In the Bookstores

Pharmacovigilance Medical Writing: A Good Practice Guide
by Justina Orleans-Lindsay;
Wiley-Blackwell Publisher, 2012.
ISBN: 978-1119967262 (paperback).
34.99 GBP. 286 pages.

A useful reference for writing pharmacovigilance documents

Like other areas of medical writing, pharmacovigilance (PV) medical writing has many detailed regulations, guidance documents, and templates associated with it. As such, there is a need for medical writers to be familiar and up-to-date with all that is involved in preparing and writing these important documents.

The author, Justina Orleans-Lindsay, describes her book as an attempt to produce 'a comprehensive manual for all PV documents submitted to regulatory authorities throughout the life-cycle of any given medicinal product…' This is an enormous task as the number of documents that are listed in the overview of the PV documents required in the EU and US regions is large. The initial overview provides us with a side-by-side comparison of the requirements for a clinical trial authorisation and an investigational new drug submission and serves as a useful reminder that, in terms of submission documents, one size still does not fit all. Although the main focus of the book is on PV medical writing in the US and Europe, a summary of the PV requirements for Japan, Canada, Australia, New Zealand, India, Singapore, and Taiwan are provided. In general, these countries follow the International Conference on Harmonisation guidance, format and standards and each is discussed in turn in a chapter entitled 'The rest of the world'. There is also a chapter on dealing with *ad hoc* safety reviews and requests from regulatory authorities.

Most regulatory medical writers are asked to write safety-related material for documents required before and after a submission has been completed. Writers may be expected to write the whole document or contribute small sections ranging from a few lines to a complete patient narrative in a clinical trial, through to writing some or all the sections for an integrated summary of safety or post-marketing update. The chapters of the book are organised across the drug development process: writing for clinical trials, writing for marketing authorisation, and writing risk evaluation and management plans, as well as writing for marketed products and *ad hoc* safety reviews. For many of the documents detailed in the book the author has provided the reader with a generic template containing headings and guidance about the type of information that should be presented under each heading. From a practical view, this makes it easy for a writer to track down the information required for writing specific documents when using this book as a reference text.

The chapter concerning writing for clinical trials provides detailed information on the Development Safety Update Report (DSUR). The evolution of this document is explained and placed in a useful historical context. The scope and general principles of the DSUR are outlined, together with advice on obtaining the relevant sources of data.

PV medical writing for marketing authorisation is a key area and in the chapter dedicated to this activity the author provides much insight into the main components devoted to safety in the Common Technical Document (CTD), the Summary of Clinical Safety (SCS; Module 2.7.4) and two other US-specific documents: the Integrated Summary of Safety (ISS) and the 120-Day Safety Update Report. Useful generic template models are provided for the SCS and ISS documents.

As well as describing the content of the different sections of the SCS and ISS the author proposes a timeline for planning and collating source data as well as listing key reviewers and their responsibilities. This is a useful place to start for those who have not completed these documents before. Her suggested timeline for either document is to allow up to 4 months from planning to finalisation. When a submission is planned for both the US and the EU the relevant summary documents are often completed in tandem, and it is difficult to put an exact timeline in place but depending on the scope and timing of data finalisation, 4 months is probably a minimum.

In the appendices section, there is some detail about the new EU PV legislation which came into

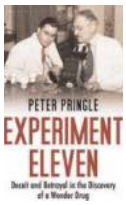
DOI: 10.1179/2047480612Z.00000000073

effect during 2012, and the author points out that for the next few years we are in a 'transition period.' To this end, she has tried to put the new EU legislation in context with a description of the revised EU legislation, and the impact it has had on other documents. For those of us not familiar with all of these changes this is a useful summary and introduction to the new legislation and will be helpful when working through this 'transition period.'

PV medical writing is considered a specialist area of medical writing by many in the medical writing profession. However, the level of involvement of a medical writer in PV medical writing often depends on the size and structure of the company, with many smaller companies requiring the medical writer to play a major part in writing most or all of the documentation. The author refers to PV medical writing 'as a discrete' discipline and separate from what she refers to as 'general medical writing'. For many medical writers this is not the case.

For those of us who consider PV medical writing as another aspect of our regulatory medical writing, there is a need to maintain current knowledge of the guidelines, templates, and requirements through continuous professional development. In my opinion, this book contributes greatly to an ability to maintain CPD in this key area of medical writing and is to be recommended.

Reviewed by Alison McIntosh
aagmedicalwriting@btinternet.com



Experiment Eleven: Deceit and Betrayal in the Discovery of the Cure for Tuberculosis
by Peter Pringle;
Bloomsbury, 2012.
ISBN-13: 978-1408814017
(Hardback).
18.99 GBP. 278 pages.

According to the official record, the 1952 Nobel Prize in Physiology or Medicine was awarded to Selman A. Waksman 'for his discovery of streptomycin, the first antibiotic effective against tuberculosis'. That by no means tells the whole story…

In an age when the word 'antibiotic' is almost invariably followed by 'resistance', it is easy to forget what a landmark the discovery of the first antibiotics was. In *Experiment Eleven*, British journalist Peter Pringle describes one of the earliest major breakthroughs in the field – the discovery of streptomycin.

Experiment Eleven is the rather tragic tale of a major dispute between a professor and his doctoral student. In the early 1940s, under the guidance of Professor Selman Waksman, Albert Schatz performed experiments to identify antibiotic-producing soil microorganisms that kill *Mycobacterium tuberculosis*, the bacterium that causes the then-incurable tuberculosis.

Pringle explains that, after 10 unsuccessful experiments, Schatz isolated two strains of *Streptomyces griseus* which produced an antibiotic that proved to be effective against pathogenic strains of *M. tuberculosis*. That antibiotic was streptomycin and it was a sensation. Waksman, who enlisted Merck & Co. to scale up its production, became something of a celebrity. Lots of lives were saved and some people made lots of money. Streptomycin even became the subject of a radio play featuring an Academy Award winner.

The initial manuscripts and patent were in both Schatz's and Waksman's names. But, according to Pringle, at some point Waksman decided that he wanted all the credit and more than his share of the money. He rewrote the story of streptomycin in a way that played down or ignored Schatz's contribution, while the institute at which Waksman worked, Rutgers College, churned out propaganda portraying him as some kind of philanthropist who had donated all his money to a new foundation. According to Pringle, Waksman was in reality pocketing a sizeable chunk of the cash. Schatz was getting next to nothing.

When Schatz found out what was going on, he sued. Pringle says that Waksman lied and repeatedly contradicted himself at a pre-trial hearing (described in *Experiment Eleven*'s longest and most fascinating chapter), and the case was ultimately settled out of court. This settlement did not, however, alter the perception that streptomycin was largely Waksman's work and the 1952 Nobel Prize in Physiology or Medicine was awarded to Waksman alone.

Interestingly, Pringle reckons that use of the passive voice in the research papers relating to streptomycin made it almost impossible to determine who had done what. Statements indicating how each author contributed to a study are a relatively new thing and, with nothing else to go on, the Nobel Committee may have placed great weight on the fact that Waksman had his name on all the key papers (Schatz did not).

Many of the issues relating to the discovery of streptomycin remain relevant today: industry

payments to researchers; what should happen to royalties from discoveries made by academics; the struggle to publish before one's competitors; and authorship and author sequence. I laughed out loud when I read the following quotation about how things used to be from Waksman's son Byron, himself a leading scientist: 'scientists who directed laboratory programs of any significance regularly appeared as senior authors on all paper emanating from their laboratories.' In my experience, this still goes on.

PhD students often have little power in such a situation because they fear they will upset their supervisor if they complain and therefore receive a bad reference, which could damage or end their scientific career. This fear is the reason Pringle gives for Schatz going along with Waksman's demands that he sign over his patent rights. If true, it ultimately made no difference: Schatz struggled to get jobs and drifted into obscurity, performing niche research.

And that was that until British microbiologist Milton Wainwright tracked Schatz down in the late 1980s, securing an interview with him in 1989. Schatz even made an emotional return to Rutgers College, which belatedly honoured him for his work.

Pringle's picture of Waksman is not that of an outstanding, creative scientist, but of a methodical workaholic. His methods seem unremarkable and he notably failed to act when presented with a test tube containing a tuberculosis strain that had been wiped out when the tube was accidentally infected with a fungus. This was in 1935 – 8 years before the isolation of streptomycin. Much is made of Waksman's absence from the lab when the key experiments were being carried out, but this merely reveals the author's apparent ignorance of the realities of bench research.

Experiment Eleven's opening passage is written in the style of a novel, but that style is quickly dropped in favour of one that is more formal yet still reader friendly and accessible to the lay audience. In fact, the book is quite a page turner. I became desperate to find out what, if any, redemption Schatz found and could not stop myself jumping forward to the last chapter.

Pedants among us may not appreciate the many typos and Pringle's use of 'bacteria' and 'algae' as singular nouns. And it's funny that he credits his readership with sufficient intelligence to understand the experiments he describes, but feels the need to explain what a parable and an IBM machine are. Still, one can only admire the thoroughness of his research and the great job he does of placing the discovery of streptomycin in its historical context, notably World War II and the Cold War.

Towards the end of the book, Pringle argues convincingly for the role streptomycin's commercialisation played in the expansion of R&D and marketing in the pharmaceutical industry. Major players began to adopt large-scale drug screening programmes, rushed to register what they hoped would be lucrative patents, and spent vast sums of money on advertising. These changes are, perhaps, Selman Waksman's other legacy.

Reviewed by Stephen Gilliver
Center for Primary Health Care Research,
Malmö, Sweden
stephen.gilliver@med.lu.se