Medicinal product regulation and product liability in UK (England and Wales): overview

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REGULATORY OVERVIEW

1. What are the main legislation and regulatory authorities for pharmaceuticals in your jurisdiction?

Legislation
The main legislation for authorisation of medicines in the UK derives from EU legislation, in particular:

- Regulation (EC) 726/2004 on the authorisation and supervision of medicines and establishing a European Medicines Agency (EMA Regulation), as amended.

The Human Medicines Regulations 2012 implement the EU legislation in the UK and contain provisions established independently of EU law and on matters of national competence (such as the supply of unlicensed medicines).

The regulatory pricing regime for medicinal products is contained in the National Health Service Act 2006 and the Health and Social Care Act 2012, together with subordinate legislation.

Regulatory authorities

Overall responsibility for pricing and reimbursement matters lies with the Department of Health.

Assessments of various aspects of patient care are conducted by the National Institute for Health and Care Excellence (NICE), which issues recommendations to the National Health Service (NHS) in England, including appraisals of health technologies based on clinical effectiveness and cost-effectiveness. Similar assessments are conducted by equivalent bodies in the devolved administrations.

The MHRA Innovation Office assists those with a novel medicine or novel approach to manufacture. The Office is the first point of call for regulatory queries about regenerative medicines (such as advanced therapy medicinal products, that is, gene therapy and somatic cell therapy products, products containing genetically modified organisms, or tissue engineered products which are defined as gene and somatic cell therapy and tissue engineered products (ATMPs)). It manages referrals to the four regulatory authorities in the field:

- MHRA.
- Human Fertilisation and Embryology Authority for gametes and embryos (HFEA).
- Human Tissue Authority for all other tissues and cells (HTA).
- The Health Research Authority which streamlines the regulation of research in the NHS in England (HRA).

2. Briefly outline how biologicals and combination products are regulated in your jurisdiction.

Biological medicines include products whose active substance may be human or animal tissue, or of microbiological origin, as well as those where a complex bioassay system is required to monitor potency. Immunological medicines, medicines derived from human blood and human plasma, biotechnology products and advanced therapy medicines are all considered to be biological medicines.

Biological medicines can generally be authorised through national marketing authorisation (MA) procedures. However biotechnology products (defined as products which are manufactured by recombinant DNA technology, products requiring genetic manipulation of cells, or monoclonal antibodies or use of hybridoma technology) and ATMPs fall outside the scope of the national MA procedure and must be authorised through the EU's centralised procedure according to the EMA Regulation.

Combination products consisting of a medicine and a medical device used for drug delivery, where both components are presented as an integrated unit, are generally regulated as medicines, except where the device component is presented separately from the medicine. The approval of such combination products must have regard to the regulatory regime for medical devices. In the case of combination products, where the medicinal component has only an ancillary function, the medical devices regime applies, but the medicinal component is separately assessed.

3. Briefly outline how medical devices and diagnostics are regulated in your jurisdiction. Is there any specific regulation of health IT issues and mobile medical applications?

each as amended. The EU has two new Regulations which have been proposed and will replace these EU directives (see http://uk.practicallaw.com/5-541-6925?q=medical+devices+regulation and http://uk.practicallaw.com/4-542-7905).

Medical devices do not require a marketing authorisation. However, before a medical device can be placed on the market, the manufacturer must ensure that the device meets the “essential requirements”, namely, the specific requirements set out in the legislation for that category of device and taking into account its intended purpose. These focus principally on the following areas:

- Health and safety,
- Product quality,
- Transportation and packaging,
- Sterility and minimising risks of contamination,
- Information for use.

To show compliance with the essential requirements, the manufacturer must follow the conformity assessment procedure. The conformity assessment procedure that a manufacturer must follow is determined according to the risk classification of the device. Lowest risk devices can be certified by the manufacturer on the basis of a self-declaration of conformity. The higher the risk category into which the device falls, the higher the level of assessment and scrutiny undertaken by notified bodies.

As of December 2014, there are five notified bodies in the UK who are competent to perform elements of conformity assessments:

- Amtac Certification Services Ltd.
- BSI Healthcare.
- Lloyd’s Register Quality Assurance Ltd.
- SGS United Kingdom Ltd.
- UL International (UK) Ltd.

Notified bodies are monitored by the MHRA, which is their competent authority and which may withdraw their designation if they are not meeting relevant requirements.

Following this assessment, the manufacturer can affix a “CE mark” to the device to show that it has undergone proper conformity assessment in accordance with the essential requirements. The CE marking enables free movement of the device in the European Economic Area without the need for further approval in each country. The manufacturer must inform a competent authority when it first places the medical device on the EU market. For certain medical devices the manufacturer must be registered with the competent authority in the EU state in which it has an office or place of business. In the UK this is the MHRA.

There are an increasing number of mobile health apps available to use for medical purposes in the UK. The definition of medical device explicitly includes software, although not all software products used in mobile health fall under the Medical Devices Regulations 2002. On 8 August 2014, the MHRA added to the existing European Commission guidelines on stand-alone software (Meddev 2.1/6 January 2012) and published its own guidance on medical device stand-alone software (including apps), explaining their regulation and providing examples of what could be considered medical devices (www.gov.uk/government/publications/medical-devices-software-applications-apps/medical-device-stand-alone-software-including-app).

The MHRA has indicated that there are a number of words likely to contribute to a determination that an app is a medical device (such as analysis, detects or monitors). A specific example given of apps that may be considered medical devices are apps that measure temperature or heart rate, or collect information entered by the user where the output affects the treatment of an individual. General disclaimers (such as “this is not a medical device”) are not acceptable if medical claims are made or implied elsewhere in the product labelling or associated promotional literature.

**PRICING, STATE FUNDING AND REIMBURSEMENT**

4. What is the structure of the national healthcare system, and how is it funded?

The UK’s national healthcare system is the NHS. It is primarily funded through general taxation, to provide healthcare that is free at the point of delivery.

With the Health and Social Care Act 2012, the structure of the NHS changed. The current structure is as follows. The Department of Health has overall responsibility for healthcare strategy. NHS England (the working name of the NHS Commissioning Board) commissions primary care services and allocates resources to clinical commissioning groups. NHS England has a budget of around GBE96.8 billion (of total national healthcare spend of around GBE170.8 billion).

NHS England is independent of government. It allocates around GBE64.8 billion a year to clinical commissioning groups (CCGs). Staffed by healthcare professionals, the 221 CCGs commission the NHS services required by their local patient populations. CCGs are monitored by NHS England, which has an overarching aim of improving health outcomes for people in England.

The NHS operates differently in the devolved nations.

5. How are the prices of medicinal products regulated?

Manufacturers are in principle able to set their own list prices. However, the total income of manufacturers is regulated by the voluntary Pharmaceutical Price Regulation Scheme (PPRS) (renegotiated every five years). Therefore, while in theory the UK is a free-price country, innovative pharmaceutical companies are heavily constrained in respect of what they can charge for their patented protected medicines.

The PPRS 2014 (effective from 1 January 2014) is an agreement between manufacturers and the Department of Health, which seeks to limit the growth of NHS spend on medicines in the five years to 31 December 2018. The PPRS 2014 recognises that the actual growth of NHS spend on branded medicines will exceed the “allowed growth”, and as such 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 GBE5 million do not have to make rebates. Moreover, manufacturers subject to the PPRS are unable to exceed profitability limits set on both Return on Capital and Return on Sales measures.

While the PPRS is a voluntary scheme, most manufacturers of patent protected medicines consent to its application on becoming scheme members. For those manufacturers not party to the PPRS (representing about 10% of branded medicines) there is a fall-back statutory scheme. While the PPRS is not legally binding, manufacturers that do not comply can be made to comply with the statutory scheme. However, despite the fact that the PPRS is a voluntary scheme a court in the UK has held that it does contain mandatory provisions.

For individual products, once manufacturers set their list price, there are tight controls on the circumstances in which that list price can be increased. While manufacturers are in principle able to set their own list prices, in practice the PPRS assumes that prices at launch will be close to their expected value as assessed by NICE.
Indeed, a recommendation in the form of a “technology appraisal recommendation” or a “highly specialised technology recommendation” from NICE is critical to the success of a drug, as the NHS is under a legal obligation to reimburse the recommended medicines. NICE does not evaluate all new medicines but evaluates medicines in relation to specific criteria (set out on its website).

For medicines which might not usually be funded by the NHS, pharmaceutical companies are increasingly using patient access and risk sharing schemes.

Generic medicines are not price-regulated, but NHS services are reimbursed for medicines dispensed at nationally set prices, which has the effect of controlling prices.

6. When is the cost of a medicinal product funded by the state or reimbursed? How is the pharmacist compensated for his dispensing services?

In-patient sector
The Health and Social Care Act 2012 sets out a statutory basis for the “national tariff”, a set of prices paid by commissioners to providers (including NHS foundation trusts and other NHS trusts) for all services carried out in the NHS. This national tariff was introduced at the end of 2013 and operates from 1 April 2014, and allows for some flexibility in pricing. The 2015/16 national tariff has not yet been finalised. Hospitals are paid based on procedures performed.

Outpatient sector
Pharmacies are reimbursed by the NHS for the products they dispense, based on the submission of NHS prescriptions and the reimbursement prices set in the Drug Tariff (or, where no reimbursement price is set in the Drug Tariff, at the manufacturer’s list price). They often purchase stock direct from pharmaceutical companies and wholesalers at lower prices and can, therefore, benefit from the marginal difference between the purchase price and the reimbursement price.

In addition, patients pay a prescription charge that is currently set at £8.20. Children, the elderly, and certain medically exempt individuals do not pay a prescription charge.

CLINICAL TRIALS

7. Outline the regulation of clinical trials.

Legislation and regulatory authorities
Clinical trials are regulated by the Clinical Trials Regulations 2004, which implement Directive 2001/20/EC on the conduct of clinical trials (Clinical Trials Directive) and Directive 2005/28/EC on good clinical practice (GCP Directive). Applications for a clinical trial authorisation are made to the MHRA. All clinical trials also require a favourable opinion from an Ethics Committee.

Authorisations
Following submission of a valid request involving a general medicine, the MHRA will conduct an initial assessment within 30 days, or within an average of 14 days if a qualifying Phase I trial, and will either:

• Accept the request for the clinical trial authorisation.
• Accept the request subject to conditions.
• Not accept the request, and provide reasons for its decision.

In the case of an acceptance subject to conditions or non-acceptance, the sponsor can submit an amended request within 14 days and the MHRA will assess within 60 days of the original request.

As part of its risk-adapted approach, the MHRA also provides a simplified notification scheme for the authorisation of most trials where the potential risk is no higher than that of standard medical care. Detailed guidance on risk adapted approaches is available on the MHRA website.

The Ethics Committee will review the:

• Trial protocol.
• Suitability of the personnel, investigator and facilities.
• Investigator’s brochure.
• Recruitment, compensation and consent of the subjects.

It has 60 days in which to form a view on the clinical trial involving a general medicine, and must then give a reasoned opinion to the sponsor and the MHRA.

For ATMPs and other biological medicines, the procedures may involve expert advisory bodies (such as the Commission on Human Medicines) and extended timelines.

Consent
Clinical trial subjects must give informed consent to be involved in the trial. Before subjects give consent, the sponsor must give them full details of the nature, significance, implications and risks of the trial. Subjects must also have had an interview with the investigating team. The consent must be evidenced in writing, in general by the subject signing the consent form. The Ethics Committee will consider the wording and information in the consent form. Detailed guidance on consent is available on the MHRA website.

Trial pre-conditions
A trial can only be started if an Ethics Committee and the MHRA conclude that the anticipated therapeutic and public health benefits justify the risks. As part of GCP, provision must be made for appropriate insurance or indemnity to cover the liability of the investigator and sponsor. Ethics Committees usually request separate insurance cover, rather than allowing a sponsor to self-insure. In addition, sponsors usually agree to provide compensation to patients for injuries under the relevant Association of the British Pharmaceutical Industry (ABPI) Compensation Guidelines.

Procedural requirements
The clinical trial must be conducted in accordance with GCP, and the terms of the protocol, clinical trial authorisation and Ethics Committee approval. Schedule 1 to the Clinical Trials Regulation 2004 sets out conditions and principles of GCP and for the protection of clinical trial subjects, including the requirements set out in Article 3 of the Clinical Trials Directive and Articles 2 to 5 of the GCP Directive. The sponsor must notify the MHRA of any serious breach of these conditions and principles or the protocol within seven days of it becoming aware of the breach.

If, following authorisation, a sponsor wishes to make any substantial changes to the terms of the clinical trial authorisation, protocol or other documents accompanying a request to the MHRA for a clinical trial authorisation or for the favourable opinion of the Ethics Committee, it must submit a further request to the MHRA and/or the Ethics Committee.

The sponsor and investigator can take appropriate urgent safety measures to protect subjects against immediate hazard to health or safety. Written notice must be given to the MHRA (as a substantial amendment) within three days of measures being taken.

The investigator must report immediately to the sponsor any serious adverse events and any adverse events identified in the protocol as critical to the evaluation of safety. The sponsor must
keep detailed records of all reported adverse events which may be required to be sent to the MHRA. Suspected unexpected serious adverse reactions (SUSARs) that are fatal or life-threatening must be reported to the MHRA and Ethics Committee as soon as possible but no later than seven days of the sponsor becoming aware.

SUSARs that are not fatal or life-threatening must be reported as soon as possible but no later than 15 days after the sponsor becomes aware.

In addition, sponsors are required to submit an annual list of suspected serious adverse reactions together with a safety report once a year, in the standardised form of a development safety update report (DSUR).

Under the UK’s self-regulatory system, the ABPI Code of Conduct for prescription medicines requires member companies and others that agree to be bound to:

- Publish all clinical trial results within one year of marketing authorisation.
- Publicly register new clinical trials within 21 days of the first clinical trial subject being enrolled.
- On 15 October 2014 the ABPI published a clinical trial disclosure toolkit which provides good practice guidance and is updated regularly in line with changes to international regulatory requirements.

On 1 January 2015, the European Medicine Agency’s (EMA) Policy 0070 on proactive publication of clinical data entered into force, and will be implemented in a number of phases. The first phase will involve the publication of clinical reports submitted to it under the centralised procedure for MAs. Policy 0070 does not replace the EMA’s reactive Policy 0043 or limit public access to documents of EU institutions or bodies provided by Regulation (EC) No 1049/2001 which continue in force. The EMA is also involved in a separate process for the proactive release of clinical study result summaries on the EU Clinical Trials Register.

8. What is the authorisation process for manufacturing medicines?

Application
Manufacturing licences are regulated by the Human Medicines Regulation 2012 which implements the Code for Human Medicines Directive and Directive 2003/94/EC on good manufacturing practice (GMP Directive). Applications for a manufacturing licence are made to the MHRA’s Inspection, Enforcement and Standards Division. There are a number of licences, including:

- Manufacture/importation licences (MIA) for licensed medicines.
- Specials manufacture licences (MS) for unlicensed medicines.
- Manufacture/importation licences (IMP) for investigational medicines to be used in clinical trials.

Wholesaler dealer licences are also regulated by the Human Medicines Regulation 2012 which implements the Code for Human Medicines Directive and reflects the EU Guidelines on Good Distribution Practice (2013/C 343/01) (GDP). The remainder of this answer considers both manufacturing and wholesale dealer licences.

Conditions
Applications for manufacturing licences and wholesale dealer licences must include the information set out in Schedule 3 of the Human Medicines Regulations 2012. The MHRA will only issue a manufacturer’s or wholesale dealer’s licence when it is satisfied, following an inspection of the site, that the information contained in the application is accurate and that the site conforms with the Human Medicines Regulation 2012 and the requirements of GMP or GDP.

In dealing with an application the MHRA will consider as appropriate the:

- Operations proposed to be carried out under the manufacturing licence.
- Premises in which those manufacturing operations will be carried out or the medicines stored.
- Equipment to be used for carrying out those manufacturing operations or equipment and facilities available for distributing the medicines.
- Qualifications of those responsible for supervising the manufacturing.
- Arrangements for keeping records in respect of the medicines manufactured or stored on or distributed from those premises.

An application for a standard variation which has the effect of altering the medicines, operations, premises, equipment, facilities or named persons under the licence may also be subject to a further inspection of the site.

Restrictions on foreign applicants
There are no specific restrictions placed on foreign applicants for manufacturer’s or wholesale dealer’s licences. However, to receive a manufacturer’s licence the site and relevant production and quality control personnel, including the Qualified Person, must be located in the UK. To receive a wholesale dealer’s licence the site and Responsible Person must also be located in the UK.

Key stages and timing
Following submission of the application for a manufacturer’s or wholesale dealer’s licence to the MHRA and a satisfactory inspection, the MHRA will issue the licence and a certificate of GMP or GDP. The MHRA may refuse to grant a licence or grant a licence otherwise than as applied for, in each case giving reasons and a period of 28 days for the applicant to respond. The timing of the application and inspection process will vary depending on how quickly an inspection can be carried out and whether any deficiencies are identified and/or information required to be provided to the MHRA. The MHRA should process applications within 90 working days.

Fee
The fees for obtaining a manufacturer’s and wholesale dealer’s licence are set out in the Medicines (Products for Human Use) (Fees) Regulations 2013, and are also listed on the MHRA website. The current standard fee for a manufacturer’s licence is £8,143 plus a £2,655 inspection fee. For a wholesale dealer’s licence the standard fee is £8,803 plus a £1,936 inspection fee.

Period of authorisation and renewals
A manufacturer’s and wholesale dealer’s licence remains in force until the licence is revoked by the MHRA or the licence is surrendered by the licence holder.

Monitoring compliance and imposing penalties
Each site is periodically inspected by the MHRA’s GMP or GDP Inspectors to assess compliance with the relevant regulatory requirements, including the principles of GMP or GDP and compliance with the Human Medicines Regulation 2012 and the provisions of the licence. A manufacturing licence holder must comply with the conditions relating to manufacture, assembly and import of medicines set out in Regulations 37 to 41 and the standard licence provisions included in the licence as set out in Schedule 4 of the Human Medicines Regulations 2012. The holder of a wholesale dealer licence must comply with the conditions set out in Regulations 43
to 45 and the standard licence provisions included in the licence as set out in Schedule 4 of the Human Medicines Regulation 2012.

Routine inspections are conducted at approximate intervals of two to three years, at the licence holder’s cost. Advance notice of inspection is normally provided, unless circumstances require that an unannounced inspection should take place.

The licence holder receives a post inspection letter identifying any deficiencies to be resolved. If an inspection identifies one or more critical deficiencies, a referral will be made to the MHRA’s Inspection Action Group (IAG). The IAG can recommend:

- Refusing, suspending or revoking the licence.
- Removing the manufacturer’s Qualified Person or Responsible Person from the licence, or referring a Qualified Person to his professional body.
- Issuing a warning letter.
- Increasing frequency of inspections.
- Requesting a meeting with MHRA.
- Referring to the MHRA’s Enforcement Group for further consideration.

Failure to comply with the terms of a manufacturing licence is a criminal offence, the penalties for which are a fine not subject to any statutory maximum and/or, if dealt with on indictment, a period of up to two years’ imprisonment.

In addition, regulations 91 to 94 of the Human Medicines Regulation 2012 set out various offences relating to Regulation (EC) 1901/2006 on medicines for paediatric use (Paediatric Regulation).

MARKETING
Authorisation and abridged procedure

9. What is the authorisation process for marketing medicines?

Application

The Human Medicines Regulation 2012 implements the Code for Human Medicines Directive and the EMA Regulation. No medicine can be placed on the market in the UK unless it has been granted an appropriate MA granted nationally by the MHRA under one of a number of procedures, or centrally by the EMA.

Applications can be submitted in one of the following ways:

- To the MHRA for a national MA.
- Through the Decentralised Procedure in a number of EU member states at the same time.
- Through the Mutual Recognition Procedure, if the applicant already has a national MA in another EU member state.

Applications can also be made to the EMA for evaluation of medicines under the Centralised Procedure. Applications which must be submitted through this procedure are:

- Certain biotechnology products.
- ATMPs.
- New active substances with certain therapeutic indications (such as cancer).
- Orphan medicines.

For some others involving a new active substance the EMA can agree to a centralised assessment where certain criteria are met (such as being a significant therapeutic, scientific or technical innovation). There are special centralised procedures for conditional authorisations and use in exceptional circumstances.

All applications must follow the common technical dossier (CTD) format, although the preferred format is the electronic Common Technical Dossier (eCTD). The summary of product characteristics (SmPC) should be submitted in the correct form using the template available on the MHRA website.

In addition to these procedures, applicants usually need to submit a paediatric investigation plan (PiP) early in the development of the medicine. The Paediatric Regulation requires applicants to submit to the EMA a PiP or, if the disease does not affect children, a waiver application. For an application for a MA to be valid the PiP agreed by the EMA’s Paediatric Committee (PDCO) must have been carried out or a relevant waiver or deferral of clinical studies granted by the PDCO. The Paediatric Regulation also created a new type of MA with ten years of market protection, the Paediatric Use Marketing Authorisation (PUMA). The PUMA may be applied for through any of the national procedures or the EMA’s centralised procedure.

The MHRA has also implemented the voluntary non-statutory early access to medicines scheme (EAMS) which aims to give patients with life-threatening or debilitating conditions access to medicines that do not yet have a MA where there is a clear unmet medical need. The first step is to obtain a promising innovative medicine designation based on data from early clinical development. An application can then be made to the MHRA for a scientific opinion on the benefit/risk balance of the medicine, based on data available at the time. If the opinion is positive, a public assessment report and EAMS treatment protocol will be published to support prescribers and patients in making decisions as to whether to use the medicine before a MA is granted. The scientific opinion lasts for one year.

Authorisation conditions

The relevant procedures for obtaining a MA are set out in Title III of the Code for Human Medicines Directive and in Title II of the EMA Regulation. Part 5 of the Human Medicines Regulations 2012 implements these requirements and, subject to regulations relating to specific medicines (such as generics), applications must be accompanied by the general and SmPC information set out in Schedule B of the Human Medicines Regulations 2012.

The MHRA can only grant the MA if it is satisfied that:

- The applicant has established the therapeutic efficacy of the medicine.
- The positive therapeutic effects of the medicine outweigh the risks to health of patients or of the public associated with the medicine.
- The application and the accompanying materials are in accordance with the legislation.
- The medicine’s qualitative and quantitative composition is as described in the application.

Variations to MAs are regulated under Regulation (EC) 1234/2008 concerning the examination of variations to marketing authorisations, as amended. The European Commission has also published guidelines for submitting variations including the change codes (C2013/2804). Major (type II) variations which have a significant impact on quality, safety and/or efficacy and minor (Type I B only) changes must be approved by the MHRA before they are made.

Key stages and timing

The MHRA must take all reasonable steps to ensure that it makes a decision to grant or refuse a UK MA before the end of 210 days beginning with the day after the application is submitted. However, this time period is suspended if requests for information are made by the MHRA, or if explanations are requested.

Applications can be fast tracked if there is compelling evidence to show the medicine is a major breakthrough in treatment of certain conditions (such as chronic, debilitating diseases where available
treatments are inadequate). Details of how to request fast tracking are set out on the MHRA’s website.

Fee

The fees are listed on the MHRA’s website (a maximum of GBR143.134, where the MHRA is the reference member state in a decentralised procedure for a new application).

Period of authorisation and renewals

MAs are granted for an initial period of five years. A renewal application must be received by the MHRA at least nine months before expiry. For renewal, the holder provides a consolidated version of the file in respect of quality safety and efficacy, including an evaluation of data contained in suspected adverse reaction reports and standardised periodic benefit risk evaluation reports (PBRERs) (previously known as a periodic safety update report (PSURs)). If the MHRA is satisfied that the positive therapeutic effects outweigh the risks and the application is granted, the renewed MA will be valid indefinitely, unless, on pharmacovigilance grounds, the MHRA considered that the authorisation should only be for another five years.

Monitoring compliance and imposing penalties

The powers of the MHRA to monitor compliance with MAs are covered by Part 16 of the Human Medicines Regulations 2012. Regulation 327 provides the legal basis for the MHRA’s powers of inspection, sampling and seizure.

In practice, the inspection of research, development and quality control laboratories, clinical trials, manufacturers, wholesalers and pharmacovigilance systems is carried out by the Inspectorate Group of the Inspection and Standards Division of the MHRA.

The regulations provide broad powers of inspection, including:

- Taking or purchasing samples of medicines and substances.
- Requesting information or documents relating to the business which are in a person’s control.
- Taking copies.
- Seizing and retaining substances or articles.
- Seizing and retaining documents and anything inspected.
- Requesting the opening of containers or packages.

It is a criminal offence to intentionally obstruct or fail to comply with a requirement under regulation 327 of an inspector, or to unreasonably fail to give any other assistance or information to an inspector. Regulations 79 to 88 of the Human Medicines Regulations 2012 also provide for the imposition of penalties for breaches of MAs as well as other failures relating to the MA and specific requirements of the legislation. In addition, various offences are set out relating to the Paediatric Regulation and withdrawal of product from the market or failure to place product in the market in regulations 89 and 90.

A person (including a company) faces a fine not subject to any statutory maximum and/or, if the matter is dealt with on indictment, a period of up to two years’ imprisonment.

Human Medicines Regulations 2012 implements those requirements. These requirements include the obligation for MA holders (MAHs) to:

- Operate and regularly audit appropriate pharmacovigilance and risk management systems.
- Monitor the safety of their medicines throughout the entire product life cycle.
- Detect any change to their risk-benefit balance.

MAHs must, as part of their pharmacovigilance systems:

- Have an appropriately qualified person responsible for pharmacovigilance located in the EU.
- Maintain a pharmacovigilance master file.
- Operate, monitor and update a risk management system for the medicine.

MAHs must record all suspected adverse reactions (SARs) of which they become aware and submit reports to the EU’s EudraVigilance database reports on all serious SARs within 15 days, and on non-serious SARs within 90 days, of becoming aware of them. In addition, the holder must submit PBRERs, usually:

- Every six months until the medicine is placed on the market;
- Every six months for the first two years after the medicine is placed on the market; and
- Once a year for the following two years.

It is a criminal offence to breach provisions of Part 11 of the Human Medicines Regulation 2012, or to provide false or misleading information pursuant to an obligation under it. Penalties are a fine not subject to any statutory maximum and/or, if the matter is dealt with on indictment, a period of up to two years’ imprisonment.

The MHRA coordinates with the EMA in relation to centrally authorised medicines and with other national regulatory authorities as part of the EU’s Co-ordination Group for Mutual Recognition and Decentralised Procedures (CMDh), to ensure the proper post approval regulatory oversight of medicines. The MHRA also operates the Yellow Card Scheme which allows healthcare professionals (HCPs) and patients to report suspected adverse incidents directly to the MHRA online.

The following are subject to increased pharmacovigilance requirements:

- Medicines containing new active substances.
- Biological medicines.
- Medicines for which a post-authorisation study (such as a safety study) is required.
- Medicines which are the subject of a conditional or exceptional approval (centralised procedure only).
- Other medicines as determined by the EMA’s Pharmacovigilance Risk Assessment Committee (PRAC).

They are labelled with a black triangle to ensure that prescribers are aware that they are subject to additional monitoring on an EU-wide basis. The up-to-date list of medicines subject to the additional monitoring regime is available on the EMA website. The EMA will keep them on the list for five years in the case of new active substances and biological medicines, or until the conditions have been fulfilled in relation to post-authorisation safety studies.

Other conditions

The MHRA can place additional obligations on the MAH as a condition of granting the MA, such as the requirement to conduct post-authorisation safety studies.

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10. What commitments and pharmacovigilance obligations apply after a company has obtained marketing authorisation? Are there further conditions concerning how the drug is distributed and accessible to patients?

Post-marketing commitments and pharmacovigilance obligations

The relevant rules on pharmacovigilance for medicines authorised through national procedures are set out largely in Title IX of the Code for Human Medicines Directive. In the UK, Part 11 of the
The MAH should notify the MHRA or (for medicines authorised centrally) the EMA, of the date on which the medicine is placed on the market in the UK. Any MA which within three years of grant does not lead to the medicine being placed on the market will cease to be valid unless an exemption is granted. If a medicine is placed on the market after authorisation, but subsequently ceases to be placed on the market in the UK for a period of three consecutive years, the authorisation will also cease to be valid.

11. Which medicines can benefit from the abridged procedure for marketing authorisation and what conditions and procedure apply? What information can the applicant rely on?

A MA application can rely on the pre-clinical and clinical data that the MHRA holds on file on already authorised medicines, or which is in the public domain, in the following circumstances.

Generic medicines
If a medicine meets the requirements for a generic product, defined in Article 10(2)b of the Code for Human Medicines Directive, it can be authorised without its own clinical and pre-clinical testing data once the data protection period for the reference medicinal product has expired.

In the UK, if a national MA was obtained for the reference medicinal product on or before 30 October 2005 the regulatory data protection period is ten years. For such MAs obtained from 31 October 2005 the regulatory data protection period is eight years, but the generic medicine cannot be placed on the market during the subsequent two year marketing protection period (the 8 +2 formula).

This marketing protection period may be extended by an additional one year if, during the first eight years, the MA holder obtains an authorisation for a new indication which is held to bring a significant clinical benefit in comparison with existing therapies. All reference medicines authorised through the centralised procedure are subject to the 8+2 formula.

Hybrid and biosimilar medicines
While certain data from a reference medicinal product may be able to be relied on, results of additional pre-clinical tests or clinical trials may be required to be submitted where a medicine does not fall within the definition of a generic product or where any of the other circumstances set out in Article 10(3) of the Code for Human Medicines Directive apply, such as changes in strength, pharmaceutical form or route of administration (referred to as a hybrid medicine).

Where a biological medicine which is similar to a reference medicinal product does not meet the conditions in the definition of generic product, owing to circumstances including those set out in Article 10(4) of the Code for Human Medicines Directive (such as differences relating to raw materials or differences in manufacturing processes), the results of additional pre-clinical tests or clinical trials must be provided as set out in Annex I of the Code of Human Medicines Directive and the related detailed guidelines.

Well-established use
If a product includes an active substance that has a well-established medicinal use (a minimum of ten years systematic use) with an acceptable level of safety, the applicant can submit appropriate scientific literature to support the safety and efficacy of the combination (Article 10a, Code for Human Medicines Directive).

Combination products
New combinations of products based on known active substances need data to support the safety and efficacy of the combination, although it is not always necessary to provide scientific references relating to the individual active substances (Article 10b, Code for Human Medicines Directive).

Informed consent
Where a MAH agrees, a second company can make use of the pharmaceutical, pre-clinical and clinical documents contained in the file of the reference product, and be granted an exact copy authorisation (Article 10c, Code for Human Medicines Directive).

12. Are foreign marketing authorisations recognised in your jurisdiction?

MAs granted in other EU member states can be recognised in the UK through the mutual recognition procedure. Under the procedure, a medicine is first authorised in one EU member state, in accordance with the national procedures of that country. Following this, further MAs can be sought from other EU member states which recognise the validity of the original assessment and national MA. The mutual recognition procedure is mainly controlled by the Code for Human Medicines Directive and national implementing laws, and is co-ordinated by the CMDh.

13. Are parallel imports of medicines into your jurisdiction allowed?

The UK operates a Parallel Import Licensing Scheme, allowing medicines authorised in other EU member states to be marketed in the UK, provided the imported medicines have no therapeutic difference from equivalent medicines authorised in the UK. The importer must submit a Parallel Import Licence application to the MHRA’s Parallel Import Section before the proposed importation. Fees are payable, and vary depending on whether the application is:

- Simple (the UK medicine and the medicine to be imported are manufactured by companies in the same group of companies or are made under licence from the same licensor, that is, they share a common origin), in which case the fee is GB£1,951.
- Complex (the UK and imported medicines do not share a common origin, and a specified additional factor is present, such as a new excipient or an active ingredient that is manufactured by a different route from the UK medicine), in which case the fee is GB£2,200.
- Standard (the UK and imported medicines do not share a common origin, but it is not considered complex), in which case the fee is GB£7,403.

Holders of intellectual property rights in a medicine that has been placed on the market in the EU by them (or with their consent) cannot generally prevent further sale or marketing of that medicine elsewhere in the EU (although under the Specific Mechanism, patent and supplementary protection certificate rights can be asserted to prevent imports of medicines from some EU member states that joined the EU later, if no pharmaceutical product patent protection was available on the date the relevant medicine was first placed on the market, provided certain criteria are met).

Trade mark owners can only object to repackaging of medicines bearing their trade marks if they have legitimate reasons to oppose further commercialisation of the medicine. Repackaging is permitted where necessary to market the medicine and where the repackaging does not adversely affect the original condition of the medicine or damage the reputation of the trade mark and of its owner. The new packaging should state by whom the medicine has been manufactured and repackaged, and the trade mark owner should be notified of the repackaging before the imported

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medicine is put on sale (and provided with a specimen repackaged medicine on request).

For information on pharmaceutical patents, trade-marks, competition law, patent licensing, generic entry, abuse of dominance and parallel imports, visit Pharmaceautical IP and Competition Law in the UK (England and Wales): overview.

RESTRICTIONS ON DEALINGS WITH HEALTHCARE PROFESSIONALS

14. What are the restrictions on marketing practices such as gifts, sponsoring, consultancy agreements or incentive schemes for healthcare establishments or individual medical practitioners?

In addition to the restrictions on promotion and other dealings imposed by the rules governing the advertising of medicines in the UK (see Question 16), promotion and other dealings such as the provision of hospitality, gifts and inducements to prescribe to HCPs or other decision makers within healthcare organisations (HCOs) are subject to the Bribery Act 2010, which is enforced by the Serious Fraud Office (SFO).

There are potentially three separate breaches of the Bribery Act which might be committed through promotion and other dealings with HCPs or HCOs:

- The "main offence" of bribing a person and accepting a bribe (sections 1 and 2).
- The "corporate offence" of failing to prevent bribery (section 7).
- Bribery of foreign public officials (section 8).

The main offence and offence of bribing a foreign public official have extra-territorial application. The Bribery Act makes no exemptions for facilitation payments. Guidance has been issued and updated by the Ministry of Justice.

The SFO has entered into a memorandum of understanding (MoU) with the ABPI and the Prescription Medicines Code of Practice Authority (PMCPA) (the body which administers the ABPI Code). The MoU covers the activities subject to the ABPI Code and states that self-regulation under the ABPI Code should be the first means of dealing with relevant complaints.

There is no statutory provision in the UK obliging companies to publicly disclose any transfers of value to HCPs or HCOs. However, under the self-regulatory system for prescription medicines, the new edition of the ABPI Code 2015 sets out the disclosure requirements, implementing the European Federation of Pharmaceutical Industries and Associations (EFPIA) Disclosure Code and HCP Code of Practice. Companies are required to document and, from June 2016, publicly disclose annually at an individual level, or if permissible on an aggregate basis (such as where recipients cannot be identified for legal reasons and in general transfers of value for research and development), certain transfers of value made directly or indirectly to HCPs and HCOs located in Europe. The transfers of value include:

- Joint working.
- Donations, grants and benefits in kind.
- Contracts between companies and HCOs.
- Sponsorship of HCPs attendance at meetings.
- Fees paid to HCPs and contributions towards the costs of meetings paid to healthcare organisations.

There will be a central platform for disclosure of transfers of value in the UK which companies must use. The template to be used is available on the PMCPA's website. Companies must have appropriate arrangements in place to lawfully disclose the information, and are encouraged to include provisions regarding consent to disclosure in new and existing contracts involving transfer of value. The ABPI has developed guidance and model contractual clauses for use by companies.

SALES AND MARKETING

15. What are the restrictions on selling medicines? Are there specific regulations for the sale of medicines on the internet, by e-mail and by mail order?

Prescription only medicines can only be sold in accordance with a prescription given by an appropriate practitioner. Both pharmacy medicines and prescription only medicines can only be sold from premises that are a registered pharmacy, and by a person who is lawfully conducting a retail pharmacy business. Sales of medicines to a member of the public in the UK on the internet, by e-mail and by mail order are not exempted from this requirement. All pharmacies in Great Britain, including those providing such services, must be registered with the General Pharmaceutical Council (GPhC).

The requirements of Title VIIIA of the Code for Human Medicines Directive relating to sale of medicines at a distance to the public are implemented by Part 12A of the Human Medicines Regulation. These requirements will come into force on 24 June 2015. Implementing Regulation (EU) 69/2014 established the common logo which must be used by all legally operating online pharmacies and approved retailers in the EU. The logo must be included on the company website and will link to national regulatory authority websites, where all legally operating online pharmacies and approved retailers will be listed. The MHRA will be the UK's regulatory authority. The GPhC already operates a voluntary internet pharmacy logo scheme in respect of pharmacies registered with it.

General Sale List medicines can be sold elsewhere than at registered pharmacies, subject to compliance with conditions relating to packaging of such medicines and the premises from which they can be sold.

ADVERTISING

16. What are the restrictions on advertising medicines?

Legislation and regulatory authority

The advertising of medicines in the UK is controlled by a combination of legislation and self-regulation. The relevant EU legislation is contained in Titles VIII and VIIIa of the Code for Human Medicines Directive which is implemented by Part 14 of the Human Medicines Regulations 2012.

The MHRA conducts a number of activities relating to advertising control. The MHRA checks advertising material for compliance with the law (vetting). Vetting may be required by the MHRA in relation to newly authorised medicines, where existing medicines are reclassified, or where previous advertising has breached advertising rules.

The MHRA also handles complaints and conducts enforcement activities in relation to non-compliant materials. A complaint may be made directly to the MHRA or any self-regulatory body such as the PMCPA, Proprietary Association of Great Britain (PAGB) and the Advertising Standards Authority (ASA). Where appropriate, and if agreed by the complainant, the MHRA may pass the complaint to the relevant self-regulatory body. Where a self-regulatory body has failed to deal with any complaint properly the MHRA will take action.

A memorandum of understanding has been entered into by the MHRA, ABPI and PMCPA which states that the MHRA focus is on
pre-vetting, dealing with complaints other than inter-company complaints and dealing with complaints that are not covered by the ABPI Code or other self-regulatory authority. Self-regulation should be the first means of dealing with complaints.

If a complaint about a broadcast advertisement is received by both the MHRA and the ASA or the ASA alone, the ASA will investigate the complaint. The ASA is a co-regulator in relation to the UK Code of Broadcast Advertising (BCAP) under contract from the Office of Communications (Ofcom) which also has enforcement powers. All radio and television advertisements must be submitted to the appropriate pre-clearance centres to comply with BCAP.

Control of the advertising of medicines by self-regulation involves the following bodies and relevant Codes of Practice, each of which includes detailed requirements which reflect and extend beyond relevant legislative requirements:

- ABPI and PMCPA - ABPI Code of Practice for prescription only medicines.
- ASA - UK Code of Non-broadcast Advertising, Sales Promotion and Direct Marketing (co-regulator of BCAP code, as above).
- The Committee of Advertising Practice (CAP) offers a free advice service for such advertisements aimed at the public.

Detailed guidance on the advertising of medicines in the UK has been published in its Blue Guide which is available on the MHRA website.

Restrictions

The restrictions applicable to advertising medicines vary depending on the intention, the context and the audience to whom the advertisement is addressed. A general restriction is that medicines cannot be advertised before the grant of their MAs or outside their licensed indication.

Advertising prescription only medicines to the general public is prohibited. To the extent it is permitted to persons qualified to prescribe or supply (PQPS), the advertising of prescription only medicines 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. Factual and non-promotional press releases are permitted, provided they also provide the appropriate context in relation to the use of the medicine and the population for which it has been authorised.

Pharmacy sale and General Sale List medicines can be advertised to the public, provided that, among other things:

- The advertisements are consistent with the SmPC and are not misleading.
- There is no suggestion that the medicine will enhance health or that the effects or side-effects of the medicine are guaranteed or the same as or better than existing named medicines.
- The advertisements do not imply that seeing a doctor or pharmacist is not necessary or quote recommendations by HCPs or celebrities.

Advertisements to the public are subject to the restrictions set out in regulations 282 to 293 of the Human Medicines Regulation 2012. The advertisements must include the particulars as set out in regulation 291 of the Human Medicines Regulation 2012 and Annex 3 of the Blue Guide.

Advertisements to PQPS, both in relation to prescription only and over-the-counter medicines, are subject to the restrictions set out in regulations 294 to 300 of the Human Medicines Regulation 2012. The advertisements must include, or if appropriate in relation to short form advertisements a specified website must include, the essential information compatible with the medicine's SmPC as set out in regulation 294 and Schedule 30 of the Human Medicines Regulation 2012 as well as Annex 4 of the Blue Guide.

Detailed guidance in relation to these restrictions is set out in the Blue Guide, as well as in the ABPI and PAGB Codes.

Internet advertising

Generally, the same rules apply to digital communications as to other forms of advertising. Advertising of medicines directed to a UK audience through the internet is therefore subject to the same controls as for other forms of advertising, including the ABPI and the PAGB Codes.

The main difference is that more issues arise in relation to the regulator's enforcement powers as the competent authorities are, in practice, only able to enforce effectively against entities with a presence in the jurisdiction. In January 2015 the PMCPA issued informal guidance on how the ABPI Code applies to digital communications. This advice confirms that digital communications must follow the general advertising principles and restrictions. The challenge for the industry is to stay away from certain risks such as off-label promotion, patient confidentiality issues and the possibility of triggering pharmacovigilance reporting obligations. In April 2013, the ABPI issued guidance notes on the management of adverse events and complaints from digital media dealing with the collection and follow up of adverse events arising through social media activities from company sponsored and non-company sponsored sites. The MHRA's Blue Guide also contains guidance.

DATA PROTECTION

17. Do data protection laws impact on pharmaceutical regulation in your jurisdiction?

The Data Protection Act 1998 (DPA) governs the processing of personal data in the UK, and implements Directive 95/46/EC on data protection. The DPA impacts many aspects of pharmaceutical regulation, including clinical trials and pharmacovigilance.

The Clinical Trials Regulation 2004 specifically refers to the requirements to comply with the DPA when conducting clinical trials, and this requirement is also included in good clinical practice guidance. Researchers in clinical trials and studies use anonymised data wherever possible, but where processing of personal data is involved, the confidentiality of records that could identify patients must be protected in accordance with the DPA and the law relating to confidentiality. Research ethics committees play an important role in ensuring that an individual's personal data are used in research in a way that is proportionate and compliant with the DPA, and that subjects give appropriate consent to such processing.

Companies are required to collect a range of information for pharmacovigilance purposes in order to ensure patient safety and to comply with regulatory obligations to report adverse reactions. This information will often include details such as the patient's age/age group, sex, weight, height, ethnicity, medical history and status. A patient's initials or an assigned ID and or date of birth are often used to identify duplicates, and the reporter name and contact details are also collected in case of a need to follow-up. Pharmacovigilance data will, therefore, often include personal data and sensitive personal data related to both the patient and the reporter, and companies are required to comply with the DPA when processing personal data for pharmacovigilance purposes. In February 2013, the ABPI published guidance to help companies performing post-marketing pharmacovigilance to comply with their obligations under the DPA, where in this setting there is no explicit consent to the processing of personal data from the data subject.
PACKAGING AND LABELLING

18. Outline the regulation of the packaging and labelling of medicines.

Legislation and regulatory authority

EU rules covering packaging and labelling of medicines are implemented by the Human Medicines Regulations 2012 and enforced by the MHRA.

Information requirements

The information specified in Part 1 of Schedule 24 to the Human Medicines Regulations 2012 must appear on the packaging of a medicine. For certain medicines, packaging must also indicate whether the medicine is intended for babies, children or adults, and any warnings or special precautions applicable to the medicine. Reduced requirements apply where the packaging is in blister pack form or is too small to display the information required.

A package leaflet must always be included in the packaging of a medicine, unless all the required information is conveyed on the packaging. As well as containing much of the information required to be displayed on the label, package leaflets must be drawn up in accordance with the SmPC and contain the information set out in Schedule 27 to the Human Medicines Regulations 2012.

Other conditions

The packaging and labelling must be in English, except where the MHRA otherwise agrees under particular circumstances.

The name of a medicine must also be expressed in Braille on the outer packaging, and the package leaflet must be available on request in formats suitable for blind and partially-sighted persons.

PRODUCT LIABILITY

19. Outline the key regulators and their powers in relation to medicine liability.

The key regulators are the MHRA for products supplied in the UK, and the European Commission, advised by the EMA, in respect of centrally authorised products.

Although there is a limited regulatory compliance defence under the Consumer Protection Act 1987 (see Question 23), if a product defect is due to mandatory compliance with regulatory requirements, the powers of the regulators do not generally bear directly on product liability in the sense of determining if civil damages should be paid. The views and actions of the regulators are not determinative of a product liability claim, but they would normally constitute relevant evidence and will form part of the circumstances taken into account in assessing if a product is defective.

The MHRA has wide ranging powers, including the power to revoke, vary, or suspend a UK MA, and to suspend the use, sale, or supply of a nationally approved product if it is unsafe, that is, if it is harmful or does not have a positive benefit to risk profile. The MHRA can take similar steps in relation to a centrally authorised product where urgent action is essential to protect human health or the environment. Under the Human Medicines Regulations 2012, criminal penalties can be imposed for breach of a wide range of obligations, including those relating to pharmacovigilance and compliance with the MA. The penalties that can be imposed vary, but in most cases the maximum penalty is an unlimited fine and/or imprisonment for up to two years.

The European Commission can, in appropriate circumstances and subject to procedures for consultation with the member states, suspend, revoke or vary a centralised authorisation. Where there is an urgent safety issue with a centrally authorised product, the Commission can order an urgent safety restriction or agree such action with the MAH. Although the Commission has power to impose financial penalties for infringements of certain obligations relating to centrally authorised medicines, most enforcement action takes place at national level via the member state competent authorities (such as the MHRA).

The European Commission also has power under Regulation 658/2007 (the Penalties Regulation) to impose financial penalties for certain infringements of requirements relating to centrally authorised products, which are committed intentionally or negligently. These financial penalties can be up to 5% of the MAH's EU turnover in the preceding business year, with further ongoing financial penalties payable based on turnover for continuing infringements.

20. Are there any mandatory requirements relating to medicine safety?

MAHs and others in the supply chain have extensive obligations to operate appropriate pharmacovigilance and risk management systems, to monitor the safety of their medicines throughout the entire product life cycle and detect any change to their risk-benefit balance (see Questions 10, 17 and 18). They are obliged to report new risks, risks that have changed, or changes to the risk-benefit balance of a medicine, both to the EMA and to the MHRA "without delay".

There are also separate procedures for reporting product defects in the sense of quality, manufacturing, and packaging or labelling defects. Any defect which could result in a recall must be reported "immediately" to the competent authority, such as the MHRA in the UK. The MHRA classifies product defects as follows:

- Class 1: the defect presents a life threatening or serious risk to health.
- Class 2: the defect may cause mistreatment or harm to the patient, but it is not life threatening or serious.
- Class 3: the defect is unlikely to cause harm to the patient, and the recall is carried out for other reasons, such as non-compliance with the MA or specification.
- Class 4: the MHRA also issues "Caution in Use" notices which are called Class 4 Drug Alerts, where there is no threat to patients or no serious defect likely to impair product use or efficacy. These are generally used for minor defects in packaging or other printed materials. "Caution in Use" notices may also be issued where a defect has been identified but due to supply concerns the product cannot be recalled; in these instances the alert will be used to provide advice to HCPs.

Similar classifications apply to defects in centrally authorised products reported to the EMA. The authorities provide guidance on the form and publication of product recall information and work closely with MAHs to ensure that recalls are effectively communicated to HCPs and patients.

Breaches of the various safety related reporting and recall requirements are subject to criminal sanctions in the UK, or in the case of centrally authorised products are subject to the administrative penalty regime operated by the European Commission (see Question 19).
21. **Outline the key areas of law applicable to medicine liability, including key legislation and recent case law.**

**Legal provisions**
Product liability claims can be brought:
- In tort for failure to take reasonable care (that is, negligence).
- In contract.

Claims can also be brought for breach of statutory duty in some circumstances.

For medicines under research, claims are often also made under the special arrangements (non-statutory) set out in compensation guidelines adopted by the members of the ABPI. Separate arrangements currently exist for Phase I studies in “healthy volunteers” and for Phase II to IV patient volunteers.

**Substantive test**
In negligence, a claimant must show that the defendant owed a duty of care, that the duty was breached, and that the breach caused damage to the claimant. Claims are usually brought against the manufacturer of a defective product, although they may also be brought against other parties in the supply chain if fault can be established.

The CPA imposes liability on the producer of a defective product for damage caused by the defect. A product is defective if it is not as safe as persons generally are entitled to expect. The safety of a product is assessed by reference to all the circumstances. This includes looking at instructions or warnings provided with the product (including the Patient Information Leaflet supplied in packs of medicines and any warnings provided on packaging) and the manner in which it has been marketed. Liability is strict: it is not necessary to prove that the manufacturer was at fault in causing the defect. The claimant need only prove a defect and a causal relationship between the defect and the injury. The CPA applies to claims arising from products placed on the market after 1 March 1988. Before this date, claims must be brought in negligence or in contract.

Liability in contract depends on the terms of the contract. Statute (the Sale of Goods Act 1979 (as amended) and the Supply of Goods and Services Act 1982) implies standard terms into all contracts for the sale of goods, unless the parties agree to exclude them. Products sold in the course of business must be of satisfactory quality and comply with the description applied to them or a sample supplied.

The seller will not be liable for faults drawn to the buyer's attention prior to the contract, or which the buyer should have detected on examination of the goods. Additional obligations apply to consumer contracts. The ability to exclude or limit liability is restricted.

22. **Who is potentially liable for defective medicines?**

In negligence, a defendant is liable if he owes (and has breached) a relevant duty of care in relation to a defective product, which has resulted in damage to the claimant. This could include, for example, distributors and sellers, in so far as their activities have an impact on the safety of the product. Prescribing physicians could also potentially be liable in negligence, for example for prescribing a medicine to a patient whose use is contra-indicated by the SmPC. Pharmacists could be liable for dispensing contrary to a doctor’s prescription.

Under the CPA it is the producer of the product who is primarily liable. This normally means the manufacturer, but an own-brand or persons who hold themselves out to be the producer may be liable instead. Further, claimants need not pursue defendants beyond the frontiers of the EU: the first importer of a product into the EU is deemed to be the producer for the purpose of the CPA. The supplier of the product (the retailer, distributor or a wholesaler) can be liable in place of the manufacturer if he fails to inform the claimant of the identity of the producer, or at least the person who supplied the product to him.

Claims for breach of contract can only be brought against the immediate supplier of the defective product to the person injured. Where medicines are supplied on prescription by the NHS, case law establishes that there is no contract between the patient and the prescribing doctor or the pharmacist dispensing the drugs. Contractual claims generally only arise where medicines are supplied privately or for products available over-the-counter.

23. **What defences are available to product liability claims?**

In the case of a claim in negligence, showing that reasonable care was taken in the development/marketing of a product is a defence. Even if, post-marketing, the product turns out to have a negative benefit to risk balance and is taken off the market, liability will not arise if the company can show that it exercised reasonable care in research and was still not able to identify the defect, having regard to the state of scientific knowledge at the time. It is also a defence if the claimant freely and voluntarily agreed to run the risk of injury in full knowledge of the nature and extent of the risk.

There are special statutory defences applicable to product liability claims brought under the CPA. A defendant will not be liable if he can show that:
- He did not supply the product.
- He did not supply it for profit and in the course of a business.
- He is not the producer.
- The defect did not exist in the product when supplied.
- In respect of component products, the defect was due to the design of the final product, or to defective specifications provided to the component producer by the producer of the final product.
- The defect is attributable to compliance with mandatory regulatory requirements. This is a narrow defence, which only applies where the defect results from something the defendant has been required by law to do or not do in relation to the product, or by a regulatory agency with power to direct certain behaviour (for example, in relation to warnings).
- The state of scientific and technical knowledge when the product was supplied was such that the producer could not be expected to discover the defect (the “development risks defence”).

Liability under the CPA and in negligence may also be limited by the principles of contributory negligence.

In contract no specific defences arise, but the claim will fail if the claimant cannot establish the breach of contract and damage due to that breach.
24. How can a product liability claim be brought?

Limitation periods
A claimant has three years from the date on which a tortious cause of action accrued (that is, the date of injury or death) or their date of knowledge of certain facts in which to bring a claim for personal injury in negligence. The date of knowledge is when the claimant is aware of the identity of the defendant, that the injury was significant, and that it was attributable in whole or part to the alleged negligence, nuisance or breach of duty. However, even where a claimant is out of time, the courts have discretion to allow the claim to proceed outside the limitation period where they consider that it is just in all the circumstances to do so.

Where the CPA applies, the claimant also has a period of three years from the date the cause of action accrues or the date of knowledge to bring a claim. However, there is a further limitation period under the CPA: ten years after the date of supply of the product the cause of action is extinguished and there is no discretion to extend.

In a claim based on contract the limitation period is six years from the date that the cause of action accrued which is, in principle, when the breach of contract arose. Special rules apply to persons under a disability, and in general, time only begins to run for limitation purposes when the claimant dies or ceases to be under a disability. However, the ten year long-stop for CPA claims still applies.

Class actions
Although there is no opt-out class action mechanism for product liability claims, the English courts do have procedures to permit the management of collective actions. The court can order that claims which give rise to common or related issues of fact or law be dealt with together under a Group Litigation Order (GLO). All claims remain individual actions in their own right, but they are noted on a group register and managed together by the court. Test cases may be selected to provide the factual basis for findings of generic importance. The outcome does not automatically determine liability in the remaining claims but, in practice, it usually provides guidance as to the likely outcome and leads to discontinuation of claims or settlement, or it simplifies resolution of the remaining litigation by focusing further proceedings on clarifying any remaining points of principle. The GLO procedure requires claimants to opt in to the litigation.

Claims can also be pursued in a representative action where one representative claimant or defendant acts on behalf of a group of individuals, but this procedure is rarely used, as it is only available where the group of litigants have the same interest in one cause of action. The court also has power to consolidate a number of individual proceedings, or to order that two or more claims should be tried together.

25. What remedies are available to the claimant? Are punitive damages allowed for product liability claims?

The usual remedy is damages. These are intended to put the claimant back in the position he would have been in had the loss/injury not occurred. In addition to expenses or loss of earnings, claimants will typically be awarded a sum to compensate them for their injury. The sum is determined by the court by reference to the circumstances of the individual claimant. Figures are contended for on the basis of precedent authority and by reference to guidelines issued by the Judicial College. The types of damages that are recoverable vary depending on the legal basis of the claim.

Punitive damages may be awarded in tortious product liability claims. However, the courts tend to award these very rarely and in cases only where the defendant’s conduct is particularly egregious. They are not generally available in respect of claims for breach of contract.

REFORM

26. Are there proposals for reform and when are they likely to come into force?

The terms of reference for the Department of Health’s Innovative Medicines and Medical Technology Review were confirmed in March 2015. It will consider how to improve the speed at which innovative medicines, devices and diagnostics get to patients. Key areas for reform have been identified as regulation, reimbursement and uptake. Among other things it will consider how to strengthen the Early Access to Medicines Scheme and consider both cost-effectiveness and affordability. Its final report is expected by December 2015.

The phased roll-out of the HRA Approval by study type will begin on 11 May 2015. The HRA Approval is a new approval that will be required for research to comment in the NHS in England. It is a new process that comprises a review by a Research Ethics Committee (where applicable) as well as an assessment of regulatory compliance and related matters. When fully rolled out it will replace the local R&D approval process.

On 16 April 2014 the new Regulation EU 536/2014 on clinical trials was adopted. It will apply no earlier than May 2016, on which date the Clinical Trials Directive will be repealed. However, sponsors will be able to elect between the requirements of the Clinical Trial Directive and the Clinical Trials Regulation for one year after it applies. The Clinical Trials Regulation contains, among other things, a new single procedure for the authorisation of clinical trials, which will replace the need for multiple submissions in EU member states and strengthened transparency requirements. Certain aspects of the application will be assessed by the Reporting member state (such as benefits for public health and risks for clinical trial subjects) while other aspects will continue to be the subject of local assessments in each member state concerned (such as informed consent). In early 2015 the EMA undertook a public consultation on how the transparency requirements would be implemented in the new EU clinical trial portal and database for which it will be responsible.

On 20 May 2015, the European Medicines Agency published a draft Guideline on the quality, non-clinical and clinical aspects of gene therapy medicinal products (EMA/CAT/80183/2014). The guideline defines scientific principles and provides guidance for the development and evaluation of gene therapy medicinal products intended for use in humans and presented for marketing authorisation. Its focus is on the quality, safety and efficacy requirements. The draft is subject to a period of public consultation which will end on 31 August 2015.

For information on pharmaceutical patents, trade marks, competition law, patent licensing, generic entry, abuse of dominance and parallel imports, visit Pharmaceutical IP and Competition Law in the UK (England and Wales): overview.

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**Professional qualifications.** Solicitor, qualified in England and Wales

**Areas of practice.** Competition; regulatory; investigations; mergers; particular focus on the life sciences sector.

**Recent/notable cases.**
Leading the process to secure competition clearance on numerous global M&A transactions, including Thermo Fisher/Life Technologies (acting for Life), which was the largest global biotech deal in history at the time (2014).

Representing clients in cartel and market investigations before the UK and EU authorities across various industries, including consumer goods, transport and energy.

Described in the Legal 500 2014 guide to leading UK competition practitioners as “one to watch”, and shortlisted for the Global Competition Review Lawyer of the Year (Under 40) for 2015.

**Professional associations/memberships.** Member of the City of London Law Society Competition Section.

**Publications.** Author of numerous competition law publications, including the UK chapter of the LBR Public Competition Enforcement Review, and the 2015 IFLR Global Merger Control guide.

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**Professional qualifications.** Solicitor Advocate, qualified in England and Wales

**Areas of practice.** Competition; regulatory; investigations; litigation; advises on competition and regulatory investigations and competition disputes.

**Recent/notable cases.** Including:

- Defending clients in investigations by authorities, guiding companies on how to prepare for and to manage on-site inspections ("dawn raids").
- Preparing competition compliance advice for clients, and assessing their potential exposure under EU and UK competition law.
- Three years as senior competition counsel at a UK sector regulator, responsible for conducting several competition and regulatory investigations.
- Advising clients on various life sciences regulatory issues, including in relation to judicial review proceedings.

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**Professional qualifications.** Solicitor Advocate, qualified in England and Wales

**Areas of practice.** Life sciences; competition; intellectual property; regulatory; litigation; investigations.

**Recent / notable experience.** Advising on issues at the interface between competition law and intellectual property rights in the life sciences sector. Advising pharmaceutical and biotech companies before the European Commission, the Court of Justice of the European Union, and the English High Court, Court of Appeal and Supreme Court, on substantive competition and regulatory law, and procedural issues. Secondment to a global pharmaceutical company advising on competition and regulatory issues.