SCHEDULE 1

CAPITAL FEES FOR APPLICATIONS FOR, AND VARIATIONS TO, MARKETING AUTHORIZATIONS, LICENCES AND CERTIFICATES

PART 4

Capital Fees for Applications for Variations of Authorizations, Licences and Registrations

Interpretation

14. In this Part of this Schedule—

"administrative variation application" means an application by a traditional herbal registration holder to vary a traditional herbal registration where the variation applied for falls within one of the following sub-paragraphs—

(a) a change of either or both of the name and the address of the holder of the registration;

(b) a change of either or both of the name and the address of a manufacturer, assembler, storer or distributor named in the registration where the change has been occasioned by the taking over of an existing business, whether by purchase, merger or otherwise, and any change of address does not involve a change of the site of manufacture, assembly or storage or of the site from which distribution takes place;

(c) the removal from the registration of details of one or more of the sites of manufacture, assembly or storage or of the sites from which distribution takes place;

"BROMI variation" means a notification of, or an application for, a variation to the terms of a marketing authorization which is not within the subject matter or scope of Commission Regulation (EC) No.1084/2003 and which—

(a) is submitted using the MHRA portal;

(b) is for a change set out in the BROMI variations guidance;

(c) complies with the conditions to be fulfilled set out in the check list which relates to that change in the BROMI variations guidance; and

(d) is accompanied by the documents which the BROMI variations guidance specifies must be provided with the application for the change;

"BROMI self-certification variation" means a BROMI variation for a change which is designated a Self Certification Procedure type in the check list in the BROMI variations guidance;

"BROMI Type IA variation" means a BROMI variation for a change which is designated a IA Procedure type in the check list in the BROMI variations guidance;

"BROMI Type IB variation" means a BROMI variation for a change which is designated a IB Procedure type in the check list in the BROMI variations guidance;

"BROMI variations guidance" means version 2.1 of the document published by the licensing authority on its website in February 2008, entitled "BROMI Dossier Requirements For Type IA And Type IB UK National Notifications" and dated November 2007(**1**);

(**1**) A copy of the guidance may be downloaded from the website at www. mhra. gov.uk or may be obtained , by writing to the licensing authority at Market Towers, 1 Nine Elms Lane, London SW8 5NQ, or by sending an email to info@mhra.gsi.gov.uk.

"complex variation application" means an application by a traditional herbal registration holder to vary a traditional herbal registration which relates to a change in the formulation of a medicinal product comprising one or more of the following changes—

(a) a change in that product's active ingredients which involves the addition of one or more active ingredients which are active ingredients from a new source;

(b) a change in that product's excipients which involves the addition of one or more TSE risk excipients from a new source; or

(c) a change which involves the addition of one or more vitamins or minerals which are vitamins or minerals from a new source where no European Pharmacopoeia certificate of suitability covering those vitamins or minerals has been submitted with the application;

"Extended Type II Complex Variation Application" means an application by a marketing authorization holder to vary a marketing authorization (not being a parallel import licence) so that the medicinal product is indicated for use—

(a) in a therapeutic area for which the product was not previously indicated for use; or

(b) in respect of an organ, or any other part, of the human body for which the product was not previously indicated for use, if the application is supported by data which comprises or includes the results of clinical trials or physico-chemical, microbiological or pharmacological and toxicological tests;

"new excipient variation application" means an application, other than a complex variation application, by a traditional herbal registration holder to vary a traditional herbal registration which relates to a change in the formulation of the medicinal product to add a new excipient;

"new indication variation application" means an application to vary a marketing authorization for a national homoeopathic product, so that product is indicated for a therapeutic use not previously covered by that authorization;

"reclassification variation application" means an application for variation of a marketing authorization which has the effect that a medicinal product to which that authorization relates—

(a) is to be available only from a pharmacy, where previously it was available only on prescription; or

(b) is to be available on general sale, where previously it was available only on prescription or only from a pharmacy;

"standard variation application" means an application by a traditional herbal registration holder to vary a traditional herbal registration which is not a complex variation application, a new excipient variation application or an administrative variation application;

"standard variation application for a homoeopathic product" means an application for a variation of a marketing authorization for a national homoeopathic medicinal product which requires—

(a) the replacement of an excipient used in the manufacture of the product;

(b) the replacement of a reagent indirectly associated with the manufacturing process of the product or which disappears from that process with a comparable reagent;

(c) a change to the qualitative composition of the container or other form of packaging immediately in contact with the product;

(d) a change to the method of manufacture of a homoeopathic stock included in the product;

(e) a change to the specification of any reagent of excipient used in the manufacture of the product;

(f) a change to the finished product specification of the product;

(g) a change to the test procedure for any raw material used in the manufacture of the product;

(h) a change to the test procedure for the product;

(i) a change to the test procedure for the container or other form of packaging immediately in contact with the product;

(j) a change to comply with a supplement to the European Pharmacopoeia or any national pharmacopoeia of a member State;

(k) a change to the shape of the container in which the product may be placed on the market;

(l) an additional pack size in which the product may be placed on the market;

(m) a change to the approved storage conditions for the product;

(n) a change to the shelf life of an unopened container of the product after the container has been opened for the first time;

(o) a change to the dimensions of an approved dosage form of the product (for example, tablets); or

(p) a change following modification to the manufacturing authorization referred to in Article 40 of the 2001 Directive;

"Type IA Application" means an application by a marketing authorization holder to vary a marketing authorization (not being a parallel import licence) which is a "minor variation" of Type IA within the meaning of Article 3.2 of Commission Regulation (EC) No. 1084/2003;

"Type IB Application" means an application by a marketing authorization holder to vary a marketing authorization (not being a parallel import licence) which is a "minor variation" of Type IB within the meaning of Article 3.2 of Commission Regulation (EC) No. 1084/2003;

"Type II Application" means an application by a marketing authorization holder to vary a marketing authorization (not being a parallel import licence) which is not—

(a) a reclassification variation;

(b) a Type IA Application;

(c) a Type IB Application;

(d) a Type II Complex Variation Application;

(e) an Extended Type II Complex Variation Application; or

(f) a change to which Annex II to Commission Regulation (EC) No. 1084/2003 applies;

"Type II Complex Variation Application" means an application for a variation of a marketing authorization, other than an Extended Type II Complex Variation Application, which relates to a change—

(a) in the formulation of a medicinal product comprising one or more of the following changes, other than a change to which paragraph 1 (changes to active substances) or paragraph 2 (changes to strength, pharmaceutical form and route of administration) of Annex II to Commission Regulation (EC) No. 1084/2003 applies—

  (i) a change which necessitates in- vivo bioavailability studies to be performed on that product,

  (ii) a change in that product's preservative system, or

  (iii) a change in that product's excipients which significantly affects the pharmaceutical or the therapeutic properties of that product; or

(b) which is considered a "major variation" within the meaning given in Article 3.3 of Commission Regulation (EC) No. 1084/2003 and which is—

(i) supported by data which comprises or includes the results of clinical trials or physicochemical, biological, microbiological or pharmacological and toxicological tests, or

(ii) accompanied by evidence relating to post-marketing experience which is information of any type described in paragraph 5.2.6 of Part I of Annex I to the 2001 Directive (clinical documentation); or

(c) in the composition, manufacture or use of a medicinal product to which—

(i) paragraph (c), (e), (g), (h), (j) or (n) of the definition of complex application in this Schedule would apply where an application for a marketing authorization is made in respect of a medicinal product, or

(ii) paragraph (i) of that definition would so apply and the change is not a variation which satisfies conditions 1, 3 and 4 specified in point 14 of Annex I to Commission Regulation (EC) No. 1084/2003 (change in the manufacturer of the active substance or starting material/reagent/intermediate in the manufacturing process of the active substance where no European Pharmacopoeia certificate of suitability is available).

Marketing authorizations

15. Subject to paragraphs 17 to 19 and 26 to 28, the fee payable under regulation 18(1) in connection with an application for a variation of a marketing authorization of a kind described in column 1 of the following table is—

(a) if the application is an eCTD format application, the fee specified in the corresponding entry in column 2 of that table;

(b) if the application is not an eCTD format application, the fee specified in the corresponding entry in column 3 of that table.

Fees for applications for variations of marketing authorizations

Column 1		*Column 2*	*Column 3*
Kind of application		*Fee payable if in eCTD format*	*Fee payable for application not in eCTD format*
1. Application where, for the purposes of Commission Regulation (EC) No. 1084/2003, the United Kingdom is the reference Member State as defined in Article 3.4 of that Regulation			
(a)	Type IA Application	£278	£292
(b)	Type IB Application	£556	£583
(c)	Type II Application	£900	£944
(d)	Type II Complex Variation Application	£14,586	£15,298
(e)	Extended Type II Complex Variation Application	£36,290	£38,062
2. Other variation applications			
(a)	BROMI Self Certification Application	£176	£178

Column 1	*Kind of application*	*Column 2* *Fee payable if in eCTD format*	*Column 3* *Fee payable for application not in eCTD format*
(b)	Type IA Application	£180	£188
(c)	BROMI Type 1A Application	£180	£188
(d)	Type 1B Application	£280	£296
(e)	BROMI Type 1B Application	£280	£296
(f)	Type II Application	£744	£778
(g)	Type II Complex Variation Application	£8,412	£8,824
(h)	Extended Type II Complex Variation Application	£25,962	£27,228
(i)	Reclassification variation Application	£8,264	£8,666

Variation of marketing authorizations

16.—(1) subject to sub-paragraph (3), if an application to vary a marketing authorization of a kind described in sub-paragraph (2) is—

(a) the first application to vary a marketing authorization;

(b) made within 5 years of the date of grant of the marketing authorization; and

(c) an application to authorise use of the medicinal product in a new therapeutic area,

the fee payable for that application is the fee payable under regulation 18(1) and the difference between that fee and the fee which would have been payable if the application had been a major application.

(2) In this paragraph a marketing authorization is one which has been granted in accordance with an application to which point 6 of part II of Annex 1 to the 2001 Directive applies or which is in respect of an orphan medicinal product.

(3) Sub-paragraph (1) and (2) shall not apply where the first application for variation of the marketing authorization relates to a therapeutic area, in respect of which the applicant would be entitled (had he not already held a marketing authorization) to apply for a marketing authorization to which point 6 of Part II of Annex I to the 2001 Directive applies or which is in respect of an orphan medicinal product.

Reclassification of marketing authorizations

17.—(1) Where an application is a reclassification variation application to which this paragraph applies, the fee payable under regulation 18(1) in connection with the application for variation of a marketing authorization is £778, unless the application is an eCTD format application, in which case the fee payable under regulation 18(1) is £744.

(2) This paragraph applies to a reclassification variation application which would have the effect that a medicinal product to which the marketing authorization relates—

(a) is to be available only from a pharmacy (where previously it was available only on prescription), if an analogous medicinal product is available only from a pharmacy or on general sale; or

(b) is to be available on general sale (where previously it was available only on prescription or only from a pharmacy), if an analogous medicinal product is available on general sale.

(3) For the purposes of this paragraph, an analogous medicinal product is a medicinal product which has a United Kingdom marketing authorization or a Community marketing authorization and which—

(a) has the same active ingredient, route of administration and use;

(b) has the same strength or a higher strength;

(c) has the same dosage or daily dosage, or a higher dosage or daily dosage; and

(d) is for sale or supply at the same quantity or a greater quantity,

as the medicinal product in relation to which the variation application is made.

Variation of marketing authorization: natural homoeopathic products

18. The fee payable under regulation 18(1) in connection with an application for a variation of a marketing authorization in respect of a national homeopathic product is—

(a) £250, where the application is a standard variation application for a homeopathic product;

(b) £388, where the application is a new indication variation application; and

(c) £127, for any other application.

Variation of parallel import licence

19.—(1) The fee payable under regulation 18(1) in connection with an application for variation of a parallel import licence is ——

(a) £8,666 if, were the marketing authorization not a parallel import licence, the application for the variation would be a reclassification variation application to which paragraph 17 of this Schedule does not apply;

(b) £176 if the application is one to which sub-paragraph (2) applies; and

(c) £360, in any other case.

(2) This sub paragraph applies where the variation applied for falls within one of the following sub-paragraphs—

(a) a change of either or both of the name and the address of the holder of the licence;

(b) a change of either or both of the name and the address of a manufacturer, assembler, storer or distributor named in the licence where the change has been occasioned by the taking over of an existing business, whether by purchase, merger or otherwise, and any change of address does not involve a change of the site of manufacture, assembly or storage or of the site from which distribution takes place;

(c) the removal from the licence of details of one or more of the sites of manufacture, assembly or storage or of the sites from which distribution takes place;

(d) the removal from the licence of details of any of the activities to which the licence relates;

(e) the removal from the licence of details of any of the medicinal products which the holder of the licence is authorized to import;

(f) the addition or deletion of the name and address of the suppliers of the medicinal product to which the licence relates, or a change in the name, the address, or both the name and address, of the suppliers of that product;

(g) unless paragraph 7 of Schedule 5 applies, a change consequential upon any or any combination of the following—

(i) a change of ownership of the United Kingdom marketing authorization in respect of which the parallel import licence was granted,

(ii) a change to the number of the United Kingdom marketing authorization in respect of which the parallel import licence was granted,

(iii) a change to the name of the holder of the United Kingdom marketing authorization in respect of which the parallel import licence was granted,

(iv) a change to the address of the holder of the United Kingdom marketing authorization in respect of which the parallel import licence was granted,

(v) a change to the number of the marketing authorization for the product in the country where the product originates,

(vi) a change of ownership of the marketing authorization for the product in the country where the product originates,

(vii) a change to the name of the holder of the marketing authorization for the product in the country where the product originates,

(viii) a change to the address of the holder of the marketing authorization for the product in the country where the product originates,

where the change has been occasioned by the taking over of an existing business, whether by purchase, merger or otherwise, if the marketing authorization was not a parallel import licence, the application for that variation would be a reclassification variation application to which paragraph 18 of this Schedule applies.

Manufacturer's authorisations and licences

20. Unless paragraph 26 applies, the fee payable under regulation 18(1)(c) or (d) in connection with an application for variation of a manufacturing authorisation or a manufacturer's licence is—

(a) £238, in the case of a manufacturer's licence referred to in paragraph 8(2) of Part 2 of this Schedule; and

(b) £476, in any other case,

unless the fee in paragraph 21 is payable.

Variation of manufacturer's authorisations and licences

21. The fee payable under regulation 18(1)(c) or (d) in connection with an application for variation of a manufacturing authorisation or a manufacturer's licence is £238 in respect of each variation applied for which constitutes a change to the authorisation or licence not requiring an inspection or medical, scientific or pharmaceutical assessment.

Wholesale dealer's licences

22. Unless the fee in paragraph 23 is payable or paragraph 26 applies, the fee payable under regulation 18(1)(c) in connection with an application for a variation of a wholesale dealer's licence is £450.

Variation of wholesale dealer's licence

23. The fee payable under regulation 18(1)(c) in connection with an application for variation of a wholesale dealer's licence is £238 in respect of each variation applied for which consists of a change to the licence not requiring an inspection or medical, scientific or pharmaceutical assessment.

Clinical trial authorisations

24.—(1) The fee payable under regulation 19(1) in connection with a notice of amendment relating to amendment to the dossier accompanying a request for authorisation to conduct a clinical trial is —

(a) £252, if the amendments relate to one of the parts of the dossier specified in sub-paragraph (2) only ;

(b) £505, if the amendments relate to two parts of the dossier specified in sub-paragraph (2) only; or

(c) £757, if the amendments relate to all three parts of the dossier specified in sub-paragraph (2) only.

(2) The parts of the dossier specified in paragraph (1) are—

(a) the part containing the summaries of the chemical, pharmaceutical and biological data relating to the medicinal product tested or used in the trial;

(b) the part containing the summaries of the non-clinical, pharmacological and toxicology data on that product; and

(c) the part containing the summaries of the available data from previous clinical trials of, and human experience with, that product.

Traditional herbal registrations

25. Unless paragraph 26 applies, the fee payable under regulation 18(1) in connection with an application for variation of a traditional herbal registration is—

(a) £247, if the application is a standard variation application;

(b) £654, if the application is a complex variation application;

(c) £7,394, if the application is a new excipient variation application;

(d) £156, if the application is an administrative variation application.

Identical variations

26. Unless paragraphs 27 or 28 apply, where more than one application by the same applicant is made at the same time for the variation of a marketing authorization, a traditional herbal registration, a manufacturer's licence, or a wholesale dealer's licence and where the applications are for identical variations, the fee payable under regulation 18(1)—

(a) in connection with the first application considered by the licensing authority is the appropriate amount specified in this Part of this Schedule;

(b) in connection with each of the other applications is 50 per cent of that amount.

Complex Variation Applications

27. Where more than one Type II Complex Variation Application or Extended Type II Complex Variation Application is made at the same time by the same applicant for the variation of a marketing authorization, the fee payable under regulation 18(1)—

(a) in connection with the first application considered by the licensing authority is the appropriate amount specified in this Part of the Schedule;

(b) in connection with each of the other applications where the applications are for identical variations and in respect of which no further medical, scientific or pharmaceutical assessment is required is the amount which would be payable if the application was a Type II Application.

Multiple reclassification variation applications

28. Where more than one reclassification variation application is made at the same time by the same applicant, each relating to medicinal products which have the same active ingredient or combination of ingredients, the fee payable under regulation 18(1)—

(a) if one or more of the applications is an application to which paragraph 17 does not apply—

(i) in connection with the first application to which paragraph 17 does not apply, is the appropriate amount specified in this Part of the Schedule,

(ii) in connection with each other application to which paragraph 17 does not apply, is £778, and

(iii) in connection with each other application to which paragraph 17 does apply, is £389;

(b) in any other case—

(i) in connection with the first application, is the appropriate amount specified in this Part of the Schedule, and

(ii) in connection with each other application, is £389.