BJHS **49**(4): 577–600, December 2016.
doi:10.1017/S0007087416001138

Pharmaceutical patenting and the transformation of American medical ethics

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Abstract. The attitudes of physicians and drug manufacturers in the US toward patenting pharmaceuticals changed dramatically from the mid-nineteenth century to the mid-twentieth. Formerly, physicians and reputable manufacturers argued that pharmaceutical patents prioritized profit over the advancement of medical science. Reputable manufactures refused to patent their goods and most physicians shunned patented products. However, moving into the early twentieth century, physicians and drug manufacturers grew increasingly comfortable with the idea of pharmaceutical patents. In 1912, for example, the American Medical Association dropped the prohibition on physicians holding medical patents. Shifts in wider patenting cultures therefore transformed the ethical sensibilities of physicians.

Introduction

In 1937 Morris Fishbein, the editor of the *Journal of the American Medical Association*, pondered the difficult question of medical patents. In an editorial published in the journal that year, Fishbein suggested that recent efforts by academic institutions to patent new drugs were in line with the ideals of benevolent medicine because they promoted the common good; pointing to the patenting of insulin over a decade earlier, he noted that 'the act of securing a patent is not in itself unethical' and argued that patenting provided a number of benefits to the public, including the ability of patent holders to ensure manufacturing standards among their licensees. In doing so, Fishbein was reacting to what he considered an outdated ethical prohibition on drug patenting within the medical community. Yet he also recognized that medical patenting led to numerous problems, including legal disputes among inventors and the 'vicious and sometimes malicious criticism of discoverers and of universities'. Perhaps most worrisome, he suggested, was the fact that patenting encouraged the development of a 'competitive spirit' that threatened 'to destroy entirely the type of cooperation in science which is responsible for much of our current progress'.[1]

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Portions of this chapter were presented at the Department of the History of Science at the University of Wisconsin–Madison, and at the Department of the History of Medicine at Johns Hopkins University. I would like to thank the participants in both discussions for their insights. I would also like to thank James F. Stark for the opportunity to contribute to this collection and the two anonymous reviewers for their helpful comments.

1 Morris Fishbein, 'Medical patents', *Journal of the American Medical Association* (1937), 109, pp. 1539–1543.

Fishbein's editorial was one small part of a broad transformation in orthodox medical thought about the ethics of drug patenting that has taken place over roughly the past two centuries. Drawing on my own previous scholarship and the work of Robert Baker, among others, in this paper I argue that during most of the nineteenth century, patents on pharmaceuticals were considered an unethical form of monopoly both by the medical community and by reputable drug manufacturers. As such, patented drugs were considered a form of quackery and roundly denounced by orthodox physicians. By the first decade of the twentieth century, however, the ethical status of pharmaceutical patents had been reconceptualized; in general, physicians now considered them an important part of the drug development process, although suspicions remained. Drug patents continued to be troubling in part because of their apparent connection to high drug prices; it was also considered unethical for physicians to directly hold patents, since doing so was assumed to threaten their commitment to science through the temptations of the market. Still, the change is unmistakable: by the first decade of the new century, drug patenting had clearly begun to recede as a topic of ethical concern within the medical community.

The ethical status of pharmaceutical patenting underwent further changes during the first decades of the twentieth century as physicians and academic scientists turned toward the use of patents to protect the public from what they considered unreliable or unscrupulous manufacturers. At the same time, both academic scientists and physicians established close working relationships with drug manufacturers as a part of their broader efforts to advance medical science. Yet, as Fishbein's editorial suggests, significant concerns about the ethics of patenting remained, in part due to the potential for patenting to foster competition among scientists. Finally, the erosion of concern about patenting accelerated in the decades immediately following the Second World War as physicians involved in research worked increasingly closely with the pharmaceutical industry. By the early 1960s the orthodox medical community had fully accepted pharmaceutical patenting as a normal and largely unproblematic part of how new drugs were developed and commercialized. Indeed, leaders in organized medicine had a tendency to defend the rights of manufacturers to patent their goods due to the assumption that patenting was necessary to encourage innovation in the industry. Ethical deliberation instead focused on other areas, such as the question of informed consent in medical research. What ethicist Albert R. Jonsen has called 'the birth of bioethics' in the 1960s and early 1970s thus took place in part through the distancing of physician concern from traditional questions about the relationship between science and monopoly.[2]

Background: pharmaceutical patents and American medical ethics during the nineteenth century

The attitudes of orthodox physicians toward patenting in the early nineteenth-century United States grew out of their broader ideas about the nature of medical science and

2 Albert R. Jonsen, *The Birth of Bioethics*, New York: Oxford University Press, 1998.

https://doi.org/10.1017/S0007087416001138 Published online by Cambridge University Press

what it meant to be a gentleman. As self-described members of what they sometimes called the 'Republic of Science', orthodox physicians believed that their efforts to advance medical knowledge were part of a larger collaborative project dedicated to the common good, one that proceeded slowly and methodically over time. They described medical science as a benevolent process based on personal sacrifice, proper character and conduct, and the sharing of information among peers. Commercialism was thus juxtaposed to the supposedly gentlemanly character of the physician, and the open circulation of knowledge about healing goods within the medical community was central both to the conduct of medical science and to the rhetorical basis of the medical community as a whole. As one physician put it in 1823, 'facts when once ascertained, and experiments when once made … are no longer the property of the individual but of the republic of science at large'.[3]

As a result, there was a fundamental equation between monopoly and quackery within orthodox medical thought. Drawing on a long tradition of hostility to nostrum vendors among English physicians, orthodox physicians in the young United States denounced quackery for what they considered to be its unscientific and predatory nature. According to this perspective, one of the defining features of quackery was its willingness to monopolize medical knowledge for selfish reasons, including through the use of patents, secrecy, and other means that seemed to interfere with the collaborative nature of medical science. The use of secret ingredients was loudly denounced because it interfered with the ability of physicians to know about the effects of the product in question; secrecy was also seen as a means of duping the public into purchasing worthless or even dangerous goods. Patents were also assumed to prevent physicians from investigating and using new products as they saw fit, inhibiting the progress of medical science and threatening the well-being of patients. Of course, pharmaceutical patenting was relatively rare in the early decades of the nineteenth century: naturally occurring substances such as minerals, chemicals and botanicals were generally assumed to not be patentable, and while formulas for medicinal cordials, elixirs and similar products could be patented, most manufacturers who wanted to protect their interests preferred to keep the ingredients of their products secret. For most physicians, however, there was little difference between patenting and secrecy when it came to drugs. Both were considered unethical forms of selfish monopoly and were clearly and unequivocally juxtaposed to medical science. Indeed, it was generally assumed that

3 'Physiology of circulation', *Medico-chirurgical Review, and Journal of Medical Science*, 1 June 1823, p. 38, quoted in Joseph M. Gabriel, *Medical Monopoly: Intellectual Property Rights and the Origins of the Modern Pharmaceutical Industry*, Chicago: The University of Chicago Press, 2014, p. 25. The first section of this paper is partially a summary of some of the arguments I made in *Medical Monopoly*; I have included this material for those readers who are unaware of my earlier work and because it is essential to the development of the argument later in the paper. On the relationship between medical science and physician character in the nineteenth-century United States see also Robert Baker, *Before Bioethics: A History of American Medical Ethics from the Colonial Period to the Bioethics Revolution*, New York: Oxford University Press, 2013; Stephanie B. Browner, *Profound Science and Elegant Literature: Imagining Doctors in Nineteenth-Century America*, Philadelphia: University of Pennsylvania Press, 2005, pp. 15–38; John Harley Warner, *The Therapeutic Perspective: Medical Practice, Knowledge, and Identity in America, 1820–1885*, Princeton, NJ: Princeton University Press, 1997.

patented remedies and quack nostrums were the same thing, and that patents should not be given out to such impositions at all. As one physician put it shortly after the Civil War,

> to monopolize medical preparations [through the use of patents or secrecy] is to grow fat on human misery. It is a part of the materialistic tendency of our age, and of the single eye we are taught by pulpit and press to have to money as the chief end of man.[4]

The prohibition on monopoly, and on medical patenting specifically, was formally incorporated into codes of ethics promulgated by the medical community in the first half of the nineteenth century. These codes typically included bans on recommending or dealing in nostrums, which included both patented goods and goods made with secret ingredients, and they sometimes included explicit bans on holding patents or prescribing patented goods; as the 1823 System of Ethics of the Medical Society of the State of New York put it, any physician or surgeon who 'practices with nostrums, secret medicines, or patent remedies, is guilty of quackery'.[5] The prohibition on patenting was also formally included in the first Code of Ethics promulgated by the American Medical Association (AMA) after it was established in 1847. The Code stated:

> Equally derogatory to professional character is it, for a physician to hold a patent for any surgical instrument, or medicine; or to dispense a secret nostrum, whether it be the composition or exclusive property of himself, or of others. For, if such nostrum be of real efficacy, any concealment regarding it is inconsistent with beneficence and professional liberality; and if mystery alone give it value and importance, such craft implies either disgraceful ignorance, or fraudulent avarice. It is also reprehensible for physicians to give certificates attesting the efficacy of patent or secret medicines, or in any way to promote the use of them.[6]

The AMA's prohibition on both holding patents and dispensing nostrums – which, despite the awkward phrasing, included patented medicines – was well within the mainstream of orthodox medical thought at the time. It was also highly influential, and medical societies across the country adopted or modified the language of the AMA's Code in their own local and state society's codes. Despite occasional controversies, an explicit prohibition on holding patents and dispensing patented goods was often a part of these codes and, in general, organized medicine in the years before the Civil

4 Anon., 'Patents in medicine and surgery,' *Medical and Surgical Reporter* (1867) 17, pp. 190–191, quoted in Joseph M. Gabriel, 'A thing patented is a thing divulged: Francis E. Stewart, George S. Davis, and the legitimization of intellectual property rights in pharmaceutical manufacturing, 1879–1911', *Journal of the History of Medicine and Allied Sciences* (2009), 64, pp. 135–172, 144.

5 Quoted in Baker, op. cit. (3), p. 94.

6 'Code of Medical Ethics', *Proceedings of the National Medical Conventions* (1847), pp. 91–106. On the 1847 code and its implications see Baker, op. cit. (3); Robert B. Baker, Arthur L. Caplan, Linda L. Emanuel and Stephen R. Latham (eds.), *The American Medical Ethics Revolution: How the AMA's Code of Ethics Has Transformed Physicians' Relationships to Patients, Professionals, and Society*, Baltimore: Johns Hopkins University Press, 1999; Robert Baker (ed.), *The Codification of Medical Morality*, vol. 2: *Anglo-American Medical Ethics and Medical Jurisprudence in the Nineteenth Century* (Boston: Kluwer Academic Publishers, 1993); John S. Haller Jr, *American Medicine in Transition, 1840–1910* (Champaign: University of Illinois Press, 1981), pp. 234–279.

War positioned itself as hostile to monopoly rights in drug manufacturing.[7] Commentators on medical ethics at the time also discussed the prohibition on medical patenting as an important part of the ethical framework of orthodox medicine. The physician Worthington Hooker, for example, described the prohibition on medical patents as reflecting 'a very just distinction between inventions in medicine and all other inventions', since 'medicine has to do with such important interests as health and life' and 'the principles of benevolence demand, that any invention or discovery in this art, should be promulgated without any hindrance'.[8]

It is not completely clear how effective these codes were at regulating physician behaviour. Many physicians did, in fact, prescribe nostrums – whether made from secret ingredients or, occasionally, patented products – because they were convenient and popular with their patients. Occasionally physicians were ostracized from the medical community for doing so, but in general the critique of monopoly was directed against manufacturers of 'secret or patent nostrums' who were accused of flooding the market with 'poisonous trash', undermining medical science, and preying on a gullible public.[9] Most manufacturers ignored the criticism, but the vociferous critique had an important effect. In the two decades immediately before the Civil War, a wing of the pharmaceutical industry self-consciously and explicitly adopted the framework of orthodox medical ethics to guide their manufacturing and advertising practices. These so-called 'ethical' manufacturers rejected the use of both patents and secret ingredients as unethical forms of monopoly; they were also careful not to advertise to the public and generally refrained from commercially introducing new goods until those goods had been thoroughly vetted by the medical community – after all, doing so seemed to prioritize commercial self-interest over the advancement of medical science. Pharmaceutical manufacturers such as E.R. Squibb & Sons (founded in 1858) and Parke, Davis, & Company (Parke-Davis, founded in 1866) thus combined a commitment to what they considered ethical market behaviour with a dedication to promoting what they considered to be scientific medicine. In doing so, they both exploited and helped to further an important market niche that was structured in part through the ethical norms of the orthodox medical community. The rejection of pharmaceutical patenting and other monopolistic practices was an essential part of this market strategy since it allowed these companies to promote their goods to the medical community without running afoul of the critique of quackery. There was some ambiguity over the question whether patents on manufacturing methods were legitimate or not, but patents on products themselves were clearly out of bounds. Parke-Davis, for example, acquired a

7 For example, *Proceedings of the State Medical Convention of the Medical Society of the State of North Carolina* (1849), pp. 9, 12. Baker, op. cit. (3), pp. 182–183, briefly discusses tensions between the Ohio and Massachusetts medical societies and the AMA over patenting; see also Haller, op. cit. (6), pp. 240–242.

8 Worthington Hooker, *Physician and Patient; or, a Practical View of the Mutual Duties, Relations and Interests of the Medical Profession and the Community*, New York: Baker and Scribner, 1849, p. 89.

9 'Nostrum venders', *Chicago Medical Journal* (February 1859), p. 127; 'Progress of medical science', *Medical Times and Gazette*, 13 March 1852, p. 270. On so-called patent medicines, the standard work is still James Harvey Young, *The Toadstool Millionaires: A Social History of Patent Medicines in America before Federal Regulation*, Princeton, NJ: Princeton University Press, 1961.

patent on a method of sugar-coating pills in 1880 without attracting negative attention, but the company also carefully refrained from keeping the ingredients of its products secret or acquiring patents on new products that it introduced, including an important line of standardized fluid extracts developed by the chemist Albert B. Lyons and commercially introduced in the early 1880s. To do so would have been to embrace quackery and risk the wrath of the medical community.[10]

The so-called ethical wing of the drug industry grew rapidly in the decades following the Civil War, fuelled in part by scientific and technological innovation within the industry. In addition to its line of standardized fluid extracts, for example, Parke-Davis sponsored botanical expeditions to California, South America and other areas to search for new botanical drugs that could be commercially introduced.[11] However, following the Civil War the rejection of monopoly proved increasingly problematic for so-called ethical manufacturers. Companies such as Parke-Davis faced growing competition from a range of new competitors that could not easily be dismissed as quacks. Chemical manufacturers that typically produced goods for other markets occasionally introduced new medicinal products; given that these companies did not primarily consider themselves to be aligned with the orthodox medical community, they cared little for orthodox medical ethics, marketed their products directly to the public, and were willing to use patents to protect their products. A growing number of small speciality manufacturers also introduced a range of therapeutic products to the market, some of which were patented as well. Most important, however, was the fact that beginning in the 1880s foreign drug manufacturers began to introduce powerful new products based on advanced techniques in synthetic chemistry. Foreign manufacturers were not shy about exploiting the fact that under US law medicines could be patented. Nor did they have concerns about subordinating scientific norms to commercial ones in the same way that so-called ethical manufacturers in the domestic industry did because they were not particularly concerned about being labelled quacks by the American medical community; unlike domestic manufacturers in the so-called ethical wing of the industry, foreign manufacturers did not assume that monopolistic practices could be equated with quackery, and they paid little attention to the criticisms of physicians along these lines. German manufacturers were especially important in this regard, introducing a wave of important new – and patented – products in the later decades of the nineteenth century, including antipyretics such as Phenacetin, Antipyrine and Aspirin.[12] These products were rapidly adopted into medical practice despite the prohibition on prescribing patented goods, in large measure because of their obvious

10 Gabriel, op. cit. (3), pp. 63–69. See also United States patent number 231,236 (1880). On Albert B. Lyons see Jonathan Liebenau, *Medical Science and Medical Industry: The Formation of the American Pharmaceutical Industry*, Baltimore: The Johns Hopkins University Press, 1987, pp. 43–44.

11 On the commercialization of drug plants from California by Parke-Davis see Gabriel, op. cit. (3), pp. 89–91. For an account of another botanical expedition supported by the company see George A. Bender, 'Rough and ready research – 1887 style', *Journal of the History of Medicine and Allied Sciences* (1968), 23, pp. 159–166.

12 Gabriel, op. cit. (3), pp. 78–98, 114–123, 139–145. On the introduction of the German synthetic drugs see also Jan R. McTavish, *Pain & Profits: The History of the Headache and Its Remedies in America*, New Brunswick, NJ: Rutgers University Press, 2004.

therapeutic utility. The equation between monopoly and quackery thus began to fracture under the weight of therapeutic innovation.

The rapidly changing drug market pushed domestic manufacturers to invest significant resources in new product development, but without an effective means of protecting this investment doing so was fraught with risk. As a result, domestic firms quickly found themselves at a distinct market disadvantage because of their inability to protect their investments in research and development. At the same time, the orthodox medical community was confronted with a series of new products that were both clearly effective and also monopolized through the use of patents. Critics within the medical community also began to critique the Code of Ethics as both outdated and stultifying, in part because of what increasingly seemed to be an outdated prohibition on patenting drugs and surgical instruments. Taken together, these trends presented a profound challenge to the ethical framework which understood monopoly and quackery as overlapping categories. In response, a small group of therapeutic reformers, some of whom were affiliated with drug manufacturers such as Parke-Davis, began to argue for the ethical legitimacy of medical patenting. Central to this process was the separation of patenting from secrecy in anti-monopoly rhetoric: reformist physicians, pharmacists and others suggested that patents were in fact the opposite of the use of secret ingredients, in that they promoted the circulation of information about products because the patent law required that details of patents be described and made publicly available; at the same time, reformers argued that patents promoted scientific innovation by allowing drug manufacturers to safely invest resources in the development of new remedies. Finally, they argued that patent law, properly applied, actually worked to suppress the manufacture and sale of quack remedies since, the theory went, those remedies were not actually patentable. As the *Medical and Surgical Reporter* put it in 1896, echoing words of physician and pharmacist Francis E. Stewart, 'A thing patented is a thing divulged. It would seem that it is not a departure from ethics for a physician to patent any medicine whose composition may involve the exercise on his part of invention.'[13]

By the end of the century a significant number of reformers in the medical community had begun to make similar arguments. These reformers suggested that patents expire after a limited amount of time and are therefore not truly a form of monopoly; that patented medicines should be distinguished from medicines made with secret ingredients, the one being ethically and scientifically legitimate and the other being an unethical form of quackery; and – most importantly – that patents might stimulate the 'inventive genius' of chemists or physicians and thereby encourage pharmaceutical innovation. Certainly, not all physicians during this period were persuaded by arguments of these types; many continued to believe that patents on medicines were ethically suspect because, as one

13 Anon., 'Editorial. patents and trade-marks,' *Medical and Surgical Reporter* (1896) 75, p. 341, quoted in Gabriel, op. cit. (3), p. 170. As I argue in *Medical Monopoly*, Francis E. Stewart, who was both a physician and pharmacist and worked closely with Parke-Davis during the 1880s, was one of the most important reformers leading this effort. See Gabriel, op. cit. (3), pp. 133–139, 164–171, 188–194. On the broader rejection of orthodox medical ethics among physicians, of which the embrace of patenting was one part, see also Baker, op. cit. (3); John Harley Warner, 'The 1880s rebellion against the AMA Code of Ethics: "scientific democracy" and the dissolution of orthodoxy', in Baker *et al.*, op. cit. (6), pp. 52–69.

physician put it, all medical knowledge is the 'common property' of the profession, and 'every fact which is discovered in medical science and art must by the finder be thrown into the common treasury'.[14] Yet for a growing number of reformers the critique of patents seemed increasingly antiquated. By the turn of the century, the prohibition on monopoly had significantly eroded under the growing realization that a product might be both monopolized and clinically effective. At the same time, scientific innovation was rhetorically linked to patenting, and to commercialism more broadly, within orthodox medical thought. As one physician put it, 'why should not the ingenuity of the profession be stimulated by the hope of reward in patenting new inventions, the same as in any other department or industry?'[15]

One result of this complex process was that domestic manufacturers in the so-called ethical wing of the industry cautiously turned toward patenting their products. Parke-Davis, for example, introduced a small number of patented drugs in the first decade of the twentieth century, the most important of which was Adrenalin. This caused little controversy; indeed, the medical press barely mentioned the issue, even after the company became embroiled in a messy court case over the patent. This is not surprising. By the first decade of the new century orthodox physicians had come to accept the fact that pharmaceutical patenting was here to stay. Some saw the issue in positive terms, others accepted the fact grudgingly, but by this point virtually no one argued that patents were by definition unethical or that manufacturers should refrain from their use. 'However much we may prefer to use unpatented drugs', noted one observer at the time, 'the fact remains that practically all the modern, synthetic drugs are so patented, and among this number are many remedies in constant, daily use, which could not be dispensed with without the serious crippling of our therapeutic resources.'[16]

As a result, the prohibition on medical patenting seemed to grow increasingly antiquated. In 1912 the prohibition on physicians holding patents was finally dropped from the Principles of Medical Ethics (formerly the Code of Ethics) of the American Medical Association. However, the 1912 Principles also declared it 'unprofessional to receive remuneration from patents for surgical instruments or medicines'.[17] This pointed to a continuation of earlier concerns that the desire to profit was in some important sense oppositional to the pursuit of science: physicians might hold patents as part of

14 L.C. Lane, 'Address of welcome to the American Medical Association', *Journal of the American Medical Association*, 23 June 1894, p. 956.

15 A.C. Simonton, 'Code of revision', *Journal of the American Medical Association*, 5 May 1894, pp. 678–679. For a rejoinder see Nathan S. Davis, 'Proposed revision of the Code of Ethics of the American Medical Association', *Journal of the American Medical Association*, 14 April 1894, p. 557.

16 Lewis A. Conner, writing in 'Report of the Committee on the Pharmacopeia', *Transactions of the Section on Practice of Medicine of the American Medical Association at the Sixteenth Annual Session* (1909), p. 325. On the adrenalin patent dispute between Parke-Davis and H.K. Mulford & Company see Gabriel, op. cit. (3), pp. 230–237; Jon Harkness, 'Dicta on Adrenalin(e): myriad problems with Learned Hand's product-of-nature pronouncements in *Parke-Davis v. Mulford*', *Journal of the Patent and Trademark Office Society* (2011) 93, pp. 363–399; Christopher Beauchamp, 'Patenting nature: a problem of history,' *Stanford Technology Law Review* (2013) 16, pp. 257–311.

17 'Principles of medical ethics', *Journal of the Indiana State Medical Association*, 15 September 1912, pp. 406–410, 407.

their efforts to develop new remedies and thereby promote the public good, but personally benefiting from such efforts threatened to undermine the pursuit of medical science and needed to be restrained. Two years later, the delegates to the annual convention of the AMA voted to give the organization's Board of Trustees the authority to hold medical patents 'as trustees for the benefit of the profession and the public, provided that neither the American Medical Association nor the patentee shall receive remuneration from these patents'.[18] The idea was short-lived – in 1916 the organization decided not to manage patents in this way – but it pointed both to the recognition that drug patents were here to stay and to continued concerns about the ability of patents to undermine the practice of medical science.

The AMA's position also reflected a growing concern about the relationship between patents and high drug prices. This concern first emerged as an important issue in the 1880s and 1890s around patented synthetic drugs introduced by German manufacturers. The fact that the United States was unusual at the time in allowing patents on pharmaceuticals meant that foreign manufacturers were able to charge significantly higher prices in the United States than they were in other countries. In 1897, for example, Phenacetin sold in the United States for one dollar an ounce, but just thirty-five cents an ounce in Canada, a price differential that was widely assumed to be made possible by the patent laws of the respective countries.[19] The issue grew more acute in the years immediately before the entrance of the United States into the First World War when the British naval blockade cut off supplies of valuable drugs manufactured in Germany. Prices for drugs protected by German patents skyrocketed, including the important new anti-syphilis drug Salvarsan. Numerous critics, including physicians, denounced the German drug industry and called for the seizure of its patents. After the United States entered the war, Congress passed the Trading with the Enemy Act which authorized the seizure of property owned by German and Austrian citizens. In 1918 an amendment to the law authorized the seizure of enemy patents and trademarks, including drug patents.[20]

Over the course of the late nineteenth and early twentieth centuries a broad transformation in medical attitudes toward pharmaceutical patents can thus be seen. Once an illegitimate form of monopoly that undermined medical science and threatened the public good, pharmaceutical patents were rendered an ethically legitimate, and perhaps even necessary, component of medical science through their potential to encourage scientific innovation. Pharmaceutical patenting was no longer juxtaposed to scientific medicine as a form of quackery; indeed, by the early twentieth century, patented goods had become an indispensable part of the practice of good medicine. Concerns about the extent of patent rights continued, most notably in terms of the relationship between patents and drug prices, but the nature of the concern was quite different than once it had been. Indeed, the concern about patents and high drug prices was

18 'Report of the Judicial Council', *Journal of the American Medical Association*, 4 July 1914, p. 106.

19 *Proceedings of the American Pharmaceutical Association at the Forty-Fifth Meeting*, Baltimore: American Pharmaceutical Association, 1897, p. 10.

20 Kathryn Steen, *The American Synthetic Organic Chemicals Industry War and Politics, 1910–1930*, Chapel Hill: University of North Carolina Press, 2014, pp. 149–156.

made possible precisely because of the assumption that patented goods were essential to the practice of medicine. Patented drugs had become important and even essential goods; the question at hand was no longer how to suppress their use. It was how to ensure access to them.

At the same time, debate about ethics and medical science shifted to other areas. For my purposes, the most important of these was the question of human experimentation and consent. Although this is not the place for a detailed history of the topic, it is worth pointing out that, during the early nineteenth century, there was little concern about human experimentation as an issue in medical ethics. Medical experiments were understood as a normal part of the gradual process through which scientific knowledge was accumulated. 'Truth-telling and consent seeking' may have been part of the American medical tradition among orthodox physicians, as Martin Pernick has argued, but negotiations between doctors and patients took place in the context of defined and explicitly hierarchical social roles that were very different than they are today. In general, physicians simply did what they believed to be appropriate as they experimented on people in their care.[21] During the late nineteenth and early twentieth centuries, however, the assumed authority of physicians to experiment on their patients came under significant strain. On the one hand, anti-vivisectionists critiqued medical researchers for subjecting patients to what they called 'human vivisection'.[22] On the other hand, a common-law tradition emerged defining surgery as technical battery, and – except in cases of emergency – legal only with the consent of the patient, whether explicit or implied, thereby exposing physicians who operated on their patients without consent to legal risk.[23] These and other changes pushed reformers in the medical community to begin to describe obtaining the consent of research subjects as an ethical duty and to work toward formulating early guidelines governing human experimentation. In 1916, for example, the American Medical Association considered amending its Principles of Medical Ethics to require the consent of research subjects, of that or their parent or guardian.[24] The AMA did not adopt the measure, but later in the year an editorial published in the *Journal of the American Medical Association* clearly asserted that consent must be obtained for human experimentation that is not intended for therapeutic purposes, noting that

21 Martin S. Pernick quoted in Sydney A. Halpern, *Lesser Harms: The Morality of Risk in Medical Research*, Chicago: The University of Chicago Press, 2004, p. 3. On human experimentation in the nineteenth-century United States see also Alexa Green, 'Working ethics: William Beaumont, Alexis St. Martin, and medical research in antebellum America', *Bulletin of the History of Medicine* (2010) 84(2), pp. 193–216; Susan E. Lederer, *Subjected to Science: Human Experimentation in America before World War II*, Baltimore: Johns Hopkins University Press, 1994, pp. 1–72.

22 'Anti-vivisectionists make hopeless fight', *Philadelphia Inquirer*, 18 May 1911, p. 6.

23 Notable legal cases in this regard include *Mohr* v. *Williams* 95 Minn. 261 (1905); *Luka* v. *Lowrie* 171 Mich. 122 (1912); *Schloendorff* v. *Society of New York Hospital* 133 NYS 1143 (1914); *Barfield* v. *S. Highland Infirmary* 191 Ala. 553 (1915). As far as I know, a detailed history of the origins of this legal concept in the United States has not yet been written, but for a general history see Ruth R. Faden and Tom L. Beauchamp, *A History and Theory of Informed Consent*, New York: Oxford University Press, 1986.

24 See Susan E. Lederer, '"The right and wrong of making experiments on human beings": Udo J. Wile and syphilis, 1917', *Bulletin of the History of Medicine* (1984) 58, pp. 380–397.

> society as now constituted will obviously not countenance any operation performed for the satisfaction of the operator or for the assurance of the investigator, whether or not for the immediate benefit of others, unless the consent of the person on whom the operation is to be performed has previously been obtained.[25]

For the public good: medical ethics and academic patenting

The so-called ethical wing of the American pharmaceutical industry embraced the use of product patents in the years following the First World War. Parke-Davis, for example, was one of the most successful firms of the time. In 1921, the company's total sales were about $20.7 million – up from just over $10 million a decade earlier – and by 1929 had reached almost $28 million.[26] This rapid growth was fuelled by many things, of course, but the tremendous success of drugs such as Adrenalin made it clear to the industry that the monopolization of scientific research held the key to dramatic profits. Parke-Davis thus acquired at least ten patents in the decade or so following the First World War on a variety of chemical substances, including barbituric acids and arsenical compounds.[27] The willingness of the company to do so points to the normalization of patenting among domestic manufacturers. It also points to the acceptance of industry patenting within the medical community, which barely noticed that the company was engaged in behaviour that would have been beyond the pale of respectability in earlier years. Patenting was now clearly within the domain of acceptable behaviour among reputable firms.

University scientists also began to patent their discoveries. Following the First World War, both academic researchers and physicians who worked at hospitals, private clinics and state institutions worked increasingly closely with the drug industry to develop and commercialize new products.[28] One of the most significant problems facing these efforts was product variability and the difficulty of manufacturing what were increasingly powerful drugs in a safe and reliable manner. Once a new drug was discovered and tested, and its therapeutic properties were announced, academic scientists and other researchers outside industry faced the difficult question of how to encourage the

25 'The right and wrong of making experiments on human beings', *Journal of the American Medical Association* (1916) 19, pp. 1372–1373.

26 'Historical financial data' (1958), Parke, Davis Research Laboratory Records, 1902–1950, Archives Center, National Museum of American History (hereafter PDR), b.5, f. BDd 1958.

27 Patents assigned to the firm following the war included US patent numbers 1,271,111 (1918), 1,286,944 (1918), 1,443,552 (1923), 1451357 (1923), 1,624,546 (1927), 1,615,870 (1927), 1,663,205 (1928), 1664123 (1928), 1,665,781 (1928), 1,717,198 (1929).

28 John Swann, *Academic Scientists and the Pharmaceutical Industry: Cooperative Research in Twentieth-Century America*, Baltimore: Johns Hopkins University Press, 1988; Jeffrey L. Furman and Megan J. MacGarvie, 'Academic science and the birth of industrial research laboratories in the U.S. pharmaceutical industry', *Journal of Economic Behavior & Organization* (2007) 63(4), pp. 756–776; Nicolas Rasmussen, 'The drug industry and clinical research in interwar America: three types of physician collaborator', *Bulletin of the History of Medicine* (2005) 79, pp. 50–80; Nelly Oudshorn, 'United we stand: the pharmaceutical industry, laboratory and clinic in the development of sex hormones into scientific drugs, 1920–1940', *Science, Technology and Human Values* (1993) 18, pp. 5–24; John Parascandola, *The Development of American Pharmacology: John J. Abel and the Shaping of a Discipline*, Baltimore: Johns Hopkins University Press, 1992, pp. 91–125; Liebenau, op. cit. (10).

development and distribution of their discovery. Simply allowing commercial firms to manufacture the product was one approach, but there was a significant risk in doing so. Commercial firms might make shoddy or inferior products, charge exorbitant prices, advertise the product unethically, or otherwise manufacture or distribute the drug in ways that the original inventor found objectionable. Even highly ethical manufacturers might not make the product according to what the original inventor considered the necessary standards; they might change the manufacturing process or ingredients in order to save costs, or have trouble standardizing their production methods, or otherwise manufacture what the original inventor considered an unsafe or inferior drug. Such variation had significant implications for the reputation of both the original inventor and the institution that they worked for. The quality of the product, and the methods that were used to sell it, had a tendency to be associated with the original inventor due to the fact that the name of the inventor – and the name of the institution that the inventor worked for – tended to follow the product through its scientific and commercial introduction. Academic scientists, and the institutions that they worked for, were thus concerned about the potential damage to their reputations that might result from the manufacture and sale of their inventions in a dubious manner. More generally, they were often concerned about the perception that manufacturers were exploiting their invention for commercial gain, and concerned that this might somehow cast a shadow on their own motives for engaging in scientific research.

In response to these difficulties, a small handful of chemists, physicians and other researchers began to patent their discoveries and assign the patents either to the institutions at which they worked or to some other affiliated institution; licenses were then issued to manufacturers for the production and commercial distribution of the drug in question. Well-known examples of this process include Walter Jacob's 1918 patent on the arsenical drug tryparsamide, which was assigned to the Rockefeller Institute for Medical Research; the 1923 patenting of insulin by Frederick Banting and his colleagues at the University of Toronto; Harry Steenbock's patent on his irradiation method of producing vitamin D at the University of Wisconsin, which he filed in 1924, and George and Gladys Dick's 1924 and 1926 patents on the scarlet fever antitoxin.[29] Overlapping concerns about manufacturing reliability and personal reputation were important factors behind the willingness of these and other researchers to patent their inventions; at the same time, an awareness of the ethical prohibition on directly holding patents within the medical community played an important part in the development of the system

29 Myriam Mertens, 'Chemical compounds in the Congo: pharmaceuticals and the 'crossed history' of public health in Belgian Congo (ca. 1905–1939)', unpublished PhD dissertation, Ghent University, 2014; Maurice Cassier and Christiane Sinding, '"Patenting in the public interest": administration of insulin patents by the University of Toronto', *History and Technology* (2008) 24, pp. 153–171; Rima Apple, 'Patenting university research: Harry Steenbock and the Wisconsin Alumni Research Foundation', *Isis* (1989) 80, pp. 375–394; Charles Weiner, 'Patenting and academic research: historical case studies', *Science, Technology, and Human Values* (1987) 12, pp. 50–62. On university patenting and academic–industrial cooperation more generally see Henry Etzkowitz, *MIT and the Rise of Entrepreneurial Science*, New York: Routledge, 2002; David C. Mowery, Richard R. Nelson, Bhaven N. Sampat and Arvids A. Ziedonis, *Ivory Tower and Industrial Innovation: University–Industry Technology Transfer before and after the Bayh-Dole Act*, Stanford, CA: Stanford University Press, 2004.

whereby patents were turned over for institutional management. As J.J.R. Macleod noted, the insulin patent was turned over to the University of Toronto in part because

> it is contrary to the traditional principles of the medical profession to restrict the production or supply of any substance that may be used for the alleviation of human suffering and is contrary to its ethical code for any physician to derive financial benefit from the sale of such substance.[30]

By the end of the decade it had become fairly common for academic researchers, including physicians, to patent their discoveries, assign those patents to either the university for which they worked or some other institution, and then license the rights to the discovery either to a single manufacturer or to a small group of manufacturers. Royalties were then typically returned to the institution at which the scientist or physician worked in order to support further scientific work. This was both a halting process and a controversial one: many academic scientists continued to believe that it was unethical for them to patent their discoveries, understanding and describing their efforts as dedicated to the public good and free from commercial influence. This perspective was particularly strong among academic physicians in elite institutions, some of whom denounced the Toronto group for patenting insulin. In 1927, for example, Parke-Davis worked closely with Harvey Cushing from Harvard to research the extracts of the pituitary gland. As a memo from the company noted, Cushing was 'bitterly opposed to the patenting of work of this kind', and he 'severely criticized the Toronto crowd for their action in regard to insulin'. Parke-Davis found Cushing's attitude exasperating, but were willing to work with him anyway based on his reputation and the assumption that having their product associated with his name would benefit them even if they could not monopolize the results of his work.[31]

The trend toward academic patenting accelerated with the onset of the Great Depression as universities and industrial manufacturers increasingly worked together in the pursuit of an entrepreneurial form of science.[32] Academic scientists and administrators recognized that patenting played an important role in the ability of the firms with which they collaborated to profit from their investment in the scientific process. Patenting also allowed universities to retain control over the commercial development of the inventions made by their faculty, and thus to enforce both manufacturing and advertising standards on the companies with which they worked. And, of course, royalties offered the promise of important revenue during a period of economic distress. Yet patenting by university scientists also raised significant concerns as the lure of financial reward seemed to encroach on the supposedly cooperative and noble goals of science – and medical science in particular. Critics suggested that patenting introduced a spirit of competition into the workplace, that it distorted the types of question scientists asked, and that it otherwise corrupted the practice of science by introducing the possibility of profit into the research enterprise. Academic patenting 'tends to shut off unselfish exchange of ideas and information', argued Alan Greg in an influential article published

30 Quoted in Cassier and Sinding, op. cit. (29), p. 154 n. 11.
31 Unclear to E.M. Houghton, 10 November 1927, PDR, b. 25, f. KJc 1922–1929.
32 The phrase 'entrepreneurial science' is taken from Etzkowitz, op. cit. (29).

in *Science* in 1933. 'It tends to kill a critical and impartial attitude, it tends to introduce quarrels and bitterness and to consume time and funds in lawsuits. It may quite naturally influence the choice of university personnel and the choice of research problems.'[33]

As a result, physicians involved in medical research sometimes had ambivalent feelings about drug patents. By this point, organized medicine had fully accepted the role of patenting in the commercial development of new drugs. Although the American Medical Association's Principles of Ethics still prohibited physicians from personally holding patents, even the most conservative physicians assumed that patenting formed an important part of the ability of drug firms to successfully develop and introduce new products. As a result, physicians who were involved in debates about how best to improve the drug market generally considered patenting an important part of the scientific and manufacturing process, and they had a tendency to defend the rights of manufacturers to enforce their patents. Drug patenting by academic researchers was also now accepted with little real opposition, although it was also assumed that the resulting patents should be turned over to the institution for which the researchers worked. However, leaders in the medical community also worried that drug patenting, and commercial ambitions more broadly, threatened to undermine the cooperative spirit that supposedly underlay medical science. They had reason to be worried. By the 1930s the possibility of accumulating profit had clearly begun to transform scientific practice. Although there was still a commitment to the open sharing of information among researchers, new forms of competition had also entered the scientific process, some of which were linked to considerations related to patenting; there was an increasing emphasis on secrecy in research design, for example, as well as on publishing material quickly in order to establish scientific priority.[34] More generally, the linkage of profit to innovation made possible through patenting meant that academic institutions increasingly seemed to be driven by financial considerations rather than scientific ones. And, of course, physicians recognized that patents allowed manufacturers to charge high prices for their goods, a significant problem during the economic crisis of the Great Depression.

Morris Fishbein's 1937 editorial in the *Journal of the American Medical Association* should be understood in this context. Like most other observers at the time, Fishbein believed that the traditional prohibition on medical patenting was outdated and that patents were a normal part of commercial drug development. Indeed, Fishbein believed that patenting conferred positive benefits on the public because of the ability of patent holders to enforce manufacturing standards on companies that licensed their products; as he noted, in reference to the patent on insulin, 'it is no secret that it became necessary to patent this discovery in order to control it'. More generally, Fishbein believed that the ethical prohibition on drug patents no longer suited the advanced state of the times. As he put it,

33 Alan Greg, 'University Patents', *Science* (10 March 1933), p. 259.

34 For example, when pharmacologist Arthur L. Tatum at the University of Wisconsin began working on barbiturates with Abbott, he suggested that 'any ideas that we have as to means of study, which are new – in other words, original ideas applicable to the problem – we feel as though should be kept confidential, at least until we say so'. Arthur Tatum to J.F. Biehn, 21 October 1929, Arthur Tatum Papers, University of Wisconsin Archives, b. 1, f. 1. On Tatum see Swann, op. cit. (28).

> our new order of living in the machine age, the development of specialization in medical practice, the incorporation of great industries for the exploitation of discoveries made in the laboratories and similar factors emphasize the need for some revision in the medical point of view concerning patents.

Yet, as I suggested earlier, Fishbein also believed that patenting had the potential to undermine the scientific process by fomenting a 'competitive spirit' that threatened to destroy the 'cooperation in science' that underlay medical progress. He also worried that patents allowed manufacturers to 'charge exorbitant prices' and thereby force physicians and other researchers to 'pay tribute to some rapacious inventor or assignee of the patent, who may even refuse to allow its use at all'. Fishbein, for example, criticized the Wisconsin Alumni Research Foundation at the University of Wisconsin for commercializing Steenbock's irradiation method and other inventions in a way that he considered unethical. 'We are assuming that the Wisconsin Foundation is more interested in industry than in science', he noted in 1933. 'Steenbock has shown how remarkably remunerative a patent may be for a fund for a university. The word has gone around that the Wisconsin University has gone royalty crazy.'[35]

The difficulties involved in what was sometimes called 'the patent question' are also illustrated by a conference the American Medical Association organized on the topic in 1939.[36] The conference brought together speakers representing a variety of different perspectives on the role of patents in scientific drug development, including John F. Anderson, president of the American Drug Manufacturers' Association and Vice President of E.R. Squibb & Sons; Torald Sollmann, chairman of the American Medical Association's Council on Pharmacy and Chemistry; and Earl Shepard Johnson, an assistant professor of sociology at the University of Chicago, who spoke on 'the public's stake in the Administration of Medical Patents'. Participants generally agreed that patents played an important role in the development of new drugs because they encouraged investment in scientific research by ethical manufacturers; as Sollman noted, 'I think all of us … realize that the introduction of a new substance by a manufacturing house is an expensive and a risky process, which, in general, could not be undertaken unless there was some degree of monopoly granted.'[37] Yet participants also suggested that commercialism was having a negative impact on university research, that patents on drugs might lead to unreasonably high prices, and that medical patents might lead to other significant problems. Participants proposed various solutions, including control of all medical patents by some central organization, yet no solution really seemed adequate to the difficult problem of how to reconcile commercialism with both the ideals of scientific cooperation on the one hand and the needs of the

35 Morris Fishbein, 'Medical patents', op. cit. (1), p. 1542; Morris Fishbein to Claude E. Forkner, 28 December 1937, Morris Fishbein Papers, University of Chicago (hereafter MFP), b. 92, f. 12; 'Copper–iron patent', 20 April 1933, MFP, b. 92, f. 13. See also 'Problem of medical patents', *Journal of the American Medical Association*, 22 July 1933, pp. 284–285; and correspondence in MFP, esp. b. 13.

36 *Report of the Conference on Medical Patents under the Auspices of the Board of Trustees, American Medical Association*, Chicago: American Medical Association, 1939.

37 Torald Sollman in *Report of the Conference on Medical Patents*, op. cit. (36), pp. 49–50.

public on the other. 'I do not know the answer any more than anyone else knows it', Fishbein noted;

> If an answer is to be found aside from government control and administration, it must be found in some voluntary activity in which all of those who are concerned come together and work out a mutually satisfactory solution which protects the rights of the inventor, the manufacturer, and the university and which at the same time keeps primarily in mind the rights of the patient and of the public.[38]

How to do so was not at all clear, yet the risks of ignoring the problem were great. As Fishbein put it not long after, 'in the scramble for patent rights, it is no profit to a university to gain the whole world and lose its own soul'.[39]

Bioethics and the eclipse of monopoly

In the two decades following the Second World War, the orthodox medical community and the pharmaceutical industry were drawn together even more tightly than they had been in earlier years. Pharmaceutical companies forged close working relationships with numerous physicians in universities, independent medical schools, state institutions and hospitals and private clinics as part of their efforts to research and develop new products. This type of cooperation was the basis for a tremendous amount of optimism about the possibilities of scientific medicine to address the problems of the day through the development of powerful new drugs. These relationships paid impressive therapeutic dividends, such as in the development of streptomycin and other antibiotics; they also decisively shaped the nature of pharmaceutical science in this period, in ways that critics today sometimes find troubling. Not surprisingly, patenting was a fundamental part of this process and complex questions related to patent law and policy occupied a significant amount of the attention of many observers of the growing alliance between the drug industry, academic researchers and the medical community. In a report on university patent policies prepared for the National Research Council in 1947, for example, Archie M. Palmer described the growing cooperation between industry and academic research units, including those housed in medical schools, and argued for the need to coordinate policies across institutions in order to effectively meet the challenges of post-war society. Noting that the American Medical Association's Principles of Medical Ethics forbade individual physicians from holding patents, Palmer pointed out that pharmaceutical patenting in the public interest was now common and that medical institutions, in particular, needed to systematize their policies in order to 'contribute, even more extensively than they have in the past, to the progress of science through the most effective utilization of their research facilities and the present short supply of scientific and technical personnel'. Palmer briefly pointed to the potentially deleterious role of commercialism in academic institutions, noting that 'new and fundamental ideas do not flourish in an atmosphere of pressure, of meeting dead-lines and achieving specific developmental objectives', but unlike Morris Fishbein a decade

38 Morris Fishbein in *Report of the Conference on Medical Patents*, op. cit. (36), p. 45.
39 Morris Fishbein, 'The insulin monopoly', *Journal of the American Medical Association* (1941), p. 112.

earlier he was not seriously concerned about the issue. Nor were the many physicians who worked closely with the industry in the decades immediately following the war. Industrial cooperation promised a bright future and there seemed little reason to think that whatever problems it might also bring could not be overcome.[40]

Central to this process was the continued transformation of the ethical framework of orthodox medicine. Patenting within the pharmaceutical industry was now considered ethically legitimate, and even necessary, as a part of the incentive structure that underlay the development of powerful new drugs. At the same time, the ethical prohibition on the clinical use of patented goods had been fully abandoned. The patent status of a product no longer had anything to say about its scientific validity or its utility in clinical practice. Finally, the ethical prohibition on physicians holding patents itself collapsed. It was increasingly acceptable for physicians to retain control of their patents themselves, as long as they did so in what was considered a responsible manner that prioritized the public good over their own financial advancement. In 1955 the American Medical Association acknowledged the changing times and revised their Principles of Medical Ethics to allow physicians to directly hold patents on medical inventions, and to receive remuneration from these patents, as long as doing so did not retard medical research or restrict the benefits from such research.[41] Perhaps more importantly, two years later the organization issued a significantly condensed version of the Principles which sought to 'eliminate superfluous wording and matters of medical etiquette' but 'retain all matters of ethics' found in the 1955 version. In doing so, the AMA explicitly stated that the Principles were simply an aid to help the enlightened physician follow his own conscience, a 'suggestion of the inexpressible' that 'may help keep ideals uppermost in mind and practice'. What had once been understood as a normative code intended to regulate physician behaviour was now a symbolic representation, and an imperfect one at that, of the individual doctor's conscience.[42]

The acceptance of patenting can also be seen in the ongoing concern about drug prices. The rising cost of drugs was a topic of considerable public concern during the 1950s, leading to charges of price-fixing and investigations by the Federal Trade Commission and other agencies into anti-competitive practices on the part of the industry.[43] Drug

40 Archie M. Palmer, *Survey of University Patent Policies, Preliminary Report*, Washington, DC: National Research Council, 1948, pp. 55, 10. The literature on the post-war American pharmaceutical industry is extensive. Works I have drawn on for my understanding of this period include Scott H. Podolsky, *The Antibiotic Era: Reform, Resistance, and the Pursuit of Rational Therapeutics*, Baltimore: Johns Hopkins University Press, 2014; Jeremy A. Greene, *Generic: The Unbranding of Modern Medicine*, Baltimore: Johns Hopkins University Press, 2014; Dominique Tobbell, *Pills, Power, and Policy: The Struggle for Drug Reform in Cold War America and Its Consequences*, Berkeley: University of California Press, 2011; Jeremy A. Greene, *Prescribing by Numbers: Drugs and the Definition of Disease*, Baltimore: Johns Hopkins University Press, 2006; David Healy, *The Antidepressant Era*, Cambridge, MA: Harvard University Press, 1999; Louis Galambos and Jane Eliot Sewell, *Networks of Innovation: Vaccine Development at Merck, Sharp & Dohme, and Mulford, 1895–1995*, New York: Cambridge University Press, 1995.

41 'Report of the Council on constitution and bylaws', *Journal of the American Medical Association* (1955) 157, p. 945.

42 'Principles of Medical Ethics – 1957', *Journal of the American Medical Association* (27 July 1957) 164, p. 1482.

43 Tobbell, op. cit. (40), pp. 71–75.

patents were frequently implicated in these charges, in part because the industry sometimes used patent cartels, restrictive licensing schemes and other patent-based monopolistic practices to manage risk, reduce competition and maintain profits. In 1953, for example, the Federal Trade Commission launched an investigation into anti-competitive practices in the antibiotics industry; the final report of the investigation, published five years later, dealt extensively with patents.[44] However, the medical community had little to say about the issue. Physicians at the time might have worried about the high price of prescription drugs, and about the price of antibiotics in particular, but their willingness to critique drug patents was limited by the growing alliance between the industry and the medical community, by their lack of knowledge about patent and anti-trust law, and most importantly by the assumption that patenting was necessary to encourage innovation – and that without drug patents the progress of American medical science would suffer.

As a result, many physicians were hostile to government efforts to limit patent rights in the drug industry. In 1958, for example, Senator Estes Kefauver launched his investigation into monopolistic practices in the drug industry as part of his broader investigation into administered prices.[45] The relationship between patents, drug prices, and what Kefauver considered to be unfair profit ratios occupied a significant part of his committee's attention, and initial drafts of proposed legislation contained language significantly weakening patent rights in the drug industry, including provisions removing patent protection for so-called 'me-too' drugs and, after three years of exclusivity, requiring patent holders to grant licenses to all qualified applicants at a maximum royalty of 8 per cent. Kefauver considered the patent provisions essential to any effort to address the problem of high drug prices, noting that 'only by modifying the patent protection for this uniquely vital industry can any adequate price reductions be achieved within the framework of a competitive, free enterprise economy'.[46] Yet as Dominique Tobbell points out, academic physicians who had forged collaborative relationships with the industry strongly opposed these provisions. Philip S. Hench, for example, was a Nobel laureate who had worked with Merck on the development of cortisone; he called the patent provisions 'astonishing' and warned against reducing the incentive for industry to invest in drug research, suggesting that doing so would undermine the nation's scientific race with Russia.[47] Other government efforts to limit patent rights in the industry were opposed

44 Federal Trade Commission, *Economic Report on Antibiotics Manufacture*, Washington, DC: United States Government Printing Office, 1958, pp. 225–257.

45 On Kefauver's investigation into the drug industry and the resulting amendments to the 1938 Food, Drug, and Cosmetic Act see Jeremy A. Greene and Scott H. Podolsky, 'Reform, regulation, and pharmaceuticals: the Kefauverr-Harris Amendments at 50', *New England Journal of Medicine* (2012) 367, pp. 1481–1483; Tobbell, op. cit. (40); Daniel Carpenter, *Reputation and Power: Organizational Image and Pharmaceutical Regulation at the FDA*, Princeton, NJ: Princeton University Press, 2010; Philip J. Hilts, *Protecting America's Health: The FDA, Business, and One Hundred Years of Regulation*, Chapel Hill: University of North Carolina Press, 2004; Richard Edward McFayden, 'Estes Kefauver and the drug industry', doctoral dissertation, Emory University, 1973.

46 Quoted in W. Steven Pray, *A History of Nonprescription Product Regulation*, New York: Pharmaceutical Products Press, 2003, p. 153.

47 Quoted in Tobbell, op. cit. (40), p. 102.

along similar lines. In his 1965 testimony opposing a proposed bill that would have granted the federal government patent rights to drugs developed using federal money, for example, Austin Smith, president of the Pharmaceutical Manufacturers Association and former editor of the *Journal of the American Medical Association*, suggested that 'the best assurance that the required investment of talent and money will be made [in developing new drugs] comes from the providing of incentive to the pharmaceutical industry in the form of reasonable ownership rights'.[48]

By the early 1960s the orthodox medical community had thus fully embraced the role of pharmaceutical patenting in the advancement of medical science, even if concerns about drug prices remained. At the same time, debate about other ethical issues took centre stage. The most important of these issues in the two decades following the Second World War was the question of human experimentation. Following the revelation of German atrocities during the war, in 1947 the American Medical Association appointed Andrew C. Ivy to formulate a set of rules governing the conduct of human experimentation in medical research.[49] Ivy's rules had a significant impact on the development of the Nuremburg Code; they also influenced the AMA's Judicial Council, which issued a simplified set of guidelines based on his rules for the conduct of human experimentation:

> In order to conform to the ethics of the American Medical Association, three requirements must be satisfied: (1) the voluntary consent of the person on whom the experiment is to be performed [must be obtained]; (2) the danger of each experiment must be previously investigated by animal experimentation, and (3) the experiment must be performed under proper medical protection and management.[50]

Of course, these rules were frequently not followed in actual practice. Researcher behaviour was guided by informal rules and expectations that only sometimes conformed to the Judicial Council's guidelines, institutional policies governing human research were largely absent, and individual investigators varied in their motives and degree of concern for their patients. Historians have documented a large number of experiments that seem difficult to justify, even from the perspective of the evolving standards of the time, but such experiments attracted little criticism from within the medical community in the two decades following the Second World War. Human experimentation was understood as a necessary part of advancing medical science and whatever harms might be inflicted on research subjects were generally considered a justifiable cost of advancing the greater good. Certainly, physicians at the time often considered obtaining consent both 'morally proper and legally prudent', as Robert Baker notes, but in general the decision about whether or not to obtain consent was left to the individual investigator.[51] Many physicians decided against it, and those who thought otherwise rarely raised the issue.

48 Quoted in 'Washington news', *Journal of the American Medical Association* (1965) 192, p. 15.

49 United States Advisory Committee on Human Radiation Experiments, *The Final Report of the Advisory Committee on Human Radiation Experiments*, New York: Oxford University Press, pp. 75–78.

50 Quoted in United States Advisory Committee on Human Radiation Experiments, op. cit. (49), p. 77.

51 Baker, op. cit. (3), p. 271.

Beginning in the early 1950s, a growing number of critics began to think about the role of informed consent in medical research. They pointed out that over the course of the past several decades it had become increasingly common to conduct medical experiments on patients that were not intended to help the patient in any meaningful sense. For these critics, non-therapeutic experimentation posed a fundamental question: how was it possible to preserve the ability of physicians to conduct the medical research obviously necessary for the advancement of science, and yet maintain the rights of the individual to be free from medical exploitation? Obtaining the consent of patients would clearly need to be at the heart of any solution, but the exact question of how patient consent and experimental science fit together was not at all clear.[52] The most important of these critics, of course, was the anaesthesiologist Henry Knowles Beecher of Harvard Medical School. Beecher became interested in the issue during the 1950s as a result of his scientific work investigating the use of placebos – and, perhaps, as a result of his own secret experiments administering hallucinogenic drugs to patients without their knowledge.[53] In 1959 he published an essay examining the question of informed consent. Beecher noted that the first rule of the Nuremburg Code was that 'the voluntary consent of the human subject is absolutely essential', but also suggested that while, 'on first reading, this sounds simple, straightforward, and absolutely to the point', further 'reflection' reveals 'certain difficulties' with the concept of patient consent, including the fact that requiring patient consent would 'effectively cripple, if not eliminate, most research in the field of mental disease' and that it would cast doubt on the study of placebos, and the difficulty – if not outright impossibility – of communicating complex scientific issues to patients, including questions related to risk. As a result, Beecher felt that the 'problems of human experimentation do not lend themselves to a series of rigid rules'.[54]

Beecher may not have approved, but such rules soon arrived. Partially in response to the thalidomide disaster, and Francis Kelly's successful effort at the Food and Drug Administration to keep the drug off the US market, legislation growing out of Kefauver's investigation of the pharmaceutical industry became law in 1962. The Kefauver-Harris Drug Amendments lacked any provisions related to patenting – in part, it should be emphasized, because of opposition from the medical community – but contained a requirement mandating that new drugs be shown to be efficacious through 'adequate and well-controlled investigations'. The exact meaning of this controversial phrase was then spelled out by the FDA, which by 1966 had promulgated a set of policies governing the conduct and structure of clinical trials. This included a requirement that all research subjects give their consent to participate in drug trials, and that

52 For example, Otto E. Guttentag, 'The problem of experimentation on human beings: the physician's point of view', *Science* (1953) 117, pp. 207–210.

53 George A. Mashour, 'Altered states: LSD and the anesthesia laboratory of Henry Knowles Beecher', *CSA Bulletin* (Winter 2009), pp. 68–74; Alfred W. McCoy, 'Science in Dachau's shadow: Hebb, Beecher, and the Development of CIA psychological torture and modern medical ethics', *Journal of the History of the Behavioral Sciences* (2007) 43, pp. 401–417.

54 Henry K. Beecher, 'Experimentation in man', *Journal of the American Medical Association* (1959) 169, pp. 461–473.

they be 'provided with a fair explanation' of the experiment and the hazards involved.[55] As David Rothman has noted, the Kefauver-Harris Drug Amendments 'unquestionably represent a new stage in the balance of authority between researcher and subject'.[56] They also provoked significant controversy among physicians involved in research, many of whom considered the new regulations governing clinical research to be unworkable and perhaps even harmful to patients. Morris Fishbein, for example, was strongly opposed to the law, including the provision requiring informed consent, calling it 'poorly conceived, grossly defective, perhaps totally unworkable, like the unfortunate armless and legless defectives that result from the actions of thalidomide'.[57]

The debate about informed consent within the medical community had little to do with the ongoing debate about patenting and drug prices that continued in other domains. In 1966, for example, Beecher published a landmark critique of what he called 'outrages' in medical research in the *New England Journal of Medicine* in which he described twenty-two recent examples of unethical research on patients.[58] The paper attracted an immense amount of attention and provoked a storm of controversy, both within the medical community and more broadly. Beecher's so-called 'bombshell' grew out of both his concerns about human experimentation and the ongoing debate about informed consent; it thus pointed to the continued transformation of ethical deliberation among physicians away from the traditional assumption that monopoly undermines the conduct of medical science and toward clinical problems and issues of other types that no longer seemed related to drug patenting. Certainly, an awareness of drug patenting as an important issue in medicine remained, both in terms of the question of price and in related areas, such as the question whether or not generic drugs are therapeutically equivalent to branded ones.[59] Yet the trend is unmistakable: concerns about drug patenting, to whatever extent they remained present within the medical community, had by this point been almost completely separated from deliberation about the ethics of scientific medicine. Beecher himself appears to have been uninterested in patents, and both his 1966 article and the broader discussion of informed consent of which it was a part had little overlap with legal and policy debates

55 '130.37 consent for use of investigational new drugs on humans: statement of policy', in *Code of Federal Regulations of the United States of America Title 21 Parts 130 to 146e Revised as of January 1, 1967*, Washington, DC: United States Government Printing Office, 1967, pp. 32–33.

56 David J. Rothman, *Strangers at the Bedside: A History of How Law and Bioethics Transformed Medical Decision Making*, New York: Basic Books, 1991, p. 94.

57 Morris Fishbein, 'The new drug laws,' MFP, b. 95, f. 14.

58 H.K. Beecher, 'Ethics and clinical research', *New England Journal of Medicine* (1966) 274, pp. 1354–1360; quote from Henry K. Beecher to Robert Kennedy, 23 September 1965, Henry K. Beecher Papers, Harvard University, b. 11, f. 37. On Beecher and his so-called 'bombshell' see Laura Stark, 'The unintended ethics of Henry K Beecher', *The Lancet* (2016) 387, pp. 2374–2375; Lara Freidenfelds, 'Recruiting allies for reform: Henry Knowles Beecher's "Ethics and Clinical Research"', *International Anesthesiology Clinics* (2007), pp. 79–103; Jay Katz, '"Ethics and Clinical Research" revisited: a tribute to Henry K. Beecher', *Hastings Center Report* (1993) 22, pp. 31–39; Rothman, op. cit. (56), pp. 70–84.

59 On the history of generic drugs in the United States, including the debate about therapeutic equivalence, see Greene, *Generic*, op. cit. (40); Tobbell, op. cit. (40); Daniel Carpenter and Dominique Tobbell, 'Bioequivalence: the regulatory career of a pharmaceutical concept', *Bulletin of the History of Medicine* (2011) 85, pp. 93–131. On the nineteenth-century origins of generic names see Gabriel, op. cit. (3).

about patents, generic drugs and drug prices then taking place in other domains. For my purposes, what is important here is not just Beecher's failure to consider the patent status of the drugs used in some of the studies he critiqued. Rather, it is the fact that debates about drug patenting and debates about how medical science should be conducted were now such clearly distinct issues that it would have been strange for him to have done so.

Conclusion: pharmaceutical patenting and ethical deliberation

Historians sometimes point to Beecher's 1966 paper as an important turning point in the change from an older-style 'medical ethics', in which deliberation about medicine and ethics was primarily the domain of the medical community, to contemporary 'bioethics', in which such deliberation takes place in additional areas, including philosophical and legal discourses.[60] Whether or not Beecher's paper deserves the vaunted place in the historiography it has been given is beyond the scope of this paper; certainly, debate about informed consent and the ethics of human experimentation was just one of a number of different issues that occupied the attention of the physicians, theologians and attorneys that made up what might be thought of as the first generation of bioethicists proper. For my purposes, what is important is not so much the exact process through which the change from medical ethics to bioethics took place, or the exact relationship between the emergence of bioethics as a domain of inquiry and technological change on the one hand or the new regulatory structures governing medical science and practice in the post-Second World War era on the other (such as the 1962 Drug Amendments). Instead, in this paper I have sought to trace the general erosion of concern among physicians interested in the ethics of their profession about drug patenting – and, by extension, other monopolistic practices. In the coming years, debates about medicine and ethics would be dominated by discussions about informed consent, organ transplantation, end-of-life care, maternal–foetal conflict, and other issues that apparently had little relation to questions of monopoly. The fact that bioethicists frequently explain the origin of their field in terms of new moral problems raised by technological change, yet generally discuss issues such as organ transplantation without reference to patenting, suggests that the evacuation of concern about monopoly from ethical deliberation extends beyond the relatively narrow story of drug innovation I describe here.

There are several exceptions to this. The first is an important debate about the ethics of patenting DNA and other forms of biological material. I have left this issue aside due to constraints of space, but patents on what, following Nikolas Rose and others, might be called 'life itself' have provoked a significant amount of debate among bioethicists.[61] The second is a debate over the ethics of patenting medical procedures, which has attracted a

60 For example, Rothman, op. cit. (56); Joel D. Howell, 'A history of the American Society for Clinical Investigation', *Journal of Clinical Investigation* (2009) 119, pp. 682–697.

61 Nikolas Rose, *The Politics of Life Itself: Biomedicine, Power, and Subjectivity in the Twenty-First Century*, Princeton, NJ: Princeton University Press, 2007. The literature on the ethics of gene patents and related issues is large, but for a useful introduction see David B. Resnik, *Owning the Genome: A Moral Analysis of DNA Patenting*, Albany: State University of New York Press, 2004.

modest amount of attention from bioethicists.[62] The most important exception, of course, is the continued concern about the relationship between patents and high drug prices. Academic physicians, bioethicists and activist groups within the medical community such as Doctors Without Borders, among others, have fiercely criticized the role of patents in maintaining high drug prices and otherwise making essential drugs unavailable to the poor. Although certainly not new, these critiques have become louder and more frequent in recent years following the introduction of extremely expensive drugs used to treat hepatitis C, cancer and other serious medical problems.[63] Since 1984, when the Drug Price Competition and Patent Term Restoration Act expedited the approval of generic drugs in the United States, what anthropologist Corrine Hayden and others have called the 'generic solution' has been thought to be the proper response to the problem of high drug prices.[64] The embrace of generic prescribing by physicians since 1984 points to a developing awareness within the American medical community that price is an important consideration in the clinical meaning of a drug, and that the ethics of medicine and the ethics of patenting cannot be fully separated from one another. So too does recent outrage over the rapidly increasing price of generic drugs themselves, provoked in part by the willingness of some manufacturers to dramatically increase the cost of drugs that have long been assumed to be within the public domain. Yet the embrace of generics should not be confused with a rejection of patenting itself. It is almost impossible to imagine a physician today refusing to prescribe a drug under patent protection that is clinically indicated for a patient simply because that drug is patented.

Defenders of the pharmaceutical industry typically respond to critiques of patenting by arguing that industry profits are exaggerated by its critics and that robust patent rights are necessary to stimulate innovation. The rhetorical importance of innovation within medical discourse, and its assumed linkage to commercial forces, have thus worked to preclude a sustained critique of pharmaceutical patents. Despite this, in recent years a growing number of physicians and ethicists have begun to suggest that there might be better methods of encouraging drug innovation that would result in the development of important new products without leading to the types of high price that characterize many drugs today. Critics also sometimes suggest that pharmaceutical patents distort the scientific process away from the goals of medicine in other ways, such as by encouraging the development and marketing of so-called 'me-too' drugs that bring

62 For example, O. Mitnovetski and D. Nicol, 'Are patents for methods of medical treatment contrary to the *ordre public* and morality or "generally inconvenient"?' *Journal of Medical Ethics* (2004) 30, pp. 470–475; Joel J. Garris, 'The case for patenting medical procedures', *American Journal of Law and Medicine* (1996) 85, pp. 85–108.

63 For example, Hagop Kantarjian and S. Vincent Rajkumar, 'Why are cancer drugs so expensive in the United States, and what are the solutions?', *Mayo Clinic Proceedings* (2015) 90, pp. 500–504; Doctors Without Borders, 'The cost of medicine: a special report', *Alert* (2015) 16(3), pp. 1–15; Aakas Kaushik Shah, Jonathan Warsh and Aaron S. Kesselheim, 'The ethics of intellectual property rights in an era of globalization', *Journal of Law, Medicine & Ethics* (2013) 41, pp. 841–851.

64 Corrine P. Hayden, 'A generic solution? Pharmaceuticals and the politics of the similar in Mexico', *Current Anthropology* (2007) 48, pp. 475–495; see also Cori Hayden, 'Distinctively similar: a generic problem', *U.C. Davis Law Review* (2013) 47, pp. 601–632.

unnecessary risks to patients or by actually retarding biomedical innovation.[65] These types of critique suggest that questions of clinical legitimacy and questions of drug patenting are beginning to be reassembled within the domain of bioethical deliberation. The fact that the scientific legitimacy of a pharmaceutical is generally conceptualized as a distinct question from whether or not that product is patented, and that as a result most physicians have little concern about drug patenting outside the issue of drug prices, suggests that since the early nineteenth century there has been a fundamental transformation in the ethical significance of monopoly rights within orthodox medical thought. Yet the fact that at least some critics of the current system are beginning to conceptualize drug patents as problematic not only due to their relation to high drug prices but also due to their relation to efficacy also suggests that, in the future, ethical deliberation may once again centre on the question of monopoly.

65 For example, Joshua J. Gagne and Niteesh K. Choudhry, 'How many "me-too" drugs is too many?', *Journal of the American Medical Association* (2011) 305, pp. 711–712; Amitava Banerjee, Aidan Hollis and Thomas Pogge, 'The Health Impact Fund: incentives for improving access to medicines', *The Lancet* (2010) 375, pp. 166–169; E. Richard Gold, Warren Kaplan, James Orbinski, Sarah Harland-Logan and Sevil N-Marandi, 'Are patents impeding medical care and innovation?', *PLoS Medicine* (2009) 7, pp. 1–5, available at http://dx.doi.org/10.1371/journal.pmed.1000208, accessed 29 June 2016; Kalman Applbaum, 'Is marketing the enemy of pharmaceutical innovation?', *Hastings Center Report* (2009) 39, pp. 13–17; Carl Nathan, 'Aligning pharmaceutical innovation with medical need', *Nature Medicine* (2007) 13, pp. 304–308, 304.