IRISH MEDICINES BOARD

GUIDE TO FEES

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

CONTENTS

ABBREVIATIONS

CHMP	Committee for Human Medicinal Products (at the European Medicines Agency)
CMS	Concerned Member State
RMS	Reference Member State
EDQM	European Directorate for the Quality of Medicines
GCP	Good Clinical Practice
GDP	Good Distribution Practice
GMP	Good Manufacturing Practice
IMB	Irish Medicines Board
MR	Mutual Recognition
MRA	Mutual Recognition Agreement
SPC	Summary of Product Characteristics
MA	Marketing authorisation

INTRODUCTION

The Irish Medicines Board is the competent authority for medicines, medical devices, blood establishments and tissue establishments. Fees for applications are laid down in Irish Medicines Board (Fees) Regulations which are made each year by the Minister for Health under section 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 a 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, as amended.

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

Codes **114**–**116** apply to mutual-recognition applications made to the IMB 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 **119** applies to applications in the decentralised procedure where Ireland is the CMS and code **123** applies to applications in the decentralised procedure where Ireland is the RMS. Fee codes **120-121** apply to each additional form and strength submitted at the same time, where Ireland is either the RMS or a CMS.

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:

€ 15,211	(Product X, 10 mg tablets)
€ 656	(Product X, 20 mg tablets)
€ 15,867	

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

€ 15,211	(Product X, 10 mg tablets)
€ 5,090	(Product X, 10 mg/5 ml oral solution)
€ 656	(Product X, 20 mg tablets)
€ 656	(Product X, 20 mg/5 ml oral solution)
€ 21,613	

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.

1.1.2 Reduced dossier - complex

Codes **131**–**143** 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, as amended: 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.

1.1.3 Reduced dossier - standard

Fee codes **151** to **163** 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, as amended: 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.

1.2 SUBSEQUENT EXTENSION APPLICATIONS

Codes **171** to **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. 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).

1.4 VARIATIONS

Variation fees are charged for each MA which is varied (i.e., per MA number), and for each change applied for, unless the changes are directly and unavoidably consequential on one main change, in which case only one fee is charged per MA. No fees charged for Type IA (immediate notification) or Type IA (annual report) variations. Fees are charged for all other variations, including safety variations, whether requested by the IMB or not.

Grouped and worksharing applications which include multiple variations will be charged in accordance with the relevant fee for each variation included in the group or worksharing application.

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

When the data are kept 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, as amended (informed consent).

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 **217** is the reduced-rate fee which applies to bulk variations for the same change to three or more MAs.

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. These fee codes also apply to the amendment to the authorisation to reflect a new paediatric indication following a Paediatric Investigation Plan.

Codes **223** and **225** are the full and reduced-rate fee codes for notifications under Article 61(3) of Directive 2001/83/EC, as amended, to change any aspect of the label or package leaflet not connected with a change to the Summary of Product Characteristics. Fee code 225 also applies to applications solely to comply with the Braille requirements of Article 56a of Directive 2001/83/EC, as amended by Directive 2004/27/EC.

Code **245** applies when the cost of multiple changes to the SPC exceeds € 7,200 per MA range.

Code **236** applies when the cost of multiple changes (changes submitted at the same time) to one SPC exceeds € 5,400.

Codes **237-239** and **246-248** refer to variations arising from the introduction of standard statements by the Pharmacovigilance Working Party of the CHMP. These fees are capped in accordance with the number of authorisations affected.

1.4.2 Mutual recognition variations

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

1.4.2.1 MR Incoming Variations

The ‘mutual-recognition incoming’ fee codes apply to MR applications where Ireland is a CMS.

Fee code **214** and the reduced rate code **215** applies to Type IB applications, i.e. those changes which are not defined as Type IA or Type II.

Code **220** is the full-rate code for incoming 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 **221** is the reduced-rate fee which applies to bulk variations of the same change to three or more MAs.

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 Summary of Product Characteristics (SPC). Fee code 226 also applies to applications solely to comply with the Braille requirements of Article 56a of Directive 2001/83/EC, as amended by Directive 2004/27/EC.

1.4.2.2 MR outgoing variations

The 'mutual recognition outgoing' fee codes **201** (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.

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 each product and each form. Fee code **232** applies to each additional strength transferred. Codes **233–234** refer to transfer between companies which are not related. These fees are applied as above.

For transfer of ownership before the MA has been granted, see section 7.1.

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:
€ 3,324 (Product X, 10 mg tablets, from Greece and Portugal)
€ 990 (Product X, 20 mg tablets, from Greece and Portugal)
€ 990 (Product X, cream, from Greece and Portugal)
€ 5,304

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. See the Application Form 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 certificates of traditional-use for herbal medicines 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 no monograph.

Codes **256** to **258** apply to mutual-recognition applications made to the IMB 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** to **263** apply to applications in the decentralised procedure where Ireland is either the RMS or a CMS.

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 **271-272** 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 out-going applications in the decentralised procedure where Ireland is the RMS
- incoming 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 **273-274** apply to incoming 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 **287-288** 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. 540 of 2007, as amended and EU Directive 2001/83/EC, as amended. 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 license, code **277** is the reduced rate fee which applies to the third and subsequent certificate**.**

Codes **278-279** apply to incoming 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.

1.10 MAINTENANCE OF AUTHORISATIONS OR REGISTRATIONS

Codes **251, 266-267** are yearly fees for each MA, which covers 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 and is not subject to variations (in the previous 36 months).

Where an MA holder has less than 10 dormant authorisations, these will be charged at the dormant rate, the balance up to 10 at the reduced rate and all other authorisations charged at the standard rate.

Where an MA holder has more than 10 dormant authorisations, these will be charged at the dormant rate, and all other authorisations charged at the standard rate.

Maintenance fees are payable annually from the date of the initial authorisation. Fees 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 BATCH SPECIFIC REQUESTS

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.

1.12 CLASSIFICATION

Codes **193** to **195** relate to requests to the Classification Committee for a determination of the medicinal product status of a product. Code **193** is the code for the first product in any request and code **194** is the reduced rate for additional products submitted at the same time, whether belonging to the same range of products or not. Where an appeal on a determination is made to the Classification Committee, code **195** applies.

1.13 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 IMB 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 IMB. The designation of a medicinal product as a service item is subject to review at any time. All post-authorisation activities (e.g., variations, maintenance of the MA) are charged at the normal rate.

2. CLINICAL TRIAL AUTHORISATIONS

Clinical trial applications are made under the European Communities (Clinical Trials on Medicinal Products for Human Use) Regulations 2004, as amended or under the Control of Clinical Trials Acts, 1987 and 1990.

Codes **336–347** refer to applications made according to Regulations 14 or 35 of the European Communities (Clinical Trials on Medicinal Products for Human Use) Regulations 2004. No fee is charged for re-applications under the Regulations of trials authorised originally under the Control of Clinical Trials Acts.

- Codes 336–340 applies to applications under Regulation 14 where Regulation 16 does not apply and are categorised into applications for Phase IV trials, applications for Phase I, II, or III trials or amendment applications.
- Codes 341–345 apply to applications under Regulation 14 where Regulation 16 does apply and are categorised into applications for Phase IV trials, applications for Phase I, II, or III trials or amendment applications.
- Code 347 refers to the submission of annual safety data.

Academic Investigations

In circumstances where there is no financial support for the conduct of the clinical trial, the investigator may be entitled to a fee waiver. This should be addressed in the application.

3. MANUFACTURER'S AUTHORISATIONS, LABORATORY APPROVALS AND WHOLESALER'S AUTHORISATIONS

3.1 MANUFACTURER'S AUTHORISATION

Code **310** applies to each application for a manufacturer's authorisation. In cases where a manufacturer holds a manufacturer's authorisations for medicinal products and for investigational medicinal products, the application fee for investigational medicinal products is reduced by 50%. There is no fee charged for the renewal of an existing authorisation.

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 directly involved in production, processing, quality control/assurance and engineering. In cases in which a manufacturer holds manufacturer's authorisations 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 manufacturing authorisations for investigational medicinal products. In cases where a manufacturer holds a manufacturer's authorisations for medicinal products and for investigational medicinal products, the annual maintenance fee for investigational medicinal products is reduced by 50%.

Code **315** applies to variations to authorisations in cases where the only change is an administrative change to the authorisation document. 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.

Applications for manufacturer's authorisations and variations to authorisations that are incorrect or incomplete and must be returned to the applicant may incur a fee of up to 10% of the application / variation fee.

Once a company is assigned a size category, that size will remain in place for the life cycle of the authorisation. The company must notify the IMB of a change in size classification. The IMB may also notify the company if our records show that there has been a change in size.

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

3.2 LABORATORY APPROVALS

Code **299** is the fee for each application for a new laboratory approval.

Code **301** applies to variations to approvals in cases where the only change is an administrative change to the approval document. Code **302** 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 approvals, the second and subsequent applications are charged at the fee code **301** rate. Please note that this only applies where the applications are submitted at the same time.

Code **300** is the annual fee payable in respect of each approval. There is no renewal of laboratory approvals.

3.3 WHOLESALER'S AUTHORISATION

Code **290** is the fee for each application for a new wholesaler's authorisation. There is no fee for the renewal of an existing authorisation.

Codes **291–93** 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 limited range of medicinal products to retail and hospital pharmacies, health boards, doctors, dentists and others.
- 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.

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. 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 non-pharmacy medicines to retail outlets.

Applications for wholesaler's authorisations and variations to authorisations that are incorrect or incomplete, and must be returned to the applicant, may incur a fee of up to 10% of the application / variation fee.
An inspection fee per member of the inspection team is payable in relation to each inspection of each site (see section 3.5 below).

3.4 TRANSFER OF OWNERSHIP OF MANUFACTURER'S OR WHOLESALER'S AUTHORISATION

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.

3.5 INSPECTIONS

Codes **371** and **372** apply to:

- inspections that form part of the evaluation of an application for a manufacturer's or wholesaler's authorisation,

- inspections that form part of an evaluation of an application for a blood establishment authorisation, or a tissue and cells establishment authorisation,
- inspections that form part of the evaluation of an application for a manufacturing authorisation for an investigational medicinal product,
- inspections of authorised manufacturers and wholesalers,
- inspections that form part of an evaluation of an application for a controlled drug licence 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 to cover any of the following activities: production, supply, and/or possession,
- inspections of marketing authorisation holders and firms involved in pharmacovigilance activities.
- good clinical practice inspections
- active substance inspections

An inspection fee per member of the inspection team is payable in relation to each inspection of each site

For the following inspections, expenses such as costs of travel, travel time and accommodation will be charged in addition to the inspection fees:

- inspections of manufacturing sites in a country that is not part of the European Economic Area,
- inspection of Good Clinical Practice (GCP); in circumstances where there is no financial support for the conduct of the clinical trial being inspected the fee will be waived,
- inspections of sites not subject to licensing under the Medicinal Products (Control of Manufacture) Regulations 2007, as amended or the Medicinal Products (Control of Wholesale Distribution) Regulations 2007, as amended, e.g., manufacturers of active pharmaceutical ingredients, 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,
- inspections performed as a result of an application to vary a licence/authorisation
- inspections in relation to controlled drug licences (see above) where the company does not hold either a manufacturer's or wholesaler's authorisation,
- engineering inspections.

3.6 EXPORT AND OTHER CERTIFICATES

Code **351** is for export and other certificates, including Certificates of Pharmaceutical Product, Free Sale Certificates, GMP Certificates for finished products and for active pharmaceutical ingredients, certificates of price, certificates of analysis and TSE declarations.

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 certificate.

Note that certificates for cosmetics and food supplements must be obtained from the Department of Health and Children.

4. BLOOD AND TISSUES ESTABLISHMENTS

Code **325** applies to each application for a blood or tissue establishment authorisation. In cases where an organisation holds either a blood or tissue authorisation 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 production, processing, quality control/assurance and engineering. In cases where an organisation holds both a blood and a tissue authorisation, the annual maintenance fee for the second licence is reduced by 50%.

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. This fee code also applies to the review of each blood bank's annual report. Where the same technical variation applies to two or more licences, the second and subsequent applications are charged at the fee code **330** rate. Please note that this only applies to where applications are submitted at the same time.

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

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

5. EXEMPT MEDICINICAL 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 € 10,000.

6. MEDICAL DEVICES

6.1 CERTIFICATES OF FREE SALE

Codes **411-412** are for certificates of free sale, up to four certificates per request. Code 412 is for urgent supply of the certificates, again up to four certificates per request. Code **413** is a charge for additional certificates, available at the time of the initial request.

6.2 REGISTRATION OF DEVICES

Code **431** is a charge for the electronic registration of an organisation which allows online registration, amendments and withdrawal of medical devices.

Codes **432-435** are annual verification fees payable in respect of each organisation that uses the online registration system and are based on the number of employees in the organisation.

Companies with less than 5 employees are not required to pay the annual verification fee provided no changes are made. In the event that changes are necessary, the administration fee (code **431**) is required to reactivate their full user access.

6.3 CLINICAL INVESTIGATIONS

Codes **451-453** apply to clinical investigations of medical devices and are based on the classification of the device. Code **454** is a charge for a technical amendment to a previously approved clinical investigation and fee code **455** is a charge for the administrative amendment (e.g., additional investigational site) to a previously approved clinical investigation.

6.4 AUDITS OF NOTIFIED BODIES AND MEDICAL DEVICE MANUFACTURERS

Codes **471** and **472** apply to all audits. An inspection fee per member of the audit team is payable in relation to each audit. Expenses such as costs of travel and accommodation will be charged in addition to the audit fee.

6.5 CLASSIFICATION

Codes **481** and **482** relate to the request to the Human Products Authorisation and Registration Department for an opinion on the classification status of a medical device. Code 481 is the code for the first device and code 482 is the reduced rate for additional devices submitted at the same time. Where an appeal on a determination is made, code **483** applies.

6.6 DESIGNATION FEE FOR A NOTIFIED BODY

Code **484** applies to applications from organisations seeking designation as a Notified Body for Medical Devices and is on a per Directive basis. The designation fee is also applied to verifications to amending directives.

Code **485** applies to applications from Notified Bodies to extend their existing scope within a specific Medical Device Directive. This fee is charged per extension.

6.7 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 IMB 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 IMB, 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 IMB 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 IMB or the Commission and the intended use of the device is in an approved therapeutic indication.

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

6.8 MISCELLANEOUS

The IMB reserves the right to charge the hourly technical rate (fee code **392**) to assess applications under Regulation 12.10 of S.I.252 of 1994.

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

7. MISCELLANEOUS FEES

7.1 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, for example, assessments outside the authorisation process, IT consultancy. These fee codes may also apply to advice provided by the IMB to professional advisors. These will be considered on a case by case basis.

Code **393** is an administration charge for non-routine administrative work e.g. photocopying requested by companies, corrections required to the authorisation documents 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.

7.2 REQUESTS FOR INFORMATION

Code **191** relates to requests to the IMB 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 Summary of Product Characteristics (SPC) for a medicinal product.

Code **192** is the fee code for each request for information made under the Freedom of Information Acts 1997 and 2003 as amended.

7.3 APPEALS

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

APPENDIX LIST OF COMPLEX VARIATIONS

The following are classified as complex variations:

Clinical changes

1. Clinical changes for which new supporting data are provided from clinical trials, pre-clinical studies, post-marketing experience or publications, including:

1.1 New indications in a therapeutic area for which the product was not previously indicated for use.

1.2 New indications in respect of an organ, any other part of the human body, or infective organism for which the product was not previously indicated for use.

Quality changes

Part S - Drug substance

2. Change in route of synthesis which can affect quality of the product, i.e. new introduction of impurities/degradation products above threshold.

Part P - Drug Product

3. Reformulation of the product - change in two or more excipients and/or change in a key excipient (e.g. preservative, release controlling excipient).
4. Change in release mechanism of the product, i.e. from immediate release to modified release.
5. Major change in manufacture of the product which affects other part of the dossier and/or requires in vivo bioavailability study.
6. Novel manufacturing process.
7. Introduction of Process Analytical Technology.
8. Any change which requires an *in vivo* bioavailability study.
9. Change in packaging material for parenteral products, e.g. vial to pre-filled syringe. Note that the addition of new packaging material, e.g. ampoule, vial etc. must be submitted as a new application.
10. Novel analytical methods not previously used.
11. Any other major change which affects more than one section in the dossier which requires further re-evaluation of the safety or efficacy of the product.
12. Change in site of manufacture of the active substance of a biological product
13. Any change in the source materials, method of manufacture of analytical procedures of a biological product which might significantly affect the quality or safety of the product.