HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Guide to
Fees for Human Products

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This guide does not purport to be an interpretation of law and/or regulations and is for guidance purposes only.

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ABBREVIATIONS

ASR	Active Substance Registration
BTO	Blood, Tissues, Organs
CHMP	Committee for Medicinal Products for Human Use (at the European Medicines Agency)
CMS	Concerned Member State
DCP	Decentralised Procedure
EDQM	European Directorate for the Quality of Medicines & HealthCare
GCP	Good Clinical Practice
GDP	Good Distribution Practice
GMP	Good Manufacturing Practice
HPRA	Health Products Regulatory Authority
MA	Marketing Authorisation
MIA	Manufacturer's/Importer's Authorisation
MR	Mutual Recognition
MRA	Mutual Recognition Agreement
RMS	Reference Member State
SmPC	Summary of Product Characteristics
WDA	Wholesale Distributor Authorisation
MDR	Medical Device Regulation
IVDR	In Vitro Diagnostic Medical Device Regulation

INTRODUCTION

The Health Products Regulatory Authority is the competent authority for medicines, medical devices, blood establishments, tissue establishments, human organs intended for transplantation and cosmetics. Fees for applications are laid down in the Health Products Regulatory Authority (Fees) Regulations which are made each year by the Minister for Health under sections 13 and 32 of the Irish Medicines Board Acts 1995 and 2006.

This guide is intended to assist applicants in identifying the correct category of fee to accompany applications for authorisation. The guide follows the order of the fees in the 'Fee Application Form' and uses the fee code numbers in that form. The fee application form should be completed and submitted with all applications.

1 AUTHORISATION OR REGISTRATION OF MEDICINES

In this section, the term 'MA range' means the marketing authorisations held by an MA holder which have the same MA company number and the same middle MA number, differing only in the end number.

1.1 New applications

1.1.1 Complex dossier, new active substance

These fees apply to medicinal products containing a new active substance not previously licensed in Ireland, and submitted under Article 8.3 of Directive 2001/83/EC.

Codes **111–113** apply to national applications.

Codes **114–116** apply to mutual recognition applications made to the HPRA where Ireland is a concerned Member State (CMS).

Code **117** applies to mutual recognition (MR) applications where Ireland is the RMS. This supplement is for the production and release of the assessment report and the handling and administration of the procedure. It is payable in addition to the appropriate national (codes **111**–**113**) fee. Only one supplement is charged for the entire MA range.

Code **124** applies to mutual recognition (MR) applications where Ireland is the RMS and where the MR application is made within 12 months of the national procedure ending.

Code **119** applies to applications in the decentralised procedure where Ireland is the CMS and code **122** applies to applications in the decentralised procedure where Ireland is the RMS. Fee codes **120** and **121** apply to each additional form and strength submitted at the same time, where Ireland is either the RMS or a CMS. Fee code **123** applies to DCP or MR applications

where Ireland is the RMS and the application involves over 15 concerned Member States. This fee is in addition to the appropriate fees for MR or decentralised applications.

Within each fee code group, the fee categories are structured in the following way: The basic fee codes apply to the initial application for the first form and strength in a range. The codes for 'each additional form at the same time' apply to each application for an additional pharmaceutical form submitted at the same time as the initial application. The codes 'for each additional strength at the same time' apply to each application for an additional strength submitted at the same time as the initial application.

Example 1, an application for one pharmaceutical form in two strengths attracts a fee of:

€22,235~~20,400~~(Product X, 10 mg tablets)
€1,110~~1,020~~ (Product X, 20 mg tablets)
€~~21,420~~23,345

Example 2, an application with two pharmaceutical forms, each form having two strengths attracts a fee of:

€22,235~~20,400~~ (Product X, 10 mg tablets)
€7,785~~7,140~~ (Product X, 10 mg/5 ml oral solution)
€1,110~~1,020~~ (Product X, 20 mg tablets)
€1,110~~1,020~~ (Product X, 20 mg/5 ml oral solution)
€~~29,580~~32,240

Code **118** applies to each additional drug master file or plasma master file submitted with the application. There is no charge for the first master file for each active substance in an application. As an alternative to drug master files, companies may submit certificates of suitability from EDQM; submission of these certificates does not attract any fee.

Booking fees for DCP applications where Ireland is the RMS
A booking fee of €1,000 is applicable to DCP applications where Ireland is the RMS and where commencement periods are pre-agreed. This fee is non-refundable and will be credited against the application fee, provided the application is received within the agreed time slot. If the HPRA, for some reason, is unable to facilitate the agreed slot, the fee will be refunded plus interest at the ECB rate plus 1%.

Pre-submission review of a dossier/application
The booking fee of €1,000 is also applicable to pre-submission procedures. This fee is non-refundable and will be credited against the full application fee.

1.1.2 Reduced dossier - complex

Codes **131**–**144** apply to applications for medicinal products containing known active substances which have already been authorised in Ireland, and which are submitted under the following articles of Directive 2001/83/EC: Article 8.3 (full), Article 10.3 ('hybrid'), Article 10.4

(similar biological), Article 10a (well-established use/bibliographic) and 10b (fixed combination). The structure of the fee codes is the same as that described in section 1.1.1.
Hybrid and generic applications for a single product range where the hybrid relates to a new strength will be charged one single hybrid fee with the appropriate additional strength fees.

1.1.3 Reduced dossier - standard

Fee codes **151**–**164** apply to applications for medicinal products containing established active substances which are already licensed in Ireland, and which are submitted under the following articles of Directive 2001/83/EC: Article 10.1 (generics, including generics referring to an EU reference product) and 10c (informed consent). The structure of the fee codes is the same as that described in section 1.1.1. Reduced dossier standard fees also apply to duplicate applications.

For repeat use procedures, the fee code **157** MR Supplement where Ireland is the RMS applies.

1.2 Subsequent extension applications

Codes **171**–**186** refer to extension applications for additional pharmaceutical forms and strengths made subsequent to the first application. The extension fee codes do not differ between applications made under different legal bases. Fee codes **173** and **174** also apply to new national line extensions following Article 29 of the Paediatric Regulation (1901/2006/EC). The structure of the fee codes is the same as those described in section 1.1.1.

1.3 Switching applications

Fee code **188** applies to a new switching application (for an active substance that is prescription only to move to over-the-counter (OTC) sale or from OTC to general sale). This fee covers all strengths but additional forms will be assessed on a case-by-case basis.

1.4 Variations

Variation fees are charged for each MA which is varied (i.e. per MA number) and for each change applied for. No fees are charged for Type IA (immediate notification) or Type IA (annual report) variations. An outgoing supplement fee is charged for MRP/DCP Type IA variations.

The outgoing IA supplement fee only applies to variations for standalone Type IA applications where Ireland are RMS and there are CMSs involved in the procedure. If no CMSs are involved in the variation, no supplement fee applies. The supplement fee applies to each product range, for example, if multiple product ranges are ~~-~~applied for, a supplement fee will be charged per product range where other CMS are involved. ~~-~~If a Type IB and IA variation is applied for where IE are RMS, there is no ~~O~~outgoing Type IA supplement fee applied to the Type IA variation.

Fees are charged for all other variations, including safety variations, whether requested by the HPRA or not.

Grouped and work-sharing applications which include multiple variations will be charged in accordance with the relevant fee for each variation included in the group or work-sharing application up to a maximum of €5,880 ~~5,395~~ (fee code **245**) per MA range, €3,800 ~~3,485~~ (fee code **236**) per MA and €6,370 ~~5,845~~ (fee code **237**) for work-sharing applications.

Reduced rates apply to bulk variations where the same change is made to three or more MAs (within an MA range). The changes to the first two MAs are charged at the full rate. For changes to only one or two MAs, each change for each MA attracts the full rate fee.

Applications for variations to authorisations that are withdrawn by the applicant will incur an administrative fee of up to 10% of the variation fee.

The variation procedure is not applicable to the transfer of an authorisation to another MA holder, for which a transfer of ownership application must be made (see section 1.5).

1.4.1 National variations

Variations to national marketing authorisations are classified according to the Commission Regulation (EC) No. 1234/2008, as minor variations Type IA and IB and major variations Type II.

Fee code **211** and the reduced rate code **212** apply to Type IB variation applications, i.e. those changes which are not defined as Type IA or Type II. Fee code **212** also applies to the re-introduction of an indication following the expiry of a patent. One fee covers the MA range.

When the supporting data are identical to the originator, no fee is charged for variations to the Part II/Module 3 data for products authorised under Article 10c of Directive 2001/82/EC, (informed consent).

A Type IB variation fee is applied to the pre-submission application for product name changes. Where the name is accepted the full fee will be credited against the cost of the variation but where the name is unacceptable, any new name will attract a fee.

Code **216** is the full-rate code for complex Type II variations, which are listed in the appendix. The code also applies to certain 'extensions' as defined in Annex I of Commission Regulation (EC) No. 1234/2008, and listed in the appendix to this guideline. Code **235** is the reduced-rate fee which applies to bulk variations for the same change to three or more MAs. For complex Type II variations relating to the assessment of the same Active Substance Master File for a number of products with the same company number, the reduced rate fee will apply to the third and subsequent products.

Codes **217** and **218** are the full and reduced-rate codes for standard Type II variations, i.e. those changes which are classified as Type II but are not listed in the appendix to this guide or in Annex I of Commission Regulation (EC) No. 1234/2008.

Codes **223** and **225** are the full and reduced-rate fee codes for notifications under Article 61(3) of Directive 2001/83/EC, to change any aspect of the label or package leaflet not connected with a change to the SmPC. Fee code **225** also applies to applications solely to comply with the Braille requirements of Article 56a of Directive 2001/83/EC.

Code **245** applies when the cost of multiple variations exceeds €5,880 ~~5,395~~ per MA range. This fee covers both national and MR applications. This fee also applies when the cost of multiple changes to the SmPC exceeds €5,880 ~~5,395~~ per MA range.

Code **236** applies when the cost of multiple variations (variations submitted at the same time) to one MA exceeds €3,800~~3,485~~. The fee covers both national and MR applications. This fee also applies when the cost of multiple changes (changes submitted at the same time) to one SmPC exceeds €3,800~~3,485~~.

Code **237** applies when the cost of a work-sharing application exceeds €6,370~~5,845~~. This fee applies to all work-sharing applications.

1.4.2 Mutual recognition variations

The fees for MR variations apply to marketing authorisations granted following a mutual recognition or decentralised procedure.

1.4.2.1 MR variations where Ireland is the CMS

The 'mutual recognition' fee codes apply to MR applications where Ireland is a CMS.

Fee code **214** and the reduced rate code **215** apply to Type IB applications, i.e. those changes which are not defined as Type IA or Type II. The reduced Type IB code **215** also applies to MR applications where Ireland is the CMS but where the change proposed does not affect the medicinal product on the Irish market.

Code **220** is the full-rate code for complex Type II variations, which are listed in the appendix. The code also applies to certain 'extensions' as defined in Annex I of Commission Regulation (EC) No. 1234/2008, and listed in the appendix to this guideline. Code **238** is the reduced-rate fee which applies to bulk variations of the same change to three or more MAs. For complex Type II variations relating to the assessment of the same Active Substance Master File for a number of products with the same company number, the reduced rate fee will apply to the third and subsequent products.

Codes **221** and **222** are the full and reduced-rate codes for incoming standard Type II variations, i.e. those changes which are classified as Type II but are not listed in the appendix to this guide. These fee codes also apply to the amendment to the authorisation to reflect a new paediatric indication following a Paediatric Investigation Plan.

Codes **224** and **226** are the full and reduced-rate fee codes for Article 61(3) notifications of changes to any aspect of the label or package leaflet which are not connected with the SmPC. Fee code **226** also applies to applications solely to comply with the Braille requirements of Article 56a of Directive 2001/83/EC.

1.4.2.2 MR variations where Ireland is the RMS

Fee code **208** is an outgoing supplement and applies to Type IA MR/DCP variations where Ireland is the RMS. This fee covers the MA range.

The mutual recognition fee codes **205** (Type II standard), **213** (Type IB) and **219** (Type II complex) apply to mutual recognition applications where Ireland is the RMS; these fees are a supplement, paid in addition to the national variation fee, and cover the MA range. These supplements will not be applied to outgoing variations where Ireland is the only country involved in a procedure.

The RMS supplement fee is applied to work-sharing applications involving nationally authorised products where the HPRA acts as reference authority for the work-sharing procedure.

1.5 Transfer of ownership

These fee codes refer to the transfer of ownership of MAs from one MA holder to another MA holder with a different legal entity.

Fee code **231** refers to the transfer of MAs to a company which is related, i.e. a 'sister', 'mother', or 'daughter' company or a common corporate body formed from a takeover or merger. This fee is applied to the first marketing authorisation within a range. Fee code **232** applies to each additional marketing authorisation within the range. Codes **233** and **234** refer to transfer between companies which are not related. These fees are applied as above.

Twice the fee code **393** applies to divestments of products where the divestment has arisen from commercial decisions. No fee applies where the change to the RMS is a result of Brexit.

For bulk transfers that are notified in advance, the first ten MAs are charged at the normal rates above and thereafter are charged at €390~~360~~ (fee code **232** or **234**) per transfer. For transfer of ownership before the MA has been granted, see section 8.1.

1.6 Renewals

There is no fee for renewal applications, however a supplement is payable for MR/decentralised applications where Ireland is the RMS. The fee code is **250** and a single supplement covers the MA range.

1.7 Parallel imports

Code **227** applies to the first pharmaceutical form and strength of a product to be parallel-imported into Ireland. A separate fee is charged for each source country applied for, whether included in the initial application or applied for subsequently.

Code **229** applies to each additional strength per country, and code **230** applies to each additional pharmaceutical form per country, whether submitted at the same time or subsequently.

Example:

€~~3,740~~4,080	(Product X, 10 mg tablets, from Greece and Portugal)
€1,2~~1~~10	(Product X, 20 mg tablets, from Greece and Portugal)
€1,2~~1~~10	(Product X, cream, from Greece and Portugal)
€6,50~~5,960~~	

Code **241** applies to the parallel import of dual-pack registration applications for products which are licensed in another Member State where the label and package leaflet of the product in that Member State is identical to the label and package leaflet of the product on the Irish market and the packaging includes the MA authorised number if the product is authorised in Ireland. Code **242** applies to each additional form and each additional strength of the product.

Code **243** refers to the transfer of ownership of parallel import licences. This fee covers the PPA range.

Fee code **244** applies to applications for parallel imports where the originator is not on the Irish market.

Parallel import variations are charged the MA variation fees where appropriate. Please refer to the HPRA 'Application for a Variation to a Parallel Import Licence' for an explanation of how these codes apply to parallel imports.

1.8 Herbal medicines

Code **253** is for an application for a traditional-use registration for herbal medicines under Article 16a of Directive 2001/83/EC, and applies to the first strength and pharmaceutical form.

Codes **254** and **255** are for applications for additional forms and strengths submitted at the same time. These codes also apply to the initial 120-day 'assessment step 1' of applications in the decentralised procedure where Ireland is the RMS. Code **264** applies to national applications where there is a monograph from the Herbal Medicinal Products Committee.

Codes **256**–**258** apply to mutual recognition applications made to the HPRA where Ireland is a CMS.

Code **259** applies to MR or decentralised applications where Ireland is the RMS. This supplement is for the production and release of the assessment report and the handling and administration of the procedure. It is payable in addition to the appropriate national fee. Only one supplement is charged for the entire range.

Code **260** applies to each additional drug master file or plasma master file submitted with the application. There is no charge for the first master file for each active substance in an application. As an alternative to drug master files, companies may submit certificates of suitability from EDQM; submission of these certificates does not attract any fee.

Codes **261**–**263** apply to applications in the decentralised procedure where Ireland is a CMS.

1.8.1 Subsequent extension applications

Codes **281**–**284** refer to extension applications for additional forms and strengths made subsequent to the first application. The structure of the fee codes is the same as those described in section 1.8.

1.8.2 National variations

The HPRA classifies variations to traditional use registrations as minor variations Type IA and IB and major variations Type II using the same classification guideline as that used for MAs.

Fee code **384** and the reduced rate code **385** apply to Type IB variation applications, i.e. those changes which are not defined as Type IA or Type II.

Code **388** is the full-rate code for complex Type II national variations, which are listed in the appendix. The code also applies to certain 'extensions' as defined in Annex I of Commission Regulation (EC) No. 1234/2008, and listed in the appendix to this guideline. Code **386** is the reduced-rate fee which applies to the third and subsequent registrations included in a bulk variation for the same change.

Codes **386** and **387** are the full and reduced-rate codes for standard Type II national variations, i.e. those changes which are classified as Type II but are not listed in the appendix to this guide or in Annex I of Commission Regulation (EC) No. 1234/2008.

Code **389** applies when the cost of multiple variations exceeds €5,1454,720. This fee covers both national and MR applications.

Code **223** and **225** are the full and reduced-rate fee codes for notifications under Article 61(3) of Directive 2001/83/EC, to change any aspect of the label or package leaflet not connected with a change to the Summary of Product Characteristics.

1.8.3 Mutual recognition variations

The following fees for mutual recognition (MR) variations apply to traditional use registrations granted following mutual recognition or decentralised procedures.

1.8.3.1 MR variations where Ireland is the CMS

Fee code **196** and the reduced rate code **197** apply to Type IB applications, i.e. those changes which are not defined as Type IA or Type II.

Code **397** is the full-rate code for complex Type II variations where Ireland is the CMS, which are listed in the appendix. The code also applies to certain 'extensions' as defined in Annex I of Commission Regulation (EC) No. 1234/2008, and listed in the appendix to this guideline. Code **199** is the reduced-rate fee which applies to bulk variations of the same change to three or more traditional-use registrations.

Code **199** and **200** are the full and reduced-rate codes for standard Type II variations where Ireland is the CMS, i.e. those changes which are classified as Type II but are not listed in the appendix to this guide.

Code **389** applies when the cost of multiple variations exceeds €5,1454,720. This fee covers both national and MR applications.

Codes **224** and **226** are the full and reduced fee codes for Article 61(3) notifications of changes to any aspect of the label or package leaflet which are not connected with the Summary of Product Characteristics.

1.8.3.2 MR variations where Ireland is the RMS

The mutual recognition fee codes **396** (Type II standard), **198** (Type IB) and **398** (Type II complex) apply to mutual recognition applications where Ireland is the RMS; these fees are a supplement, paid in addition to the national variation fee.

The fees for all other applications are the same as for MA applications, as described in section 1 of this guide.

1.9 Homeopathic product registration and authorisation

1.9.1 New homeopathic applications

Codes **271** and **272** are for applications for certificate of registration for homeopathic medical products under the simplified registration scheme. The codes apply to:

- national applications
- 'assessment step 1' of applications in the decentralised procedure where Ireland is the RMS
- decentralised applications where Ireland is a CMS

Each pharmaceutical dosage form of a product requires a separate application form and a separate fee irrespective of the stock or potency used. An application for a series of dilutions (potencies) derived from the same stock or stocks are treated as a single application, provided all dilutions are mentioned in the same application.

Codes **273** and **274** apply to MR applications where Ireland is a CMS.

Code **275** applies to MR applications where Ireland is the RMS. This supplement is for the production and release of the assessment report and the handling and administration of the 90-day mutual recognition procedure. It is payable in addition to the appropriate national fee (**271** or **272**), either when the initial national application is made or before the 90-day mutual recognition procedure begins. Only one supplement is charged for the entire range.

1.9.2 New homeopathic applications national rules scheme

Codes **287** and **288** apply to new applications for authorisation under the national rules scheme. These fees cover authorisations of homeopathic medicinal products, as provided for under S.I. No. 540 of 2007, and EU Directive 2001/83/EC. The national rules scheme covers homeopathic medicinal products that have indications and therefore do not qualify for the simplified registration scheme.

1.9.3 Homeopathic registrations and national rules scheme variations

Code **276** is for national variation applications. For bulk variations for the same change to two or more certificates, authorisations or licenses, code **277** is the reduced rate fee which applies to the third and subsequent certificate.

Codes **278** and **279** apply to MR variation applications where Ireland is a CMS.

Code **280** is a supplement fee which applies to MR variation applications where Ireland is the RMS. Only one supplement is charged for the entire range.

Code **204** applies when the cost of multiple variations to the master file exceeds €2,495~~2,290~~.

1.10 Maintenance of authorisations or registrations

Codes **251**, **266** and **267** are yearly fees for each MA, which cover~~s~~ all aspects of routine dossier management and maintenance, including the work associated with on-going pharmacovigilance activities. A reduced fee (code **251**) is applied to the first ten MAs and fee code **266** is applied to the subsequent MAs. Fee code **267** applies to MAs which are deemed to be dormant.

Dormant authorisations are defined as MAs where the product is not marketed (excluding temporary cessation) as notified to the HPRA by 01 January of each year. Notification can be made by submitting a Marketing Status Notification form.

Where an MA holder has less than ten dormant authorisations, these will be charged at the dormant rate, the balance up to ten at the reduced rate and all other authorisations charged at the standard rate.

Where an MA holder has more than ten dormant authorisations, these will be charged at the dormant rate, and all other authorisations charged at the standard rate.

Authorisations or registrations that are withdrawn before 01 May will not be charged a maintenance fee for that year. MAs withdrawn on 01 May and after that date will be charged a full year's fee.

Maintenance fees are payable annually and are invoiced to MA holders during the course of the year.

A reduced maintenance fee (code **252**) applies to parallel import licences. Fee code **269** applies to the maintenance of dual pack registrations.

A reduced annual maintenance fee (code **249**) also applies to homeopathic products.

An annual maintenance fee (code **268**) applies to herbal medicines.

1.11 Enforcement fees – marketing authorisation holder and parallel import licence holder

Fee codes **317**–**320** are yearly fees for MA and parallel import licence holders which cover the enforcement activities undertaken by the HPRA. Enforcement fees are payable annually. The fees are invoiced to companies during the course of the year.

Fee codes **317**–**320** are related to the number of MAs or parallel import licences held by the company, which is determined on the same basis as for the annual maintenance fees. MA or parallel import licence holders pay the MA or parallel import licence holder fee in addition to any manufacturing/wholesaler fee.

1.12 Batch-specific requests

Code **381** is applicable ~~-~~to requests to market specific batches of a medicinal product. The fee is payable per MA. ~~Code **381** is applicable to applications for permission to carry out emergency over-labelling of a batch of a medicinal product for the Irish market or for requests to market specific batches of a medicinal product. The fee is payable per MA.~~

Where the change is identical across a number of MAs only one batch-specific fee will apply.

Code **382** applies to requests to over-label a Malta batch which is the same or similar to the product on the Irish market. This fee also applies to requests to rework or over-label Irish superseded stock to bring it in line with a recently approved variation or the currently approved MA/PA.

Code **383** is a reduced fee for the re-application of a batch request where the request is identical to the original application. In the event that a MAH is contacted by the HPRA due to shortages of a different company's product, and the MAH proposes to submit a BSR for their product to ensure continuity of supply to patients, the reduced fee code 383 (€610~~560~~) will apply for that BSR.

1.13 National scientific advice

An applicant can request national scientific advice at any stage of product development in preclinical, quality and clinical sections in line with our guide for national scientific and regulatory advice (see www.hpra.ie).

Code **240** applies to advice requested in a single area of quality or preclinical development.

Code **246** applies to advice requested in the clinical development section only.

Code **247** applies to situations where advice is requested in two sections from preclinical, quality or clinical in any combination.

Code **248** applies when an applicant requests advice in all three sections.

1.14 Classification

Codes **193, 195 and 201** relate to requests to the Borderline Products Committee for a determination of the medicinal product status of a product. Code **193** is the code for a classification request and the fee applies per product. Code **201** relates to complex classification requests. When the classification involves a novel product requiring detailed consideration of more than one potential regulatory framework~~,~~ or a complex product requiring consideration of multiple components to determine the overall classification of the product or consultation with

European colleagues it may be considered as a complex classification. Where an appeal on a determination is made to the Borderline Products Committee, code **195** applies.

1.15 Service items

Code **190** applies to service items, i.e. applications for radiopharmaceuticals and medicinal products with severely limited but important uses for which no alternative authorised product exists. The designation of a product as a service item must be agreed with the HPRA in advance of the submission. A turnover cut-off is also considered and companies should be prepared to divulge their expected turnover when discussing the application for service item status with the HPRA. The designation of a medicinal product as a service item is subject to review at any time.

2 CLINICAL TRIAL AUTHORISATIONS

The new Clinical Trials Regulation (Regulation No. 536/2014) ~~will be~~was implemented on 31 January 2022 and new clinical trial applications can now be ~~then~~ submitted under this legislation.

New clinical trial applications can continue to be made under the European Communities (Clinical Trials on Medicinal Products for Human Use) Regulations 2004 but only ~~during the first year post implementation.~~until 31 January ~~31~~st~~,~~ 2023.

~~-~~After this date, all new applications must be submitted under the Clinical Trials Regulation (Regulation No. 536/2014). ~~-~~Applications submitted under the Clinical Trials Regulation are subject to a single fee which includes HPRA scientific and National Research Ethics Committee (NREC) ethical assessment. ~~-~~This fee is payable to the HPRA, and a portion is then transferred to the NREC National Office to cover the independent process of research ethics review by the NREC.

Substantial amendments to authorised clinical trials can be submitted under the Clinical Trial Regulations 2004 during the ~~three year~~ transition period up to 21 January ~~23~~1st~~,~~ 2025. ~~.~~

2.1 Request for Authorisation under Regulation 14 of the Clinical Trial Regulations 2004

Codes **338** – **339** refer to applications made according to Regulations 14 of the European Communities (Clinical Trials on Medicinal Products for Human Use) Regulations 2004, and apply to all phases of trials. After 31 January ~~31~~st ~~/01/~~2023, fee codes **338 – 339** will no longer be operational.

Codes **340** and **346** apply to substantial amendment applications. One amendment fee will cover a number of changes submitted at the same time to the same clinical trial. Where an amendment relates to more than one trial, an amendment fee will be charged per trial.

The fees for drug safety update reports and reviews of annual safety data apply as outlined in section 2.3 below.

2.2 Request for Authorisation under Clinical Trial Regulations - Regulation No. 536/2014 (single fee for HPRA scientific and NREC ethical assessment)

2.2.1 Applications with an investigational medicinal product dossier (IMPD)

Code **1001** applies to mono-national applications (i.e. Ireland only). Code **1004** is a supplement where Ireland subsequently becomes the reporting member state for a mono-national trial.

Code **1002** applies to applications where Ireland is the reporting member state. Code **1005** will apply to second and subsequent waves.

Code **1003** applies to applications where Ireland is a concerned member state and initial, transitional or additional applications.

Code **1006** is a reduced fee applied to all non-commercial/academic trials.

2.2.2 Applications with no IMPD or with a simplified IMPD

Codes **1006** – **1010** refer to new clinical trial applications with no IMPD or with a simplified IMPD, for example, a low intervention trial. The structure of the fee codes is the same as that described in section 2.2.1.

2.2.3 Substantial modifications (Parts I & II or Part I only) – with the addition of a new IMPD

Code **1011** applies to mono-national substantial modifications with the addition of a new IMPD.

Code **1012** applies to substantial modifications where Ireland is the reporting member state.

Code **1013** applies to substantial modifications where Ireland is a concerned member state.

Code **1014** is a reduced fee for substantial modifications to all non-commercial/academic trials.

2.2.4 Substantial modifications (Parts I & II or Part II only) – other

Codes **1014 -1017** refer to other substantial modifications. The structure of the fee codes is the same as that described in section 2.2.3.

2.2.5 Substantial modifications (Part II only)

Codes **1018-1019** apply to substantial modifications to part II only. Code **1019** is a reduced fee for substantial modifications to non-commercial/academic trials.

2.3 Drug Safety Update Reports – review of annual safety data

Code **347** refers to the submission of an annual safety report or a drug safety update report (DSUR).

Code **348** refers to the submission of a drug safety update report or an annual safety report where ~~the HPRA~~Ireland is the lead Member State under a work-sharing procedure or Safety Assessment Member State (saMS).~~.~~

2.4 Appeal of a Clinical Trial Decision

Codes **1020**-**1021** refers to an appeal of a clinical trial decision.

3 MANUFACTURERS'/IMPORTERS' AUTHORISATIONS AND WHOLESALE DISTRIBUTOR AUTHORISATIONS

3.1 Manufacturers'/importers' authorisations

Code **310** applies to each application for a manufacturer's/importer's authorisation (MIA). In cases where a manufacturer holds a MIA for medicinal products and a second for investigational medicinal products (with the same legal entity), the application fee for investigational medicinal products is reduced by 50%.

Codes **311**–**314** are annual maintenance fees payable in respect of each authorisation and are related to the size of the facility based on the numbers of 'relevant employees', defined as those employees directly involved in production, processing, quality control/assurance and engineering. In cases in which a manufacturer holds MIAs for medicinal products for both human and veterinary use, the total number of relevant employees will determine the site size, and the fee per annum is 1.5 times the single authorisation fee.

Code **314** is the annual maintenance fee for a MIA for investigational medicinal products. In cases where a manufacturer holds a MIA for medicinal products and for investigational medicinal products, the annual maintenance fee for investigational medicinal products is reduced by 50%.

Code **349** is the annual maintenance fee for a homeopathic manufacturer.

Note: A company is assigned a size category at the application stage. The company must notify the HPRA of a change in size classification. The new classification will be assigned to the company from the date of notification. The HPRA may also notify the company if our records show that there has been a change in size.

Code **315** applies to variations to authorisations in cases where the only change is an administrative change to the authorisation document. A single administrative fee will also apply when the application submitted includes multiple variations to remove various entries from an MIA (e.g. contract manufacturers, contract laboratories, imported products, QP). Code **316** applies to variations involving technical assessment, e.g. requiring inspection or review of supplementary data. Where the same technical variation applies to two or more authorisations, the second and subsequent applications are charged at the fee code **315** rate. Please note that this only applies where the applications are submitted at the same time.

Fee codes **315** and **316** also apply to variations to GMP certificates issued to manufacturers of active pharmaceutical ingredients.

When adding and removing a qualified person or doing the same for other key personnel, fee code **316** applies and covers both changes, as they are consequential. This only applies when the addition and removal are covered within the same application. Removal of any other named person(s) will be charged at the administrative fee code **315**.

Code **315** applies to immediate notification variation applications of IMP MIA Annex 3 and 4 where contract manufacturers and contract laboratories are located in the EU/EEA. Code **316** applies to variations of IMP MIA for Annex 3 and 4 where contract manufacturers and contract laboratories are located outside of the EU/EEA.

Code **335** applies to expedited assessments of IMP/Human/Vet MIA variations for Annex 3 and 4 (contract manufacturers and contract laboratories). The expedited process is limited to the variation types relating to Annex 3 and 4. Where the same expedited variation applies to two or more authorisations, the second and subsequent applications will be charged at the administrative variation fee code **315**.

Applications for MIAs and variations to authorisations that are incorrect or incomplete may incur a fee of up to 10% of the application/variation fee.

Code **371** and **372**: An inspection fee per day/hour per member of the inspection team is payable in relation to each inspection (see section 3.5 below).

3.2 Wholesale distributor authorisations

Code **290** is the fee for each application for a new wholesale distributor authorisation (WDA).

Codes **286** and **291–293** are the annual fees payable in respect of each authorisation and are related to the size of the site:

- Code **291** refers to a large full-line wholesaler supplying a wide range of medicinal products to other wholesalers, retail and hospital pharmacies, health boards, doctors, dentists and others.
- Code **292** refers to a medium full-line or short-line wholesaler supplying a moderate range of medicinal products to retail and hospital pharmacies, health boards, doctors, dentists and others.
- Code **286** refers to a small short-line wholesaler supplying a limited range of medicinal products to a limited range of customers, typically retail and hospital pharmacies.
- Code **293** refers to a minor site supplying medicinal products which may be legally sold in non-pharmacy outlets only to retail outlets such as grocery and newsagents. This code also refers to a 'Procure & Supply' wholesaler. These wholesalers operate on the basis of taking ownership and selling medicinal products onwards. They do not directly store medicinal products.

Code **294** applies to variations to authorisations in cases where the only change is an administrative change to the authorisation document. Code **295** applies to variations involving technical assessment, e.g. requiring inspection or review of supplementary data. No fee applies to an administrative variation that is consequential to a technical variation, e.g. the addition and removal of a responsible person. Where the same technical variation applies to two or more authorisations, the second and subsequent applications are charged at the fee code **294** rate. Please note that this only applies where the applications are submitted at the same time. A reduced fee (code **296**) applies to technical variations to minor site authorisations where the authorisation holder trades in supplying medicinal products only to retail outlets such as grocery and newsagents.

Code **378** relates to classification requests received from wholesalers to determine if a product may be regarded as a medicinal product. The fee covers a maximum of 10 products.

Applications for new WDAs and variations to authorisations that are incorrect or invalid will be considered incomplete and may incur a fee of up to 10% of the application/variation fee.

An inspection fee per day/hour per member of the inspection team is payable in relation to each inspection (see section 3.5 below).

3.3 Active substance manufacturers, importers and distributors and brokers of medicinal products

Code **376** applies to the registration of importers and distributors of active substances and fee code **334** applies to the registration of manufacturers. One fee applies to consequential registrations listed below:

- Manufacture of active substance and distribution of only those active substances manufactured at the site to other sites.
- Importation of active substances and distribution of only those active substances to other sites.

Code **376** also applies to the registration of brokers of finished medicinal products.

Codes **356** and **359** relate to notification of changes to the Active Substances Register. Code **356** relates to the notification of administrative changes. Code **359** relates to immediate notification of a change which may have an impact on the quality or safety of the active substance. One fee covers all changes made in the same application.

Codes **377**, **379** and **380** are annual maintenance fees payable by each registered distributor, importer or manufacturer of active substances.

Code **350** applies to notifications of changes to the register of brokers of finished medicinal products.

3.4 Transfer of ownership of authorisations, approvals and registrations

Codes **321** and **323** apply to the transfer of an authorisation to a company which is related, i.e. a 'sister', 'mother', or 'daughter' company or a common corporate body formed from a takeover or merger. Codes **322** and **324** refer to transfers between unrelated companies.

Codes **321** and **322** also apply to the transfer of a blood, tissues establishment or organ authorisation.

Codes **323** and **324** also apply to the transfer of registrations granted to an active substance manufacturer, importer or distributor or to a broker of medicinal product.

3.5 Inspections

Codes **371** and **372** apply to:
- inspections that form part of the evaluation of an application for a MIA or WDA
- inspections that form part of an evaluation of an application for a blood establishment authorisation, a tissue establishment authorisation or an organ establishment authorisation
- inspections that form part of the evaluation of an application for a MIA for an investigational medicinal product

- inspections of authorised manufacturers, establishments and wholesalers
- inspections of contract laboratories named in manufacturers' authorisations
- inspections that form part of an evaluation of an application for a controlled drug licence or registration to cover any of the following activities: production (including active and finished product), supply, and/or possession
- inspections that form part of an evaluation of an application for a scheduled substance licence or registration to cover any of the following activities: production, supply, and/or possession
- inspections of manufacturers or distributors of precursor chemicals
- inspections of marketing authorisation holders and firms involved in pharmacovigilance activities
- good clinical practice inspections
- inspections of active substance manufacturers
- inspections of brokers of medicinal products, active substance importers and distributors
- inspectorate evaluation of third country sites
- remote inspections ~~/~~ distant assessments
- inspections of manufacturers of investigational medicinal products that are exempt from requiring manufacturer's authorisations. The fee may be waived ~~for~~ when the process inspected supports non-commercial/academic clinical trials.

An inspection fee per day/hour per member of the inspection team is payable in relation to each inspection of each site.

In addition to the fees for each day of the inspection, travel time (maximum of five hours per inspector for travel within Ireland) will be charged together with the cost of expenses, including travel costs and subsistence for the following inspections:

- inspections of sites in a country that is not part of the European Economic Area; accommodation costs will also be charged along with the above expenses for these inspections
- inspections of Good Clinical Practice (GCP); in circumstances where there is no financial support for the conduct of the clinical trial being inspected the fee is waived; the inspection fees for clinical research centres that conduct a mixture of commercial and non-commercial trials is reduced by 80%
- inspections of sites not subject to authorisation or registration, e.g. marketing authorisation holders, firms involved in pharmacovigilance activities
- inspections of contract laboratories
- inspections conducted in response to suspected non-compliance with the principles of GXP, e.g. follow-up inspections, for-cause inspections
- inspections performed to evaluate an application to vary a licence/authorisation or registration
- inspections performed to review engineering installations
- inspections relating to controlled drug and precursor chemical~~s~~ licences or registrations where the company does not hold either a manufacturer's or wholesaler's authorisation may

only be charged ~~do not incur a charge for travel time but~~ the costs of the inspector's expenses, such as subsistence~~, may be applied on a case-by-case basis.~~

3.5.1 Cancellation/Reschedule fees for inspections

Fee code **390** is applicable to non-routine inspections requested by a MIA/WDA/BTO/ASR authorisation holder~~/proposed authorisation holder~~ or applicants. This fee applies to an authorisation holder who gives less than 4four~~3~~ weeks cancellation/rescheduling notice.

3.6 Export and other certificates

Code **351** is for export and other certificates, including ~~Certificate~~ certificate of a ~~Pharmaceutical~~ pharmaceutical ~~Product~~product, ~~Free~~ free ~~Sale~~ sale ~~Certificates~~certificates, GMP ~~Certificates~~ certificates for finished products and for active pharmaceutical ingredients certificates of analysis and TSE declarations. There is no charge for certificates provided in relation to mutual recognition agreements (MRAs) on GMP inspection.

Code **352** is for urgent supply of the above certificates.

There is no fee charged for GMP certificates that are issued on satisfactory conclusion of an inspection. Fee codes **351** or **352** apply to requests for the reissue of a post-inspection GMP certificate.

Codes **353**–**355** are the fees for the issue of free sale certificates for cosmetics.

Note: certificates for food supplements must be obtained from the Department of Health.

3.7 Enforcement fees

Fee codes **303**–**308** are fees payable annually for manufacturers and wholesalers which cover the enforcement activities undertaken by the HPRA. The fees are invoiced to companies during the course of the year.

Fee codes **303**-**308** are related to the size of the site. The size of the site will be determined on the same basis as for the annual maintenance fees.

Companies classed as both manufacturer and wholesaler are charged the higher of the two applicable charges.

3.8 ~~3.8~~ Clinical Trials Regulation – Register of Exemptions (Article 61(5))

Code **265** applies to the registration of IMP manufacturing processes that are exempt from requiring manufacturer's authorisations. -If the process relates to non-commercial/academic clinical trials, the fee may be waived.

Code **270** relates to notification of amendments to the registered details.

4 BLOOD AND TISSUE ESTABLISHMENTS AND ORGAN AUTHORISATIONS

Code **325** applies to each application for a blood ~~and~~ or tissue establishment or organ authorisation. In cases where an organisation holds either a blood or tissue or organ authorisation (with the same legal entity) the application fee for a second authorisation is reduced by 50%. Codes **326**–**329** are the annual maintenance fees payable in respect of each authorisation and relate to the size of the facility based on the numbers of 'relevant employees' defined as those directly involved in operations of the establishment, e.g. donation coordination, processing and quality control/assurance. In cases where an organisation holds more than one authorisation, the annual maintenance fee for the second authorisation is reduced by 50%.

Code **333** applies to organisations who have less than five employees and a turnover of less than €300,000. This is a reduced annual maintenance fee payable in respect of each authorisation and applies to the first four years of the authorisation.

Code **330** applies to variations to authorisations in cases where the only change is an administrative change to the authorisation document. Code **331** applies to variations involving technical assessment, e.g. requiring inspection or review of supplementary data. Where the same technical variation applies to two or more authorisations, the second and subsequent applications are charged at the fee code **330** rate. Please note that this only applies where applications are submitted at the same time.

Fee code **330** also applies to the review of each blood bank's annual report and to non-routine import and export notifications.

Code **332** applies to the formal appeal to a decision to refuse, amend or revoke a blood or, tissue establishment or organ authorisation.

Applications for variations to blood or tissue or organ authorisations that are incorrect or incomplete ~~will~~ may be returned to the applicant and may incur a fee of up to 10% of the application/variation fee.

Code **371** and **372** are the inspection fees per day/hour per member of the inspection team payable in relation to each inspection (see section 3.5).

Code **285** applies to the assessment of devices incorporating non-viable human tissues. This is a fee for the provision of a scientific opinion to a notified body on the non-viability of the

cells/tissues, donation, procurement testing and the risk of the incorporation of the tissues or cells.

5 EXEMPT MEDICINAL PRODUCTS

Codes **297** and **298** apply to notifications of exempt medicinal products. These fees are charged annually based on the number of product notifications made in the calendar year. These fees are capped at €12,245~~11,235~~.

6 COSMETICS

6.1 Inspections of cosmetic product responsible person, manufacturers and distributors

Codes **374** and **375** apply to inspections of cosmetic product responsible person, manufacturers and distributors. In relation to for cause inspections, a fee per member of the inspection team will be applied in addition to expenses for costs of travel and accommodation. For routine inspections, a fee per member of the inspection team will only be applied if there are five or more employees working at the site subject to inspection.

Codes **353**–**355** (Section 3.6) are the fees for the issue of certificates of free sale.

7 PRECURSOR CHEMICALS

Code **309** applies to each application in respect of an import licence, export licence, Category 2 or 3 registrations or per class of drug applicable to a Category 1 annual licence.

8 MISCELLANEOUS FEES

8.1 Technical and administrative services

Codes **391** and **392** are daily and hourly charge-out rates which apply when the services of technical staff are sought, e.g. assessments outside the authorisation process, IT consultancy. These fee codes may also apply to advice provided by the HPRA to professional advisors. These will be considered on a case-by-case basis.

Code **391** also applies to small countries with medicines shortages, where the HPRA will act as RMS in a repeat use procedure subject to the CMS accepting an administrative procedure.
Code **393** is an administration charge for non-routine administrative work, e.g. photocopying requested by companies, corrections required to the authorisation documents, queries relating to the legal basis under which products are authorised, ad-hoc queries, etc. This code is also used for the transfer of an application for a MA before the MA has been granted. Where there are two or more MAs in the product range, twice the code **393** fee is charged for the entire MA range.

8.2 Requests for information

Code **191** relates to requests to the HPRA for information, e.g. for information from the medicinal products database. The fee is payable per request. A reduced fee of €15 applies to requests to provide the SmPC for a medicinal product.

8.3 Appeals

Code **394** is the fee for a formal appeal to a decision of the Authority of the HPRA; it is refundable to the applicant if the appeal is successful.

9 MEDICAL DEVICES

9.1 Certificates of free sale or letters confirming the location of a manufacturing facility in Ireland

Code **411** is a charge for certificates of free sale or for letters confirming the location of a manufacturing facility in Ireland, which includes up to four certificates per request.
Code **413** is a charge for additional certificates/letters available at the time of the initial request.

Code **414~~XXX~~** is a charge for the issuance of a letter confirming the registration of a device or a list of devices with the HPRA.~~Code is a charge for the generation of a letter confirming that medical devices are registered with the HPRA.~~

9.2 Registration of devices

Code **431** is a charge for the initial ~~online~~ registration of a manufacturer, authorised representative, economic operator~~s~~ and assembler, system and procedure pack producer or steriliser placing devices on the market or putting devices into service in Ireland. ~~-~~Where an economic operator is already registered with the HPRA ~~in the context of the Directives~~, they will not be charged a second administrative fee when they register in the context of the ~~R~~regulations or when additional roles are added.~~Where an entity is required to subsequently register under a different medical device regulatory framework or where the entity has to register an additional role the fee will not be charged again.~~

Note: Where an ~~E~~economic ~~O~~operator ~~/ E~~ntity is required to register on Eudamed and this registration requires validation by the HPRA, no ~~online~~ registration fee is charged in this instance. A record of the registration is taken by the HPRA and this is considered, where applicable, in the calculation of our annual fees.
~~There is no fee associated with the Eudamed validation by the HPRA. Additional roles to a registration are not chargeable.~~

9.3 Annual fee for manufacturers, system and procedure pack producers and manufacturing facility located in Ireland

Codes **458–462** and **470** are annual fees payable by each manufacturer (as defined by the legislation) (definition – Appendix II), system and procedure pack producers or a manufacturing facility (definition – Appendix II) located in Ireland. The fees charged are related to the size of the organisation based on the numbers of 'relevant employees', defined as those employees directly or indirectly involved in the design, manufacture, testing, supply, regulatory, governance

and application of the quality management system for the devices manufactured. The annual fee is charged to cover the cost of the HPRA's market surveillance activities.

Where an entity that acts as both a manufacturer (as defined by the legislation) and a manufacturing facility at the one address, the entity will only be charged the fee associated with a manufacturer (as defined by the legislation).

~~No fees are charged to health institutions or registered charities who act as manufacturers, system and procedure pack producers or a manufacturing facility.~~

Where one organisation has multiple manufacturers (as defined by the legislation), system and procedure pack producers or manufacturing facilities based in Ireland, the organisation will be charged per manufacturer or system and procedure pack producer or manufacturing facility to a maximum fee of €61,200.

9.4 Annual fee for authorised representatives

Codes **438-440** and **464** are annual fees payable by each authorised representative of devices. These fees are charged per non-EU manufacturer and are based on the risk class of the manufacturer's devices. The fees are structured to reflect the important roles and responsibilities of the authorised representative, the number of non-European based manufacturers the authorised representative represents, as well as the risk class and the complexity of the devices. The annual fee is charged to cover the cost of the HPRA's market surveillance activities for both the activities of the authorised representative and the non-European based manufacturer.

Fee code **464** – Type I authorised representative relates to authorised representatives that represent non-EU manufacturers who manufacture Class I devices (MDD/MDR) and/or general category IVDs (IVDD)/Class A (IVDR). This fee is capped at €5,500 (fee code **439**).

Fee code **438** - Type II authorised representative relates to authorised representatives that represent non-EU manufacturers who manufacture Classes IIa, IIb, III devices (MDD/MDR), active implantable devices, self-test IVD, Annex II IVD (IVDD) or Class B, C and D (IVDR). This fee is capped at €7,500 (fee code **440**).

An authorised representative who represents a non-EU manufacturer who manufactures a mix of Type I and Type II devices will be charged fee code **438**. The fees for an authorised representative who represents both non-EU manufacturers with low risk devices and non-EU manufacturers with high risk devices the authorised representative will be charged the Type I or Type II fee for each non-EU manufacturer. This fee is capped at €7,500 (fee code **440**).

9.5 Annual fee for distributors and importers

Codes **465**–**468** and , **479** ~~**480**~~ are annual fees payable by each distributor and importer of devices. The fees are related to the size of the organisation based on the total turnover relating to the device business only.

Where an entity acts as both a distributor and importer, one annual distributor's/importer's fee will be charged, and for entities with a turnover of more than ~~€500,000~~3 million an additional fee (fee code **479**)- is charged to reflect the dual responsibilities~~. Fee code **479** only applies to entities with an annual turnover greater than €3 million. Where the entity's turnover is less than €500,000, the additional fee code **480** will apply.~~ will be applied.

Where entities recognised in the manufacturer section 9.3 above also act as distributors of devices to the Irish market for the purpose of intercompany distribution (from other EU and ~~non EU~~non-EU sites) and distribution of third party devices, these fees apply.

Where an entity is recognised as a manufacturer, authorised representative and/or a distributor/importer, separate fees will be charged up to a maximum of €61,200.

9.6 Annual fee for notified body

Code **469** is the annual fee payable by a notified body. The fee covers the continued maintenance of a notified body's designation and its required continuous monitoring.

9.7 Clinical investigations and IVDR performance studies

Codes **451**–**45**2323 apply to clinical investigations of devices and are based on the classification of the device. Code **450** applies to post-market clinical follow-up investigation notifications under MDR Article 74(1), notification of performance study involving companion diagnostic IVD using left over samples under (IVDR Article 58(2), notifications of performance study within the intended purpose of an IVD bearing a CE mark under IVDR Article 70(1)) and notifications associated with MDR Aarticle 74(1), and Article 82. Code **450** also applies to notifications of substantial modifications to previously submitted notifications mentioned above. and IVDR Article 70(1). Code **453** will only be valid until the date of application of the MDR (May 2021).

Code **449** applies to performance studies under the IVDR and IVDR Article 70(2) studies. Code **447** applies to post-market performance follow-up notifications under IVDR Article 70.

Code **454** is a charge for a substantial modification and a technical amendment to a previously approved clinical investigation/performance study. and fee code **455** is a charge for the non-substantial amendment (e.g. additional investigational site) to a previously approved clinical investigation/performance study.

No fees are charged for clinical investigations which are carried out in academic settings with limited funding, e.g. where there is no commercial funding; this will be determined on an individual case basis.

Code **456** applies to the resubmission of clinical investigation applications/performance studies which have been either objected to, withdrawn and resubmitted, or have lapsed. Code **457** is a reduced fee for resubmission of clinical investigation/performance study applications from clinical/academic sponsors.

9.8 Audits of notified bodies, device manufacturers and distributors

Codes **471** and **472** apply to audits of device manufacturers and distributors. In relation to 'for-cause audits' the audit fee per member of the audit team along with expenses, such as, costs of travel and subsistence, is payable in relation to each audit. For proactive surveillance audits, a fee per member of the audit team is payable if there are more than five employees working at the audited site. Fees and expenses for proactive surveillance audits of device manufacturers and distributors with less than five employees can be waived in certain circumstances. In the case of audits that are conducted remotely, additional charges for expenses will not apply.

Codes **471** and **472** apply to the on-site designation assessment, any further assessments required as part of the designation (e.g. additional assessments to confirm corrective actions), surveillance assessments and witnessed audits. The audit fee per member of the HPRA audit team along with expenses, such as, costs of travel and subsistence, is payable in relation to each audit. In the case of assessments that are conducted remotely, additional charges for expenses will not apply. This fee is charged separately to the ~~D~~designation fee (code 484).

9.9 Determination of classification within the medical devices regulations

Code **481** relates to the request to the Medical Devices department for a determination of classification within the medical devices regulations.

Code **492** relates to complex classification requests. When the classification involves a device, which is novel or part of a combination product or incorporates a new novel technology, it may be considered as a complex classification. Where a request requires additional technical review requiring technical and/or regulatory input to reach a determination, or where it requires consultation with EU colleagues, it may be considered as a complex classification.

Where an appeal on a determination of a classification opinion is made, code **483** applies.

Code **437** applies where the HPRA are required to arbitrate between the manufacturer and the notified body on the classification or qualification of a product.

9.10 Designation fee for a notified body

Code **484** applies to applications from organisations seeking designation as a notified body for devices and is on a per directive or r~~R~~egulation basis. The designation fee is also applied to verifications to amending directives or r~~R~~egulations -and to~~. The designations fee is also applied to the re-assessment of the notified body under the new D~~device R~~regulations[1]. This fee is charged separately to any fees relating to any associated inspections/audits (fee codes **471** and **472**).

Code **485** applies to applications from notified bodies to extend their existing scope within a specific ~~Medical~~ medical ~~Device~~ device ~~Directive~~ directive or ~~Regulation~~regulation. This fee is charged per extension.

Code **484** also applies to designation renewals of notified bodies under the Implementation Regulation 920 of 2013 and the new Device Regulations 745 and 746 of 2017.

[1] Regulation (EU) 745/2017 on medical devices (MDR) and Regulation (EU) 746/2017 on *in vitro* diagnostic medical devices (IVDR)

9.11 Medicinal product/device - drug consultations

Codes **486**–**490** relate to the fees for drug consultations on drug/device combination products where a notified body in the EEA requests the HPRA to assess the drug component of the device. Code **486** is for drug consultations on a novel drug substance which has not been approved for use in a medicinal product or a device in Ireland either by the HPRA, or by the European Commission in the case of medicinal products authorised by the Commission.

Code **487** is for drug consultations on a drug substance which has been approved for use in a medicinal product or device by the HPRA or the EU Commission but the intended use of the device is in a therapeutic indication which is not approved. Code **488** is for drug consultations on a drug substance which has been approved for use in a medicinal product or device by the HPRA or the Commission and the intended use of the device is in an approved therapeutic indication.

Drug consultation variations are covered by codes **489** and **490**.

Fee codes **486-490** also apply to the assessment of devices that are composed of substances that are absorbed by or locally dispersed in the human body and that are systematically absorbed to achieve their intended purpose.

9.12 Summary evaluation reviews

Codes **495** and **496** relate to fees for ~~Summary~~ summary ~~Evaluation~~ evaluation ~~Reviews~~ reviews under Commission Regulation (EU) No: 722/2012 which concern requirements laid down by the Council Directives with respect to active implantable devices and devices manufactured utilising tissues of animal origin.

9.13 Assessments under Article 59 of the MDR and Article 54 of the IVDR~~9.12 of IVDD~~

Code~~s~~ **417**~~5 417~~ relate~~s~~ to assessments conducted under Article 59 of the MDR and Article ~~9.12~~54 of the IVD~~RD~~. ~~The fees are based on the risk class and the complexity of the devices involved in the application.~~

Assessments for a 'certificate' that covers multiple devices/device groups will be assessed on a ~~case by case~~case-by-case basis.

A discretionary waiver of the fee will apply when a submission for assessment is made on compassionate grounds for a single patient, single and multiple use of the same device. Multiple applications for the same device in multiple patients will incur fees. Each application will be subject to conditions and a validity period.

~~When a submission for assessment is made on compassionate grounds for a single patient no fee will apply.~~

9.14 European Union Reference Laboratories (EURLs)

Code **420**~~XXX~~ is a charge for the HPRA's verification of a European Union Reference Laboratory~~ies~~ (EURL~~s~~) designation application~~s~~. This verification is conducted prior to the application being submitted by the laboratory to the European Commission.

There is no refund of this fee in the case that the designation application is unsuccessful.

~~A discretionary waiver of the fee will apply when a submission for assessment is made on compassionate grounds for a single patient, single and multiple use of the same device. Multiple applications for the same device in multiple patients will incur fees based on the class of the devices included. and this will be independent of the type of applicant. Each application will be subject to conditions and a validity period.~~

9.15 Miscellaneous

Codes **473** and **474** are daily and hourly charge-out rates which apply when the services of technical staff are sought, e.g. assessments ~~outside the authorisation~~conducted as part of the HPRA processes. These fee codes may also apply to advice provided by the HPRA to professional advisors. These will be considered on a case-by-case basis. The HPRA reserves the right to charge the hourly technical rate to assess applications under Regulations S.I. No. 547 of 2017, S.I. No. 261 of 2021, S.I. No. 691 of 2021, S.I. No. 256 of 2022, S.I. No. 365 of 2022 and the associated amendments. ~~252 of 1994, S.I. No. 253 of 1994, S.I. No. 304 of 2001 and S.I. No. 547 of 2017.~~

Code **475** is an administration charge for non-routine administrative work, e.g. photocopying requested by companies, corrections required to the authorisation documents, queries relating to the legal basis under which products are authorised, ad-hoc queries, etc.

Code **491** relates to requests to the HPRA for information, e.g. for information from the medical device database. The fee is payable per request.

APPENDIX I LIST OF COMPLEX VARIATIONS

The following are classified as complex variations:

Quality Changes – I Active Substance

B.I.a.1 Change in the manufacturer of a starting material/reagent/intermediate used in the manufacturing process of the active substance or change in the manufacturer (including where relevant quality control sites) of the active substance, where no Ph. Eur. Certificate of Suitability is part of the approved dossier

b) Introduction of a new manufacturer of the active substance that is supported by an ASMF.
c) The proposed manufacturer uses a substantially different route of synthesis or manufacturing conditions, which may have a potential to change important quality characteristics of the active substance, such as qualitative and/or quantitative impurity profile requiring qualification, or physico-chemical properties impacting on bioavailability.
d) New manufacturer of material for which an assessment is required of viral safety and/or TSE risk.

B.I.a.2 Changes in the manufacturing process of the active substance

b) Substantial change to the manufacturing process of the active substance which may have a significant impact on the quality, safety or efficacy of the medicinal product.

B.I.e.1 Introduction of a new design space or extension of an approved design space for the active substance, concerning:

a) One unit operation in the manufacturing process of the active substance including the resulting in-process controls and/or test procedures.
b) Test procedures for starting materials/reagents/intermediates and/or the active substance.

B.I.e.2 Introduction of a post approval change management protocol related to the active substance

Quality Changes – II Finished Product

B.II.a.3 Changes in the composition (excipients) of the finished product

b) Other excipients.
2. Qualitative or quantitative changes in one or more excipients that may have a significant impact on the safety, quality or efficacy of the medicinal product.
4. Any new excipient that includes the use of materials of human or animal origin for which assessment is required of viral safety data or TSE risk.
5. Change that is supported by a bioequivalence study.

B.II.a.5 Change in concentration of a single-dose, total use parenteral product, where the amount of active substance per unit dose (i.e. the strength) remains the same

B.II.b.3 Change in the manufacturing process of the finished product, including an intermediate used in the manufacture of the finished product

b) Substantial changes to a manufacturing process that may have a significant impact on the quality, safety and efficacy of the medicinal product.

B.II.c.3 Change in source of an excipient or reagent with TSE risk

b) Change or introduction of a TSE risk material or replacement of a TSE risk material from a different TSE risk material, not covered by a TSE certificate of suitability.

B.II.d.3 Variations related to the introduction of real-time release or parametric release in the manufacture of the finished product

B.II.e.1 Change in immediate packaging of the finished product

b) Type of container or addition of a new container.
2. Sterile medicinal products and biological/immunological medicinal products.

B.II.g.1 Introduction of a new design space or extension of an approved design space for the finished product, excluding biologicals, concerning:

a) One or more unit operations in the manufacturing process of the finished product including the resulting in-process controls and/or test procedures.
b) Test procedures for excipients/intermediates and/or the finished product.

B.II.g.2 Introduction of a post approval change management protocol related to the finished product

Safety, Efficacy and Pharmacovigilance changes

C.I.4 Variations related to significant modifications of the Summary of Product Characteristics due in particular to new quality, pre-clinical, clinical or pharmacovigilance data – SmPC sections 4.2, 4.3 or 5.1. One complex fee is charged if the additional changes applied for are consequential to the main change.

C.I.6 Change(s) to therapeutic indication(s)

a) Addition of a new therapeutic indication or modification of an approved one. (Note: complex fee not charged for a modification)

Other categories of variations where there are substantial changes may be complex and will be considered on a case-by-case basis.