

Setting the standards for medicines — the British Pharmacopoeia

The British Pharmacopoeia, published annually, is the only comprehensive collection of standards for UK medicinal substances. Ged Lee, Matilda Vallender and Stephen Young discuss the history behind and the current work that produces the British and European pharmacopoeias

The British Pharmacopoeia (BP), which is now published annually, is the only comprehensive collection of standards for UK medicinal substances. It contributes to the overall control of the quality of medicinal products by providing an authoritative statement of the standard that a product is expected to meet at any time during its period of use. The publicly available and legally enforceable pharmacopoeial standards are designed to complement and assist the licensing and inspection processes, and are part of the system for safeguarding public health. The BP is an essential reference for all individuals and organisations involved in pharmaceutical research, development, manufacture and testing of medicines.

History of the BP

The regulation of medicinal products by officials in the UK dates back to the reign of Henry VIII (1491–1547). The Royal College of Physicians of London had the power to inspect apothecaries' products in the London area and destroy defective stock. The first list of approved drugs with information on how they should be prepared was the London Pharmacopoeia published in 1618. The first edition of the BP was published in 1864 and it was one of the first attempts to harmonise pharmaceutical standards across different countries, by merging the London, Edinburgh and Dublin pharmacopoeias.

The 1968 Medicines Act established the legal status of the British Pharmacopoeia Commission and of the BP as the UK standard for medicinal products under section 4 of the Act. The BP Commission continues

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the work of the earlier commissions appointed by the General Medical Council. A commission was first appointed by the GMC when it was made statutorily responsible, under the Medical Act 1858, for producing a BP on a national basis.

Legal status of pharmacopoeias

There are two pharmacopoeias that have legal status within the UK — the BP and the European Pharmacopoeia (Ph Eur).

The European Pharmacopoeia The legal basis for the Ph Eur is the Council of Europe Convention on the elaboration of a European Pharmacopoeia, an international treaty signed by member states. There were eight founder countries in 1964 and currently 34 countries are parties to the Convention as individual states together with

the EU. A further 17 European and non-European countries plus the World Health Organization have observer status at the European Pharmacopoeia Commission (EPC). Monographs of the Ph Eur are legally enforced in the countries which are signatories to the Convention, and they are enforced in the EU through Directive EC 2001/83.¹

Preparation of the Ph Eur is the responsibility of the EPC. The technical secretariat of the EPC is part of the Council of Europe's European Directorate for the Quality of Medicines and Healthcare which is located in Strasbourg. The UK participates at all stages of Ph Eur monograph development and revision via UK membership of the Groups of Experts, and through the UK delegation to the EPC.

The Ph Eur contains monographs for pharmaceutical substances, general monographs for formulated dosage forms and individual monographs for vaccines, immunosera and radiopharmaceutical preparations. The monographs of the Ph Eur apply to substances used in either human or veterinary medicines, or in both. The Ph Eur also contains individual monographs of vaccines for veterinary use. Other than vaccines and immunosera and radiopharmaceuticals, there are no monographs for individual dosage forms in the Ph Eur.

The British Pharmacopoeia The monographs of the BP are legally enforced by the Medicines Act 1968. Where a pharmacopoeial monograph exists, medicinal products sold or supplied in the UK must comply with that monograph.

All the monographs and texts of the Ph Eur are reproduced in the BP. These include the monographs for pharmaceutical substances, general monographs, and individual monographs.

The BP Commission is responsible for preparing new editions of the BP and the BP (Veterinary) and for keeping them up to date. Under Section 100 of the Medicines Act, the BP Commission is also responsible for selecting and devising British Approved Names.

The BP Commission is comprised of experts from the pharmaceutical industry, academia, regulators and hospital pharmacy and, in addition, there are two lay members. There are also seven expert advisory groups that advise on and finalise the BP texts (three of these advise on medicinal chemicals and the remainder on antibiotics, pharmacy, herbal and complementary medicine, nomenclature and unlicensed medicines) and four panels of experts on inorganic chemistry, biological products (including blood products and immunological products), microbiology and radiopharmaceuticals that provide advice in these fields when necessary.

In contrast to the Ph Eur, the BP contains monographs for individual dosage forms. This allows the BP to define standards for individual medicinal products on the UK market.

The BP also develops and publishes standards for products such as unlicensed medicines, and herbal and complementary medicines, that would not be otherwise subject to any quality standard that could be legally enforced.

Production of the BP

The BP comprises six volumes. The contents of these volumes are given in Panel 1. In contrast to the Ph Eur, the BP contains individual monographs for dosage forms (Vol III) and monographs for veterinary substances and individual dosage forms are published in a separate volume (Vol V).

The BP is now integrated into the work of the Medicines and Healthcare products Regulatory Agency. The BP is prepared by the Pharmacopoeial Secretariat of the MHRA working in collaboration with the BP Laboratory, the BP Commission and its expert advisory groups. The development of pharmacopoeial standards receives input from relevant industries, hospitals, academia, professional bodies and governmental sources, both within and outside the UK.

The BP Laboratory provides analytical and technical support to the BP. Its major functions are:

- Development of new pharmacopoeial monographs — the laboratory undertakes the development and validation of qualitative and quantitative test methods for new monograph specifications for publication in the BP, and refines and revalidates test methods for existing BP monographs
- The BP chemical reference substance (BPCRS) — the laboratory is responsible for the procurement, establishment, maintenance and sale of BPCRSs and the catalogue currently contains approximately 500 BPCRSs, which are needed as standards for monograph tests in both the BP and the BP (Veterinary).

2008 British Pharmacopoeia

The BP 2008 was published on 28 August 2007. It comes into force on 1 January 2008 and supersedes the BP 2007. This edition, to-

Panel 1: Contents of volumes I–VI of the BP 2008

Volumes I and II	Medicinal substances
Volume III	Formulated preparations, blood-related products, immunological products, radiopharmaceutical preparations, surgical materials and homeopathic preparations
Volume IV	Appendices, infrared reference spectra, supplementary chapters and index
Volume V	British Pharmacopoeia (Veterinary) 2008
Volume VI	CD-ROM version of BP 2008 and BP(Vet) 2008

gether with its companion edition, the BP (Veterinary) 2008, incorporates all the monographs of the fifth edition of the Ph Eur as amended by supplements 5.1 to 5.8 and contains approximately 3,100 monographs including 49 new monographs of national origin and 60 new monographs from the Ph Eur. In addition to the new monographs, several of the supplementary texts and chapters have been reviewed and revised, editorial changes, including colour printing, have been introduced and new areas of work have been added.

Supplementary texts The supplementary chapter on dissolution testing of solid oral dosage forms has been revised to give consistency with internationally harmonised guidance notes. All new monographs included in the BP 2008 and subsequent editions will apply the harmonised dissolution criteria.

Information on the BP policy for monograph initiation is included in a supplementary chapter for the first time.

A new chapter on pharmacopoeial quantitative analysis has been introduced. Sections on pharmacopoeial calculations and titrimetric analysis are provided for the benefit of analysts and information on indicator colour changes is given with examples of colour change intervals for common indicators, printed in colour for the first time.

Unlicensed medicines The primary focus of the BP has been the provision of standards for licensed medicinal products. However, the use of unlicensed medicines in the UK is increasing and becoming more widespread and so standards for those products are also necessary.

The general chapter on unlicensed medicines has been revised and expanded. It now gives the background to the use of unlicensed medicines in the UK; it provides guidance to prescribers, manufacturers and suppliers on the legal and ethical considerations for unlicensed medicines and also provides guidance on standards for the preparation and manufacture of unlicensed medicines.

A new general monograph for unlicensed medicines provides mandatory quality requirements that are generally applicable to all unlicensed medicines. It also includes labelling requirements.

The BP 2008 contains 10 new monographs for unlicensed medicines. These are

identified by the statement “There are currently no licensed formulations in the United Kingdom” in the text of the monographs.

Traditional herbal medicines In support of the new regulatory requirements for registration of traditional herbal medicinal products,² seven new monographs for herbal materials and processed herbs used in traditional Chinese medicines (TCM) are published. The monographs define only the quality of the materials; safety and efficacy have not been assessed.

Homoeopathic preparations As part of another new initiative to support the simplified registration scheme for the regulation of homoeopathic products,³ five new monographs for homoeopathic stocks and mother tinctures are included in the BP 2008. As with TCM, the monographs define only the quality of the materials; safety and efficacy have not been assessed.

A truly global resource

Since its first publication in 1864, the distribution of the BP has grown throughout the world. Now used in over 100 countries with exposure in most continents of the world, the BP is setting the standard for pharmaceutical compliance across the globe. In Australia and Canada it is still a legally enforced national standard and it is used by competent authorities throughout Europe and the Commonwealth to advise and complement the licensing and regulation of medicines.

While addressing the requirements for standards of medicines in the UK, the needs of this wider market are also recognised. By continuing to include monographs for pharmaceutical substances and active pharmaceutical ingredients alongside monographs for individual finished dosage forms, the BP is meeting these needs by providing users with one comprehensively indexed compendium of pharmacopoeial standards for medicines for human and veterinary use.

References

1. Directive 2001/83/EC The Community Code relating to Medicinal Products for Human Use.
2. Directive 2004/24/EC amending as regards to Traditional Herbal Medicinal Products, Directive 2001/83/EC.
3. Directive 2004/27/EC amending Directive 2001/83/EC on the Community Code relating to medicinal products for human use.