage that they need not appear as commercial actors, as the remedy was distributed under the label of the producer. In each case, cooperation was stipulated by contracts governed by private law. Indeed these contracts, when the contractual periods were over, caused conflicts; for instance between Behring and *Farbwerke Höchst* about the contract modalities to be negotiated (Throm 1995).

The mix of scientific work and economic interests also led to conflicts between colleagues, especially when personal and scientific relationships were tightly interwoven and no or only insufficient contractual agreements had been made. In the aftermath of the successful development of the diphtheria serum, Behring had several conflicts with his scientific collaborators and friends about the commercial exploitation of the remedy. The quarrels were about the question of how much each respective scientist had contributed to the joint work, and in which way this contribution was compensated or appreciated. All these different relations of trust between the scientist and his industrial partner, the medical community, the general public, and his co-workers had to be balanced out. The example of the development and exploitation of the diphtheria serum illustrates the connectedness and fragility of trust, and demonstrates the importance of trust as a category for the analysis of legal matters in the history of science.

Farbwerke Hoechst, doc. 678. Draft and contract 20 Dec. 1892, *Behring Archive*, University of Marburg, 8-01; Throm 1995: 44, 49.

14 Niklas Luhmann emphasizes that trust is also a risky »advance payment« and only this risk makes trust possible (Luhmann 2000).

Beside the debates on priority before the advent of patent law, the question of resources is an important, but less discussed issue. As described above, until the 1880s medical science was understood by orthodox physicians as an accumulation of data and knowledge about therapeutic cures. With the rise of the chemical industry, the implementation of bacteriology, and experimental laboratory medicine, growth of knowledge was no longer obtained by the exchange of data collected in the medical practice or at the bedside—rather knowledge was produced.

With the emergence of bacteriology and biochemistry in the last third of the 19th century, the acquisition of expensive technical devices and the creation of laboratory facilities became a precondition for research. Furthermore, the extensive consumption of animals for in vivo experiments and the need for chemical compounds in bacteriology or chemotherapy caused high expenses. The funding of larger series of experiments became a great challenge for institutions focused on research. For this reason, these institutions tried to find money to fund experiments in addition to their regular budget. The chemical industry funded experiments directly as well as indirectly through the provision of chemicals, as I will show in the next section. However, the chemical industry did not support research for altruistic reasons, but expected to benefit from the investment. A problem in this relationship was the short-term costs for institutions in contrast to prospective long-term and uncertain profits, again an issue of trust and future expectations. It seems that patenting balanced and institutionalized these different expectations and needs in the most satisfactory way for all parties. In the following section, I will illustrate how science and industry were related to each other, and describe the role of patents within, and their influence on, the research process.

Patents and science in action. The importance of patents at the *Institute for Experimental Therapy* and the *Georg Speyer House*

In November 1898, Paul Ehrlich, director of the *IET*, thanked the *Badische Anilin- und Soda-Fabrik* (*BASF*) for sending him dyestuffs. He told them that he was intending »to turn again more intensively to my

old favorite field of histological and biological staining,« and he asked for future support.[15] As a consequence, the dyestuff producers sent Ehrlich newly developed products, asking if he would test their therapeutic impact or histological staining properties. Ehrlich also, after having consulted catalogues or patent announcements,[16] ordered new dyestuffs.[17] At the *IET*, the director and his co-workers tested the therapeutic or toxic effects of the dyestuffs and the arsenic compounds on several parasitic pathogens in vitro or in vivo. If the experiments showed promising results, Ehrlich organized clinical trials by contacting familiar or friendly clinicians.

If the clinical trials were unsuccessful or only partly successful because the preparations caused side-effects, Ehrlich sometimes suggested a change in their composition. Since the turn of the century, the director of the *IET* had been cooperating with a number of dyestuff producers and chemists, mainly *Farbwerke Höchst* and the dye-works *Leopold Casella & Co.* After the foundation of the *GSH*, a private chemotherapeutical research institute affiliated with the *IET*, chemists from the *GSH* cooperated extensively with their colleagues at *Farbwerke Höchst* and *Casella & Co.* Some *GSH* chemists were even partly paid by the industry, or chemists from the *Speyer House* worked temporarily at the industrial plants. The companies also provided chemical compounds. Arthur Weinberg, together with his brother owner of *Casella & Co.,* was a member of the

15 Paul Ehrlich to *BASF*, 15 Nov. 1898, RAC PEC Box 4.

16 See the request for the patent specification 30 A 189110, Paul Ehrlich to the *Imperial Patent Office*, 29 Nov. 1907, Copybook XXIII, RAC PEC, Box 25; the request for patent publications about a procedure for an arsenic-acid preparation of Wilhelm Adler; and about a procedure for the production of a secondary Diazo dyestuff of the *Anilinfabrication AG* in Berlin, Paul Ehrlich to the *Imperial Patent Office*, 9 July 1909, RAC PEC, Copybook XXVI, Box 25.

17 See his letter to the *Gesellschaft Chemische Industrie in Basel* (*CiBa*) in February 1903 asking for batches with reference to the *Färberzeitung* (Dyer journal) and the patents mentioned therein.

board of trustees of the *Speyer Funding Society*. Weinberg also became a personal friend of Ehrlich, and helped to close financial gaps in the institute's budget. In return, the *GSH* tested the therapeutic impact and staining capabilities of chemical compounds and made new research results available to *Casella & Co.* and *Farbwerke Höchst*.

Particularly around 1900, when no chemist was yet working at the institute Ehrlich directed, he cooperated with chemists he was close with, as well as with his nephews, the chemists Georg Pinkus and Franz Sachs, both of whom were working as assistants at Emil Fischer's laboratory. Ehrlich regularly sent written instructions to his nephew Franz Sachs urging him to read patent specifications or to assess and modify experiments.[18] In some cases these experiments produced successful results. In such cases Ehrlich urged Sachs to finish the patent specifications.[19]

Mentions of patents are regularly found among Ehrlich's notes and instructions to his staff members. On the one hand, Ehrlich told them about certain patents they were supposed to read and assess.[20] For example, between September 1912 and the beginning of 1913 we find instructions on the completion of patents (Block No. 5037) and on applications for patents (Block Nos. 5143, 5169), a reminder that *Farbwerke Höchst* was supposed to extend the patents on arsphenamine with metal compounds (Block No. 5376), and a reminder that the Maynerack patent

18 For example he asked whether Franz Sachs could pass by the *Imperial Patent Office* to inspect the patent application for water-soluble and unstained fuchsin preparations: Paul Ehrlich to Franz Sachs, 12 May 1905, RAC PEC Copybook XVII, Box 24; request, to inspect the patent for *Farbwerke Höchst's* akridiniume dyestuff, October 1902, RAC PEC, Box 20.

19 For the correspondence between Franz Sachs und Paul Ehrlich from the late 1890s to 1903/1904, see the archive of *Leo Baeck Institute*, New York.

20 In April 1909 he requested copies of patents mentioned in the *Chemikerzeitung* held by the companies *Soc. Commerciale du Carbure de Calcium*, *Farbwerke Höchst*, *Kalle Biebrich*, and *Ludwig Wilhelm Gans* as well as a patent on medical yeast for injections held by the Italian life scientist Maurizio Ascoli, RAC PEC Box 25, Copybook XXVI.

should be discussed with Alfred Bertheim and Paul Karrer, two of Ehrlich's co-workers,[21] as well as a note saying that *Farbwerke Höchst* was supposed to deliver arsenic sulfide, to »mate [it with the] mixed compounds,« so that they would be able to check the possibility of having it patented.[22]

If the experiments at the *GSH* produced promising results, he urged his staff members to write a patent specification. For example, Ludwig Benda, a staff member of the *GSH* who was working on the premises of the *Casella* company,[23] informed Paul Ehrlich in May 1910 regarding Trypaflavin and Diaminokridin that the application for a patent had passed the preliminary tests and would be handed in soon.[24] Benda continued that Arthur von Weinberg had not yet applied for trademark protection because he was of the opinion that this would be done by *Farbwerke Höchst*. On another occasion, Paul Ehrlich sent a patent specification to Ludwig Benda, requesting him to »produce small samples of the two described azo dyes of naphtion acid and H acid« to test their capabilities[25] of staining tissue and sterilizing pathogens. Similarly, Alfred Bertheim was instructed to finish the recipe for the production of urea, so that it could be sent to the *Vereinigte Chemische Werke* in Charlottenburg as soon as possible.[26]

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21 See the note for a meeting with Robert Kahn and Alfred Bertheim concerning the application of some reduction preparations to be saved as soon as possible, March 1907, RAC PEC, Box 28.

22 All notes and instructions (so-called blocs/pads) between mid-September 1912 and end of February 1913, RAC PEC Box 20.

23 Benda's salary was paid partly by the *GSH* and partly by *Casella & Co*.

24 Ludwig Benda (letterhead *Casella & Co*.) to Paul Ehrlich, 26 May 1910, RAC PEC Box 1 Folder 4.

25 Another example: Ehrlich informed Benda (2 April 1909) that the dyestuff Tryparosan had been tested in Heidelberg successfully, RAC PEC Box 1 Folder 4.

26 Likewise Bertheim should prepare the patent for urea, see Paul Ehrlich to Richard Kahn (Head of Chemical Department), 12 Nov. 1906, RAC PEC Box 27.

Instructions on patents indicate the close cooperation between science and industry. The *Vereinigte Chemische Werke*, for example, agreed to extend experiments on atoxyl. They also advised being wary of imitators and recommended securing patents.[27] The mention of patents in the instructions shows the significance of patents at and for the *GSH*. As soon as there were any prospects of successful commercial exploitation, an application was made for a patent on the newly developed substance. This is not very surprising if one looks at the legal constitution of the *GSH*.

Initial capital for the *GSH* had been donated by banker's widow, Franziska Speyer, in memory of her husband's death. The founding contract from 1906 provided that the board of trustees of her foundation, the *Georg und Franziska Speyer'sche Studien Stiftung* would have the right to depose of all inventions made at the *GSH*. The director transferred the rights to all arsenic compounds suitable to fighting parasitic diseases first to the *Vereinigte Chemische Werke* and later to *Farbwerke Höchst* and *Casella & Co*. The industrial partner was responsible for production and distribution. The agreement stipulated that the industrial cooperation partner officially apply for patents on any new developments and methods. The research was to be funded in the main by the foundation's endowment capital and, in addition, indirectly by the cooperation partner who was to provide manpower, material, and laboratory space. The industrial partner would then take over commercial exploitation and the *GSH* as well as its staff members were to receive a contractually fixed share of the net profits.[28] Thus, the *Speyer House* and its director were interested in applying for as many patents as possible.

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27 *Vereinigte Chemische Werke Charlottenburg* to Paul Ehrlich, 5 Sep. 1906, RAC 650.3 Eh 89 Martha Marquardt Collection, Box 2.

28 The *GSH* was supposed to receive thirty percent. After the expiration of the 15-year contract, both contracting parties were free to commercialize the products or preparations. The patents were the property of both parties, but the trademark was owned by the *Vereinigte Chemische Werke*. RAC PEC Box 1 Folder 45.

The organization of the application process was based on the division of labor. The technical details of the application were outlined by *GSH* scientists and the application was then handed over to the industrial cooperation partner. The company's legal department and research and development department completed the application by adapting it to the formalized structure defined by the *Imperial Patent Office*. Unclear issues of content were clarified in letters between the legal department or the research and development department and members of the *GSH*; otherwise, the *GSH* made no official appearance. The correspondence was solely between the company and the *Patent Office*. Civil servants of the *Imperial Patent Office* checked the patent application as to originality. If nobody entered an objection within a certain period of time, the patent became valid.[29]

Already shortly after synthesizing it, Ehrlich applied for a patent on arsphenamine in June 1909 (Ehrlich and Bertheim 1910). In the course of the following year, the preparation proved to be efficient in the treatment of syphilis, and in December 1910 it was marketed by *Farbwerke Höchst* under the label »Salvarsan.« Profits from *Salvarsan* sales were enormous and totaled in the millions, because *Farbwerke Höchst* also patented the preparation in other countries and secured a worldwide monopoly. The *GSH*, Paul Ehrlich, and those staff members who had contributed to developing the preparation also benefitted financially, as they were entitled to a percentage of the net profits. The importance of patents for the *GSH* became obvious when the income from *Salvarsan* decreased rapidly during the First World War. When at the beginning of the war the export of *Salvarsan* was banned, the chemical-pharmaceutical industry in North America, Britain, France, and Japan ignored the patent and started their own production of the drug. Consequently, the director

29 See Fleischer 1984; Seckelmann 2006. The practical process is described in Gaudillière 2008b using the example of *Schering*.

of the *GSH* lamented to a member of the board of trustees that no money was coming in from foreign patents.[30]

For *Farbwerke Höchst*, the contractual cooperation with scientists like Paul Ehrlich became a model for the organization of research and development.[31] Whereas *Farbwerke Bayer* established their own research and development department, *Farbwerke Höchst* supported independent scientists whose developments they marketed.[32]

Although the application for a patent provides more clarity regarding the legal and commercial exploitation of an invention, there was still a potential for conflicts. Ehrlich started to argue with the *Vereinigte Chemische Werke* after their business relationship came to an end.

> Now I intend to have some patent fun with my opponents, those from Charlottenburg, who gave me the run-around and tried to fool us by prematurely launching our acetylate oxyl. They have had two compounds patented whose absolutely easy production I suggested to them two years ago. As my experts tell me, legally the case is absolutely clear, and I think we will be able to have the patents transferred to ourselves.[33]

Alongside questions about the exploitation of inventions were many more open questions. The next section will explore the broad potential

30 Paul Ehrlich to Ludwig Darmstädter, 27 Oct. 1914, RAC PEC Box 1 Folder 8.

31 Christina Ratmoko (2010) describes a similar example of this form of cooperation in the 1920s and 1930s between Leopold Ruzicka and the Swiss company *Chemische Industrie Basel* (*CiBa*) that led to the successful development and marketing of sex hormones. For the cooperation between scientific/clinical experts and the pharmaceutical industry in the North American context, see Rasmussen 2005.

32 See Wimmer 1994. Until the early 1920s, the research and development department at *Farbwerke Höchst* acted more like a mediator between the legal department and the scientists.

33 Paul Ehrlich to Lord Moulton, end of November/early December 1908, RAC PEC Copybook XXV, Box 25.

of conflicts by again taking up the discussion of Friedmann's remedy for tuberculosis.

Economic capital and public trust. The patenting of Friedmann's tuberculosis remedy

In March 1913, the President of the *Imperial Health Office* gave a detailed report to the State Secretary of the Interior on Friedmann's tuberculosis remedy. He stated that Max Piorkowski, on Friedmann's behalf, had bred a strain of so-called turtle tuberculosis bacteria already in 1903 from the lungs of a turtle that had died of tuberculosis. The bacterial culture seemed to be similar to bovine or human tuberculosis pathogens. Guinea pigs that had been injected with this culture showed symptoms of tuberculosis, but did not die of it. Since resuming the experiments, Friedmann had been very secretive and had not left the culture he had bred with anybody else. However the attempt to have the remedy produced by *Farbwerke Höchst* failed in 1905. Staff members from the company's biological department had come to the conclusion that the remedy had no therapeutic effect whatsoever. In the following years, Friedmann continued work on the remedy, until in 1912 he believed he had achieved a breakthrough.[34]

This remedy was not at all a curiosity. Since Edward Jenner had propagated vaccination with cowpox lymph as a preventive measure against smallpox at the end of the 18th century, there had been repeated attempts to fight other diseases in this way. In the 1880s, Louis Pasteur and members of his staff had succeeded in developing vaccines against chicken pox, cholera, anthrax, and rabies from attenuated bacteria cultures, and in 1890 Robert Koch had made an attempt to develop a rem-

34 See President of the *Imperial Health Office* to the State Secretary of the Interior, 22 March 1913. Report concerning Friedmann's remedy against tuberculosis. Report and evaluation of the therapeutic results and their historical development (hereafter report concerning Friedmann's remedy), Geheimes Staatsarchiv Preußischer Kulturbesitz (Prussian Secret State Archives), 1. Hauptabteilung, Rep. 76 VIII B, Nr. 4176 (hereafter GStA PK 4176); Werner 2002; Hüntelmann 2008.

edy for tuberculosis, called tuberculin, which was based on the same principle (Porter 1997; Bynum et al. 2006). Since the mid-1890s, a number of sera and vaccines against human or animal diseases had been developed and marketed.

Friedmann's tuberculosis remedy was similar as regards production and composition to these organic pharmaceuticals, such as vaccines against typhus and cholera, which were based on modified bacteria cultures. What made Friedmann's tuberculosis remedy special was that attenuated living cultures (that were supposed to be avirulent) were injected, and critics worried that possibly the bacteria culture might regain its original virulence, thus becoming a danger for the patient.[35]

In July 1911, Friedmann applied for a patent for his remedy, or rather for his method. According to the *Imperial Health Office*, his application was very general and vague. Friedmann had not restricted his patent to »turtle bacteria« but had formulated his claims as broadly as possible, speaking generally of »tuberculosis bacteria and other acid-resistant bacteria.« The virulence of the bacteria cultures was supposed to be attenuated by means of continued inoculation in an artificial culture medium.[36]

> Somewhat vaguely he stated that bacteria, which after longer periods (about 8-12 months) in the bodies of animal species related to humans […] and extracted again, will have a considerably increased protective and healing value.[37]

After further processing, the tuberculosis cultures would then be used in the form of an emulsion or a suspension that had to be injected. The

35 See the President of the *Imperial Health Office* to the State Secretary of the Interior, 22 March 1913. Report concerning Friedmann's remedy. GStA PK 4176.

36 Ibid.; Patent application of 19 July 1911, displayed in public on 14 Nov. 1912, objection to be entered by 13 Jan. 1913, Patent No. F 32742; Piorkowski 1913.

37 See the President of the *Imperial Health Office* to the State Secretary of the Interior, 22 March 1913. Report concerning Friedmann's remedy. GStA PK 4176.

patent was supposed to include not only living, but also dead bacteria. Friedmann's patent should cover the cultures and their further uses which, as the President of the *Imperial Health Office* remarked, would also concern pharmaceuticals such as tuberculin.[38]

The *Health Office* was particularly critical towards a method that was supposed to use living avirulent tuberculosis pathogens. This method, the office argued, bore the danger that a transfer of virulent bacteria could not be avoided, especially because no preservative, such as carbolic acid which would kill adverse bacteria, was added. This danger appeared serious as Friedmann had not documented any test series with animals and clinical trials had only been conducted regarding one certain method which was complicated and difficult to comprehend and evaluate.[39]

The application for a patent and the comments by the President of the *Imperial Health Office* illustrate the difficulties regarding applications for patents on remedies, especially those of biological origin. The patent was not meant for an individual end product, but for methods of using tuberculosis bacteria as a basis for the production of remedies. Friedmann had extended the description of his method so far that his claim covered methods using attenuated, dead, or living tuberculosis pathogens. Furthermore, his application included the modification of pathogens by passaging them through animals and the use of intermediate products such as the cultures themselves. Finally, it included methods such as processing tuberculosis pathogens into emulsions or suspensions to be injected, or creams for external use (inunction). In short, his patent application included every possible known method of developing a tuberculosis remedy on the basis of biological and organic substances. This would have secured Friedmann a legal monopoly on the production of

38 Ibid.; Patent of 19 July 1911, Patent No. F 32742.

39 See the President of the *Imperial Health Office* to the State Secretary of the Interior, 22 March 1913. Report concerning Friedmann's remedy. GStA PK 4176. Concerning the difficult and complex application process and the controversial human experiments see Hüntelmann 2008.

these biologicals. Thus it is no surprise that objections were raised to his application.

Max Piorkowski, who had cultivated the turtle tuberculosis bacteria on Friedmann's behalf a decade earlier, also raised objections to the latter's patent application. His justification mixed personal reasons with those of public interest. Piorkowski referred to patent laws that excluded pharmaceuticals from patent protection. However, the status of tuberculosis pathogens as a remedy was unclear. On the one hand, he said, living bacteria were of immunizing nature even if they were unprocessed; on the other hand they were not a priori a protective and healing substance. The preliminary examiner on behalf of the patent office had objected that Friedman's claim to a method of producing protective and healing substances to fight tuberculosis was not new, but was already in general use. Piorkowski criticized the application for being so complex and extensive »that a monopoly for the breeding of tuberculosis bacilluses would be granted and that in the future it would be impossible for any researcher to further fructify this branch of bacteriology« (Piorkowski 1913).[40] The only new thing was the tubercle lesions within the turtle, and these had developed naturally and had only coincidentally got into Friedmann's hands. If anybody, it was Piorkowski who was entitled to a patent, as it had been he who had bred the turtle tuberculosis pathogen (Piorkowski 1913).

With his extensive patent application Friedmann had gone beyond the pale in several respects. His contemporaries and colleagues gained the impression that he wanted to monopolize organic preparations based on bacteria for tuberculosis treatment (Möller 1913). This impression was exacerbated by what the scientific community saw as Friedmann's promotion efforts. The presentation of his remedy to the medical community was accompanied by a press campaign which, in the opinion of his

40 Likewise, A. Möller (1913) criticized Friedmann for obviously wanting to monopolize the treatment of tuberculosis with bacterial preparations.

contemporaries, had been initiated by Friedmann.[41] His expert colleagues objected to his offensive manner of marketing the remedy, which corresponded to the extensive patent and the assumed monopolization of bacteria preparations. If advertising a remedy was a taboo among physicians, a press campaign was considered a violation of physicians' morals.[42] In contrast to his extensive patent application he had been very secretive about the production method and the composition of his remedy so that his colleagues accused him of quackery and of merchandising a secret remedy. The suspicion that this press campaign only served considerations of private profit made an even more disastrous impact, as Friedmann publicly proclaimed himself an altruist and claimed that he had no intention of making profits from the remedy. At the same time, he severely criticized his critics' economic interests. Friedmann assumed that they opposed his remedy simply because they were only interested in making money with useless therapeutics and sanatoriums (Werner 2002; Hüntelmann 2008). Whatever reasons were in the end decisive, the patent application was rejected.

Wrapping up—the relation between patent law, priority, property, and trust in a broader context

Friedmann's tuberculosis remedy illustrates the ambivalence of patenting pharmaceuticals in the German Empire. And the examples of the *IET* and the *GSH* demonstrate the role and the importance of patents and patent law within the research process in the first decade after 1900. In both case studies, economic interests were closely connected to notions such as trust, intellectual property rights, and scientific priority.

Patents were supposed to reward the inventor for his work and to protect his inventions and developments from imitators; to protect intellec-

41 Confidential report by Otto Kiliani to the Imperial German Consul General, Horst Falcke, 5 Oct. 1913. GStA PK, Nr. 4176.

42 Regarding the official ostracism of advertisements in the medical field and the manifold attempts to undermine professional ethical norms see Binder 2000.

tual property. Although patent law was supposed to provide more clarity in respect to the legal and commercial exploitation of an invention, this does not mean that the question of priority as concerns inventions had been clarified. The objection by Max Piorkowski and others show that the development of a pharmaceutical was also connected to questions of originality, the rights of first invention, and related quarrels about priority.

Securing exploitation rights by way of patent protection is based on a different strategy than claiming priority. For example, whereas Behring published the results of his work as early as possible to claim priority for a development, in applying for a patent there was no necessity for publication. On the contrary, this would have been an obstacle. If earlier we found hints among Ehrlich's instructions and correspondence that results should be published as soon as possible to preempt competing teams, their number declines to the same degree as the number of demands for patent applications increases. In the latter case, publication was less advisable than keeping confidentiality until the patent application was submitted. Accordingly, Ehrlich published the results on the synthesis of arsphenamine only one year after the patent application was submitted. The criticism of Friedmann's tuberculosis remedy was based primarily on the fact that he would not tell about the method and the composition of the remedy as long as the application procedure was ongoing.

Whereas priority quarrels took place in journals and in front of the expert public, it was lawyers, producers and inventors who were involved in patents quarrels. After all, the priority quarrel happened ex post, i. e. the two inventors derived their claims from earlier publications to justify their claim to priority, whereas the patent quarrel happened before patent protection was decided.

Pharmaceuticals were admittedly excluded from patent protection in the German Empire, but both examples nevertheless deal with the patenting of pharmaceuticals. The patenting applications for chemical intermediate products necessary to produce pharmaceutical end products illustrate how this exemption was circumvented. Friedmann tried to avoid patent

law by patenting all different means of processing bacteria cultures to protect his prospective tuberculosis remedy.

But this practice raised questions about the status of biological materials and chemical preparations. Were, for instance, organic preparations and bacteria cultures, minerals and vegetable raw materials »normal« commodities or pharmaceuticals? Bacteria were supposed to become both a remedy and a public good, making it difficult to patent (Gabriel 2009; Cassier 2009; Bud 2009).

The state was another actor in the patenting of pharmaceuticals. The *Imperial Patent Office* and the public health administration were key figures. While the patent office was generally the executive body that examined applications and granted or denied patents, public health authorities were involved especially (and exclusively) in the patenting of pharmaceuticals. The state had to balance several bio-political aims. In the case of Friedmann's tuberculosis remedy, bacteria cultures were considered to be a public health risk *and* at the same time a prospective remedy for a widespread infectious disease. For this reason, information about the remedy was a sine qua non and the *Imperial Health Office* discussed and evaluated any related public health risk that might result from its use. The development of an effective and harmless remedy could only be guaranteed by its critical examination and confirmation by the scientific community.

In order to combat probable public health risk, the state had a bio-political interest in the development of new remedies. Patent protection provided producers with an opportunity to inform the public about the drugs they invented while at the same time protecting them. But the simultaneity of give and take was precarious and a matter of trust. The development of a remedy that would have been well received by the medical community required the publication of information about the invention in advance, but this made the reproduction of the invention possible. For this reason, Friedmann hesitated to publish information about his remedy until he had applied for a patent. However, due to a lack of information, the public and the medical community were skeptical about the remedy. The discussion of Friedmann's tuberculosis remedy was linked to the tensions between public trust and secret remedies,

between tradition and progress. Friedmann's failed patenting process illustrates the significance of public trust and transparency, as well as the necessary reciprocity of trust.

Trust also played an important role in the relationship between scientists doing experimental research, as in the example of Ehrlich and the industry. The cooperation between the chemical industry and science had changed by the end of the 19th century. The chemical industry became enormously dynamic in this period and the realm of industrial research had been established through patent law. Beyond this, chemical companies provided scientists with material and in return, the latter transferred the rights to useful results to the industry. In this way, both parties benefited from the cooperation and the exchange of knowledge. The industry paid in advance for the scientists' ever more costly experiments; in return, new developments were patented and exploited commercially by the industry. Patents, to compensate for unreliable returns at an indeterminate future date, provided a possibility for enterprises to legitimate short-term expenses and investments. According to how the relationship is organized, the inventor receives a contractually fixed share of the profits; the industry appears to the public as the beneficiary, and the life-scientist is spared a conflict with medical ethos. However, for this contractual relationship too, trust plays an important role for a fruitful cooperation. Providing financial and other support for the scientists is a credit of trust, connected to the expectation and the promise that at some time in the future the scientist will develop a market-ready product. Against this background, as shown by the example of the *IET* laboratories, patents became an important driving force for inventions.

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