

how to navigate adverse political systems and help to change unfair societies, not only by reading remarkable memoirs but by studying public health histories done by professional historians.

Marcos Cueto

Casa de Oswaldo Cruz, Fiocruz, Brazil

doi:10.1017/mdh.2019.16

William Green, *Contraceptive Risk: The FDA, Depo-Provera, and the Politics of Experimental Medicine* (New York: New York University Press, 2017), pp. ix + 322, \$89, hardback, ISBN: 9781479876990.

William Green's expertise in constitutional law and pharmaceutical drug policies, combined with his obvious commitment to the protection of civil liberties, makes this a unique and very valuable history of a three-month injectable contraceptive that continues to raise important and sometimes disturbing questions. US drug law requires that new drugs be shown to be safe and effective for their intended uses, but how to meet these legal requirements has been subject to refinement over the years since Depo-Provera came onto the market. Green knows that there is no such thing as an entirely safe drug. The Food and Drug Administration (FDA) has acted with this knowledge since its founding, but only in the later twentieth century did the public become more aware and understanding of the fact that assurances of absolute drug safety do not exist and that knowing and managing risks is key to approving a useful and effective drug. When one considers the move from testing in a small, carefully controlled patient population to general use by physicians under their own expertise as medical practitioners, the status of Depo-Provera is more easily understood. As Green shows, however, almost nothing about Depo-Provera conforms to a 'normal' new drug study and approval paradigm, from its development and pre-market testing to its recurrent, controversial and somewhat atypical FDA drug reviews extending over decades.

Depo-Provera had been approved as safe for medical uses other than birth control around 1960. Prior to 1961, new drugs had to demonstrate only that they were safe before receiving FDA approval for marketing. In 1961, however, a new drug known as thalidomide, which originated in Germany and was prescribed to pregnant women, turned out to be a potent teratogen, leaving babies who survived with severe birth defects. Beginning in 1962, countries around the world revisited their new drug protocols. The US responded by creating a new science of regulatory statistics to ensure that approved drugs were not only safe but also effective for their intended use. Placebo-controlled, double-blinded studies were dubbed the 'gold standard' of the drug-approval process. It took a full decade to issue workable regulations regarding safety and efficacy study requirements for new drugs, and it was not until 1973 that the Supreme Court upheld the FDA's authority in the field. This meant that Depo-Provera remained on the market and available to physicians. Efficacy studies conducted at Grady Hospital in Atlanta had experimental authorisation from the FDA to study the drug in women in their family-planning clinic. However, Johns Hopkins had no such permission to study the drug in male sex offenders. Green notes that neither group of human subjects gave informed consent to participate in a trial.

Over its twenty-five-year drug-approval process, according to Green, medical officers at the FDA had concerns about the drug's carcinogenic potential and osteoporosis association

following monkey and beagle studies. This concern, however, was not shared by the FDA's leadership, whose perspectives are not closely examined or questioned outside of the paradigm of societal concerns about world overpopulation. In 1974, the drug was approved for limited contraceptive use; in 1978, however, the drug was denied a general marketing licence following an intra-agency review, Congressional scrutiny and opposition by consumer groups, women's organisations and activists.

This denial was upheld in 1986, and Upjohn withdrew its new-drug application (NDA). By 1987, it was clear how widespread its use as a contraceptive had become. In 1992, the drug was approved conditional on post-market studies of the risk of osteoporosis. Green claims, however, that the FDA then turned a blind eye for twelve years to its unapproved contraceptive use, until the results of the osteoporosis hearings led to a black-box warning and a recommendation that its use be limited to two years to minimise the risk.

So while Green resists primarily blaming the FDA for problems with the drug, his principal reliance on oral-history interviews with a limited number of eyewitnesses and former regulators as well as Congressional-hearing records fails, to my mind at least, to offer adequate historical perspective and context for the regulatory process at critical points in the new-drug-approval process, which was undergoing monumental changes beginning in the 1960s. Green's charge that the agency failed to manage Depo-Provera's risks in experimental use, however, overestimates the agency's ability to do so and fails to examine the oversight role that institutional review boards may or may not have played.

Bureaucratic and legal concerns are one thing, but Green tells a tripartite story of regulation, litigation and criminal sentencing. His biographical account of Anne McMurdo explores patient litigation, with a focus on her thirteen-year journey through the Florida court system claiming that Upjohn was negligent in its warnings about the drug's dangers – in her case excessive bleeding that led to a hysterectomy. McMurdo is a poster child for litigation surrounding medical liability and contributory negligence on the part of the drug's manufacturer, multiple physicians who continued to prescribe it and the surgeon who was not informed of the drug's use or side effects and elected to perform a hysterectomy. Initially, her first doctor 'made the difficult decision' to give her the injectable contraceptive 'off label' to prevent an unwanted pregnancy rather than allow her to chance another pregnancy in spite of unofficial, but known, concerns about possible carcinogenic risks. It should be kept in mind that during this period this 'special category' of women with 'special needs' had very clear connotations. They were largely urban African American women, such as those in the clinic at Grady Hospital in Atlanta, and poor white Appalachian women at family-planning clinics. Known, but rarely acknowledged, this 'special category' also included poor women with mental and physical impairments.

Green's final chapter, though, is perhaps the most disturbing and defies easy summary. It is essentially the story of how an oral contraceptive for women became a viable, court-ordered form of chemical castration for men, imposed on/offered to former prisoners convicted of child molestation and released under probation and parole protocols. Its unapproved use in the criminal-justice system operates outside of all investigational-new-drug (IND) boundaries and the oversight of the FDA. Instead, as Green shows through a succinct but important historical overview, the 'risk managers' are no longer medical officials but rather state criminal-court judges, legislators and corrections officers.

Green's book, with all of its complicated political, systemic and legal issues, is certainly a cautionary tale, full of worries about a 'complex, weak, and flawed' system filled with

'competing powerful interests'. It is well worth reading as a unique case study of a unique drug at a unique point in history.

Suzanne Junod

US Food and Drug Administration, USA

doi:10.1017/mdh.2019.18

Londa Schiebinger, *Secret Cures of Slaves: People, Plants, and Medicine in the Eighteenth-Century Atlantic World* (Stanford, CA: Stanford University Press, 2017), pp. xiii + 234, \$24.95, paperback, ISBN: 978150360291.

Secret Cures of Slaves is a book about flux. Not so much the diarrhoea and dysentery which were an inevitable part of plantation life, but the fluid nature of knowledge exchange in the Caribbean in the eighteenth century. The book presents a series of medical dramas involving the plants used to combat tropical pathogens. The effects of disease and attempted cures were played out on the bodies of the indigenous Caribbean inhabitants, the transported slaves and their descendants, white soldiers and sailors and, on occasion, members of the elite white population. Londa Schiebinger has written previously on the role of botany, *materia medica* and knowledge networks in the Atlantic world. She has investigated how knowledge did and did not pass between the free and the colonised and enslaved. Plants may have travelled across to the Old World, but understandings of their power to heal or work on the body could be held back, protecting the limited agency of the enslaved. Here Schiebinger combines these interests with concerns about human experimentation and the testing of cures and prophylactic interventions in the colonial Caribbean. Though parts of the book have appeared elsewhere as book chapters and journal papers, *Secret Cures* has a strong narrative to pull together what can (and cannot) be known of the flow of information within the Caribbean and across the Atlantic to Europe and West Africa, what she terms the 'Atlantic World medical complex' (p. 1).

In her analysis, the eighteenth-century Caribbean is turned into a laboratory for exploring how doctors independently, and at the behest of plantation owners, generated, researched and tested cures for diseases such as fevers, yaws and tetanus, and sought to prevent smallpox and yaws by inoculation. The division of the Caribbean between competing European powers who administered and paid their medics in differing ways provides a valuable source of contrast for the generation and circulation of knowledge. It reinforces how knowledge transfer could both follow patterns associated with language and national identity and move between colonial cultures when islands and plantations changed hands. This reinforces the sense of flux in a region made of large and small islands and the mainland colonies on the northern coast of South America. Schiebinger focuses on distinctions between Britain and France, but looks forward to future work involving other colonial powers in the region.

The example of the experimental testing of a European and a slave cure for yaws on the island of Grenada is particularly well worked. Schiebinger's research throws into doubt the simple assumption that a slave cure was one generated in Africa and transferred along with the enslaved to the Caribbean. Yaws was perceived as a distinctly African affliction, so turning to 'Negro *Materia Medica*' (p. 9) made sense. This was particularly so in the eighteenth century when the now well-attested faith in local knowledge to combat tropical diseases was still respected. In the case of the Atlantic world medical complex, local knowledge was both African and Caribbean, as well as a blending of the