The Life Sciences Law Review

Editor
Richard Kingham

Law Business Research

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EDITOR'S PREFACE

It is a pleasure to serve as the editor of the first edition of *The Life Sciences Law Review*, which aims to provide an overview of legal issues of special interest to pharmaceutical, biotechnology and medical device companies in 27 jurisdictions. The life sciences sector is of vital importance to the health and well-being of persons around the world. Innovative manufacturers play a key role in the discovery and development of new therapies, while generic manufacturers serve an equally important function by ensuring availability of inexpensive products once patents and regulatory exclusivity periods expire. Throughout the lifespan of a drug or device – from the earliest discovery stage, through non-clinical tests and clinical trials, the governmental approval process, and after entry to the market – lawyers play a central role as advisers to the industry.

We have sought to organise the regulatory discussion in each national entry to correspond roughly to the key stages of product development: the regulatory classification of the product, which determines requirements for approval; non-clinical studies and clinical trials; compassionate use prior to approval; product pre-clearance; regulatory incentives for investment in drug development; post-approval controls; manufacturing; promotion; distribution; legal status; imports and exports; special rules on controlled substances; and enforcement.

In addition to product pre-clearance procedures, many jurisdictions impose requirements for approval of pricing or reimbursement of pharmaceuticals and, to a lesser extent, devices. These are addressed in the entry for each country. We also set out basic information on administrative and judicial remedies, controls on financial relationships with prescribers and payors, special liability systems, and transactional and competition issues that are specific to pharmaceuticals and medical devices.

Finally, each chapter identifies issues of current interest in the jurisdiction. These include, for example, plans to increase transparency in the regulatory process without undermining protection of intellectual and industry property; efforts to adapt traditional regulatory systems to new and emerging technologies, such as companion diagnostics, gene therapy and cell processing; and implementation of regulatory pathways for

'biosimilars' as patents expire for the first generation of biotechnology-derived medicinal properties. As these and other issues develop, we expect to devote additional attention to them in future editions.

I wish to thank all of the contributors who have made this publication possible. They are an impressive group, and it is a privilege to be associated with them in this enterprise.

Richard Kingham

Covington & Burling LLP
Washington, DC
March 2013

Chapter 26

UNITED KINGDOM

Grant Castle and Sarah Cowlishaw[1]

I INTRODUCTION[2]

Medicines for human use are regulated primarily by the Human Medicines Regulations 2012[3] ('the Medicines Regulations'). The Medicines Regulations implement EU Directive 2001/83/EC[4] and most other EU medicines laws into UK law. The Medicines Regulations also consolidated most UK medicines legislation – including the majority of the Medicines Act 1968 – into one statutory instrument to provide a comprehensive regime for the authorisation, manufacture, import, distribution, advertising, sale and supply of medicinal products for human use. However, the Medicines Act 1968 continues to regulate some aspects, such as pharmacies and the dispensing of medicines.

Medical devices are regulated by the Medical Device Regulations,[5] which implement the three EU Medical Devices Directives[6] into UK law.

The Medicines and Healthcare products Regulatory Agency ('MHRA'), an executive agency of the Department of Health, is the UK's national competent and

1 Grant Castle is a partner and Sarah Cowlishaw is an associate at Covington & Burling LLP.

2 This chapter summarises the UK regimes governing medicines and medical devices. Since the UK is an EU Member State and has implemented the EU medicines and medical devices regimes, this chapter will not repeat much of the substantive content of the EU chapter. This chapter will focus on unique features of the UK regimes and should be read in conjunction with the EU section.

3 The Human Medicines Regulations 2012 (SI 2012/1916).

4 Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use, as amended.

5 The Medical Devices Regulations 2002 (SI 2002/618), as amended.

6 The Active Implantable Medical Devices Directive 90/385/EEC, the Medical Devices Directive 93/42/EEC, and the In Vitro Diagnostic Medical Devices Directive 98/79/EC.

enforcement authority for the regulation of medicinal products and medical devices. However, the 'licensing authority' is responsible for the grant, renewal, variation, suspension and revocation of licences, authorisations, certificates and registrations under the Medicines Regulations. The licensing authority comprises either or both of the Secretary of State for Health and the Minister for Health, Social Services and Public Safety, acting on the advice of the MHRA. Likewise, the Secretary of State exercises certain powers under the Medical Devices Regulations.

II THE REGULATORY REGIME

i Classification

The MHRA has primary responsibility for determining whether borderline products are medicinal products or medical devices. It does so on a case-by-case basis having regard to the legal definition of a medicinal product and a medical device set out in EU law and implemented in the UK.

The MHRA's Borderline Section considers each product on its merits and any information that may have a bearing on the product's status, for example, its mode of action, pharmacological properties of the product's ingredients, the claims made for the product, whether there are any similar regulated products on the market, and how the product is presented through labelling, packaging, promotional literature and advertisements.

The Borderline Section provides informal, written advice on classification in response to specific enquiries about potential borderline issues. However, it will also exercise its enforcement powers following complaints about a particular product or based on its review of a product. In the latter scenario, the Borderline Section has a range of powers available to it to require removal of the product from the market (e.g., because it is an unlicensed medicine or a medical device that does not conform to the Medical Devices Regulations). However, the MHRA's usual approach is to serve a provisional determination notice advising that the MHRA considers the product a medicinal product or a medical device. A provisional determination must set out the reasons for the Agency's position and the options available to the person served with the notice should that person disagree with the determination. The options include the right to request an independent (advisory) review panel to review the determination and associated documentation. After considering the panel's advice, the MHRA makes a final determination. There is no right of appeal against a final determination, other than via the courts and judicial review. It is a criminal offence not to comply with the conditions of a final determination.

ii Non-clinical studies

The Animals (Scientific Procedures) Act 1986[7] implemented Directive 2010/63/EU[8] into the UK law from 1 January 2013. It permits research involving animals only in

7 Animals (Scientific Procedures) Act 1986 (c. 14), as amended.

8 Directive 2010/63/EU of the European Parliament and of the Council of 22 September 2010 on the protection of animals used for scientific purposes.

premises licensed by the Home Office, by appropriately qualified staff and in accordance with procedures designed to minimise animal pain and suffering.

The Good Laboratory Practice Regulations 1999[9] transpose Directive 2004/10/EC[10] into UK law. They require that all animal studies be conducted in accordance with sound standards of GLP. These standards reflect the Organisation for Economic Co-operation and Development ('OECD') requirements.

iii Clinical trials

Medicines

Clinical trials of medicines for human use are regulated under the Medicines for Human Use (Clinical Trials) Regulations 2004[11] ('the Clinical Trial Regulations'), which implement the EU Clinical Trials Directives 2001/20/EC[12] and 2005/28/EC[13] into UK law. Clinical trials of medicinal products in humans are generally only permitted if the MHRA has granted a clinical trial authorisation ('CTA') and an ethics committee has issued a favourable opinion. However, a notification scheme is available in the UK for trials involving medicinal products authorised in any EU Member State if the trial relates to the licensed range of indications and dosage form, or involves off-label use that is established practice and supported by published evidence.

CTA approval process

Applicants for a CTA must first have obtained a EudraCT number and must then submit the relevant application form and investigational medicinal product dossier ('IMPD') to the MHRA. The MHRA aims to assess applications within 30 days from receipt of a valid application, but there are accelerated review times for certain studies. The Agency aims to review applications for Phase I trials in healthy volunteers within 14 days and there is also a 14-day notification scheme for clinical trials that involve an authorised medicinal products and meet certain conditions.

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9 The Good Laboratory Practice Regulations 1999 (SI 199/3106), as amended.

10 Directive 2004/10/EC of the European Parliament and of the Council of 11 February 2004 on the harmonisation of laws, regulations and administrative provisions relating to the application of the principles of good laboratory practice and the verification of their applications for tests on chemical substances.

11 Medicines for Human Use (Clinical Trials) Regulations 2004, as amended (SI 2004/1031).

12 Directive 2001/20/EC of the European Parliament and of the Council on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use, as amended.

13 Commission Directive 2005/28/EC of 8 April 2005 laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use, as well as the requirements for authorisation of the manufacturing or importation of such products.

Applications for a positive ethics committee opinion are usually considered in parallel with applications for a CTA and are made via the National Research Ethics Service, which is part of the Health Research Authority.

All investigational medicinal products must have been manufactured or imported by the holder of a manufacturer's authorisation in the European Economic Area ('EEA'). The manufacturer or importer must ensure that a qualified person has performed batch release of the products for clinical-trial use, which is only possible if the product is in accordance with an appropriate standard of good manufacturing practice ('GMP') and if the product conforms with the specifications in the IMPD.

Sponsors must submit reports of suspected unexpected serious adverse reactions (both UK and non-UK) relevant to a UK trial to the MHRA and the relevant research ethics committee. There also is a requirement to submit annual safety reports. They must provide investigators with information on safety issues relevant to whether they enrol patients or allow them to continue with the study.

The Clinical Trial Regulations require sponsors to provide adequate insurance or indemnity to cover liabilities that may arise in relation to the clinical trial. The MHRA expects that a sponsor's insurance policy or indemnity will reflect the form recommended by the Association of the British Pharmaceutical Industry ('ABPI') Clinical Trial Compensation Guidelines. The ABPI has also published specific insurance and compensation guidelines for Phase I clinical trials.

Notification process

Following receipt of a valid notification submission, the MHRA will send sponsors an acknowledgement letter to say that the trial may go ahead after 14 days from receipt of the notification, if the MHRA has not raised any objections. This means that the acknowledgement letter will act as the authorisation.

If the MHRA raises an objection to the notification, the submission is treated as a standard request for authorisation and an assessment is carried out in the usual way with a timeline of 30 days from the receipt of the original notification.

Medical devices

Clinical investigations of medical devices are governed by the Medical Devices Regulations. In addition to obtaining research ethics committee approval, the manufacturer must notify the MHRA prior to the conduct of a clinical investigation involving a non-CE-marked medical device. The MHRA assesses notifications within 60 days of receipt of a complete notification.

There is a different process for performance evaluation of a non-CE-marked *in vitro* diagnostic medical device ('IVD'). Manufacturers must draw up a declaration and follow the procedure set out in Annex VIII of the IVD Directive and must also register details of the IVD for performance evaluation with the MHRA.

Manufacturers must report serious adverse events involving a device under clinical investigation to the MHRA. The MHRA requires manufacturers to provide insurance for subjects in clinical investigations of medical devices.

iv Named-patient and compassionate use procedures

Medicines

Regulation 167 of the Medicines Regulations implements the named-patient exemption under Directive 2001/83/EC into UK law. It allows the supply of unlicensed medicines in response to a *bona fide* unsolicited request by a health-care professional to meet the unmet clinical needs of an individual patient. Medicinal products supplied under the named-patient exemption are known as 'specials'. A special may not be advertised (although price lists may be made available) and they should not be supplied if an equivalent authorised product is available. The responsibility for patient safety remains with the prescribing clinician.

If a special is manufactured in the UK, the manufacturer must hold a manufacturer's (specials) licence granted by the MHRA. Importers of specials must hold the appropriate wholesale dealer's or manufacturer's authorisation. In addition, importers must notify the MHRA 28 days prior to importing a special.

There are record-keeping requirements and serious adverse drug reactions must be reported to the MHRA.

The compassionate use exemption under Article 83 of Regulation (EC) 726/2004 applies directly in the UK.

Medical devices

The Medical Devices Regulations permit the supply of custom-made medical devices that meet the essential requirements but have not been CE-marked, and also devices that do not meet the essential requirements, provided that the MHRA authorises their use.

The use of an individual non-complying medical device, for a single named patient, is permitted only in exceptional circumstances, for example, where no alternative CE-marked devices are available or where it has been demonstrated that the morbidity or mortality of patients is significantly reduced with the use of the device in question as compared to those using alternative available treatment. The MHRA requires that an application be made for each patient, which includes information from the manufacturer and relevant clinician.

v Pre-market clearance

Medicines

Regulation 46 of the Medicines Regulations implements Article 6(1) of Directive 2001/83/EC, which requires that a medicinal product has a marketing authorisation prior to being placed on the market. It is an offence for any person to sell or supply, or offer to sell or supply an unauthorised medicinal product or a medicinal product otherwise than in accordance with the terms of a marketing authorisation.

The MHRA is the UK national competent authority for review of marketing authorisation applications under the national, mutual recognition and decentralised procedures, although the relevant ministers acting through the licensing authority grant the authorisations.

Medical devices

The EU chapter summarises the conformity assessment and CE-marking procedures for medical devices. Since there is little regulatory pre-market review and approval of medical devices (with the exception of European Medicines Agency review of devices incorporating medicinal products and blood products), the MHRA has no involvement in the process leading up to CE-marking.

However, the Medical Device Regulations require that manufacturers and authorised representatives based in the UK that are placing class I or custom-made devices on the market to register details of themselves and the medical devices with the MHRA. Manufacturers or authorised representatives for IVDs must register themselves and their IVDs via the EU database, Eudamed.

vi Regulatory incentives

Medicines

The Medicine Regulations implement the EU periods of eight years' regulatory data exclusivity (during which generic applicants cannot file) followed by two years' market exclusivity (during which regulators may review generic applications, but generic manufacturers cannot launch) under Directive 2001/83/EC for products for which qualifying national applications were submitted after 30 October 2005. For complete free-standing applications submitted on or before that date, UK marketing authorisation holders would benefit from 10 years of data exclusivity protection, during which generic applicants cannot file. These regulatory exclusivity periods begin when the product is first approved anywhere in the EEA, not necessarily in the UK.

The additional data exclusivity provisions for 'orphan medicinal products' and for products with paediatric indications developed in accordance with an approved paediatric investigation plan under Regulation (EC) No. 141/2000[14] and Regulation (EC) No. 1901/2006,[15] respectively, apply directly.

In the UK, the Intellectual Property Office is responsible for granting supplementary patent certificates for medicinal products that meet the criteria under Regulation (EC) No. 469/2009.[16]

Medical devices

UK legislation does not provide specific regulatory exclusivity periods for medical devices. A device may be protected by a UK patent, if it satisfies the requirements for patentability under the Patents Act 1977.[17] A UK patent is granted initially for four years

14 Regulation (EC) No. 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products.

15 Regulation (EC) No. 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No. 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No. 726/2004.

16 Regulation (EC) No. 469/2009 of the European Parliament and of the Council of 6 May 2009 concerning the supplementary protection certificate for medicinal products.

17 Patents Act 1977 (c. 37), as amended.

and is renewable annually thereafter up to a maximum of 20 years from the filing date of the patent application.

vii Post-approval controls

The UK's post-approval controls over marketing authorisation holders for medicines and manufacturers of medical devices closely mirror the EU requirements.

Transfer of marketing authorisations for medicines

Marketing authorisation holders may apply to the MHRA to 'transfer' ownership of their marketing authorisations to third parties. If satisfied that the recipient is suitable to hold the approval, the MHRA will grant the transferee a new marketing authorisation. It will usually also allow the original authorisation to remain in force for a transitional period. This avoids interruptions in supply by allowing a product in the name of the original authorisation holder to be placed on the market until the new product is widely available.

Revocation, suspension or variation of marketing authorisations

The licensing authority, acting through the MHRA, has the power to revoke, suspend or vary a marketing authorisation. Companies that are unhappy with the proposal have the right to appeal to the appropriate committee, then to an independent review panel in accordance with Schedule 5 of the Medicines Regulations. However, these procedures do not apply when the product is centrally approved or has been subject to either the mutual recognition procedure, the decentralised procedure or an EU referral. Under those circumstances, the relevant procedures are governed by EU law.

viii Manufacturing controls

The substantive requirements governing the manufacture of medicinal products, including the need for a manufacturing or import authorisation, a qualified person and compliance with GMP, are discussed in the EU chapter.

The MHRA regulates pharmaceutical manufacturing operations within the UK, although the licensing authority actually grants, suspends and revokes manufacturing authorisations. The MHRA will conduct inspections of manufacturing facilities pre-authorisation and periodically thereafter.

Changes to UK manufacturing and wholesale distribution authorisations require variations to be submitted to the MHRA. A change of name of the licence holder, if it remains the same legal entity, requires a simple administrative notification to the MHRA. Transfers of authorisations from one legal entity to another require submission of a change of ownership application signed by both the transferor and the transferee. The MHRA will only accept such change of ownership applications if there is no substantive change to premises, operations or personnel. If there are any substantive changes, the MHRA will treat the application as an application for a new licence.

ix Advertising and promotion

Medicines

The Medicines Regulations implement the EU advertising rules into UK law. These include the general requirements that advertisements should not be misleading, that they should be substantiated and that they should be accompanied by appropriate prescribing information. There is also a prohibition on pre-approval or off-label promotion of medicines, advertisements of prescription-only medicines to the general public, and illegal inducements to prescribe. Guidance from the MHRA called the Blue Guide on Advertising and Promotion of Medicines ('the Blue Guide') supplements the Regulations and is intended to provide additional clarification on the interpretation and application of the law. The MHRA is the statutory enforcement body for these rules and requires pre-vetting of advertising material in some circumstances, for example, new active substances granted marketing authorisations.

The statutory scheme is supported by a long-standing system of self-regulation based on the ABPI Code of Practice for the Pharmaceutical Industry ('the ABPI Code'). The ABPI Code is enforced by a self-regulatory body called the Prescription Medicines Code of Practice Authority ('PMCPA'), which adjudicates complaints by competitor companies and individuals, but can also bring proceedings itself.

The ABPI Code governs the advertising of prescription-only medicines to health professionals, relevant administrative staff and to the general public. It only applies to companies that are members of the ABPI or that have formally agreed to abide by the ABPI Code. The success of this self-regulatory scheme has meant that the MHRA has not needed to exercise its statutory enforcement powers against legitimate pharmaceutical companies for nearly 30 years.

The provisions of the ABPI Code are consistent with the Medicines Regulations and in some instances more stringent. For example, under the ABPI Code, promotional material must not be issued unless its final form has been certified by two persons on behalf of the company. One of the two persons should be a registered medical practitioner or a UK-registered pharmacist. It also significantly limits companies' ability to provide promotional aids and seeks to regulate certain company interactions with the National Health Service ('NHS').

Medical devices

The UK has no specific device advertising legislation, with the exception of the HIV Testing Kits and Services Regulations 1992[18] that make it an offence to advertise or promote HIV testing kits to the general public. Medical device advertising is subject to general advertising rules, requiring that advertisements be substantiated, factual, balanced and not misleading.

The Association of the British Healthcare Industries ('ABHI') has incorporated advertising guidelines into its Code of Business Practice ('the ABHI Code'). The provisions of the ABHI Code only apply to ABHI members and companies that have

18 HIV Testing Kits and Services Regulations 1992 (SI 1992/460).

formally agreed to abide by the ABHI Code. There is a complaints procedure, but at the time of going to press, the Complaints Adjudication Panel has yet to hear a complaint.

x Distributors and wholesalers

Medicines

As under EU law, distributors of medicinal products must hold a wholesale dealer's licence, and must operate appropriate facilities and staff under the supervision of an appropriately qualified responsible person. They must comply with good distribution practices and maintain appropriate batch records.

The Medicines Regulations define wholesale dealing as 'selling or supplying it, or procuring, holding or exporting it for the purposes of sale or supply,' to a person who receives it for the purposes of selling or supplying it, or administering it or causing it to be administered to a human being. Thus, sale of a medicine without physically handling the product constitutes wholesale dealing, for which a distributor's authorisation is required.

The licensing authority, acting through the MHRA, is responsible for issuing, suspending and revoking wholesale dealer's licences in the UK. The MHRA will conduct inspections prior to the grant of such a licence and then periodically thereafter.

Medical devices

The UK has no specific rules governing the distribution or wholesale of medical devices.

xi Classification of products

Medicines

The Medicines Regulations presuppose that new medicinal products are generally restricted to use under medical supervision and made available only on prescription. There is also scope for imposing additional restrictions, such as requiring that certain products are prescribed only by specialists, or in hospitals. Non-prescription status is appropriate only for products with an appropriate level of safety and where self-diagnosis and treatment is appropriate without a health-care professional's intervention or supervision.

There are two classes of non-prescription or over-the-counter drugs in the UK. Consumers must obtain pharmacy supply products bearing the designation 'P' from pharmacies, where they are dispensed under the supervision of a registered pharmacist. General sale list products may be sold through general retail channels, such as supermarkets, convenience stores, petrol stations and the like. These products bear the designation 'GSL'.

Medical devices

There are no UK rules governing the classification of medical devices that restrict their sale to the public.

xii Imports and exports

The UK's regulations governing the import and export of medicinal products reflect those at the EU level. Unless products are intended only for trans-shipment via the UK,

they must be imported by the holder of a manufacturer's authorisation. Products may only be exported by authorised manufacturers or distributors.

xiii Controlled substances

The Misuse of Drugs Act 1971[19] and subordinate legislation including the Misuse of Drugs Regulations 2001[20] implement the UN Single Convention on Narcotic Drugs 1961 and the UN Convention on Psychotropic Substances 1971 into UK law. A 'domestic licence' is required to produce, possess, supply or offer to supply any controlled substance. Any person that intends to import or export a controlled substance must also obtain an import or export licence for the particular consignment, as applicable. The Home Office is responsible for issuing controlled substances licences in England and Wales. A domestic licence holder may only supply controlled substances to persons authorised to possess such drugs, for example, registered pharmacists.

xiv Enforcement

Medicines

Breach of the Medicines Regulations is in most cases a criminal offence, and the MHRA has an Enforcement Division that considers and manages prosecutions. When the MHRA identifies a potential breach of the legislation, a letter is sent to the individual outlining the Agency's provisional view. The letter will generally list the potential breach or breaches and any public health risk identified where appropriate, along with any action the MHRA requests the company to take. The process to resolve such issues tends to be informal, with individuals agreeing to take voluntary action, so prosecutions are rare. Offences under the Medicines Regulations are usually triable either way (i.e., in summary proceedings before magistrates or on indictment before a Crown Court judge and jury, depending on the seriousness of the breach). They usually carry a penalty of a fine not exceeding £5,000 per offence on summary conviction or an unlimited fine and the possibility of up to two years in jail on indictment. From 1 April 2013, the £5,000 maximum statutory per offence fine will become uncapped.

When the PMCPA Panel rules there is a breach of the ABPI Code under the self-regulatory scheme, the company concerned must give an undertaking not to repeat the offending advertisement or activity. The company must also pay an administrative charge; a charge of £3,000 per matter where it accepts the Panel's decision that it breached the Code. The charge increases to £11,000 per matter where the member appeals the Panel's decision and is unsuccessful. At the conclusion of a case, the PMCPA will also publish a detailed case report in its Code of Practice review and on its website.

Medical devices

The MHRA is responsible for ensuring compliance with the Medical Devices Regulations. For enforcement purposes, an offence under these Regulations is often treated as

19 Misuse of Drugs Act 1971 (c.38), as amended.

20 Misuse of Drugs Regulations 2001 (SI 2001/3998), as amended.

a breach of a safety regulation under the Consumer Protection Act 1987.[21] A person who contravenes the Medical Devices Regulations is liable for a penalty of six months' imprisonment or a £5,000 fine per breach, which is scheduled to become uncapped in April 2013.

The main sanction under the ABHI Code for non-compliance is negative publicity. An administrative charge is also payable. However, there have been no complaints procedures under the Code and the level of the administrative charges payable has not yet been determined.

III PRICING AND REIMBURSEMENT

The NHS is primarily funded by general taxation. The NHS consists of four individual systems: the NHS England, National and Social Care in Northern Ireland, NHS Scotland and NHS Wales. In England, the Department of Health controls the NHS.

i Medicines

The NHS pricing and reimbursement process is essentially a free pricing model for innovative medicines. There are separate schemes for generic medicines. Manufacturers set the reimbursement price of products, usually having consulted the Department of Health. This price is published in the Drug Tariff. The Secretary of State has the power to impose price reductions under the National Health Service Act 2006, but has not done so because most companies participate in a voluntary Pharmaceutical Price Regulation Scheme ('PPRS') (for branded medicines). In addition, the National Institute for Health and Clinical Excellence ('NICE') assesses medicinal products to determine if they are cost effective and should be reimbursed by the NHS. NHS health service providers are expected to make funding available for products recommended by NICE.

ii Pharmaceutical Price Regulation Scheme

The PPRS is a voluntary arrangement negotiated between the Department of Health[22] and the branded pharmaceutical industry represented by ABPI. The ABPI negotiates the PPRS approximately every five years and agrees a price reduction that participants must deliver during the term of the next scheme. The reduction is based largely on profits companies have generated on NHS sales. Participants may deliver the price reduction in a number of ways, for example, through uniform price reductions, by selectively reducing the price of certain products and even by making a payment in lieu of a proportion of the reduction.

21 Consumer Protection Act 1987 (c. 43), as amended.

22 Pursuant to the powers conferred upon the Department of Health by Section 262 of the National Health Service Act 2006 (c. 41).

iii National Institute for Health and Clinical Excellence

NICE performs technology appraisals of medicines and medical devices and draws up clinical guidelines to assist the NHS in England and Wales. There are analogous procedures for other parts of the UK.

Under the National Health Service Act 2006, NHS entities should reimburse medicines used in accordance with a favourable appraisal determination, but are not precluded from reimbursing products that NICE has not recommended.

NICE appraises individual or multiple products, technologies and procedures and develops guidelines on the instructions of the Department of Health or the Welsh Assembly Government. Where necessary, it commissions an independent academic centre known as an assessment group to review available evidence, including submissions by manufacturers, and prepare an evaluation report. A NICE appraisal committee then produces an appraisal consultation document ('ACD'), which includes NICE's provisional view on the cost-effectiveness of a product and its recommendations. NICE has a fairly rigid approach to assessing cost effectiveness. It determines the quality-adjusted life year ('QALY') associated with a technology and uses that to calculate the cost per QALY saved (i.e., incremental cost-effectiveness ratio ('ICER')). NICE will favour interventions with a lower ICER. If the ICER is less than £20,000, NICE will usually recommend reimbursement. For ICERs up to £30,000, it will often exercise its discretion to recommend a product, but above this threshold, it is unlikely to recommend a product unless there are extenuating circumstances. Stakeholders and commentators have four weeks to comment on the ACD. After considering comments on the ACD, the appraisal committee makes its final recommendations in the final appraisal determination ('FAD'). Stakeholders can appeal against the final recommendations in the FAD to the NICE Appeal Panel. If there are no appeals, or an appeal is not upheld, the final recommendations are issued as NICE guidance.

iv Medical devices

There is no formal scheme in the UK that governs the pricing and reimbursement of medical devices. Some devices are listed in the Drug Tariff, but these are largely consumable devices used by outpatients. Many other devices are reimbursed as part of the cost of NHS procedures. However, NICE performs some technology appraisals of medical devices.

IV ADMINISTRATIVE AND JUDICIAL REMEDIES

In the UK, it is possible to challenge the decisions of national public authorities, such as the MHRA or NICE, by judicial review. This is a procedure by which courts examine the decisions, actions or failures to act of a public body, subject to general principles of administrative law. Before seeking judicial review, the applicant must have exhausted all other avenues of redress, such as internal or administrative appeal procedures. In addition, the relevant act and body must be amenable to review; the claimant must have 'sufficient interest in the matter to which the application relates',[23] or legal standing; and

23 Section 31(3) of the Senior Courts Act 1981 (c. 54).

the claim must be commenced 'promptly and in any event not later than three months after the grounds to make the claim first arose'.[24]

The grounds for judicial review are constantly evolving but, in general, the courts will consider whether decisions or acts of a public body are illegal, irrational or procedurally unfair.[25]

There are three specific discretionary remedies for judicial review proceedings: quashing orders, prohibiting orders and mandatory orders. A claimant may also seek a declaration, a stay or injunction and, in certain circumstances, damages. Claimants typically seek a quashing order to set aside the public body's decision, together with a mandatory order directing the public body to take the decision again in accordance with the court's judgment.

Where national judicial review proceedings involve matters of EU law, national courts may refer questions of EU law to the Court of Justice of the European Union ('CJEU'). The CJEU will issue a preliminary ruling, which the national court can use as a basis for its judgment.

V FINANCIAL RELATIONSHIPS WITH PRESCRIBERS AND PAYORS

i Medicines

Regulations 293–300 of the Medicines Regulations implement into UK law the EU rules on the promotion of medicinal products and also interactions between pharmaceutical companies and health-care professionals. The legal position in the UK concerning communications or activities of pharmaceutical companies involving prescribers and payors is therefore the same as in the EU, and contains a broad prohibition on the offer to health-care professionals of unlawful inducements to prescribe. However, the prohibition excludes financial trade practices, such as discounts, that were in common usage in the industry on 1 January 1993.

The Blue Guide and the ABPI Code clarify or establish additional requirements governing interactions with payors and prescribers. For example, the ABPI Code also governs the offer of inducements to administrative staff and prohibits promotional aids, except for stationery associated with meetings and inexpensive items for patient support. The ABPI Code also contains guidelines governing certain interactions between companies and NHS entities.

ii Medical devices

There are no specific UK rules that govern the interaction between medical devices companies and health-care professionals.

The ABHI Code includes guidelines and a question-and-answer document on the minimum standards device companies should comply with when interacting with

24 Civil Procedure Rules 1998 (SI 1998/3132) Part 54.5(1).

25 *Council of the Civil Service Unions v. Minister for the Civil Service* [1985] A.C. 374. List of grounds for review cited is not exhaustive and may be added to in the future.

health-care professionals, including payors. The provisions of the ABHI Code are based on the EU code of practice, the Eucomed Code, and therefore the national principles reflect the EU position on ethical communications and interactions with prescribers and payors.

iii Anti-bribery legislation

Most health-care professionals, administrative staff and payors in the UK will be government officials, employees or contractors. Companies should therefore also be mindful of anti-bribery legislation, such as the UK Bribery Act 2010.

VI SPECIAL LIABILITY OR COMPENSATION SYSTEMS

i Medicines

With the exception of a specific vaccine injury compensation scheme and the implementation of EU rules governing compensation for clinical-trial related injuries, there are no specific pharmaceutical injury compensation rules in the UK.

The Vaccine Damage Payments Act 1979 ('VDPA') provides a statutory compensation scheme for individuals who can demonstrate that they have suffered a severe mental or physical disability caused by a vaccination against a specific disease. The VDPA scheme applies only to vaccinations for specified diseases listed in the VDPA or diseases recommended by the Secretary of State for Health as falling under the scope of the VDPA scheme.[26] The diseases are typically those for which vaccination is recommended.

Under the VDPA, individuals must show that they were at least 60 per cent disabled by the vaccination to be entitled to a tax-free payment of £120,000. The scheme is rarely used because of the requirement for 60 per cent disability before a claim can be made and limitation periods under UK law.

ii Medical devices

There is no national scheme or system to compensate individuals injured by medical devices.

VII TRANSACTIONAL AND COMPETITION ISSUES

i Competition law

Since the UK is an EU Member State and because the provisions of the UK Competition Act 1998 closely reflect those found in Articles 101 (anti-competitive agreements) and 102 (abuse of dominant market position) of the Treaty on the Functioning of the European Union, many of the considerations and issues outlined in the EU chapter apply equally in the UK.

The Office of Fair Trading ('OFT') is the body with responsibility for policing activities that affect trade within the UK, or regions within the UK. It has bought a number of proceedings against companies in the life sciences sector. For example, the

26 Section 2 of the VDPA 1979 (c. 17), as amended.

OFT found that Genzyme abused its dominant position by bundling the list price of its drug, Cerezyme, with the price of home-care services. The OFT imposed directions requiring that the NHS list price for Cerezyme be a stand-alone price for the drug, exclusive of any home-care services, and that the price at which the drug was supplied to third parties be no higher than the stand-alone price for the drug.

Napp Pharmaceuticals and other manufacturers have been investigated for the price fixing of opiate drugs. The OFT found that Napp abused a position of dominance approaching monopoly in the UK market for the supply of morphine tablets by charging excessively low, predatory or exclusionary, prices in the hospital segment of the market, and excessively high prices in the community segment of the market. The OFT ordered Napp to cut the price of its morphine products to the community and reduce the difference between community and hospital prices.

In 2005, the OFT undertook a review of the PPRS to assess whether the PPRS was the most effective means of securing value for money for the NHS. While the OFT did not find the PPRS anti-competitive *per se*, it queried whether the price of drugs under the PPRS reflected their therapeutic value.

ii Transactional issues

The considerations and issues outlined in the EU chapter apply equally in the UK.

VIII CURRENT DEVELOPMENTS

As an EU Member State, developments in the UK regimes governing medicines and medical devices will be driven largely by developments at the EU level.

At the purely national level, there is a growing realisation that NICE technology appraisal methodologies struggle to deal with products for smaller patient populations and those used towards the end of a patient's life, for example, in the oncology space. Possible replacements include a value-based pricing scheme, or one that seeks to reward innovation.

There are also signs that the MHRA is adopting a more aggressive enforcement stance, particularly where non-compliance causes, or has the potential to cause, a public health concern.

Appendix 1

ABOUT THE AUTHORS

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Grant Castle is a partner in the London office of Covington & Burling practising in the areas of life sciences regulatory law, with an emphasis on pharmaceutical and medical device regulation and associated compliance issues. He has assisted clients with a wide range of regulatory and compliance issues and has participated in formal and informal advertising, commercial practices, good manufacturing practices, good clinical practices, drug safety and pharmacovigilance proceedings before the European Medicines Agency, national authorities, courts and self-regulatory bodies.

He speaks and lectures frequently on compliance issues in both the pharmaceutical and medical device areas at the University of Surrey, the University of Wales and Cranfield University. He received a BSc in Chemistry with first class honours from Imperial College of Science, Technology and Medicine in London in 1991 and a PhD in Organic Chemistry from Trinity College, University of Cambridge in 1994.

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