The Life Sciences Law Review

Fifth Edition

Editor
Richard Kingham

Law Business Research

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EDITOR'S PREFACE

The fifth edition of *The Life Sciences Law Review* covers a total of 37 jurisdictions, providing an overview of legal requirements of interest to pharmaceutical, biotechnology and medical device companies. The chapters are arranged to describe requirements throughout the life cycle of a regulated product, from discovery to clinical trials, the marketing authorisation process and post-approval controls. Certain other legal matters of special interest to manufacturers of medical products – including administrative remedies, pricing and reimbursement, competition law, special liability regimes and commercial transactions – are also covered. Finally, there is a special chapter on international harmonisation, which is of increasing importance in many of the regulatory systems that are described in the national chapters.

Now, more than ever, it is important for leaders in the pharmaceutical and medical device industries and their advisers to be knowledgeable about the laws and regulations in major jurisdictions around the world. In the past year, there have been significant developments in the regulation of drugs and medical devices, especially in the United States, where a new law – the 21st Century Cures Act – was passed at the end of 2016. There are prospects for further developments in the coming year. The new president and the Republican-controlled Congress will consider legislative measures affecting the pharmaceutical and medical device sectors, including proposed repeal of the Affordable Care Act, continuing inquiries into pricing of medical products and reauthorisation of user fee laws that fund a substantial part of the drug and device approval processes. The United Kingdom will initiate formal proceedings to begin the process of withdrawing from the European Union, with potential consequences for the medical products sectors. Other jurisdictions, including China and India, are considering reforms to their regulatory systems for medicinal products.

Each of the chapters has been written by leading experts within the relevant jurisdiction. They are an impressive group, and it is a pleasure to be associated with them in the preparation of this annual publication.

Richard Kingham
Covington & Burling LLP
Washington, DC
March 2017

Chapter 15

IRELAND

Colin Kavanagh and Ciara Farrell[1]

I INTRODUCTION

i Regulatory framework

The regulatory framework for medicinal products in Ireland is based on Directive 2001/83/EC on the Community code relating to medicinal products for human use (as amended) (the Community Code). This was implemented in Ireland by the Irish Medicines Board Act 1995 (as amended) (IMB Act) and domestic regulations, most notably the Medicinal Products (Control of Placing on the Market) Regulations 2007 (S.I. 540/2007) (as amended) (Marketing Regulations).

The regulatory framework for medical devices in Ireland is based on the following directives that have been transposed into Irish law; Directive 93/42/EEC concerning medical devices, Directive 90/385/EEC on active implantable medical devices (as amended) and Directive 98/79/EC on *in vitro* diagnostic medical devices (IVD Directive) (as amended). National legislation transposing those Directives (as amended) include the European Communities (Medical Devices) Regulations 1994 (S.I. 252/1994) (as amended in 2001, 2002 and 2009), the European Communities (Active Implantable Medical Devices) Regulations 1994 (S.I. 253/1994) (as amended in 2009), the European Communities (In-Vitro Diagnostic Medical Devices) Regulations 2001 (S.I. 304/2001) (as amended in 2012), the European Communities (Medical Devices) (Reclassification of Breast Implants) Regulations (S.I. 358/2003) 2003, the European Communities (Medical Devices) (Tissues of Animal Origin) Regulations 2003 (S.I. 554/2003) and the European Communities (Medical Devices) (Reclassification of Hip, Knee and Shoulder Joint Replacements) (Amendment) Regulations 2007 (S.I. 92/2007) (collectively, the Medical Devices Legislation).

1 Colin Kavanagh is a partner and Ciara Farrell is an associate at Arthur Cox.

ii Regulatory authorities

The Health Products Regulatory Authority (HPRA; formerly the IMB) (www.hpra.ie) is the competent authority responsible for regulating medicinal products, medical devices, cosmetics and other health products in Ireland. The National Standards Authority of Ireland (NSAI) is the notified body in Ireland approved by the HPRA to carry out conformity assessment procedures to ensure compliance with the Medical Devices Legislation. The HPRA's main areas of responsibility are:

a ensuring the quality, safety and efficacy of medicinal products (including veterinary medicinal products) available in Ireland, participating in systems designed to do so throughout the EU, and monitoring the quality of medicinal products and their manufacturing and distribution processes;

b acting as competent authority for the implementation of EU and national legislation relating to blood, blood components, tissues, cells and medical clinical research, and cosmetics;

c regulating medical devices on the Irish market;

d regulating the protection of animals used for scientific purposes; and

e regulatory functions in respect of organs intended for transplantation.

II THE REGULATORY REGIME

i Classification

The decision as to whether a product will be deemed a medicinal product, a medical device or other regulated product will largely depend on the particular intended use of the product, as assigned by the manufacturer, and on the demonstrated mode of action. In arriving at any decision in regard to classification the applicant must provide the HPRA with sufficient information about the product and its intended usage including all promotional material. This includes not only labels, leaflets and all advertising materials but also any websites linked to such literature. In the event that the HPRA determines that the product could potentially be a medicinal or other product, the product may be referred to the HPRA Classification Committee, which meets once a month and is responsible for assessing the classification of products where their classification is not obvious, including those that are borderline medical devices or medicinal products. Alternatively, classification requests for borderline products may be sent directly to the Classification Committee as opposed to being referred by the HPRA.

Decisions of the Classification Committee can be appealed to the HPRA Management Committee, which may request the advice of the Advisory Committee on Human Medicinal products (ACHM) set up under the IMB Act. The decision of the Management Committee is final.

ii Non-clinical studies

Non-clinical studies such as non-interventional studies are not regulated by the applicable laws and guidance for clinical trials in Ireland. They do not require the positive opinion of an ethics committee. There is, however, general legislation that applies, such as data protection legislation, the common law on consent for medical treatment and research, animal welfare protection laws and good laboratory practice.

Directive 2010/63/EU was transposed into Irish law in December 2012 by the European Union (Protection of Animals used for Scientific Purposes) Regulations 2012 (S.I 543/2012) (as amended). This legislation aims to improve the welfare of animals used for scientific purposes and to promote the principles of the 3Rs – replacement, reduction and refinement:

a Replacement refers to the use of alternative methods which substitute the use of animals for scientific purposes. Where replacement is not possible, animal use must only be permitted where justified and where the expected benefits outweigh the potential adverse effects.

b Reduction measures must be applied so as to minimise the number of animals used in each research project.

c Refinement measures must also be applied to enable procedures to be carried out in the most humane manner possible and to minimise pain, suffering, distress and lasting harm.

European Communities (Good Laboratory Practice) Regulations 1991 (S.I. 4/1991) (as amended) give effect to Commission Directive 2004/10/EC, which requires certain testing on chemicals to be carried out in accordance with the Principles of Good Laboratory Practice. The Irish National Accreditation Board has statutory responsibility for the enforcement of these regulations.

iii Clinical trials

Medicinal products

Clinical trials in Ireland are regulated by the European Communities (Clinical Trials on Medicinal Products for Human Use) Regulations 2004 to 2009 (Clinical Trial Regulations), which implement Directive 2001/20/EC on the conduct of clinical trials (Clinical Trials Directive) and Directive 2005/28/EC on good clinical practice for medicinal products for human use (GCP Directive).

The Clinical Trial Regulations apply to clinical trials conducted in human subjects and involving investigational medicinal products (IMP). On 16 April 2014, the new Clinical Trials Regulation (Regulation No. 536/2014) was adopted. It will repeal the Clinical Trials Directive and its aim is to simplify and harmonise the authorisation of clinical trials across the EU. The new Regulation is expected to enter into force six months following the full functionality of a new EU Database and single online EU Portal created under the new Regulation. Clinical trials will, however, continue to be conducted in accordance with the Clinical Trials Directive until the new regulation becomes applicable.

Authorisations

A clinical trial authorisation (CTA), issued by the HPRA, must be obtained by a sponsor or person authorised to act on his or her behalf prior to commencing a clinical trial. An investigational medical product dossier should be submitted to the HPRA providing clinical and non-clinical supporting data for the investigational medicinal product together with evidence of the favourable ethics committee opinion and the sponsor's EudraCT number (see 'Trial preconditions' below).

Informed consent

The sponsor must obtain each trial subject's informed consent and inform each trial subject of the trial procedure, and his or her right to withdraw at any time. Other conditions apply in accordance with the requirements of the applicable data protection legislation and the Clinical Trials Regulations. Documentation relating to these matters must be submitted to the ethics committee for opinion before the application for a CTA is made to the HPRA (see below).

Trial preconditions

The following items must be satisfied before a clinical trial can commence:

a the sponsor, or the person authorised to act on his or her behalf in relation to the trial, is established in the EU;

b the sponsor has registered with the European Economic Area (EEA) system for monitoring drug safety, EudraVigilance;

c a favourable ethics committee opinion in relation to the trial protocol has been obtained;

d HPRA has granted a CTA; and

e insurance and indemnity cover for the conduct of the trial has been obtained.

To facilitate the effective initiation of clinical trials and the removal of administrative barriers a single HSE clinical trial indemnity form (CTIF) has been agreed between the State Claims Agency and the Irish Pharmaceutical Healthcare Association (IPHA) for the conduct of industry-led clinical trials in Ireland. The CTIF is applicable to the conduct of any industry sponsored clinical trial in any HSE hospital in Ireland. Use of the HSE CTIF, which refers to the IPHA clinical trial compensation guidelines, provides the assurance that the company sponsoring a clinical trial will, without legal commitment, adhere to the following guidelines in the event of injury caused to a patient attributable to participation in the trial in question.

Medical devices

Devices carrying the CE mark may be freely marketed anywhere in the European Union.[2] Clinical assessments are usually required before non-CE marked medical devices may enter the Irish market. In order for any clinical investigation to commence in Ireland, approval from the HPRA is required along with a positive opinion of an ethics committee. Note that certain clinical investigations, such as those using CE-marked devices within their intended purpose, may not require review by the HPRA. This must be assessed on a case-by-case basis.

Typically applications are submitted by commercial sponsor's (e.g., medical device manufacturers). By this application, the manufacturer is proposing to conduct an investigation to gather the necessary clinical data to demonstrate the basic safety and performance of their device. The HPRA reviews the regulatory, technical and clinical aspects of the application. The HPRA reviews applications to conduct clinical investigations in Ireland in parallel with the appropriate ethics committee review. The final opinion of the HPRA will be provided within 60 days of the application with an initial opinion issued within 30 days.

2 Where the medical device is to be exported outside of the European Economic Area, it will be necessary to apply to the HPRA for a Certificate of Free Sale.

There is no specific legislation relating to clinical investigations involving *in vitro* diagnostic medical devices. Rather, *in vitro* diagnostic medical devices have to undergo performance evaluation as specified under Annex VIII of Directive 98/79/EC on *in vitro* diagnostic medical devices.

iv Named-patient and compassionate use procedures

Medicinal products

Named-patient programmes

Regulation 2 of Schedule 1 of the Marketing Regulations regulates named-patient programmes in Ireland. Under the Marketing Regulations, a named-patient programme permits the sale or supply of a medicinal product in response to a *bona fide* unsolicited order, formulated in accordance with the specifications of a practitioner for use by his or her individual patients on his or her direct personal responsibility, in order to fulfil the special needs of those patients.

To avail of the programme, the following conditions must be satisfied:

a receipt of an unsolicited order from a registered healthcare provider (HCP);
b the product must be supplied to the order or prescription of the requesting HCP;
c the product is only provided to the HCP's individual patient; and
d the provision of the product is supervised under the direct personal responsibility of the HCP.

There is no formal authorisation for establishing a named-patient programme in Ireland. However, wholesalers and manufacturers that receive or import exempt medicinal products intended for distribution in Ireland under a named-patient programme must notify the HPRA of this fact within two working days of receipt of the consignment. There are a number of exceptions to this notification requirement, all of which depend on the specific supply chain. Packaging and labelling requirements will apply along with fees and record keeping obligations in terms of pharmacovigilance and quality defects.

Compassionate use

Medicinal products for use in an authorised clinical trial are exempt from the requirement to be subject to a marketing authorisation (MA). The HPRA does recognise the option of an Expanded Access Programme (EAP) for patients who have been treated with a medicinal product during a clinical trial and wish to continue treatment. If, however, the EAP fulfils the definition of a clinical trial, it is required to be authorised as such under the applicable Irish legislation. In the event that it does not fulfil the definition of a clinical trial, the medicinal product can only be supplied via a named-patient programme. This essentially means that EAPs are only recognised in Ireland if they are authorised as clinical trials and meet all applicable legislation governing clinical trials.

Medical devices

Custom-made medical devices that meet the essential requirements but are not CE-marked can be marketed in Ireland and, in exceptional circumstances, non-CE marked medical devices that do not meet the essential requirements. In both instances, the HPRA must authorise such uses.

v Pre-market clearance

Medicinal products

The placing of medicinal products on the market in Ireland is regulated by the Marketing Regulations. Subject to certain exceptions (including the compassionate use exemption and clinical trial supplies), a medicinal product cannot be placed on the market in Ireland unless a marketing authorisation (MA) has been granted for that product by the HPRA or, where appropriate, the European Commission. An MA can be obtained through the following procedures:

a National procedure: an application is submitted to the HPRA and, if granted, the MA entitles the marketing authorisation holder (MAH) to place the medicinal product on the Irish market.

b Mutual recognition procedure: if the medicinal product has received an MA in another EEA Member State (Reference Member State), the MAH can apply to one or more other Member States (Concerned Member State) to recognise that authorisation. If a product has received an MA in another member state, the MAH can apply to the HPRA to mutually recognise that authorisation in Ireland.

c Decentralised procedure: this can be used if the product has not yet received an MA in a member state, and the applicant wishes to apply for simultaneous authorisation in two or more Member States. The applicant nominates one of the states as the Reference Member State, whose competent authority examines the application in full and prepares a report for the competent authorities of the Concerned Member States. The HPRA is the competent authority for these applications in Ireland.

d Centralised procedure: a Community MA, which is valid throughout the EEA, can be obtained by applying to the EMA, through the centralised procedure governed by Regulation (EC) No. 726/2004 on the authorisation and supervision of medicinal products and establishing a European Medicines Agency (as amended) (EMA Regulation). Following a positive assessment by the EMA, an MA is granted by the European Commission. The Centralised Procedure is compulsory for certain medicinal products.

Medical devices

The conformity assessment and CE marking procedures for medical devices discussed in the EU chapter also apply in Ireland. Apart from the registration requirement below, there is little additional regulatory pre-market review and approval by the HPRA.

The Medical Device Regulations require that certain persons placing devices on the market must register their contact details and details of their devices with the HPRA. This requirement applies if that person has a registered place of business in Ireland and if that person:

a manufactures Class I or custom-made medical devices and places them on the market under his or her own name, or trading name;

b manufactures custom-made active implantable medical devices and places them on the market under his or her own name, or trading name;

c manufactures *in vitro* diagnostic medical devices and place them on the market under his or her own name, or trading name;

d fully refurbishes Class I devices or labels one or more ready-made devices, with a view to placing these on the market under his or her own name;

e places medical devices bearing the CE marking on the market, in a system or a procedure pack;

f sterilises, for the purpose of placing on the market, systems or procedure packs or other CE-marked medical devices designed by the manufacturers to be sterilised before use; or

g is the designated European authorised representative for a manufacturer that does not have a registered place of business in the European community, and who places on the market devices within the above-listed categories.

vi Regulatory incentives

Medicinal products

An application for authorisation of a generic of a medicinal product or similar biological product can be made to the HPRA eight years after authorisation of the reference product (i.e., the original product), when the period of data exclusivity for the reference product expires. If the application for the reference product was made before 30 October 2005, and the application was not in respect of a Community MA, the period is reduced to six years.

Once authorised, a generic or similar biological product cannot be placed on the market for ten years (depending on the exclusivity period available for the reference medicinal product) following authorisation of the reference product. This is extended to 11 years if, during the first eight years after the grant of the initial MA for the reference product, the holder of that MA is granted an authorisation for a new therapeutic indication of significant clinical benefit in comparison to existing therapies.

In Ireland, the Irish Patents Office is responsible for granting supplementary protection certificates for medicinal products that meet the criteria under Regulation (EC) No. 469/2009.

Medical devices

There is no specific regulatory exclusivity for medical devices in Ireland. Medical devices may be protected by a patent granted by the Irish Patents Office under the Patents Act 1992 (as amended) (the Patents Act). Patents granted under the Patents Act can be for 20 years (full-term patent) or ten years (short-term patent).

vii Post-approval controls

Medicinal products

The Irish requirements concerning post-approval controls reflect those discussed in the EU chapter.

Additional information to the HPRA

In addition to the requirements for MAHs discussed in the EU chapter, MAHs are required by the Marketing Regulations to inform the HPRA of certain information, including the date that the medicinal product is placed on, or removed from, the market, and any new information that may influence the evaluation of the benefits and risks of the medicinal product.

Transfer of marketing authorisations

An MA may be transferred from the existing authorisation or licence holder to another holder using a transfer procedure. A transfer may occur before a product is authorised or

after authorisation, to a company related to the existing holder or to an unrelated company. An MA can be transferred within six weeks upon receipt of a valid application by the HPRA. Products can be transferred either before authorisation or once authorised. Transfer applications are subject to the national procedure, even if the product has been authorised via the mutual recognition procedure.

Medical devices

The Irish requirements concerning post-approval controls reflect those discussed in the EU chapter.

viii Manufacturing controls

Medicinal products

Manufacturing is regulated by the S.I. 539/2007 Medicinal Products (Control of Manufacture) Regulations 2007 (as amended) (the Manufacturing Regulations).

The manufacture and importation of medicinal products is subject to the holding of an authorisation. This is known as a manufacturing import authorisation (MIA). In order to obtain an MIA, an application is made to the HPRA. The manufacturer is required to provide certain documentation as part of the application that will be verified for accuracy by the HPRA, which may include an inspection of the site where the activities take place. There is no restriction on foreign applicants to apply for an MIA. However, the HPRA only issues manufacturing authorisations for Irish manufacturing or importation sites. Applications must be granted or refused by the HPRA within 90 days.

The requirements governing the information to be submitted as part of the application and those required to ensure the validity of the authorisation (e.g., a qualified person and the principles of good manufacturing practice (GMP)) are discussed in the EU chapter.

The HPRA is responsible for monitoring compliance with manufacturing authorisations and GMP requirements. The HPRA can:

a enter and inspect sites;
b inspect and copy records;
c conduct tests or examinations at the site; and
d take samples for testing.

The HPRA can investigate whether a manufacturer or importer has obtained an authorisation and is complying with it, and has, at his or her disposal, the qualified person approved by the HPRA who meets the requirements and is fulfilling his or her obligations.

Medical devices

Apart from the registration requirement discussed in subsection v, *supra*, the Irish requirements concerning the manufacture of medical devices are similar to those discussed in the EU chapter.

ix Advertising and promotion

Medicinal products

The advertising of medicinal products is regulated by the Advertising Regulations. The Advertising Regulations are enforced by the HPRA. Non-compliant advertisements can be required to be withdrawn and the person responsible for the advertisement may be required to publish a corrective statement. Breach of the Advertising Regulations is a criminal offence

under the IMB Act. The Consumer Protection Act 2007 and the European Communities (Misleading and Comparative Marketing Communications) Regulations 2007 also apply to general advertising and commercial practices.

Self-regulation plays an important role and members of the IPHA must comply with the Code of Practice for the Pharmaceutical Industry (the IPHA Code) for prescription and non-prescription medicinal products, and the Code of Standards of Advertising Practice for the Consumer Healthcare Industry (the IPHA Consumer Code) for non-prescription medicinal products.

The IPHA Code fully reflects the standards of the European Federation of Pharmaceutical Industries and Associations Code on the Promotion of Prescription-only Medicines to, and Interactions with, Healthcare Professionals. The IPHA Code and the IPHA Consumer Code apply only to those pharmaceutical companies that have voluntarily agreed to be members of the IPHA. The Irish Generic Medicines Association (IGMA), the industry body representing manufacturers of generic medicinal products, has published the Code of Practice on Advertising of Medicinal Products (Edition 1, 2010), a similar code based on the Regulations and the Directive.

The Advertising Standards Authority for Ireland (ASAI) has published a Manual of Advertising Self-Regulation with the Code of Standards for Advertising, Promotional and Direct Marketing in Ireland (the ASAI Code). The ASAI Code applies to the advertising of medicinal products, with the exception of specialised marketing communications addressed to the medical, veterinary and allied professions. The Broadcasting Authority of Ireland has produced a General Commercial Communications Code, which applies to advertising broadcasts on radio or television channels licensed in Ireland.

Medical devices

The Medical Devices Legislation does not specifically regulate the advertising of medical devices.

The Irish Medtech Code of Ethical Business Practice (the Medtech Code) is a self-regulatory code and is binding on all Irish MedTech (formerly IMDA) members and Irish Medical and Surgical Trade Association (IMSTA) members. This Code is not underpinned by legislation.

The Medtech Code has been developed by Irish MedTech and the IMSTA and is largely based on that of MedTech Europe (formerly Eucomed and the European Diagnostic Manufacturers Association), the European medical technology industry association. A new common Code of Ethical Business Practice was adopted by MedTech Europe, in a move to put forward clearer and more stringent self-regulation. The new code will replace the current codes of business practice and will be known as the MedTech Europe Code of Business Practice, which will become binding for Irish MedTech members on 1 January 2018. It will set the minimum standard by which industry members operate across Europe.

x Distributors and wholesalers

Medicinal products

Wholesaler's distribution licence

The wholesale or distribution of medicinal products is subject to the possession of a wholesale distribution licence (WDL), as outlined in the Medicinal Products (Control of Wholesale Distribution) Regulations 2007 to 2013. The relevant competent authority in Ireland is the HPRA. The activities that require a WDL are as follows:

a 'procuring' is understood as obtaining, acquiring, purchasing or buying medicinal products from manufacturers, importers or other wholesale distributors;

b 'holding' is understood as storing medicinal products; and

c 'supplying' is understood as all activities of providing, selling, donating medicinal products to wholesalers, pharmacists, or persons authorised or entitled to supply medicinal products to the public.

Medical devices

There are no specific rules concerning the wholesale or distribution of medical devices in Ireland.

xi Classification of products

Prescription-only medicinal products can only be dispensed by a person lawfully conducting a retail pharmacy business, and must be dispensed by or under the personal supervision of a registered pharmacist according to a prescription issued by a registered medical practitioner, a registered dentist or, in certain circumstances, a registered nurse.

Certain non-prescription drugs (as set out in the Medicinal Products (Prescription and Control of Supply) Regulations 2003, as amended (S.I. 540/2003)) can only be sold from a pharmacy under the supervision of a registered pharmacist. General sale products can be placed on general sale, which means that they can be sold in a pharmacy and in any other outlet that is not a pharmacy, for example a supermarket.

The supply of prescription-only medicinal products in Ireland by mail order is prohibited. Supply by mail order is defined as both:

a any supply made, after solicitation of custom by the supplier, or by another person in the supply chain inside or outside Ireland; and

b without the supplier and the customer being simultaneously present and using a means of communication at a distance, whether written or electronic, to convey the custom solicitation and the order for supply.

Medical devices

There are no such similar restrictions on medical devices in Ireland.

xii Imports and exports

The Irish rules governing the import and export of medicinal products and medical devices reflect those at EU level.

An MIA is required for the importation of medicinal products from outside the EEA into Ireland. Applications are made to the HPRA, and must include details of the:

a applicant;

b relevant medicinal products and pharmaceutical forms;

c proposed operations;

d premises, equipment and facilities; and
e site master file.

There must be a 'qualified person' for batch release, who ensures that each batch complies with the law, GMP, the manufacturer's authorisation and the MA or equivalent (such person must be nominated by the applicant.) Each applicant must give a written undertaking to comply with the conditions of the authorisation, if granted.

Products may only be exported by authorised manufacturers or distributors.

xiii Controlled substances

Medicinal products that contain controlled substances as set out in Misuse of Drugs Acts and the Misuse of Drugs Regulations 1988 (as amended) require a controlled drug licence. In Ireland, controlled substances are listed in the Misuse of Drugs Acts and the Misuse of Drugs Regulations 1988 (as amended). Depending upon which Schedule of the regulations the controlled substance is listed in, a manufacturer may be required to obtain a controlled drug licence from the HPRA before the company can legally sell the products to third parties in Ireland. Controlled drugs licences can take between two to eight weeks to obtain.

xiv Enforcement

Medicinal products

A breach of the applicable medicinal product regulations, in most cases, constitutes a breach of Section 32 of the IMB Act, which means that the offending entity shall be guilty of an offence and liable to a fine or imprisonment, or both.

For a summary conviction, a fine not exceeding €2,500 or a term of imprisonment of one year, or both, may be imposed. In addition, on summary conviction, the District Court has discretion to award costs to the HPRA. On indictment, for a first time offence, a person shall be liable to a fine not exceeding €120,000 or a term of imprisonment not exceeding 10 years, or both. For a second and subsequent offence, a fine not exceeding €300,000 or a term of imprisonment not exceeding 10 years, or both, may be imposed. A Section 32 offence can be prosecuted by the Minister for Health, the HPRA, the Pharmaceutical Society of Ireland or the health board in whose functional area the offence was committed. If an offence is committed by a corporate body and is proven to have been committed with the consent or connivance, or is attributable to the neglect, of any person who is an officer or shareholder (if the shareholder manages the corporate body), this person may be personally liable for the offence.

If there is a breach of the self regulatory IPHA Code, the IPHA Code Council, who is responsible for overseeing breaches, may decide to:

a ask the company concerned to cease the practice found to be in breach of the IPHA Code and take all necessary steps to avoid a similar breach in the future;
b reprimand the company for the breach of the IPHA Code;
c order the recovery of material found to have been in breach of the IPHA Code;
d order the correction of inaccurate information by way of direct contact with relevant healthcare professionals or by publication, in the medical or pharmaceutical press, of a corrective notice in terms approved by the IPHA Code Council and Appeals Board;
e order the immediate publication of the decision in whole or in part and specify how and to whom the decision is to be sent. This is in addition to the inclusion of details of the decision in the annual Code of Practice Publication of Findings report;

f in the case of difficult or persistent breaches of the IPHA Code, refer the matter to the Minister for Health; or

g recommend to the IPHA Board of Directors that the offending party be suspended or expelled from the IPHA.

Administrative fees may also be charged. All findings are published at least once a year and are made available to: all members of the IPHA; all non-IPHA member Code signatories; the Minister for Health or Department of Health; and the HPRA.

Medical devices

If an authorised officer appointed by the HPRA has reasonable grounds for suspecting that an offence under the Medical Device Regulations has been committed on any premises, he or she may seek a search warrant from the District Court to search said premises. Any person or body corporate found guilty of an offence under these Regulations shall be liable on summary conviction to imprisonment for up to six months or a fine, or both. When an offence is committed by a body corporate with the consent, connivance or by the negligence of any person who is a director, manager, secretary or other officer of that body corporate, such person may also be personally liable.

If there is a breach of the self-regulatory Irish MedTech Code, the Board of Irish MedTech responsible for overseeing breaches may decide to:

a issue a formal letter of reprimand to the member company;

b issue a formal letter of reprimand to the member company and also recommend to suspend that member company from membership of Irish MedTech for a specified period or to impose conditions for readmission; or

c recommend to expel the offender from Irish MedTech.

Administrative fees will also be charged.

III PRICING AND REIMBURSEMENT

The Health (Pricing and Supply of Medical Goods) Act 2013 (as amended) (the Health Act) and the newly agreed 2016 IPHA Framework Agreement (discussed below) are the key documents regulating the prices of medicinal products in Ireland.

Medicinal products dispensed in the community are funded by the state, through reimbursement of the pharmacist, where the patient in question is eligible under one of the reimbursement schemes, and where the medicinal product being dispensed is eligible for reimbursement.

i Reimbursement schemes

The HSE Primary Care Reimbursement Service (PCRS) operates a General Medical Services (GMS) Scheme in addition to a number of other community reimbursement schemes (Community Drug Schemes) under which it reimburses primary care contractors, including pharmacists, for the cost of providing health services and medicinal products to the public.

The GMS Scheme provides free general medical services, including access to doctors, surgeons, dentists and medicinal products, to those who cannot afford such services. The Community Drug Schemes include the Drugs Payment Scheme, the Long-Term Illness Scheme, the High Tech Drugs Scheme and the EEA Scheme, among others.

ii Pricing

In setting the price for a listed medicinal product, the HSE is required to take into account:

a the ability of suppliers of the relevant items to meet patient demand;

b the value for money provided by the relevant items;

c the equivalent relevant prices (if practicably available) of the relevant items in all other Member States where one or more than one of the relevant items is marketed;

d the relevant prices of therapeutically similar items; and

e the resources available to the HSE; and

f the terms of any agreement in place (whether entered into before, on or after the commencement of the Health Act) between the HSE and any representative body of the suppliers of drugs, medicinal products, or medical or surgical appliances, where the agreement relates, whether directly or indirectly, to the price of one or more of those items. This final point requires the HSE to take into account the terms of the agreements entered into by the HSE with the IPHA and with the IGMA (formerly the Association of Pharmaceutical Manufacturers in Ireland), the industry body representing manufacturers of generic medicinal products (see subsection iii, *infra*).

iii IPHA Framework Agreement

The IPHA Framework Agreement, which came into effect on 1 August 2016 and will operate for four years, only applies to IPHA member companies that are listed in Schedule 2 of the agreement. It governs the pricing and supply of medicinal products that are included on the HSE Reimbursement List, supplied to, or reimbursed by, the HSE, state-funded hospitals or any other publicly funded entities and state agencies providing similar services (hospital medicinal products) or subject to an application for inclusion on the Reimbursement List, or for supply or reimbursement as a hospital medicinal product.

The new agreement introduces five additional EU Member States bringing the proposed price of a product in line with the average ex-factory price in 14 Member States. The IPHA Agreement includes an annual downward only price realignment which commenced on 1 August 2016, and on 1 July for each subsequent year. The price realignment will be set as the average ex-factory price of the 14 Member States for patented medicinal products, and for off-patent medicinal products for which there is no identical pharmaceutical form available for prescription within the reimbursement schemes, to the currency-adjusted average price to the wholesaler in the nominated EU Member States in which the medicinal product is available. The price of a medicinal product that has lost patent protection and for which a generic product has become available, will fall by 50 per cent from the original ex-factory price. Patent-expired biological products are subject to a 20 per cent reduction in price once a biosimilar enters the market.

Significantly, the Agreement has introduced the involvement of the Department of Health in the decision-making process when reviewing products that cannot be funded from within existing HSE resources, such as products that exceed the budget impact or a certain cost-effectiveness threshold. HSE leadership assess a product at first instance and, if the HSE cannot reimburse the product, the HSE can inform the Department of Health who may apply to the government to request consideration of funding for the product.

iv Reimbursement procedure

A medicinal product is eligible for reimbursement if it: has a current MA; is approved for reimbursement by the HSE; is prescribed by a doctor; or is dispensed by a doctor or pharmacist.

New medicinal products for which an MA has been granted may become reimbursable within 75 days of application to the HSE for reimbursement approval, subject to certain exceptions. New and existing technologies that are of high cost or that may have a significant impact on the Irish healthcare budget may be referred by the HSE for pharmacoeconomic assessment.

Payments to pharmacists are regulated by HSE Community Pharmacy Contractor Agreements and the Health Professionals (Reduction of Payments to Community Pharmacy Contractors) Regulations 2013 (S.I. 279/2013).

v Medical devices

Reimbursement of medical devices is conducted through the Aids and Appliances Scheme operated by the Health Services Executive. Increasingly health technology assessments are playing a role, with the Health Information Quality Authority (the body with responsibility for conducting HTAs in Ireland) producing two sets of guidelines in 2010: the Guidelines for Budget Impact Analysis of Health Technologies in Ireland and the Guidelines for the Economic Evaluation of Health Technology in Ireland.

IV ADMINISTRATIVE AND JUDICIAL REMEDIES

Public decisions made by administrative bodies such as the HPRA, NSAI and the HSE may be judicially reviewed by the High Court. In a judicial review, generally the court is not concerned with the merits of the decision but rather with the lawfulness of the decision-making process (i.e., how the decision was made and the fairness of it). Applicants must demonstrate 'sufficient interest' in the proceedings and that they have an arguable case (i.e., the case has grounds).

The High Court will examine the decision and how it was reached and will decide whether or not it was unconstitutional or illegal. There are a number of various grounds upon which an application for judicial review in this jurisdiction may be based. Where the Court is satisfied that there are grounds for quashing a decision to which the application relates, the Court may, in addition to quashing it, remit the matter to the authority concerned with a direction to reconsider it and reach a decision in accordance with the findings of the Court.

The High Court may also quash or cancel the decision by issuing an order known as *certiorari*. The High Court can also order a decision-maker, who is obliged to make a decision but has failed or refused to do so, to actually make the decision – this is known as an order of *mandamus*. An order of prohibition may also be granted in appropriate circumstances (i.e., an order prohibiting a decision-maker from making a decision). Other orders that are available include declarations, injunctions of an interim, interlocutory or permanent nature, or an award of damages. There are certain time frames for submitting an application for leave to apply for judicial review.

V FINANCIAL RELATIONSHIPS WITH PRESCRIBERS AND PAYERS

i Medicinal products

The promotion of medicinal products to healthcare establishments and professionals is governed by the Medicinal Products (Control of Advertising) Regulations 2007 (Advertising Regulations) and, for IPHA Members, the IPHA Code.

The rules reflect those of the EU with the broad prohibition on gifts (including promotional aids), pecuniary advantages or benefits in kind supplied, offered or promised to persons qualified to prescribe or supply by a pharmaceutical company, subject to any regulations for the time being in force relating to prices, margins and discounts.

The IPHA Code also provides specific detailed guidance on interactions with HCPs in Ireland. For instance, items of medical utility aimed directly at the education of healthcare professionals and patient care are not considered gifts and can therefore be supplied, provided they are inexpensive and do not offset the cost of routine business practice of the recipient.

A further update to the IPHA Code took effect from 1 January 2015, and requires that direct and indirect transfers of value (subject to limited exceptions) from pharmaceutical companies to healthcare professionals and healthcare organisations are documented and publicly disclosed by pharmaceutical companies. Public disclosures commenced in 2016 in respect of transfers of value occurring in 2015.

The Prevention of Corruption Acts 1906 to 2010 and the Ethics in Public Office Acts 1995 (as amended) and the Civil Service Code of Standards and Behaviour are also relevant. Holders of certain public positions (including senior personnel within the HSE, HPRA, and the Department of Health and in voluntary hospitals) must disclose certain interests to the Standards in Public Office Commission. These include gifts or the provision of travel facilities, living accommodation, meals or entertainment above a certain threshold in any given year, or both. While responsibility for compliance rests with the recipient of the gift, the provider of the gift can be requested to assist the Standards in Public Office Commission in its investigations, and failure to do so can be a criminal offence.

ii Medical devices

There are no Irish laws or regulations governing interactions between prescribers and payers.

However, the Irish MedTech Code governs all interactions between medical technology companies who are members of Irish MedTech and healthcare professionals, including payers, and it is supplemented by detailed guidelines that clarify and distinguish between appropriate and inappropriate activity in areas such as:

a appropriate support of scientific and educational conferences;
b legitimate consulting agreements with HCPs;
c provision of educational grants and charitable donations; and
d provision of modest hospitality and gifts.

The Code aims to ensure interactions between industry and healthcare professionals cannot be misused to influence, through undue or improper advantages, purchasing decisions, nor should such interactions be contingent upon sale transactions or use or recommendation of products.

VI SPECIAL LIABILITY OR COMPENSATION SYSTEMS

The purchaser or a user of medicinal products or medical devices can seek recourse for regulatory and legal infringements through the Irish courts (i.e., using product liability rules). In Ireland, liability for defective products falls under four main categories: statute, tort, contract and criminal. The principal product liability statute in Ireland is the Liability for Defective Products Act 1991. This Act provides for a strict liability regime, making a producer of the defective product liable in damages in tort for damage caused wholly or partly by a defect in the product. A purchaser or user may also sue in tort for any reasonably foreseeable damage caused to them, or in contract where the pharmaceutical or device was not of merchantable quality.

In Ireland, compensation schemes have been set up in circumstances where an organ of the state may have liability. Such schemes are ad hoc, rather than statutorily required. The State Claims Agency manages these schemes. An example of a compensation scheme includes the Hepatitis C Compensation Tribunal.

VII TRANSACTIONAL AND COMPETITION ISSUES

i Competition law

Irish competition law is based on equivalent EU competition law and is interpreted and applied by analogy. There is no equivalent under Irish competition law to Regulation (EU) No. 316/2014 on the application of Article 101(3) of the Treaty on the Functioning of the European Union to categories of technology transfer agreements (the Technology Transfer Block Exemption Regulation) but Irish competition law would be interpreted in a manner consistent with it. Specific issues have not arisen in any reported Irish competition law cases involving technology transfer licensing agreements or patent licensing.

Arrangements that prevent, restrict or distort competition in trade in any goods or services in Ireland are prohibited and are rendered void (Section 4(1), Competition Act 2002 (as amended)). Horizontal agreements between competitors involving price-fixing, market sharing or output limitation would constitute a serious cartel offence in breach of Section 4(1), which would be investigated and prosecuted on a criminal standard.

Vertical agreements between pharmaceutical suppliers and independent wholesalers and agreements between wholesalers and retailers can also fall under Section 4(1), particularly where there is resale price maintenance, and are likely to be investigated and enforced on a civil standard. To date, neither the Competition and Consumer Protection Commission (CCPC) nor its predecessor, the Competition Authority, has conducted a cartel investigation in the pharmaceutical sector. Apart from public enforcement, parties who claim to be aggrieved by a competition law infringement can take proceedings in the Irish courts and claim damages. There are no reported private competition law actions in the pharmaceutical sector to date.

ii Abuse of a dominant position

Abuse by one or more undertakings of a dominant position in trade for any goods or services in Ireland or any part of Ireland is prohibited (Section 5(1), Competition Act 2002 (as amended)). Therefore, dominant undertakings should exercise caution when engaging in certain practices. For example, a refusal to supply pharmaceutical products could be deemed to be an abuse of a dominant position unless there is an objective justification. Abuse of dominance cases are likely only to be investigated and enforced on the civil standard. Neither

the CCPC nor the Competition Authority, at the time, has reported abuse of dominance cases in the pharmaceutical sector. We are aware of one private action where a drug wholesaler was accused of abusing a dominant position in a region of Ireland by discontinuing supply to a pharmacist. The case was settled.

iii Transactional issues

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

VIII CURRENT DEVELOPMENTS

There are a number of developments at the EU level that will have considerable impact on Ireland's regulatory regime as an EU Member State, most notably the new Medical Device Regulations, the Data Protection Regulation and the Clinical Trials Regulation.

There are signs of increased levels of criticism in recent years in terms of prices of medicinal products and the resulting costs to the state, which culminated in delays in pricing and reimbursement approvals and protracted negotiations on the new IPHA Framework Agreement. In light of the changes in the new Agreement and a changing political landscape, there will be a greater onus on companies to be more prepared and informed on how to navigate the reimbursement process in Ireland.

Appendix 1

ABOUT THE AUTHORS

COLIN KAVANAGH

Arthur Cox

Colin is a partner and head of the life sciences group at Arthur Cox. Colin advises Irish and multinational pharmaceutical, medical device, biotech, cosmetic, food, beverage and agribusiness companies in Ireland on a wide range of corporate, commercial, regulatory, intellectual property and promotional matters, both as part of their day-to-day sourcing, supply chain, manufacturing and sales activities but also in relation to their involvement in corporate transactions.

Colin is also a partner in the corporate and commercial department, with a broad-based commercial practice and a particular focus on life sciences. He advises a broad spectrum of clients on commercial, regulatory and intellectual property matters relating to the life sciences industry. Colin's corporate and commercial practise focuses principally on commercial arrangements between companies and corporate reorganisations across a wide range of industries.

CIARA FARRELL

Arthur Cox

Ciara is a regulatory and compliance specialist advising clients on European Union and Irish regulatory matters applicable to medical devices, medicinal products, food law and cosmetics throughout their entire life cycle. This includes assisting clients in classification of their products, establishment of a pathway to authorisation and marketing of their products in the EU (including related regulatory obligations), pharmacovigilance obligations, promotion and marketing of products, sales agreements, clinical trial agreements, adverse event reporting, product withdrawals, data privacy obligations, conduct of compliance and anti-bribery investigations and regulatory due diligence. She also challenges national authority and EU institution decisions concerning classification and marketing of medicinal products and medical devices.

Ciara also assists life sciences clients in the preparation, drafting and review of numerous agreements including clinical study agreements, pharmacovigilance agreements, CRO agreements, European Authorised Representative Agreements, distribution agreements and sales and promotion agreements.

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