United Kingdom

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Organisation and financing of health-care

1 How is health-care in your jurisdiction organised?

The United Kingdom (UK) health-care system comprises both public and private services.

Since 1999, the UK provision of health-care is devolved to the administrations of each of the UK's four constituent countries. Public health-care is provided through the National Health Service (NHS) in England and by equivalent bodies in Northern Ireland, Scotland and Wales. The NHS was founded in 1948 with the aim of providing free health-care at the point of use to the whole population. The Secretary of State for Health is ultimately responsible for the provision of medical services, but discharges this role through the hospitals, clinics and related institutions (some of which may be privately run) contracted by NHS Trusts and Health Authorities and statutory bodies called Clinical Commissioning Groups (CCGs) created under the Health and Social Care Act 2012. The Health and Social Care Act 2012 made fundamental changes to the core structure of the NHS so that, from 1 April 2013, clinical commissioning groups (CCGs) within NHS England and local area teams share the responsibilities of commissioning health-care services for patients. CCGs in turn contract to obtain the services of general practitioners (GPs) for use in the community and pharmacy services, and will tender for the supply of certain medicines and clinical services. NHS England is an independent body, at arm's length to the government. Its main role is to set the priorities and direction of the NHS and to improve health and care outcomes for people in England.

Private health-care may be provided for those individuals who take out such cover in parallel to the NHS. It is generally used as a complement to NHS services, in particular with respect to non-emergency services or elective procedures.

2 How is the health-care system financed in the outpatient and in-patient sectors?

Publicly funded health-care accounts for approximately 83 per cent of total health-care expenditure in the UK, with the remaining 17 per cent of UK health-care expenditure funded privately.

With the exception of some charges (including lower-than-cost fees for prescriptions, optical services and dental services for non-exempt patients) the UK public health system offers inpatient and outpatient services which are free at the point of use for all UK residents.

Public health-care expenditure in Northern Ireland, Scotland and Wales is decided by their respective devolved governments, while NHS expenditure in England is determined by the UK government. For 2016/17, planned NHS expenditure amounts to approximately £118.3 billion. This expenditure (and its equivalents in the devolved jurisdictions) is funded by:

- general taxation (80 per cent);
- national insurance contributions, which are payments made by workers and employers towards the cost of certain state benefits (18.8 per cent); and
- user charges (1.2 per cent).

The private health-care sector in the UK is funded largely by private insurance. It operates its own clinics and hospitals, and may sometimes subcontract its services to the NHS. Certain practitioners in specialist areas work in the NHS as well as in private hospitals and clinics.

Compliance – pharmaceutical manufacturers

3 Which legislation governs advertising of medicinal products to the general public and health-care professionals?

The advertising of medicinal products in the UK is controlled by a combination of legislation and self-regulation through industry associations' codes of practice.

Part 14 of the Human Medicines Regulations 2012 (the UK Regulations) contains the key statutory provisions relating to medicines advertising, and serves to implement Titles VIII and VIIIa of EU Directive 2001/83/EC on the advertising of medicines for human use. Minor amendments to the UK Regulations were made by the Human Medicines (Amendment No. 2) Regulations 2014. In addition to the UK Regulations, the following legislation regulates particular aspects of medicines advertising in the UK:

- the Bribery Act 2010 contains certain provisions which are relevant to interactions between industry and HCPs, government officials and other stakeholders;
- the Enterprise Act 2002 implements certain provisions on the enforcement of Title VIII of EU Directive 2001/83/EC;
- the Cancer Act 1939 prohibits certain advertisements for cancer treatments; and
- the Trades Descriptions Act 1968, the Business Protection from Misleading Marketing Regulations 2008/1276 and the Consumer Protection from Unfair Trading Regulations 2008/1277 contain provisions governing advertising practices generally.

Supplemental guidance to the UK Regulations has been issued by the Medicines and Healthcare Products Regulatory Agency (MHRA) in its '*Blue Guide*'. Part 14 of the UK Regulations and the Blue Guide set out different requirements depending on whether the advertising in question is aimed at the general public or to health-care professionals (HCPs).

In addition to the legislative framework, a self-regulatory system for medicinal product advertising is operated by the Association of the British Pharmaceutical Industry (ABPI) and the Proprietary Association of Great Britain (PAGB). The ABPI's Code of Practice and the PAGB's Consumer Code regulate the advertising of prescription only medicines (POMs) and the advertising of over-the-counter medicines respectively. The MHRA works with the Advertising Standards Authority (ASA), the UK's independent regulator on matters relating to general advertising across all media, and the Committee of Advertising Practice (CAP), the body responsible for writing and maintaining the UK advertising codes.

4 What are the main rules and principles applying to advertising aimed at health-care professionals?

Consistent with EU pharmaceutical law, as a general rule, advertising of an unlicensed medicine is prohibited. Nor can a medicine be promoted outside its licensed indication(s). All medicines advertising must be consistent with the approved summary of product characteristics (SmPC) of the product.

Insofar as the advertising of medicines to HCPs who are persons qualified to prescribe or supply (PQRS) medicines is concerned, regulations 294 to 300 of the UK Regulations set out requirements relating

to a variety of activities including internet advertising, the provision of samples and the conduct of medical sales representatives.

The advertising of POMs to PQRS must be accurate, balanced, fair, objective and unambiguous. It must be based on an up-to-date evaluation of all the evidence and reflect that evidence clearly. It must not mislead, either directly or by implication, and must be sufficiently complete to enable the recipient to form their own opinion of the therapeutic value of the medicine.

All advertisements of medicinal products aimed at PQRS must contain the essential information set out in regulation 294 and schedule 30 of the UK Regulations. These requirements include an obligation of the marketing authorisation holder to:

- state one or more of the licensed indications in the advertisement;
- list the active ingredient(s);
- summarise the main points in the SmPC relating to dosage, method of use, adverse reactions, precautions, relevant contraindications and, (where it is not obvious) method of administration;
- state the actual product name, active ingredients, licence number, the name and address of the licence holder and the cost of the product; and
- refrain from stating or implying that a medicines is 'safe' or 'new' (except in certain specified circumstances).

Regulation 300(1) of the UK Regulations moreover prohibits the supply, offer or promise of any gift, pecuniary advantage or benefit to HCPs in connection with the promotion of medicinal products, unless it is inexpensive and relevant to medical practice. Breach of regulation 300(1) is a criminal offence.

5 What are the main rules and principles applying to advertising aimed at the general public?

Regulations 282 to 293 of the UK Regulations govern advertising aimed at the general public.

The advertising of POMs to the general public is prohibited. Factual and non-promotional press releases relating to POMs are permitted, as long as their content is newsworthy and they provide an appropriate context relative to the use of the medicine and the population for which it is authorised.

Over-the-counter and General Sale List medicines may be advertised to the public subject to certain requirements set out in regulation 291 of the UK Regulations and the guidance provided in Annex 3 of the Blue Guide, including that the advertisements:

- are consistent with the SmPC of the medicines concerned and are not misleading;
- refrain from suggesting that the medicine will enhance the health of a person not suffering from a disease or injury, or that the effects of the medicine are guaranteed or the same as or better than another identifiable treatment;
- refrain from implying that medical consultation is unnecessary or quote recommendations by HCPs or celebrities; and
- are not directed principally at persons aged under 16.

The UK Regulations also set out rules concerning the form and content of advertisements aimed at the public. Products must be clearly identified as medicinal products, and information regarding the correct use of the product and an express invitation to read the SmPC must be included. Pursuant to regulation 293 of the UK Regulations, the sale or supply of medicinal products to the public for promotional purposes is also prohibited.

6 What are the most common infringements committed by manufacturers with regard to the advertising rules?

The MHRA Advertising Standards and Outreach Unit's latest tenth annual report notes that 170 complaints were received by the MHRA in 2015. This is a reduction from the number of complaints received in 2014 (193) and reflects an ongoing downward trend. Consistent with previous years, over 80 per cent of complaints received by the MHRA concerned advertising of prescription-only medicines to the public. Complaints regarding advertisements of botulinum toxin products (eg, Botox, featured particularly prominently). An increase was also observed in the number of complaints received about advertising in social media such as Facebook and Twitter.

The issues reported to the PMCPA are of a more varied nature. These complaints relate to various forms of interactions between pharmaceutical companies and other stakeholders, including advisory board and other meeting arrangements, the provision of hospitality to HCPs, journal advertisements and discount schemes.

7 Under what circumstances is the provision of information regarding off-label use to health-care professionals allowed?

It is a breach of the UK Regulations to issue promotional material for a licensable medicine before the licence is granted, or for the off-label use of a licensed product that goes beyond the scope of its licence.

In exceptional circumstances, limited factual information regarding new treatments which are expected to give rise to significant changes in costs (compared to the costs of currently available treatments) may be disseminated by manufacturers to persons with responsibility for health budgetary decisions, such as health authorities. Manufacturers may also provide relevant factual information concerning unlicensed medicines or off-label use where this is required by certain national public advisory bodies.

The general prohibition on advertising of unlicensed medicines does not prevent the communication of a factual answer to an unsolicited question about an unlicensed medicine or off-label use. However, manufacturers must take care not to engage in activities which appear to be designed to solicit such questions, which would likely be regarded as promotion and therefore in breach of the UK Regulations.

Under the UK Regulations, licensed manufacturers and suppliers of unlicensed medicines (specials) may send out price lists to HCPs to whom the price of specials may be relevant. No product claims should be included in the price list. Typically, a price list would include the active ingredient, strength, dosage form, pack size and price for each product listed.

Companies may promote the service they provide but any proactive display of information about specials, for example at a conference stand, is likely to be seen as promotional.

The ABPI Code (Supplementary Information to Clause 3) recognises that the promotion of medicines at international meetings held in the UK may sometimes pose problems with regard to medicines or indications for medicines that are not licensed in the UK although they are licensed in another major industrialised country. The display and provision of promotional material for such medicines is permitted, subject to certain conditions being met.

8 Which legislation governs the collaboration of the pharmaceutical industry with health-care professionals? Do different rules apply regarding physicians in the outpatient and in-patient sector?

The pharmaceutical industry's collaboration with HCPs is governed by a combination of UK domestic law (implementing EU law) and industry self-regulatory regime. The self-regulatory regime is provided in guidance notes and codes of practice. The governing regulatory framework does not distinguish between the outpatient and in-patient sectors and therefore apply equally to all practising physicians.

In addition to the UK Regulations (see question 3), the instruments (statutory or otherwise) that are particularly relevant to guiding collaborations between the pharmaceutical industry and HCPs in the UK include:

- the Medicines for Human Use (Clinical Trials) Regulations 2004 (as amended), which govern the conduct of clinical trials;
- the Data Protection Act 1998, which ensures the protection of patients' and clinical trial subjects' personal data;
- the Bribery Act 2010;
- ABPI Code of Practice and guidance notes
- Clause 20 of the 2016 ABPI Code, which addresses joint working between pharmaceutical companies and the NHS;
- the ABPI Guidance Notes on Joint Working Between Pharmaceutical Companies and the NHS and Others for the Benefit of Patients (2009)
- ABPI Quick Start Reference Guide for NHS and Pharmaceutical Industry Partners (2012); and
- the ABPI guidance Joint Working with the Pharmaceutical Industry, guide and case studies (2013);

- the General Medical Council's 'Good Medical Practice' guidance (2013), which provides guidance to doctors on standards of professional conduct and medical ethics;
- the General Pharmaceutical Council Standards of Conduct, Ethics and Performance (2012); and
- the Department of Health and NHS Best Practice Guidance on Joint Working between the NHS and Pharmaceutical Industry and Other Relevant Commercial Organisations (2008).

9 What are the main rules and principles applying to the collaboration of the pharmaceutical industry with health-care professionals?

All collaborations between the pharmaceutical industry and HCPs must in principle be for the benefit of patients, although the arrangement may also benefit the parties to the collaboration. Collaborations should typically take place at an organisational level rather than with individual HCPs.

The ABPI Code sets out rules regarding gifts, inducements, promotional aids and hospitality provided to members of the UK health professions. There must never be any benefit provided to such persons by way of an inducement to prescribe, supply or recommend a medicine. Hospitality must also be strictly limited to the main purpose of any event in connection with which the hospitality is offered, and the level of subsistence offered must not exceed the level that the recipients would normally pay for themselves.

Sponsorships by pharmaceutical companies must be disclosed, and declarations of sponsorships made in publications must be sufficiently prominent to ensure that readers are aware of it at the outset.

The UK Regulations do not include a requirement for companies to make publicly available information about payments or other transfers of value provided to HCPs, patient organisations or health-care organisations. These requirements have been agreed by the industry on a voluntary basis under the ABPI self-regulatory system.

10 What are the most common infringements committed by manufacturers with regard to collaboration with health-care professionals?

As indicated at question 6, complaints received by the PMCPA concern a variety of interactions between manufacturers and HCPs. The PMCPA's published case reports confirm that complaints commonly involve the arrangements and conduct of meetings with HCPs, such as advisory board meetings, misleading promotional materials or promotional events which are disguised as educational seminars.

11 What are the main rules and principles applying to the collaboration of the pharmaceutical industry with patient organisations?

Regulations 280 to 293 set out the restrictions on advertising aimed at and interactions with the general public, which includes patients and patient organisations. Clause 27 of the ABPI Code (enforced by the PMCPA) sets out the conditions under which pharmaceutical companies may collaborate with patient organisations.

When working with patient organisations, pharmaceutical companies must ensure that its involvement is documented by a written agreement between the parties and that all of the arrangements comply with the ABPI Code. This includes the need to declare sponsorship and the prohibition on advertising (POMs) to the public. Pharmaceutical companies' members of the ABPI must make publicly available, at a national or European level and on an annual basis, a list of patient organisations to which they provide financial support and/or significant non-financial support.

Restrictions apply with respect to the use of a patient organisations' logo or proprietary material. Companies must also not seek to influence the text of patient organisation material in a manner favourable to its own commercial interests. However, this does not preclude a company from correcting factual inaccuracies.

12 Are manufacturers' infringements of competition law pursued by national authorities?

Yes. Alleged infringements of UK or EU competition law may be the subject of complaints to the Competition and Markets Authority (CMA), a body established under the Enterprise and Regulatory Reform Act 2013. The CMA may also investigate a matter of its own volition.

13 Is follow-on private antitrust litigation against manufacturers possible?

Yes. Actions for civil remedies may be brought in the High Court by anyone with sufficient interest, such as a competitor, supplier or customer who has suffered loss or damage as a result of an alleged infringement of UK or EU competition law. These actions may be stand-alone or follow-on, and the available remedies include damages and/or an injunction.

In addition, any person who has suffered loss or damage as a result of an infringement of UK or EU competition law may bring a damages action before the Competition Appeal Tribunal (CAT). These are follow-on actions only. Claims on behalf of individuals may also be made to the CAT by certain recognised representative bodies acting on behalf of identified consumers.

14 What are the main mandatory anti-corruption and transparency rules applicable to pharmaceutical manufacturers?

As indicated in question 8, interactions and arrangements involving the provision of hospitality, gifts and inducements to prescribe to HCPs (or other decision-makers within healthcare organisations) are also subject to the Bribery Act 2010. Three particular offences thereunder should be borne in mind, namely:

- bribing or accepting a bribe from another person (sections 1 and 2);
- failing to prevent bribery (only corporate bodies) (section 7); or
- bribing a foreign public official (section 6).

The Bribery Act 2010 is enforced by the Serious Fraud Office (SFO). The SFO has issued a memorandum of understanding with the ABPI and the PMCPA, which confirms that the SFO sees self-regulation under the ABPI Code as the first means of dealing with complaints relating to the issues under the scope of the ABPI Code. Although both bodies deal with complaints whatever their source, the SFO focus is on dealing with complaints not covered by the ABPI Code and which meet its criteria of serious fraud.

Closely interlinked with the Bribery Act is the Procurement Directive 2004/18/EC, which provides for a sanction of debarment from public procurement to any candidate who has been convicted of an offence, of which the authority is aware. In the UK, the debarment from public procurement is discretionary where a company is convicted of failing to prevent bribery by an associated person. However, it is mandatory if a company is convicted of active bribery.

Compliance – medical device manufacturers

15 Is the advertising of medical devices and the collaboration of manufacturers of medical devices with health-care professionals and patient organisations regulated as rigorously as advertising and collaboration in the pharmaceuticals sector?

The rules relating to medical devices are similar to, but less detailed and less onerous in some aspects, than those relating to the pharmaceuticals sector. It has been said that the reason for the seemingly more relaxed approach is presumably due to a lower risk of misuse as compared to medicines.

Similar to the pharmaceuticals sector, the rules applicable to medical devices also derive from a combination of legislation and self-regulation. The Medical Devices Regulations 2002 implement the EU Medical Devices Directives and although they address issues of labelling, display, information to be supplied and the CE mark, they do not regulate advertising material per se. The current Medical Devices Directives are subject to a legislative amendment, which was approved by the European Parliament ENVI committee on 15 June 2016. The European Parliament is expected to agree the new Regulation this year, allowing it to come into effect by the end of 2016 or early 2017. The advertising of medical devices is therefore primarily governed by general consumer legislation, such as the Sales of Goods Act 1979, the Consumer Protection from Unfair Trading Regulations 2008 and the Business Protection from Misleading Marketing Regulations 2008.

The self-regulatory regime for medical technology or devices sector is primarily controlled by the Association of British Healthcare Industries (ABHI) in accordance with the principles set out in its Code of Business Practice, which requires any advertising of medical devices to be accurate, balanced, fair, objective and unambiguous. The ABHI Code, along with the Eucomed Code of Ethical Business Practice, govern collaborations and other interactions between medical device manufacturers and HCPs. The Bribery Act 2010 is also applicable to this industry sector.

Pharmaceuticals regulation

16 Which legislation sets out the regulatory framework for granting marketing authorisations and placing medicines on the market?

The granting of marketing authorisations and the placing of medicines on the UK market is governed by the UK Regulations. The UK Regulations implement the relevant EU law concerning granting of marketing authorisations. The relevant procedures are set out in Title III of Directive 2001/83/EC and Title II of Regulation (EC) No. 726/2004 (as amended). In addition, Regulation (EC) No. 1901/2006 addresses the authorisation of medicinal products for paediatric use, while Regulation (EC) No. 1394/2007 contains specific rules concerning the authorisation, supervision and pharmacovigilance of advanced therapy medicinal products.

17 Which authorities may grant marketing authorisation in your jurisdiction?

In the UK, the MHRA is the competent authority for the grant of national marketing authorisations. It is responsible for applications made through the national, mutual recognition or decentralised procedures (see question 18).

The European Medicines Agency (EMA), established by Regulation (EC) No. 726/2004, is the European executive agency responsible for evaluating marketing authorisations submitted through the centralised procedure. It is currently based in London. The EMA advises the European Commission and EU/EEA member states on all matters concerning supervision of medicinal products.

18 What are the relevant procedures?

A medicine can be authorised for marketing in the UK through the following alternative regulatory routes:

- the centralised procedure (CP);
- the decentralised procedure (DCP);
- the mutual recognition procedure (MRP), and
- the national procedure.

CP, DCP and MRP are regulatory procedures created under EU pharmaceutical law that seek to achieve harmonisation and coherence of the regulatory decision on granting and supervision of a marketing authorisation.

A successful CP application results in a single marketing authorisation that is valid in all EEA countries. Applications through the CP are submitted directly to the EMA for scientific evaluation. The scientific evaluation is assisted by the EMA's relevant scientific committee(s) resulting in adoption of an opinion, which will form the basis for the European Commission to issue a binding Commission decision. The European Commission serves as the EU licensing authority to grant marketing authorisations through CP in the EU.

The CP is the mandatory procedure where the application concerns a medicinal product that falls within the scope of Annex to Regulation 726/2004, namely:

- advanced-therapy medicinal product (ATMPs) such as gene therapy, cell therapy and tissue-engineered products;
- medicines derived from biotechnological processes;
- orphan medicines (medicines intended to treat rare human diseases); and
- new active substances with particular therapeutic indications (for example, cancer or HIV/AIDS).

Where a product does not fall within one of the categories referred above, companies may nevertheless use the CP provided that: (i) the new medicine concerned represents a significant therapeutic, scientific or technical innovation; (ii) if its authorisation would be in the interest of public or animal health; or (iii) if the medicine is a generic version of a medicine previously authorised through the CP.

Pharmaceutical companies may apply for the authorisation of a medicine through DCP that has not yet been authorised in any EEA country to be simultaneously authorised in multiple EEA countries (provided that the medicine does not fall within the mandatory scope of the CP). A reference member state leads the assessment of the DCP application and provides the other member states with a draft assessment report and a SmPC. The reference member state liaises with the member states where the applicant wishes to market the product. When an agreement is reached, the application is approved by the individual member states concerned resulting in the grant of national marketing authorisations. If an agreement to approve the application is not reached within 210 days, the matter is referred to the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) (if the medicine is intended for human use) and potentially to the Committee for Medicinal Products for Human Use (CHMP).

The MRP is used in cases where a marketing authorisation has already been granted in one EEA country (this country would become the reference member state for MRP purposes) and an additional marketing authorisation is progressively granted in one or more other EEA countries. Similar to the DCP, the reference member state produces an assessment report and a SmPC for review and approval by the concerned member states. Provided there is no objection, the existing marketing authorisation is recognised and additional marketing authorisations are granted on that basis. If there is disagreement, the matter is referred to the CMDh and then the CHMP.

Provided that the product does not fall within the scope of the mandatory CP and that there is no commercial interest for the product to be marketed in the other EEA countries, an application for marketing authorisation may be submitted nationally to the competent authority. In the UK, the competent authority is the MHRA. In practice, the national procedure is of limited application for new innovative products.

19 Will licences become invalid if medicinal products are not marketed within a certain time? Are there any exceptions?

Other than in exceptional cases where the MHRA has granted an exemption on grounds of public health, a UK marketing authorisation will cease to be in force if the product to which it relates is not placed on the market in the UK within the first three years following the date on which it was granted (see regulation 67 of the UK Regulations). A marketing authorisation will also be invalidated if the product to which it relates has been placed on the market but has not been sold or supplied for a period of three consecutive years.

20 Which medicines may be marketed without authorisation?

Part 10 of the UK Regulations specify exemptions to the general requirement for a marketing authorisation. A medicine may be marketed, notwithstanding that a marketing authorisation has not been granted, in limited circumstances including:

- if the product is supplied in response to an order from a HCP for use by his or her individual patient on a special needs basis (specials) (see question 21);
- if the medicine is manufactured and assembled in accordance with the instructions of a HCP; or
- if the product is manufactured by mixing authorised medicinal products with other authorised medicinal products, or with substances that are not medicinal products, provided that any authorised medicinal products used are subject to general sale.

There are also exemptions in relation to ATMPs prepared on a non-routine basis, and certain radiopharmaceuticals.

Products supplied under these exemptions cannot be advertised and must be manufactured and controlled according to specific requirements including proper record-keeping in relation to their supply.

The UK also operates a parallel import licensing scheme, which allows medicines authorised in other EEA countries to be marketed in the UK provided that the imported products have no therapeutic difference from equivalent products authorised in the UK. Companies wishing to import medicinal products must submit a Parallel Import Licence application to the MHRA's Parallel Import Section (unless they

are products authorised through the CP, in which case the application for parallel distribution should be made to the EMA).

21 Are any kinds of named patient programmes in place? If so, what are the requirements for pre-launch access?

Yes. Pursuant to the UK Regulations, an unlicensed medicine may be prescribed to an individual patient (often called 'named patient supply', although the patient does not, in fact, have to be named by the HCP seeking supply of the unlicensed product), subject to certain conditions in circumstances where a patient has a special need for the medicine and there is no existing alternative. This may be appropriate if the medicine is still undergoing clinical trials and a marketing authorisation has not yet been granted, or in respect of uncommon diseases where there are no suitable medicines available. This provision implements article 5(1) of Directive 2001/83/EC.

In addition, the UK government launched the Early Access to Medicines Scheme (EAMS) in 2014. This is a voluntary, non-statutory scheme that runs in parallel to the UK Regulations, and is intended to allow patients to access innovative unlicensed or off-label medicines earlier than the current marketing authorisation procedures permit. The scheme applies to medicines that target life threatening or seriously debilitating conditions for which there are no existing treatments, or where existing treatments are unsatisfactory. However, there must be sufficient quality, safety and efficacy data available to show that the risk or benefit profile of the product is positive, and that the medicine represents a significant advance in the treatment of an unmet need. As a result, products will normally be eligible for EAMS only after completion of Phase III clinical trials.

Pricing and reimbursement of medicinal products

22 To what extent is the market price of a medicinal product governed by law or regulation?

The prices of branded health service medicines supplied for use in the UK (whether for use in the outpatient or in-patient sectors) are controlled through the Pharmaceutical Price Regulation Scheme (PPRS) or the parallel statutory scheme.

The PPRS is a voluntary scheme agreed between the Department of Health and the ABPI under Section 261 of the National Health Service Act 2006 (the 2006 Act). The scheme is renegotiated about every five years; the current version of the PPRS is the 2014 scheme.

The PPRS is adhered to by members of the ABPI and non-members who have voluntarily agreed with the Department of Health to be subject to it. Scheme member companies are exempted from statutory price regulation by reason of their voluntary compliance with the PPRS. While companies are in principle free to set their own list prices, in practice the PPRS assumes that prices at product launch will be approximate to the product's anticipated value as assessed by National Institute for Health and Care Excellence (NICE) in England (and its equivalents in the devolved countries) pursuant to a technology appraisal recommendation. Price increases proposed by scheme member companies must be approved by the Department of Health and be compliant with the PPRS regime. Although the PPRS does not explicitly fix prices for branded medicines, companies with sales to the NHS that exceed a set value threshold are required to submit data on those sales from which a determination will be made as to the amount to be reimbursed. The PPRS requires manufacturers to make quarterly rebate payments at pre-agreed levels. These rebates are payable subject to certain conditions; for example, manufacturers with sales to the NHS of less than £5 million do not have to make rebates.

The statutory scheme, under sections 262–264 of the 2006 Act, is set out in the Health Service Branded Medicines (Control of Prices and Supply of Information) No. 2 Regulations 2008 (as amended). The statutory scheme is applicable only to POMs. All companies supplying branded health service medicines who are not members of the PPRS (representing about 10 per cent of branded medicines), are automatically subject to the statutory scheme. At the time of preparing this manuscript, Health Service Medical Supplies (Costs) Bill was presented to Parliament on Thursday 15 September 2016. The Bill has been prepared in recognition of the fact that the mechanism of controlling prices in the statutory scheme is less effective in terms of the level of saving it makes than the mechanism in the voluntary scheme, leading to some companies leaving the voluntary scheme in favour of the statutory scheme.

There is no price regulation of generic medicines. However, NHS services are reimbursed for medicines dispensed at nationally set prices, which has the effect of controlling prices.

23 Must pharmaceutical manufacturers negotiate the prices of their products with the public health-care providers?

See question 22.

24 In which circumstances will the national health insurance system reimburse the cost of medicines?

There is no formal reimbursement step required before medicines may be prescribed for NHS patients. However, usage of medicinal products is controlled through inclusion in local formularies defined by CCGs or NHS Trusts. In England, NICE carries out appraisals of certain new products (and existing products in some cases) and issues recommendations based on health technology appraisals based upon an assessment of clinical and cost-effectiveness in order to determine whether such products should be used to treat NHS patients. Such recommendations are important for products to be adopted by CCG or NHS Trust formularies. In practice, a medicinal product which is not included on the relevant formulary will unlikely be used or its use is limited to very exceptional circumstances.

Pharmacies are reimbursed by the NHS for the actual cost of products they dispense, based on the published price of medicines as set out in the Drug Tariff (or, where no reimbursement price is set in the Drug Tariff, at the manufacturer's list price). This is the case in both the outpatient and in-patient sectors.

NHS Trusts are paid by their local CCGs, based on procedures actually performed, and the cost of the procedure is fixed in the 'national tariff', which includes standard medicines, but not many high cost products (these are instead charged separately). The statutory basis for the national tariff is the Health and Social Care Act 2012.

HCPs can issue an NHS prescription for licensed and unlicensed products (in the case of 'specials' and any prescribed off-label use), except in respect of those that feature on the 'blacklist'. The blacklist can be found at schedule 1 to the NHS (General Medical Services Contracts) (Prescription of Drugs, etc) Regulations 2004 and is reproduced in part XVIIIA of the Drug Tariff. It primarily lists health supplements and cosmetic treatments, for which the patient must pay as the cost of dispensing is not reimbursed by the Department of Health.

24 If applicable, what is the competent body for decisions regarding the pricing and reimbursability of medicinal products

Overall responsibility for pricing and reimbursement matters lies with the Department of Health. However, as indicated in questions 22 and 24, NICE (and its equivalents in the devolved jurisdictions) conducts assessments which form the basis of recommendations to the NHS regarding the clinical and cost effectiveness of medicinal products.

26 Are manufacturers or distributors of medicinal products statutorily obliged to give a discount?

No, there is no statutory requirement for manufacturers or distributors to offer discounts on the medicinal products they supply.

However, as indicated in question 22, the PPRS and the various statutory powers under the National Health Service Act 2006 indirectly regulate the prices set by manufacturers for the supply of products to the NHS by regulating profits that pharmaceutical companies are allowed to make on their sales. Discounts by pharmaceutical manufacturers and distributors are, however, common practice in the UK.

Medicine quality and access to information

27 What rules are in place to counter the counterfeiting and illegal distribution of medicines?

The Falsified Medicines Directive 2011/62/EU (FMD) came into force in the EU on 2 January 2013. It introduced harmonised, pan-European measures to ensure that medicines are safe and that the trade in medicines is rigorously controlled. The new rules include:

- obligatory safety features, comprising a unique identifier and an anti-tampering device, on the outer packaging of some medicines (these were detailed in Commission Delegated Regulation (EU)

Update and trends

- The EU's General Data Protection Regulation (GDPR) was on track to come into effect on 25 May 2018. However, the Information Commissioner's Office has confirmed that the UK government needs to consider the impact of the result of the Brexit referendum on the GDPR. There is accordingly some uncertainty as to whether, and if so to what extent, the UK's current Data Protection Act 1998 will be overhauled by the GDPR.
- The EAMS (see question 21) has been in place since April 2014, and aims to give patients with life threatening or seriously debilitating conditions access to medicines that do not yet have a marketing authorisation when there is a clear unmet medical need. Under the scheme, the MHRA will give a scientific opinion on the benefit o risk balance of the medicine, based on the data available when the EAMS submission was made. The process involves a two-stage evaluation, which requires applicants to first obtain a promising innovative medicine (PIM) designation, after which an EAMS opinion will be issued. By the end of September 2016, the MHRA had received a total of 32 applications for PIM designation and it had granted PIM designation to 20 of these.
- In November 2014, the UK government commissioned the Accelerated Access Review with the aim of speeding up access to innovative drugs, devices and diagnostics for NHS patients. The final report was published on 24 October 2016. It makes recommendations of establishing streamlined mechanisms for prioritising emerging technologies, working with innovators to accelerate approvals and aligning national organisations to enhance the NHS's ability to rapidly adopt the right innovations.
- The EU's new Clinical Trials Regulations (EU Regulation No. 536/2014) was published in the EU's *Official Journal* in May 2014, and will come into effect by October 2018. In the UK, the MHRA confirmed on 1 August 2016 that the UK is assessing the potential impact on its regulatory framework of the decision to leave the EU, but that the MHRA currently continues with its programme for implementing the Clinical Trials Regulations. A consultation on the MHRA's proposals for 'Risk proportionate approaches in clinical trials' was issued at the same time.
- As indicated at question 15, the existing medical devices legislation is in the process of being overhauled and it is likely that new EU legislation will come into effect by the end of 2016 or early 2017. In a position statement issued by the MHRA in the wake of the Brexit referendum on 27 June 2016, the MHRA confirmed that its preparations with respect to incorporating in the UK the new EU medical devices legislation will continue. More generally, the MHRA committed to continue to play a full and active role in European regulatory procedures for medicines.
- The new requirements, contained in industry self-regulation, concerning disclosure of transfers of value by pharmaceutical companies to HCPs (see question 9) have yielded its first year of published results. On 30 June 2016, the ABPI published details of payments or benefits in kind – made to HCPs and health-care organisations in the UK – on a publicly accessible database. The new database (available at www.disclosureuk.org.uk) shows payments made by 109 pharmaceutical companies in the UK. The data shows that the pharmaceutical industry spent a total of £340.3 million on working with HCPs and health-care organisations in 2015; the majority (67%) of this amount related to activities connected with the research and development of new medicines.

2016/161 which was published in the *Official Journal* on 9 February 2016 and becomes directly applicable on 9 February 2009);
- a common, EU-wide logo to identify legal online pharmacies;
- tougher rules on the controls and inspections of producers of active pharmaceutical ingredients; and
- strengthened record-keeping requirements for wholesale distributors.

The bulk of the FMD was transposed in the UK by the Human Medicines (Amendment) Regulations 2013, which became effective on 20 August 2013. However, provisions relating to safety features were carved out and do not have to be implemented until 9 February 2019.

Owners of certain intellectual property rights can impede the production and supply of counterfeit medicines by taking private civil actions against infringers, or by applying to restrict the importation of suspected counterfeit goods under Regulation (EU) No. 608/2013. The UK customs authority, HMRC, is responsible for reviewing applications and detaining suspected counterfeit products at the UK border. The owner of the intellectual property rights that the goods are alleged to infringe may then elect to commence proceedings.

More generally, the MHRA has powers under the UK Regulations to investigate cases and, where appropriate, bring criminal prosecutions in respect of the sale and supply of unlicensed medicines.

28 What recent measures have been taken to facilitate the general public's access to information about prescription-only medicines?

As part of its 'Pharmaceutical Package', the European Commission aims to provide for a clear framework for the dissemination of information by marketing authorisation holders about their prescription-only

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medicines to the general public. In view of this aim, the European Commission published a legislative proposal in December 2008 concerning the provision of information to patients. However, following protracted but ultimately unsuccessful negotiations, the proposal was abandoned in May 2014. The UK authorities have not publicised any intention to take additional measures to facilitate the general public's access to information about POMs.

29 Outline major developments to the regime relating to safety monitoring of medicines

The EU legal framework of pharmacovigilance for medicinal products for human use is provided for in Directive 2001/83/EC for all medicinal products authorised under EU pharmaceutical law, and Regulation (EC) No. 726/2004 for centrally authorised products. The legislation was amended by Regulation (EU) No. 1235/2010 and Directive 2010/84/EU. The changes introduced by the Directive were transposed into UK law by the UK Regulations, while Regulation (EU) No. 1235/2010 is directly applicable.

The new pharma co-vigilance legislative package has applied since July 2012 across all EEA countries. The regulatory tools made available under the revised legislation include risk management plans, post-authorisation studies, signal detection and management at EU level, periodic safety update reports assessment and reviews of medicines through referrals. The legislation creates a Pharmacovigilance Risk Assessment Committee (PRAC), which is responsible for assessing and monitoring safety issues for human medicines.

Under the new legislative package, marketing authorisation holders are also required to maintain a pharma co-vigilance system master file (PSMF) that is permanently available for submission or inspection by the national competent authority.

The process of reporting adverse drug reactions (ADR) is in the process of being centralised through electronic submissions to the EudraVigilance database. Previously, reports were made via the individual national competent authority. Since September 2013, it has been mandatory to display a black inverted triangle on the product information of medicines that are being monitored particularly closely by regulatory authorities. With this measure, the European Commission aims to improve the safety of medicines and to highlight to patients the importance of reporting suspected ADRs.

Vaccination

30 Outline your jurisdiction's vaccination regime for humans.

The Department of Health administers the UK's national immunisation programme, and has set out relevant considerations and guidance in it publication *Immunisation Against Infectious Disease* (also known as the Green Book).

Vaccination is not mandatory, and explicit consent must be obtained before any immunisations are administered. The NHS has issued a recommended vaccination schedule for children up to the age of 18, adults over the age of 65 and people who fall into certain risk groups (for example, pregnant women and health-care workers). Certain travel vaccines are usually provided free-of-charge by the NHS (for example, hepatitis A, typhoid and cholera vaccines) whereas other travel vaccines must be arranged privately (for example, yellow fever vaccination).

GPs must maintain a record of patients' vaccination history, which may require them to draw on information from other health-care bodies and institutions to produce a vaccination history. Individuals administering vaccinations must have received training in the management of anaphylaxis, and must have immediate access to appropriate equipment and to adrenaline (epinephrine).

The reimbursement regime surrounding vaccinations is governed by the General Medical Services Contract (GMS contract) made pursuant to the NHS (General Medical Services Contracts) Regulations 2004. This contract acts as the basis for arrangements between the NHS Commissioning Board and providers of general medical services in England. Under the GMS contract, vaccines and immunisations have been paid for through various mechanisms depending on which services a practice provides. Most payments are made through the 'global sum', although certain directed enhanced services for patients at risk of infection are reimbursed separately. The global sum is a distribution of the NHS core funding to practices according to the needs of their registered list of patients and the costs of providing services defined as 'essential' and 'additional' services in the GMS contract.

NHS statistics indicate that, in 2014/15, roughly 92 per cent of children in the UK completed the recommended immunisations by the age of two years, with little variation between the four nations across all vaccines.

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