Intellectual Property Office

BL O/141/14

31 March 2014

COUNCIL REGULATION (EC) 469/2009
CONCERNING THE CREATION OF A
SUPPLEMENTARY PROTECTION CERTIFICATE
FOR MEDICINAL PRODUCTS

APPLICANT Cerus Corporation

ISSUE Whether applications SPC/GB/07/043 and SPC/GB/07/044 meet the requirements of Article 2 and Article 3(b) of the Regulation

HEARING OFFICER Dr L Cullen

DECISION

Introduction

1 This decision relates to two applications for supplementary protection certificates SPC/GB/07/043 and SPC/GB/07/044 which were filed on behalf of Cerus Corporation (the "applicant") on 9 August 2007.

2 The documents filed in support of these two SPC applications are summarised in Table 1.

Background

3 The basic patent upon which these SPC applications are based is EP(UK) 0707476 B1 entitled "*Compounds for the photodecontamination of pathogens in blood*", which was filed on 24 June 1994, with a priority date of 28 June 1995, and was granted by the European Patent Office (EPO) on 14 February 2007. The expiry date of this patent is 23 June 2014.

4 This patent describes a method of inactivating pathogens in blood products in the presence of ultraviolet light, without significantly affecting the function of the blood product or causing mutagenicity.[1] It describes methods to inactivate pathogens in blood products, in particular, methods to inactivate viruses, prior to the use of these blood products *in vivo* and *in vitro*. In contrast with previous approaches, the method requires only short irradiation times and there is no need to limit the concentration of molecular oxygen present. The patent describes (i) photoactivation devices; (ii)

[1] See discussion in basic patent EP(UK) 0707476 B1, see for example [0002], [0007]-[0011], [0014], [0016], [0067], [0069], [0075], [0076], [0090] and [0091] ; text of patent also available via https://register.epo.org/application?number=EP94922020

synthesis of photoactive compounds; (iii) binding of such compounds to nucleic acid; (iv) inactivation of pathogen contaminants; and (v) preservation of biochemical properties of the material treated.

SPC/GB/07/043

5 Form SP1 filed with the first SPC application SPC/GB/07/043, and dated 8 August 2007, indicates that the applicant is seeking to protect the following product "*Platelet preparation obtainable by addition, and subsequent photoactivation, of amotosalen or its salt, to a suspension of platelets in plasma".*

6 The Marketing Authorisation supplied in support of SPC/GB/07/043, was EC Design Examination Certificate No. G7 02 05 16178 063, dated 31 May 2002, which was issued by TUV PRODUCT SERVICE GmbH in Munich, Germany, which identifies itself as an appropriate Certification body. This certificate was issued in accordance with Annex II, Section 4, of Directive 93/42/EEC concerning Medical Devices. It was issued to Baxter Healthcare Corporation (with a US address) and its European representative (in France) was identified. It identifies the product and model as follows:

Product	Medical Disposables
Model(s)	Pathogen Inactivation Disposables for - INTERCEPT (Amotosalen Photochemical Treatment) System for Platelets

7 This design certificate indicates that the product referred to fulfils the "*relevant provisions of the Directive*" (in this case, '*Directive'* refers to the Medical Devices Directive, also referred to as MDD, MedDevDir or Directive 93/42/EC))[2]. It also indicates that the certificate is based on the examination of the technical design documentation submitted (by the client) and the detailed results of this examination are provided in the associated Test Report identified by reference number 70001907. A copy of this report was also filed with this SPC application. This Technical report, which runs to 30 pages in total), on its cover page, identifies the client as Baxter Healthcare Corporation (with a US address) and its places of manufacture in Europe (one in Belgium and one in France) and then identifies its subject matter as the following:

Test subject	Pathogen Inactivation Disposables for INTERCEPT Amotosalen Photochemical Treatment System for Platelets
Test Specification	Council Directive 93/42/EEC of 14 June 1993 concerning medical devices (MDD) (see footnote 2)
Purpose of Examination	EC-Design examination according to the MDD annex II.4 (see footnote 2)
Test Result	The product mentioned above shows that the essential requirements according to the MDD annex I are fulfilled.

[2] MDD or Medical Devices Directive or MedDevDir or Directive 93/42/EEC or Council Directive 93/42/EEC of 14 June 1993 concerning medical devices.

Table 1: Summary of documents filed in support of SPC applications SPC/GB/07/043 and SPC/GB/07/044

SPC APPLICATION	***SPC/GB/07/043***	***SPC/GB/07/044***
Product Definition Applied for	***Platelet preparation obtainable by addition, and subsequent photoactivation, of amotosalen or its salt, to a suspension of platelets in plasma***	***Plasma preparation obtainable by addition to plasma, and photoactivation, of amotosalen or its salt***
PROPOSED AS MARKETING AUTHORISATION		
EC Design Examination Certificate (according to Annex II, Section 4 of Directive 93/42/EC)	G7 02 05 16178 063	G7 06 09 60562 004
Date	31 May 2002	21 November 2006
Valid until	29 May 2007	28 September 2011
Product	Medical Disposables	Blood Processing Devices Pathogen Inactivation Disposables
Model(s)	Pathogen Inactivation Disposables for - INTERCEPT (Amotosalen Photochemical Treatment) System for Platelets	INTERCEPT (Amotosalen Photochemical Treatment) System for Plasma
Notified Body	TUV PRODUCT SERVICE GmbH in Munich, Germany	TUV SUD PRODUCT SERVICE GmbH in Munich, Germany,
Technical/Test report no.	70001907	70113942
Date	23 May 2002	03 November 2006
Test Subject	Pathogen Inactivation Disposables for INTERCEPT Amotosalen Photochemical Treatment System for Platelets	INTERCEPT Blood System for Plasma
PATENT		
Basic Patent	EP 0707476 B	
Title	"*Compounds for the photodecontamination of pathogens in blood*",	
Expiry Date	23 June 2014	

SPC/GB/07/044

8 Form SP1 filed with the second SPC application SPC/GB/07/044 indicates that the applicant is seeking to protect the following product "*Platelet preparation obtainable by addition to plasma, and photoactivation, of amotosalen or its salt".*

9 The Marketing Authorisation supplied in support of SPC/GB/07/044, was EC Design Examination Certificate No. G7 06 09 60562 004. This was also issued in accordance with Annex II, Section 4, of Directive 93/42/EEC on Medical Devices. The certification body in this case was TUV SUD PRODUCT SERVICE GmbH in Munich, Germany, and the certificate also includes a statement that "*TUV SUD PRODUCT SERVIVE GmbH is a Notified body according to Council Directive 93/44/EEC concerning medical devices with identification no. XXX*". This certificate refers to the applicant (Cerus Corporation) as the manufacturer and identifies the product and model covered by the certificate as follows:

Product	Blood Processing Devices Pathogen Inactivation Disposables
Model(s)	INTERCEPT (Amotosalen Photochemical Treatment) System for Plasma

10 A technical report identified by the reference number 70113942 and dated 2006-11-03 was also attached to this certificate. On the first, or cover, page of this report, it identifies the client as Baxter Healthcare Corporation (with a US address) and its place of manufacture in Europe (in France) and then identifies its subject matter as the following:

Test subject	"INTERCEPT Blood System for Plasma"
Test Specification	The essential requirements of Council Directive 93/42/EEC of 14 June 1993 concerning medical devices (MDD)
Purpose of Examination	EC-Design examination according to the MDD annex II.4 (see footnote 2)
Test Result	The requirements of the test specifications are fulfilled.

11 The examiner considers these two SPC applications do not comply with the conditions for obtaining a supplementary protection certificate in that the marketing authorisations filed in support of these applications do not comply with Article 3(b) of Council Regulation (EEC) No 1768/92 of 18 June 1992 concerning the creation of a supplementary protection certificate for medicinal products ("the SPC Regulation"). This article requires that the marketing authorisation is "***granted in accordance with Directive 2001/83/EC*** *or Directive 2001/82/EC as appropriate*" (my emphasis).

12 In addition, the examiner considers that these applications are out of scope as they do not relate to medicinal products subject to an "administrative authorisation procedure as laid down in Directive 2001/83/EC of the European Parliament and the Council of 6 November 2001 on the Community code relating to medicinal products for human use."

13 There has been an extensive correspondence between the applicant and examiner concerning these SPC applications comprising detailed argument and analysis while referring to a significant number of supporting documents.

14 The applicant has sought to convince the examiner that an EC declaration of conformity issued on the medical devices referred to above under the procedure as laid down in Directive 93/42/EEC is equivalent to an authorisation to place a product on the market as a medicinal product under the **procedure as laid down in Directive 2001/83/EC** of the European Parliament and the Council of 6 November 2001 on the Community code relating to medicinal products for human use." Thus the applicant considers that the EC declaration of conformity issued under Directive 93/42/EEC is equivalent to an authorisation to place a product on the market as a medicinal product granted in accordance with Directive 2001/83/EC and thus meets the requirement under Article 3(b) of the SPC regulation.

The Relevant Law and its interpretation

The SPC Regulation

15 Council Regulation (EEC) No 1768/92 of 18 June 1992 concerning the creation of a supplementary protection certificate for medicinal products, which was in force when the SPC applications in question were applied for, has been codified and superceded by Council Regulation (EC) 469/2009 concerning the creation of a supplementary protection certificate for medicinal products, hereafter referred to as the SPC Regulation. Article 22 of Council Regulation (EC) 469/2009 makes clear that references to Council Regulation (EEC) No 1768/92 shall be construed as references to Council Regulation (EC) 469/2009 and shall be read in accordance with the correlation table for recitals and Articles in Annex II of Council Regulation (EC) 469/2009. In this decision, the relevant article from the codified regulation is referred to.

16 Recitals 2-5, 9 and 10 of the SPC Regulation state (emphasis added):

> *'(2) Pharmaceutical research plays a decisive role in the continuing improvement in public health.*
>
> *(3) Medicinal products, especially those that are the result of long, costly research will not continue to be developed in the Community and in Europe unless they are covered by favourable rules that provide for sufficient protection to encourage such research.*
>
> *(4) At the moment, the period that elapses between the filing of an application for a patent for a new medicinal product and authorisation to place the medicinal product on the market makes the period of effective protection under the patent insufficient to cover the investment put into the research.*
>
> *(5) This situation leads to a lack of protection which penalises pharmaceutical research.*
>
> *…*
>
> *(9) The duration of the protection granted by the certificate should be such as to provide adequate effective protection. For this purpose, the holder of both a patent and a*

certificate should be able to enjoy an overall maximum of 15 years of exclusivity ***from the time the medicinal product in question first obtains authorisation to be placed on the market in the Community****.*

(10) All the interests at stake, including those of public health, in a sector as complex and sensitive as the pharmaceutical sector should nevertheless be taken into account. For this purpose, the certificate cannot be granted for a period exceeding five years. ***The protection granted should furthermore be strictly confined to the product which obtained authorisation to be placed on the market as a medicinal product****.'*

17 Article 1 of the SPC Regulation provides the definition of 'product ' and 'medicinal product':

For the purposes of this Regulation, the following definitions shall apply:

(a) 'medicinal product' means any substance or combination of substances presented for treating or preventing disease in human beings or animals and any substance or combination of substances which may be administered to human beings or animals with a view to making a medical diagnosis or to restoring, correcting or modifying physiological functions in humans or in animals;

(b) 'product' means the active ingredient or combination of active ingredients of a medicinal product;

.....

18 Article 2 of the Regulation defines the scope of the regulation (emphasis added) and reads:

Any product protected by a patent in the territory of a Member State and subject, prior to being placed on the market as a medicinal product, to an administrative authorisation procedure as laid down in Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use *or Directive 2001/82/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to veterinary medicinal products may, under the terms and conditions provided for in this Regulation, be the subject of a certificate.*

19 Article 3 of the Regulation which defines the conditions for obtaining a certificate (emphasis added) reads as follows:

A certificate shall be granted if, in the Member State in which the application referred to in Article 7 is submitted and at the date if that application:

(a) the product is protected by a basic patent in force;

(b) a valid authorisation to place the product on the market as a medicinal product has been granted in accordance with Directive 2001/83/EC or Directive 2001/82/EC, as appropriate;

(c) the product has not already been the subject of a certificate;

(d) the authorisation referred to in point (b) is the first authorisation to place the product on the market as a medicinal product"

20 Article 8(1)(b) of the SPC Regulation which concerns the content of an application for an SPC reads as follows (emphasis added):

The application for a certificate shall contain:

(a) .....

(b) a copy of the authorisation to place the product on the market, as referred to in Article 3(b), in which the product is identified, containing in particular the number and date of the authorisation ***and the summary of the product characteristics listed in Article 11 of Directive 2001/83/EC*** *or Article 14 of Directive 2001/82/EC;*

The Medicinal Products Directive – Directive 2001/83/EC[3,4]

21 The Medicines Directive has undergone a number of amendments since it came into force[5]. The references to Articles and other parts of the Medicines Directive below are to the form of the directive that was in force when the SPC applications in question were made in August 2007[6].

22 Article 1 of Title 1 of this directive provides the following definitions

2. Medicinal product*:*

(a) Any substance or combination of substances presented as having properties for treating or preventing disease in human beings; or

(b) Any substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis.

3. Substance*:*

Any matter irrespective of origin which may be:

— human, e.g.

human blood and human blood products;

— animal, e.g.

micro-organisms, whole animals, parts of organs, animal secretions, toxins, extracts, blood products;

— vegetable, e.g.

micro-organisms, plants, parts of plants, vegetable secretions, extracts;

— chemical, e.g.

elements, naturally occurring chemical materials and chemical products obtained by chemical change or synthesis.

---

[3] MPD or MedProdDir or Dir 2001/83/EC or Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use.

[4] Directive 2001/83/EC updates and replaces original Council Directive 65/65/EEC of 26 January 1965 which was the first directive to deal with such medicinal products and is also the directive referred to in Council Regulation EEC/1768/92 which has been codified and superceded by Council Regulation EC/469/2009.

[5] See full entry for Directive 2001/83/EC on EurLex European legislation website at http://eur-lex.europa.eu/Result.do?T1=V1&T2=2001&T3=83&RechType=RECH_naturel&Submit=Search

[6] See consolidated version of Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use, dated 26 January 2007), on EurLex website at Http://Eur-Lex.Europa.Eu/Lexuriserv/Lexuriserv.Do?Uri=Consleg:2001l0083:20070126:En:Pdf

23 Title III of this directive concerns placing medicinal products on the market and includes Articles 6-39, Chapter 1 of this title is entitled ‘Marketing Authorization’ and includes Articles 6-12. Article 6 reads (emphasis added):

> ***No medicinal product may be placed on the market of a Member State unless a marketing authorisation has been issued by the competent authorities of that Member State in accordance with this Directive*** *or an authorisation has been granted in accordance with Regulation (EC) No 726/2004,.....*

24 Article 8 of the medicines directive reads (emphasis added):

> *1. In order to obtain an authorization to place a medicinal product on the market regardless of the procedure established by Regulation (EEC) No 2309/93,* ***an application shall be made to the competent authority of the Member State concerned****.*
>
> *2. A marketing authorization may only be granted to an applicant established in the Community.*
>
> ***3. The application shall be accompanied by the following particulars and documents, submitted in accordance with Annex I:***
>
> *(a) Name or corporate name and permanent address of the applicant and, where applicable, of the manufacturer.*
>
> *(b) Name of the medicinal product.*
>
> *(c) Qualitative and quantitative particulars of all the constituents of the medicinal product, including the reference to its international non-proprietary name (INN) recommended by the WHO, where an INN for the medicinal product exists, or a reference to the relevant chemical name.*
> *(ca) Evaluation of the potential environmental risks posed by the medicinal product. This impact shall be assessed and, on a case-by-case basis, specific arrangements to limit it shall be envisaged.*
>
> *(d) Description of the manufacturing method.*
>
> *(e) Therapeutic indications, contra-indications and adverse reactions.*
>
> *(f) Posology, pharmaceutical form, method and route of administration and expected shelf life.*
>
> *(g) Reasons for any precautionary and safety measures to be taken for the storage of the medicinal product, its administration to patients and for the disposal of waste products, together with an indication of potential risks presented by the medicinal product for the environment.*
>
> *(h) Description of the control methods employed by the manufacturer.*
>
> *(i) Results of:*
> *— pharmaceutical (physico-chemical, biological or microbiological) tests,*
> *— pre-clinical (toxicological and pharmacological) tests,*
> *— clinical trials.*

(ia) A detailed description of the pharmacovigilance and, where appropriate, of the risk-management system which the applicant will introduce.

(ib) A statement to the effect that clinical trials carried out outside the European Union meet the ethical requirements of Directive 2001/20/EC.

(j) A summary, in accordance with Article 11, of the product characteristics, a mock-up of the outer packaging, containing the details provided for in Article 54, and of the immediate packaging of the medicinal product, containing the details provided for in Article 55, together with a package leaflet in accordance with Article 59.

(k) A document showing that the manufacturer is authorised in his own country to produce medicinal products.

(l) Copies of any authorisation obtained in another Member State or in a third country to place the medicinal product on the market, together with a list of those Member States in which an application for authorisation submitted in accordance with this Directive is under examination. Copies of the summary of the product characteristics proposed by the applicant in accordance with Article 11 or approved by the competent authorities of the Member State in accordance with Article 21. Copies of the package leaflet proposed in accordance with Article 59 or approved by the competent authorities of the Member State in accordance with Article 61. Details of any decision to refuse authorization, whether in the Community or in a third country, and the reasons for such a decision. This information shall be updated on a regular basis.

(m) A copy of any designation of the medicinal product as an orphan medicinal product under Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products (..), accompanied by a copy of the relevant Agency opinion.

(n) Proof that the applicant has the services of a qualified person responsible for pharmacovigilance and has the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.

The documents and information concerning the results of the pharmaceutical and pre-clinical tests and the clinical trials referred to in point (i) of the first subparagraph shall be accompanied by detailed summaries in accordance with Article 12.

The Medical Devices Directive (MedDivDir, MDD) - Directive 93/42/EEC[2]

25 The Medical Devices Directive has undergone a number of amendments since it first came into force[7]. The references below to Articles and other parts of the Medical Devices Directive are to the form of the directive that was in force when the SPC

[7] Council Directive 93/42/EEC of 14 June 1993 concerning medical devices – see full entry for this directive on EurLex European legislation website at http://eur-lex.europa.eu/Notice.do?val=294514:cs&lang=en&list=335843:cs,329393:cs,329392:cs,317994:cs,294514:cs,293822:cs,&pos=5&page=1&nbl=6&pgs=10&hwords=).

applications in question were made in August 2007[8]. It is noted that this directive underwent its most recent amendment shortly after the applications for these SPCS were made in September 2007[7].

26 Directive 93/42/EEC, as amended ("the Medical Devices Directive or MDD"), relating to medicinal devices in general[9], in its preamble and recitals identifies its essential objective thus:

> *"Whereas medical devices should provide patients, users and third parties with a high level of protection and attain the performance levels attributed to them by the manufacturer; whereas, therefore, the maintenance or improvement of the level of protection attained in the Member States is one of the essential objectives of this Directive*;"

27 This directive then goes on to outline the relationship between this directive and the Medicinal Products Directive as follows (emphasis added):

> "*Whereas certain medical devices are intended to administer medicinal products within the meaning of Council Directive 65/65/EEC of 26 January 1965 on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products;*
> *whereas, in such cases, the placing on the market of the medical device as a general rule is governed by the present Directive and the placing on the market of the medicinal product is governed by Directive 65/65/EEC;*
> *whereas if, however, such a device is placed on the market in such a way that the device and the medicinal product form a single integral unit which is intended exclusively for use in the given combination and which is not reusable, that single-unit product shall be governed by Directive 65/65/EEC;*
> *whereas a distinction must be drawn between the above mentioned devices and medical devices incorporating, inter alia, substances which, if used separately, may be considered to be a medicinal substance within the meaning of Directive 65/65/EEC;*
> ***whereas in such cases, if the substances incorporated in the medical devices are liable to act upon the body with action ancillary to that of the device, the placing of the devices on the market is governed by this Directive;***
> ***whereas, in this context, the safety, quality and usefulness of the substances must be verified by analogy with the appropriate methods specified in Council Directive 75/318/EEC of 20 May 1975 on the approximation of the laws of the Member States relating to analytical, pharmaco-toxicological and clinical***

[8] See consolidated version of Directive 93/42/EEC of 14 June 1993 concerning medical devices, dated 20 November 2003, on EurLex website at http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CONSLEG:1993L0042:20031120:EN:PDF.

[9] There are three directives which concern themselves with Medical Devices and which are often referred to together in the various guidance and discussion documents regarding the borderline between the authorisation process for medicinal products and that for medical devices. In addition to Council Directive 93/42/EEC (MDD) referred to in footnote 7 above, the other two medical devices directives are: (i) *Council Directive 90/385/EEC of 20 June 1990 relating to active implantable medical devices (AIMDD)* (http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CONSLEG:1990L0385:20071011:EN:PDF); and (ii) *Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on In Vitro Diagnostic Medical Devices (IVDMDD)* (see http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CONSLEG:1998L0079:20090807:EN:PDF).

standards and protocols in respect of the testing of proprietary medicinal products;"

28 The references to Directive 65/65/EEC in the extract above should be read as references to Directive 2001/83/EC[10]. Similarly, the reference to Directive 75/318/EEC in this extract should also be read as a reference to Directive 2001/83/EC[10.] At the time when the two SPC applications in question were made, Directives 65/65/EEC and Directive 75/318/EEC had been replaced by Directive 2001/83/EC. Thus, all references to these two older directives in the following paragraphs, including extracts from the relevant EU legislation should be read as a reference to Directive 2001/83/EC.

29 The recitals to Directive 93/42/EC also indicate that a clinical investigation may be necessary to establish compliance with the requirements of the directive:

> *Whereas **the confirmation of compliance with the essential requirements may mean that clinical investigations have to be carried out under the responsibility of the manufacturer**; whereas, for the purpose of carrying out the clinical investigations, appropriate means have to be specified for the protection of public health and public order;*

30 Article 1 of Directive 93/42/EC entitled 'Definitions, Scope' defines a medical device in the following manner (see part (2)):

> "2. For the purposes of this Directive, the following definitions shall apply:
>
> (a) 'medical device' means any instrument, apparatus, appliance, material or other article, whether used alone or in combination, including the software necessary for its proper application intended by the manufacturer to be used for human beings for the purpose of:
> — diagnosis, prevention, monitoring, treatment or alleviation of disease,
> — diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap,
> — investigation, replacement or modification of the anatomy or of a physiological process,
> — control of conception
>
> and which does not achieve its principal intended action in or on
> the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means; ..."

31 This article, in parts 3, 4, 4a and 5(c), then goes on to define the scope of the Medical Devices Directive as follows (emphasis added):

> ***3. Where a device is intended to administer a medicinal product within the meaning of Article 1 of Directive 65/65/EEC, that device shall be governed by the present Directive, without prejudice to the provisions of Directive 65/65/EEC with***

[10] Council Directive 65/65/EEC of 26 January 1965 on the approximation of provisions laid down by law, regulation or administrative action relating to medicinal products and Council Directive 75/318/EEC of 20 May 1975 on the approximation of the laws of Member States relating to analytical, pharmaco-toxicological and clinical standards and protocols in respect of the testing of proprietary medicinal products, are among the ten directives which were codified into a single text in Directive 2001/83/EC (see also footnotes 3-6 above)

regard to the medicinal product. If, however, such a device is placed on the market in such a way that the device and the medicinal product form a single integral product which is intended exclusively for use in the given combination and which is not reusable, that single product shall be governed by Directive 65/65/EEC. The relevant essential requirements of Annex I to the present Directive shall apply as far as safety and performance related device features are concerned.

4. ***Where a device incorporates, as an integral part, a substance which, if used separately, may be considered to be a medicinal product within the meaning of Article 1 of Directive 65/65/EEC and which is liable to act upon the body with action ancillary to that of the device, that device must be assessed and authorized in accordance with this Directive****.*

4 a. Where a device incorporates, as an integral part, a substance which, if used separately, may be considered to be a medicinal product constituent or a medicinal product derived from human blood or human plasma within the meaning of Article 1 of Directive 89/381/EEC (1) and which is liable to act upon the human body with action ancillary to that of the device, hereinafter referred to as a 'human blood derivative', that device must be assessed and authorised in accordance with this Directive.

5. ***This Directive does not apply to****:*
(a) ....;
(b) ....:
(c) ***medicinal products covered by Directive 65/65/EEC****, including medicinal products derived from blood as covered by Directive 89/381/EEC;*
(d).....

32 Article 3 entitled 'Essential Requirements' states (emphasis added):

"*The devices must meet the essential requirements set out in Annex I which apply to them,* ***taking account of the intended purpose of the devices concerned."***

33 Article 9, entitled 'Classification' reads as follows (emphasis added):

*"****1. Devices shall be divided into Classes I, IIa, IIb and III. Classification shall be carried out in accordance with Annex IX****.*

2. In the event of a dispute between the manufacturer and the notified body concerned, resulting from the application of the classification rules, the matter shall be referred for decision to the competent authority to which the notified body is subject.

3. The classification rules set out in Annex IX may be adapted in accordance with the procedure referred to in Article 7 (2) in the light of technical progress and any information which becomes available under the information system provided for in Article 10."

34 Article 11, entitled 'Conformity Assessment Procedures', is also relevant for the purposes of this case. Article 11(1)(a), 11(1)(b), 11(9) and 11(11) in particular state as follows:

"1. In the case of devices falling within Class III, other than devices which are custom-made or intended for clinical investigations, the manufacturer shall, in order to affix the CE marking, either:

(a) follow the procedure relating to the EC declaration of conformity set out in Annex II (full quality assurance); or

(b) follow the procedure relating to the EC type-examination set out in Annex III, coupled with:

(i) the procedure relating to the EC verification set out in Annex IV;
or
(ii) the procedure relating to the EC declaration of conformity set out in Annex V (production quality assurance).

.....

9. Where the conformity assessment procedure involves the intervention of a notified body, the manufacturer, or his authorized representative established in the Community, may apply to a body of his choice within the framework of the tasks for which the body has been notified.

.....

11. Decisions taken by the notified bodies in accordance with Annexes II and III shall be valid for a maximum of five years and may be extended on application, made at a time agreed in the contract signed by both parties, for further periods of five years."

35 Article 15 entitled 'Clinical Investigation' states that (emphasis added):

"1. In the case of devices intended for clinical investigations, the manufacturer, or his authorized representative established in the Community, shall follow the procedure referred to in Annex VIII and notify the competent authorities of the Member States in which the investigations are to be conducted.

2. In the case of devices falling within Class III and implantable and long-term invasive devices falling within Class IIa or IIb, the manufacturer may commence the relevant clinical investigation at the end of a period of 60 days after notification, unless the competent authorities have notified him within that period of a decision to the contrary based on considerations of public health or public policy.

Member States may however authorize manufacturers to commence the relevant clinical investigations before the expiry of the period of 60 days, in so far as the relevant ethics committee has issued a favourable opinion on the programme of investigation in question.

3. In the case of devices other than those referred to in the second paragraph, Member States may authorize manufacturers to commence clinical investigations, immediately after the date of notification, provided that the ethics committee concerned has delivered a favourable opinion with regard to the investigational plan.

4. The authorization referred to in paragraph 2 second subparagraph and paragraph 3, may be made subject to authorization from the competent authority.

5. The clinical investigations must be conducted in accordance with the provisions of Annex X. *The provisions of Annex X may be adjusted in accordance with the procedure laid down in Article 7 (2).*

6. The Member States shall, if necessary, take the appropriate steps to ensure public health and public policy.

7. The manufacturer or his authorized representative established in the Community shall keep the report referred to in point 2.3.7 of Annex X at the disposal of the competent authorities.

8. The provisions of paragraphs 1 and 2 do not apply where the clinical investigations are conducted using devices which are authorized in accordance with Article 11 to bear the CE marking unless the aim of these investigations is to use the devices for a purpose other than that referred to in the relevant conformity assessment procedure. The relevant provisions of Annex X remain applicable."

36 This Directive also comprises a number of Annexes (12 in total) which provide greater detail on how the various procedures covered by the Medical Devices Directive work. Of these 12, five are relevant to the present case, Annexes I, II, III, IX and X.

37 Annex I entitled "EC Declaration of Conformity (Full Quality Assurance procedure)' describes in detail the essential requirements that devices must meet (see Article 3 of the Directive) in order to qualify for the CE marking and, as a result, for free movement within the Community.

38 Sections 1-6 of Annex 1, under Part I entitled 'General Requirements', read (emphasis added):

"1. The devices must be designed and manufactured in such a way that, when used under the conditions and for the purposes intended, they will not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety.

2. The solutions adopted by the manufacturer for the design and construction of the devices must conform to safety principles, taking account of the generally acknowledged state of the art.

In selecting the most appropriate solutions, the manufacturer must apply the following principles in the following order:
— eliminate or reduce risks as far as possible (inherently safe design and construction),
— where appropriate take adequate protection measures including alarms if necessary, in relation to risks that cannot be eliminated,
— inform users of the residual risks due to any shortcomings of the protection measures adopted.

3. The devices must achieve the performances intended by the manufacturer and be designed, manufactured and packaged in such a way that they are suitable for one or more of the functions referred to in Article 1 (2) (a), as specified by the manufacturer.

4. The characteristics and performances referred to in Sections 1, 2 and 3 must not be adversely affected to such a degree that the clinical conditions and safety of the patients and, where applicable, of other persons are compromised during the lifetime

of the device as indicated by the manufacturer, when the device is subjected to the stresses which can occur during normal conditions of use.

5. The devices must be designed, manufactured and packed in such a way that their characteristics and performances during their intended use will not be adversely affected during transport and storage taking account of the instructions and information provided by the manufacturer.

6. Any undesirable side-effect must constitute an acceptable risk when weighed against the performances intended."

39 Section 7 of Annex 1 entitled 'Chemical, Physical and Biological properties', in part II of this Annex under the title 'Requirements regarding Design & Construction' reads as follows (emphasis added):

"**7.1 The devices must be designed and manufactured in such a way as to guarantee the characteristics and performances referred to in Section I on the 'General requirements'. Particular attention must be paid to:**

— the choice of materials used, particularly as regards toxicity and, where appropriate, flammability,

— the compatibility between the materials used and biological tissues, cells and body fluids, taking account of the intended purpose of the device.

7.2. The devices must be designed, manufactured and packed in such a way as to minimize the risk posed by contaminants and residues to the persons involved in the transport, storage and use of the devices and to the patients, taking account of the intended purpose of the product. Particular attention must be paid to the tissues exposed and to the duration and frequency of exposure.

7.3. The devices must be designed and manufactured in such a way that they can be used safely with the materials, substances and gases with which they enter into contact during their normal use or during routine procedures;
if the devices are intended to administer medicinal products they must be designed and manufactured in such a way as to be compatible with the medicinal products concerned according to the provisions and restrictions governing these products and that their performance is maintained in accordance with the intended use

7.4 Where a device incorporates, as an integral part, a substance which, if used separately, may be considered to be a medicinal product as defined in Article 1 of Directive 65/65/EEC and which is liable to act upon the body with action ancillary to that of the device, the safety, quality and usefulness of the substance must be verified, taking account of the intended purpose of the device, by analogy with the appropriate methods specified in Directive 75/318/EEC.

(.....)."

40 Annex II describes the system that the manufacturer needs to put in place to ensure that the devices they produce meet the necessary standard. This is referred to as the EC Declaration of Conformity - Full Quality Assurance System. In Sections 1 and 2, it states that:

"1. The manufacturer must ensure application of the quality system approved for the design, manufacture and final inspection of the products concerned, as specified in Section 3 and is subject to audit as laid down in Sections 3.3 and 4 and to Community surveillance as specified in Section 5.

2. The declaration of conformity is the procedure whereby the manufacturer who fulfils the obligations imposed by Section 1 ensures and declares that the products concerned meet the provisions of this Directive which apply to them.

The manufacturer must affix the CE marking in accordance with Article 17 and draw up a written declaration of conformity. This declaration must cover a given number of the products manufactured and be kept by the manufacturer."

The references to sections quoted above are to the relevant sections in Annex II of Directive 93/42/EEC. I also note that this Annex refers to the term 'products' rather than devices.

41 Section 3 of Annex II entitled 'Quality System' states at Section 3.1 that:

"*The manufacturer must lodge an application for assessment of his quality system with a notified body*."

This section then goes on to list all the elements that must be included in such an application and all documentation that the system needs to be able to collect and provide.

42 Section 4 of Annex II entitled 'Examination of the design of the product' states at Sections 4.1-4.3 that (emphasis added):

"4.1. In addition to the obligations imposed by Section 3, the manufacturer must lodge with the notified body an application for examination of the design dossier relating to the product which he plans to manufacture and which falls into the category referred to in Section 3.1.

4.2. The application must describe the design, manufacture and performances of the product in question. It must include the documents needed to assess whether the product conforms to the requirements of this Directive, as referred to in Section 3.2 (c).

***4.3. The notified body must examine the application and, if the product conforms to the relevant provisions of this Directive, issue the application with an EC design-examination certificate.** The notified body may require the application to be completed by further tests or proof to allow assessment of conformity with the requirements of the Directive. The certificate must contain the conclusions of the examination, the conditions of validity, the data needed for identification of the approved design, where appropriate, a description of the intended purpose of the product.*

In the case of devices referred to in Annex I, section 7.4, first subparagraph, the notified body shall, as regards the aspects referred to in that section, consult one of the competent bodies designated by the Member States in accordance with Directive 65/65/EEC before taking a decision. The notified body will give due consideration to the views expressed in this consultation when making its decision. It will convey its final decision to the competent body concerned.

In the case of devices referred to in Annex I, section 7.4, second subparagraph, the scientific opinion of the EMEA must be included in the documentation concerning the device. The notified body will give due consideration to the opinion of the EMEA when making its decision. The notified body may not deliver the certificate if the EMEA's scientific opinion is unfavourable. It will convey its final decision to the EMEA.

(.....)'

43 Annex III describes the EC Type-Examination procedure, which, as part 1 of this Annex indicates, '*is the procedure whereby a notified body ascertains and certifies that a representative sample of the production covered fulfils the relevant provisions of this Directive*.' As noted, the procedure is carried out by Notified Bodies.

44 Annex IX entitled 'Classification Criteria' outlines the rules to be used to decide what classification class your medical device falls into, i.e., class **I, IIa, IIb,** or **III** . The conformity assessment procedure that has to be followed depends on the class of the device under consideration. Of relevance to the present case is rule 13 which indicates that.

45 Annex X entitled 'Clinical Evaluation' is concerned with how to decide if the characteristics and performances referred to in Sections 1 and 3 of Annex I are met.

46 Sections 1 and 2 of Annex X indicate that the overall purpose of clinical evaluation is as follows (emphasis added):

"1. General provisions

1.1. **As a general rule, confirmation of conformity with the requirements concerning the characteristics and performances referred to in Sections 1 and 3 of Annex I under the normal conditions of use of the device and the evaluation of the undesirable side-effects must be based on clinical data in particular in the case** of implantable devices and **devices in Class III**. Taking account of any relevant harmonized standards, where appropriate, the adequacy of the clinical data must be based on:

1.1.1. either a compilation of the relevant scientific literature currently available on the intended purpose of the device and the techniques employed as well as, if appropriate, a written report containing a critical evaluation of this compilation;

1.1.2. or **the results of all the clinical investigations made, including those carried out in conformity with Section 2.**

(.....)

2. **Clinical investigations**

2.1. *Objectives*
The objectives of clinical investigation are:
— to verify that, under normal conditions of use, the performance of the devices conform to those referred to in Section 3 of Annex I, and
— to determine any undesirable side-effects, under normal conditions of use, and assess whether they constitute risks when weighed against the intended performance of the device.

(.....)"

I note in particular, that Section 1.1. refers to the use of this clinical evaluation step in the case of devices in Class III.

Guidance on how the Medical Devices Directive and the Medicinal Products Directives interact

47 The European Commission has produced a set of Guidelines relating to questions of application of EC Directives on medical devices[11]. Guidance document entitled "*MEDICAL DEVICES: Guidance document - Borderline products, drug-delivery products and medical devices incorporating, as an integral part, an ancillary medicinal substance or an ancillary human blood derivative"* deals specifically with the issue of deciding whether or not a product is to be dealt with under the Medical Devices Directive or under the Medicinal Products Directive.[12] The current version of this guideline is MEDDEV 2.1/3 rev 3. None of these guidelines are legally binding, since (as the guideline makes clear in its foreword) only the European Court of Justice can give an authoritative interpretation of Community law, such as the Directive on Medical Devices. However, the guideline has been developed by an expert group including experts from the Competent Authorities of the Member States, the European Commission, as well as industry trade associations and, as a consequence, it is anticipated that these guidelines will be followed within the Member States and, therefore, ensure uniform application of relevant Directive provisions. Thus, although not legally binding, a guideline such as this represents the clearest indication of how the experts in the field of medical devices regulation consider these issues should be addressed.

48 This guideline notes (see foreword on page 1) that it is a revision of an earlier version, MEDDEV 2.1/3 rev 2, which was dated July 2001. The latest revision of this MEDDEV guideline was carried out to incorporate the amendments to Directive 93/42/EEC introduced by Directive 2007/47/EC which have applied since 21 March 2010[7]. This is the version which the applicant has quoted from in their correspondence referred to below. However, as the SPC applications in this case were made before this date and relate to EC Design Examination Certificates issued under the version of the Medical Devices Directive that was in force before these amendments took effect, I consider that it is necessary to take account of the guidance that was available at that date, i.e., version MEDDEV 2.1/3 rev 2.

[11] The Guidance MEDDEVs are guidelines to promote a common approach by manufacturers and Notified Bodies involved in the conformity assessment procedures according to the relevant annexes of the Medical Devices Directives, and by the Competent Authorities charged with safeguarding Public Health. For a full list of the Guidance MEDDEVs see http://ec.europa.eu/health/medical-devices/documents/guidelines/index_en.htm.

[12] For the current version of this MEDDEV Guideline see http://ec.europa.eu/health/medical-devices/files/meddev/2_1_3_rev_3-12_2009_en.pdf; this document also refers to the earlier version of this MEDDEV Guideline.

Issue to be decided

49 The issue to be decided is whether or not an approval gained for a medical device that **"***incorporates, as an integral part, a substance which, if used separately, may be considered to be a medicinal product within the meaning of Article 1 of Directive 65/65/EEC* [i.e. Directive 2001/83/EC] *and which is liable to act upon the body with action ancillary to that of the device***"** under Directive 93/42/EEC fulfils the necessary condition for the grant of an SPC under Article 3(b) of the SPC Regulation that "*a valid authorisation to place the product on the market as a medicinal product has been granted in accordance with Directive 2001/83/EC"*.

50 It is appropriate at this point to observe that the role of the IPO as the body responsible for granting SPCs in the UK (see Article 9 of the SPC Regulation) is to determine if the applications for SPCs received meet the requirements of the SPC regulation, in particular, Article 3. If so, an SPC shall be granted (see Article 10 of the SPC Regulation). The SPC is granted for a period, calculated using the algorithm outlined in Article 13, for a product that is covered by a patent and is the active ingredient (or combination of active ingredients) in a medicinal product which has been authorised for human use under Directive 2001/83/EEC. The SPC is designed to compensate the applicant for the loss of the term of their patent while gaining the necessary regulatory approval to place the medicinal product comprising this product on the market. The IPO is not involved in the regulatory processes that lead to the grant of a marketing authorisation for a medicinal product. The later is the responsibility of the Medicines and Healthcare Products Regulatory Agency (MHRA) at the national level in the UK[13] and of the European Medicines Agency (EMA) at the Community wide level[14]. The analysis below is based on my consideration and comparison of Directives 2001/83/EC and Directive 93/42/EEC, in the forms that were in force when the applications were made, and my consideration of all the materials on file.

The Medical Devices Directive, Dir 93/42/EEC – how it works

51 In relation to discussion and analysis below regarding the issue to be decided, it is necessary to be aware of the following features regarding how the Medical Devices Directive, Directive 93/42/EEC, works.

(i) The Medical Devices Directive was introduced into the EU after the first Medicinal Products Directive, Directive 65/65/EEC, which has now been superceded by Directive 2001/83/EC (see Article 28 of Dir 2001/83/EC). It is designed to sit alongside but not to overlap with the Medicinal Products Directive 2001/83/EC. Provisions have been included in the Medical Devices Directive to explain how these two directives work alongside each other – for example, in the recitals and in Articles 1(3), 1(4), 1(4a) and 1(5) [see above].

[13] See MHRA website at http://www.mhra.gov.uk/index.htm#page=DynamicListMedicines

[14] See EMA website at http://www.ema.europa.eu/ema/index.jsp?curl=pages/home/Home_Page.jsp&mid=

(ii) The Medical Devices Directive describes the various ways by which manufacturers of medical devices can demonstrate that their products, i.e. the medical devices, meet the requirements laid down by this directive. Devices which meet these requirements are identified by addition of the CE mark to the device as well as to the labelling and packaging to indicate that they are in conformity with these requirements and thus they can be freely marketed and traded within the European Community. The procedure is referred to as the conformity assessment procedure and it is used to demonstrate and verify that the device is in conformity with the essential requirements of the Directive and that this conformity has been verified.

(iii) Devices which meet the essential requirements of the Directive must bear the CE marking of conformity when they are placed on the market. This marking is also accompanied by the identification number of the notified body (see below) responsible for implementation of the relevant conformity assessment procedure.

(iv) Medical Devices are subject to a classification system – as indicated in the recitals (see above) and Article 9 and Annex IX of Directive 93/42/EEC – which is based on determining "*the vulnerability of the human body taking account of the potential risks associated with the technical design and manufacture of the devices*". There are four classes of devices and the conformity assessment procedures for each class vary in significance and requirements based on the greater vulnerability of the human body arising from the manufacture and use of these devices. In relation to this case, it is necessary to note that Class III is the classification set aside for the most critical devices which constitute a high risk potential and for which explicit prior authorisation with regard to conformity is required for them to be placed on the market.

(v) The conformity assessment procedure to be followed for each class of device is outlined in Article 11 of Directive 93/42/EC. There are two options for a Class III device described in Article 11(1)(a) and 11(1)(b). For the purposes of this decision, I note that the conformity assessment procedure referred to in Article 11(1)(a) was followed for both medical devices.

(vi) The conformity assessment procedure is carried out by a notified body – as defined in Directive 93/42/EC (see Article 16 and Annex XI). Any body that meets the requirements laid down can be designated as a notified body by a Member State. The manufacturer can select which notified body they want to use based on the tasks relating to procedures under Article 11 of the Directive that the notified body has been designated for. The notified body carries out a technical assessment of the all the material submitted by the manufacturer to demonstrate that their device conforms to the requirements of this directive. If this technical assessment is favourable, the manufacturer can attach the CE mark to his device and place it on the market. In this case, the notified body was TUV from Germany.

(vii) A clinical evaluation in accordance with the provisions laid down in Annex X of the Directive is necessary to show conformity for devices in Class III (see Article 15 and Part 1.1 of Annex X). 'Clinical Evaluation' is the term used in

the Medical Devices Directive to describe the process by which confirmation of conformity is established. This clinical evaluation will involve clinical investigations which, as Part 2.1 of Annex X indicates, have the following objectives:

1. to verify that, under normal conditions of use, the performance of the device conforms to those referred to in Section 3 of Annex I, i.e. "*The devices must achieve the performances intended by the manufacturer and be designed, manufactured and packaged in such a way that they are suitable for one or more of the functions referred to in Article 1(2)(a), as specified by the manufacturer*", and

2. to determine any undesirable side-effects, under normal conditions of use, and assess whether they constitute risks when weighed against the intended performance of the device.

52 The above summary relates to how Directive 93/42/EEC was working at the time that the SPC applications were made and under which the EC Design Examination Certificates and associated documents have been approved and issued. As noted already, Directive 93/42/EEC underwent additional and quite significant amendment in September 2007 from Directive 2007/47/EC which came into force on 20 March 2010[15].

Views of the Applicant and the Examiner

53 I will first provide a summary of the main points made in arguments presented by the applicant and the examiner before presenting my analysis and conclusions regarding the issue to be decided.

The Applicants View

54 The applicant is seeking the grant of an SPC for the amotosalen-treated platelet product and another for the amotosalen-treated plasma product using the EC conformity assessment procedure carried out for a class III medical device under Directive 93/42/EEC (MedDevDir) instead of a marketing authorisation granted under Directive 2001/83/EC. The applicant considers that a conformity assessment procedure which involves a clinical evaluation of the medicinal product by a competent body[16], as well as an assessment of the device in which that medicinal product is used, is equivalent to an administrative procedure as laid down in Directive 2001/83/EC.

55 Their reasons for this view can be summarised as follows:

[15] See footnote 7 and associated entry on EurLex website for details of amendment history of Directive 93/42/EEC.

[16] A competent body is a body in each member state recognised for the grant of marketing authorisations for medicinal products under Directive 2001/83/EC. It is not the same as a notified body under Directive 93/42/EC

(a) Part 4 and Part 4A of Article 1 of Directive 93/42/EEC (MedDevDir) in conjunction with the first two paragraphs of Article 7.4 of Annex 1 clearly establish the relationship between the MedDevDir (Directive 93/42/EEC) and the MedProdDir (Directive 2001/83/EC). From this, it is clear that, whereas the device itself (which includes the substance) is assessed and authorised in accordance with the MedDevDir, the substance is also subject to an assessment which accords with Directive 2001/83/EC. The applicant considers that the authorisation of their devices under MedDevDir equates to the authorisation of the substances produced and contained in the devices in accordance with MedProdDir. This, they argue, follows from the requirement in Annex 1, 7.4 of MedDevDir that the properties of the substances be verified "*by analogy with the appropriate methods specified in Directive 75/318/EC* [i.e., Directive 2001/83/EC]"

(b) A purposive interpretation of Article 3(b) of the SPC Regulation, rather than a literal one, means that the assessment of the quality, safety and usefulness of the substance incorporated in each device (which is the same one – amotosalen) by analogy with the methods specified in Directive 2001/83/EC can be deemed to be equivalent with the grant of a marketing authorisation for a medicinal product pursuant to Directive 2001/83/EC (MedProdDir). The quality, safety and usefulness of the amotosalen-treated plasma and platelet products obtained from the respective device were considered by an appropriate national regulatory authority, i.e., member state competent body, prior to issue of the approvals under Directive 93/42/EEC. The EC Design Certificates which have been submitted in support of each of these SPC applications includes in essence two approvals, one for the device itself (not covered by the SPC Regulation) and one for the therapeutic substance, in the case of SPC/GB/07/043, the amotosalen-treated platelet product, in the case of SPC/GB/07/044, the amotosalen-treated plasma product).

(c) Guidance issued by the European Commission concerning *"Borderline products, drug-delivery products and medical devices incorporating, as an integral part, an ancillary medicinal substance or an ancillary human blood derivative*" [17] states that in the situation, such as the present one, where you have a medical device with an associated ancillary medicinal substance then the documentation that the notified body needs to provide to the competent authority in order to gain approval for the medical device need to fulfil the following condition:

> "*For new active substances and for* ***known substances in a non-established purpose, comprehensive data is required to address the requirements of Annex I to Directive 2001/83/EC****. The evaluation*

[17] This guidance document entitled "MEDICAL DEVICES: Guidance document - Borderline products, drug-delivery products and medical devices incorporating, as an integral part, an ancillary medicinal substance or an ancillary human blood derivative" is one of a series coordinated by the European Commission which provides guidance to allow a common position to be taken on issues related to the EC Directives on Medical Devices. For the full document see http://ec.europa.eu/health/medical-devices/files/meddev/2_1_3_rev_3-12_2009_en.pdf; This reference also provides access to earlier versions of this document

of such active substances would be performed in accordance with the principles of evaluation of new active substances."

The two devices and their associated ancillary medicinal substance which are the subject of these two SPC applications fall into this group.

(d) The devices are already in use, or in process of being put into use, in a number of countries, e.g. Spain, Portugal, Italy and Belgium. It is not credible that the blood products – plasma or platelets – could be used therapeutically within the EC unless the approvals if each device by the respective certificates G7 06 09 60562 004 and G7 02 05 16178 063 also implied an approval of the medicinal products commensurate with approval under Directive 2001/83/EC (MedProdDir). The issue of these certificates already indicates that the regulatory authorities are satisfied that the medicinal products produced in the authorised devices fulfil the requirements of Directive 2001/83/EC.

(e) The IPO has previously granted an SPC on the basis of an authorisation issued under the MedDevDir (SPC/GB98/013 in relation to Hylan B) and there was no basis on which to change this practice at the IPO. A number of other national jurisdictions have also granted SPCs based on an authorisation obtained under Directive 93/42/EC or one of the other directives concerning medical devices[9], for example, in the Netherlands (*Genzyme v Dutch IPO*); in Italy, an SPC has been granted in relation to the present case; in Germany (German Federal Court decision, Patent Docket 14W (Pat) *12/07 Yttrium-90 Glass Microspheres*). In the latter case, the German Federal Court found that an EC-certificate granted under Directive 90/385/EEC relating to active implantable medical devices (AIMD Directive) would be sufficient to support an SPC application, and that this device authorisation included an authorisation granted pursuant to MedProdDir for the active substance in the device. The applicant considers that the same reasoning applies to an EC-certificate granted under the MedDevDir, i.e., for medical devices in general.

(f) The medicinal substance in the device, amotosalen or its salt, has been subjected to an assessment of a standard and rigour comparable with that used to assess a novel medicinal product. This was carried out by the French competent body, AFSSAPS, in relation to the EC Certificate for the amotosalen-treated plasma product filed in support of SPC/GB/07/044 and details of this assessment is provided in the technical report which accompanies this certificate; and by the Irish Medicines Board in relation to EC Certificate for the amotosalen-treated platelet product filed in support of SPC/GB/07/043 and details of this assessment is provided in the technical report which accompanies this certificate. As these bodies have experience in dealing with the assessment of novel medicinal products under the MedProdDir, they will have applied this expertise and approach when assessing amoptosalen as part of the assessment procedure under the MedDevDir. The actual work carried out to evaluate these devices under MedDevDir by the two national competent bodies (French AFSSAPS and Irish Medicines Board) involves a medical assessment and assessment of clinical data obtained from tests conducted in accordance with the standards and protocols prescribed by MedProdDir. This provides an assessment of the

preclinical and clinical verification of safety, quality and usefulness of the active substance. Without the substance that if used on its own would meet the definition of a medicinal product under Directive 2001/83/EC, successfully meeting these criteria, the certificate for the device could not have been issued.

(g) In the present case, if the SPC application is rejected, this is a harsh outcome in view of the extensive preclinical and clinical programs conducted to satisfy the regulatory bodies responsible for the assessment of the medicinal substance in each device by analogy to the methods specified in Annex I of MedProdDir. Furthermore, the applicants state that they have experienced a significant delay in exploiting their patent because of the need to carry out extensive regulatory testing in order to meet the requirements for a class III device as well as to assess the substance incorporated in the device as an innovative medicinal product. The SPC regulation was implemented to compensate holders of patents for the loss of term they experience while gaining the necessary regulatory approval.

(h) The applicant had no choice but to obtain authorisation for the INTERCEPT Blood System as a Medical Device in each case. They did not have the choice to seek authorisation of the medicinal product in the device under the Medicinal Products Directive. As such, it is not appropriate to then say that the applicant has to have an authorisation under the MedProdDir as this choice is not available to him.

56 In addition, the applicant also suggested that examiner consider whether the product definition "amotosalen or a salt thereof" was an appropriate one for either application, as a possible way to progress this case

The Examiners view

57 As mentioned briefly above, the examiner considers that these two SPC applications do not comply with the conditions for obtaining a certificate because the authorisations filed in support of these applications do not comply with Article 3(b) of the Regulation, which requires that the authorisation is "***granted in accordance with Directive 2001/83/EC*** *or Directive 2001/82/EC as appropriate*" (my emphasis).

58 In addition, the examiner considers that these applications are out of scope as they do not relate to medicinal products subject to an "**administrative authorisation procedure as laid down in Directive 2001/83/EC** of the European Parliament and the Council of 6 November 2001 on the Community code relating to medicinal products for human use."

59 The reasons for the examiner's view can be summarised as follows:

(a) The devices authorised in G7 06 09 60562 004 and G7 02 05 16178 063 "*incorporate as an integral part a substance which, if used separately, may be considered to be a medicinal product…"* and thus each requires the applicant to seek an authorisation under the Directive 93/42/EEC and not Directive 2001/83/EC. As part of the overall process for approval of a device under Directive 93/42/EC, the "quality safety and usefulness of the substance"

incorporated in the device must be verified by analogy with the methods in Directive 2001/83/EC. This is not the same as a marketing authorisation with a full Summary of Product Characteristics (SmPC) which is derived from a consideration of the safety, quality and efficacy of a medicinal product.

(b) A consideration of the MedProdDir and the MedDevDir shows that products to which these directives apply will not be authorised under more than one regulatory code. Thus products are only authorised under the medicinal products code if they are considered "medicinal products". It is thus relevant and a matter of fact that the subjects of the present SPC applications have not have been considered medicinal products and thus they are not the subject of authorisations under the medicinal products directive.

(c) In accordance with directive 93/42/EC, the MHRA, as the relevant competent authority in the UK, carries out an evaluation, on request, on behalf of a Notified Body where a medicinal substance is to be incorporated into a medical device. Following this evaluation the MHRA issues an opinion on the quality, safety and clinical benefit v risk arising from the incorporation of that substance into the device. That opinion, provided to the Notified Body, does not constitute a marketing authorisation and is not based on a full assessment of the quality, safety and efficacy of the medicinal substance component or of the medical device in its entirety. It is the responsibility of the Notified Body to take account of that opinion in deciding whether to issue its certification for the device which incorporates this medicinal substance. It is the view of the examiner that the assessment undertaken to provide an opinion in accordance with Article 1(4) of MedDevDir (93/42/EC) is not the same as a full medicinal marketing authorisation and accordingly cannot be considered to be equivalent to a medicinal marketing authorisation under the MedProdDir.

(d) Article 2(2) of MedProdDir (2001/83/EC) sets a clear demarcation between what is a medicinal product and what is not, in order to resolve any doubt in favour of the more rigorous regulation. The examiner considers that the regulator can decide if an active should be evaluated having regard to 2001/83/EC or another directive such as 93/42/EC. If the two codes under these directives could have the same affect it would appear that this choice is unnecessary at least in respect of borderline products. Thus the choice in favour of authorisation having regard to one or other of the codes furthermore sets the requirements and benefits (such as an SPC) that may result. Insofar as the present device and product combination is covered by MedDevDir (93/42/EC) it would appear that it is the regulator's intention to prohibit access to MedProdDir and hence an SPC.

(e) Each application for an SPC to the IPO has to be dealt with on the merits of that case, the decisions of other National Offices who grant SPCs in the European Community and the earlier practice at this Office, while they are persuasive, are not binding. In addition, there has also been a decision from the German courts which has found that an EC certificate could not constitute an authorisation in accordance with 2001/83/EC for the purpose of granting an SPC. This relates to the Hylan A and Hylan B products which was also the subject of applications and litigation in UK and Netherlands. The German

Court upheld the decision of the German Patent and Trademark Office not to grant SPC in this case because the approval procedure under Directive 93/42/EC could not be considered to have the same features as the approval procedure under Directive 2001/83/EC.

(f) European legislators have had a number of opportunities to provide that medical device and product combinations covered by EC certificates of conformity with a route to SPC protection. There have been 3 occasions since MedDevDir (93/42/EC) came into force that MedProdDir (2001/83/EC) has been amended and no such clear reference has been included. Instead, a selection of guidance documents have been developed by the European Commission and experts in the field of Medical devices and medicinal products authorisation to show how these different pieces of EU legislation work alongside each other and which one applies and which one does not in such circumstances. This indicates that the two systems are considered to be separate and do not overlap.

Analysis

60 On the face of it the answer to the question whether or not the procedure used for approval to place a medicinal device on the market in Europe under Directive 93/42/EC is equivalent to the procedure used for approval to place a medicinal product on the market in the Europe Community under Directive 2001/83/EC for the purposes of meeting the requirements of Article 3(b) of the SPC regulation is a very straightforward one. A medical device is not the same as a medicinal product although both are used for the same purpose – to treat human beings – and, as a consequence, it is appropriate that both have to be subjected to some form of authorisation process to confirm that they do treat human beings in the manner proposed and that they do not have any unacceptable consequences from their use. Article 2 of the SPC regulation indicates that the scope of the regulation applies only to medicinal products which have been subject of an approval procedure under Directive 2001/83/EC. Article 3(b) of the SPC regulation makes clear that "a valid authorisation" for a medicinal product under Directive 2001/83/EC is required. Thus an approval for a device under Directive 93/43/EEC is one granted under a different piece of EU legislation than that required by the SPC regulation and therefore is not relevant for the purposes of granting an SPC.

61 The literal interpretation of the requirements of the SPC Regulation in this manner has some attraction. It is simple and transparent in keeping with the purpose of the regulation as laid down in its Explanatory Memorandum to this regulation[18]. However, despite this attraction, I do not consider that I can reject each of these SPC applications simply on the basis that this application is outside the scope of the SPC regulation under Article 2. It is a well established principle of EU law that it is necessary to take account of the purpose and objectives behind the EU legislation in

[18] See Explanatory Memorandum entitled 'Proposal for a Council Regulation (EEC) concerning the creation of a supplementary protection certificate for medicinal products, COM(90), 101 final – SYN 255, 11 April 1990.

question – the so-called teleological approach[19]. The purpose of the SPC regulation has been discussed previously in the UK courts[20] and in the many references to the CJEU that have been made concerning the interpretation of this regulation[21].

62 Following a teleological approach prompts me to take a closer look at the type of authorisation that the applicant has provided in support of their SPC applications. The approval being cited in support of each SPC application relates to a class III medical device which incorporates, as an integral part, a substance, which if used separately, may be considered to be a medicinal product within the meaning of Article 1 of Directive 65/65/EEC [i.e., now Directive 2001/83/EC], and which is liable to act upon the body with action ancillary to that of the device. Thus, a substance which would fall within the definition of a medicinal product is involved.

63 However, if, having taken account of the purpose and objectives of the SPC Regulation and the two relevant Directives, my conclusion is that the EC Design Examination Certificate cannot be deemed equivalent to a valid marketing authorisation under Directive 2001/83/EC and so fulfil the requirement of Article 3(b) of the SPC regulation, then the applications will also be outside the scope of this Regulation under Article 2 which requires that, in order to qualify for an SPC, a product has to be the subject of an administrative authorisation procedure under Directive 2001/83/EC. In this situation, the conclusion from the teleological interpretation would be the same as that suggested by a literal interpretation.

Approval process for Class III Medical Devices under Directive 93/42/EEC

64 Approval under Directive 93/42/EC using the conformity assessment procedure (see Article 11(1)(a)) for class III medical devices, such as those at issue in the current case, involve as part of this procedure, an assessment of the medicinal product that is incorporated in the medical device. This involves, as referred to in Annex I, section 7.4, of Directive 93/42/EEC, an assessment of "*the safety, quality and usefulness of the substance*" while "*taking account of the intended purpose of the device*". As Annex II, section 4.3 (second sub paragraph) indicates the notified body responsible for carrying out the conformity assessment procedure, will consult one of the competent bodies designated by the Member States in accordance with Directive 65/65/EEC (now Directive 2001/83/EC) and, before taking any decision, "*will give due consideration of the views expressed in this consultation*".

65 As a consequence, the applicant argues that, because the approval process, i.e. the conformity assessment procedure, that resulted in the issue of the EC design examination certificate for each of the devices concerned in this case, has involved

[19] See discussion of teleological approach and references to relevant case law in paras 14 & 15 of IPO decision BL O/389/09 (Neurim) at http://www.ipo.gov.uk/pro-types/pro-patent/pro-p-os/o38409.pdf.

[20] See *Draco A.B.'s SPC application* [1996] RPC 417 which also refers to House of Lords decision in *R. v. Henn, R. v. Darby* [1981] A.C. 850 and to paragraphs 2.266 and 2.268 of Volume 51 of Halsbury's Laws of England (4th edition).

[21] See, for example, para 27 of C-482/07 *AHP* at http://curia.europa.eu/juris/document/document.jsf?text=&docid=73083&pageIndex=0&doclang=EN&mode=lst&dir=&occ=first&part=1&cid=194830

as part of that process, a clinical assessment of the medicinal product incorporated in the device using the principles of Directive 65/65/EEC [i.e., Directive 2001/83/EC] then it is entirely appropriate to consider that such an approval process is suitable to meet the requirements of Article 3(b) of the SPC regulation.

66 In determining whether or not the EC Design Examination Certificates included with these two SPC applications meet the criterion under Article 3(b) of the SPC regulation for a valid authorisation to place the medicinal product on the market in the community, it is necessary for me to consider the relationship between the Medical Devices Directive and the Medicinal Products Directive. In particular, I need to consider the circumstances where a medicinal product, as defined in Article 1 of the SPC regulation, is involved.

67 'Product' is not a term that is included in the definitions in Article 1 of the Medical Devices Directive, so I take it to have its usual meaning in the English language, i.e., a product of a process of manufacture or assembly which in this case will be a process of manufacture of a medical device. This term, in relation to Annex II of Directive 93/42/EEC, does not have the same meaning as 'product' as defined by Article 1(b) of the SPC regulation. It is also worth noting that when Directive 93/42/EEC refers to 'product' in the context of medicinal product, it refers to the definition of medicinal product provided in Directive 2001/83/EC or its predecessor Directive 65/65/EEC. The definition of 'medicinal product' in the Medicinal Products Directive, Directive 2001/83/EC, differs slightly from that in the SPC regulation. However, I consider that there is no material difference between these definitions and that, for our purposes, they relate to the same thing. As Article 2 of the SPC regulation makes clear, if a medicinal product has been approved under Directive 2001/83/EC, it is eligible for protection under the SPC regulation.

Has a medicinal product been authorised under Directive 93/42/EC?

68 The applicant has identified the product for which it is seeking an SPC, in the case of SPC/GB/07/043, as "*Platelet preparation obtainable by addition, and subsequent photoactivation, of amotosalen or its salt, to a suspension of platelets in plasma"* and in the case of SPC/GB/078/044, as ""*Plasma preparation obtainable by addition to plasma, and photoactivation, of amotosalen or its salt".*

69 However, if we consider what is the product that has been identified as meeting the requirements of Directive 93/42/EC, the situation is a little more complicated and it is necessary to look at this in a little more detail. In both cases, the EC Design Certificates identify the products they cover as 'Disposables'. For EC Design Certificate G7 02 05 16178 063 this is '*Medical Disposables*' and for G7 06 09 60562 004, this is '*Blood Processing Devices Pathogen Inactivation Disposables'*. In both cases, these EC Design Certificates then go on to refer to the 'Model' they relate to, the former relates to '*INTERCEPT (Amotosalen Photochemical Treatment) System for Platelets*' and the latter to '*INTERCEPT (Amotosalen Photochemical Treatment) System for Plasma'*. I conclude from this that the EC Design Examination Certificates filed in support of these applications each relate to a device, referred to as the INTERCEPT (Amotosalen Photochemical Treatment) System, that comprises a number of elements that make up the system, all of which are disposable.

70 A technical report was filed with each of these EC Design Examination Certificates. As noted above, the notified body produces these technical reports as part of the conformity assessment procedure. Each technical report identifies the 'Test Subject' that they relate to as the 'INTERCEPT Amotosalen Photochemical Treatment System', in the case of G7 02 05 16178 063, for use with platelets and, in the case of G7 06 09 60562 004, for use in plasma.

71 Technical report no. 70001907, filed with G7 02 05 16178 063 in support of SPC/GB/07/043, is the earlier of the two technical reports filed with these applications (see Table 1) and, in Section 1.1 entitled 'Intended Use'; it explains how the INTERCEPT Amotosalen Photochemical Treatment System works for Platelets. It is used *ex-vivo* (i.e., outside the body) to prepare and store pathogen and leukocyte reduced buffy coat platelets. The device uses a synthetic psoralen molecule, identified as S-59 or Amotosalen, which, when illuminated with Ultraviolet (UV) light, reacts with the pyrimidine bases present in the DNA or RNA of any viral or bacterial contaminants in the platelet solution to form irreversible covalent bonds. The Amotosalen is capable of reversible intercalation into the helical regions of DNA and RNA and it is only when it is illuminated with Ultraviolet (UV) light, that it reacts with the pyrimidine bases present in DNA or RNA to form irreversible covalent bonds. This results in the photo-degradation of the amotosalen and any DNA or RNA containing species in the treated sample. Viral or bacterial species that have reacted with the amotosalen in this irreversible manner will no longer be able to function or replicate. The platelets obtained using this INTERCEPT Amotosalen Photochemical Treatment System are stored and used for patients with various clinical conditions that require transfusions. The Device includes the ultraviolet illuminator, a solution of amotosalen as a hydrochloride salt and various storage containers and a compound adsorption device (CAD) which uses a separation medium (beads) to remove residual amotosalen and photochemical degradation products from the platelet mixture. This treated and purified platelet suspension can be stored for up to five days

72 This report, in Section 4.6 entitled 'Clinical Data', states (under the Discussion and Summary [see point 4.]):

> "*In accordance to the requirements of the Directive 93/42/EEC (MDD), Annex 11.4.3, the drug component S-59 was assessed by the competent authority. Especially the pharmaco-toxicological aspects and conclusion of the competent authority has to be taken into consideration to come to a final decision. This was done by the Irish Medicines Board (...)*"

and [in point 5.] that

> "*Based on the data provided by the assessment report of the Irish Medicines Board the safety of the device is demonstrated. From the clinical point of view the benefit-to-risk ratio is considered to be acceptable*."

73 Technical/Test report no. 70113942, filed with G7 06 09 60562 004, in support of SPC application SPC/GB/07/044, indicates that the INTERCEPT Amotosalen Photochemical Treatment System for Plasma works in essentially the same way as the INTERCEPT Amotosalen Photochemical Treatment System for Platelets. The device, for all practical purposes, involves the same components and uses the same

synthetic psoralen molecule identified as S-59 or Amotosalen. In this case the report indicates at Section 4.11 entitled "Drug/medical device combination (Annex I.7.4)"

> *"see 4.15 Clinical Data*
> *The drug component Amotosalen has been assessed by the French competent authority AFSSAPS"*

It provides more detail at Section 4.15 entitled "Clinical Data (Annex I.1, I.6, 1.14)" as follows:

> "*Discussion and Summary*
>
> 1. *The manufacturer detailed sufficiently the clinical need for pathogen-inactiviating systems for plasma protection.*
> 2. *The Intercept Blood System for Plasma is effective in reduction of viruses, bacterial species and pararsites. This is specified and more detailed within the labelling/IFU of this product.*
> 3. *The performance and safety of the Intercept processiing set for platelets were confirmed by post market data*
> 4. *The performance and safety of the plasma specimens treated by the Intercept Blood System were demonstrated in the clinical setting of 42 healthy subjects and 203 patients.*
> 5. *It could be demonstrated by the manufacturer that the results gained in the clinical trials can be transferred [to] the commercial version of the Intercept Blood System"*

74 Both technical reports also make clear that the device in each case is classified as a Class III device according to the classification rules in Annex IX of Directive 93/42/EEC.[22]

75 Based on the above technical reports, I consider that the devices that have been approved under the medical devices directive are disposable devices which deliver a platelet preparation or plasma preparation that can be stored and used for transfusion purposes and which have a significantly reduced likelihood of causing infection because pathogens therein have been destroyed and removed. The device in each case provides the means to obtain a purified preparation after a sample of plasma or platelets has been removed from the body, the amotosalen has been added to it, it has then been subjected to photo-chemical illumination and the resultant preparation has each been subjected to a physical treatment step to remove the products formed in the photo-illumination step and thus yield a solution which is, in the case of G7 02 05 16178 063, a purified solution containing platelets, and, in the case of G7 06 09 60562 004, a purified solution of plasma. The amotosalen is involved once the sample has been removed from the human body where it is added to the platelets or plasma, photo-illuminated and the resultant photochemical degradation products are removed.

76 I do not consider that the product definitions as originally applied for in relation to SPC/GB/07/043 and SPC/GB07/044 are appropriate. These definitions, while they correctly summarise the product that is obtained using each device, they do not

[22] The relevant classification rules from Annex IX of Directive 93/42/EEC are special rules 13 and 18, (see Annex IX, Part 4.1 and 4.5)

identify what is the active substance or product for which the SPC is sought under Article 1(b). The amotosalen or its salt is not a part of the platelet preparation or plasma preparation obtained after use of the appropriate device. These preparations are what is left after the amotosalen has been added, illuminated, allowed to react and then removed. The SPC regulation provides for an SPC in relation to the product, i.e., active ingredient or active substance in the medicinal product that has been authorised for human use under Directive 2001/83/EC.

77 If the amotosalen was used separately, I agree that it would fall within the meaning of Article 1 of Directive 2001/83/EC, as a medicinal product, because it has the properties of being able to intercalate into the helical regions of DNA and RNA which occurs in humans as well as in bacteria and viruses. Thus if exposed to ultraviolet light, it would likely exert a 'pharmacological or metabolic action'. My understanding is that this substance is acting on the human body in a manner ancillary to the device because, it carries out its action on any viral and bacterial contaminants in the samples outside the body (in order to remove them from the platelets or plasma), and the resultant reaction products are removed from the platelet or plasma solution that the device produces, before either of these products is then used to treat the human body, i.e. to provide a transfusion. The amotosalen does not act directly on the human body. The applicant refers to a number of trials of both devices that were conducted in clinical setting with healthy subjects and patients to confirm that the device works as intended, e.g., can treat and store plasma and platelets, does not have any side-effects or risks that outweigh its benefits.

78 Thus, the competent body in each case was asked to provide an opinion to the notified body (TUV) in relation to amotosalen, which is present in both devices as a hydrochloride solution. In line with Annex I, section 7.4; Annex II, Section 4.3 (second subparagraph) and Annex X, Section 2.1, of Directive 93/42/EC, the clinical investigation in relation to each of the devices involving amotosalen would thus have to consider and establish, for example, what is the likelihood and impact of residual unused amotosalen in the platelet or plasma preparations coming into contact with a patient. Would there be any undesirable side-effects that could arise and what is the risk of such side-effects occurring when the device is operating under normal conditions of use and based on the performance of the device intended by the manufacturer.

79 Thus, in my view, I consider, **if** an SPC was to be granted in this case, it should be for amotosalen alone or a salt of amotosalen, e.g. the hydrochloride salt. I consider this to be the product, in the meaning of Article 1(b) of the SPC Regulation. The applicants acknowledges this possibility in their letter dated 23 December 2013, requesting a written decision from the Office based on the papers on file. In this letter the applicant suggested that, as an alternative product description, the SPCs applied for be granted for "amotosalen or a salt thereof". The applicant also indicated that if this was acceptable, they would withdraw the second of the two applications (SPC/GB/07/044) at a later date because they acknowledged (rightfully in my view) that in that circumstance both SPCs applied for would relate to the same active substance.

Relationship between Medicinal Products Directive (Directive 2001/83/EC) and the Medical Devices Directive (Directive 93/42/EEC)

80 In Directive 93/42/EEC, there are a number of specific references to the approval procedure for medical devices that involve substances which, if used separately, may be considered to be a medicinal product within the meaning of Article 1 of 2001/83/EC[23]. It is clear from these extracts that for devices which also involve a substance that is, or may be considered as, a medicinal product under the Medicinal Products Directive, the approval process is that outlined in Directive 93/43/EC and not that outlined under the Medicinal Products Directive. There is only one situation under which Medicinal Products Directive takes precedence as described in Article 1(3), second sub paragraph (see above). A device, such as in the present case, which incorporates, as an integral part, a substance which, if used separately, may be considered to be a medicinal product within the meaning of Article 1 of Directive 2001/83/EC is not assessed and authorised under both directives, it is only assessed and authorised under one, i.e. the Medical Devices Directive (Directive 93/42/EC).

81 This recognises the fact that the process for conformity assessment of a medical device is designed to exist alongside but not to overlap with the process for authorising a medicinal product, i.e., one is not required to gain approval under both directives in the situation where a substance incorporated in the device would meet the definition of a medicinal product. This would be a double burden on applicants. Approval under one directive only is required. However, I consider that it also follows from this that approval under the medical devices system, cannot be considered to fulfil the requirements of both codes. The assessment of the substance incorporated in the devices is not a full assessment under Directive 2001/83/EC (see Annex I). It is, however, necessary to demonstrate that the device as a whole can be used with this substance in a manner that is safe and does not cause problems while the device fulfils its intended purpose and also that the benefits of doing so outweigh, the risks. Thus, I consider that the opinion from the competent body is based on what is necessary to approve a device not on what is necessary to approve a medicinal product under Directive 2001/83/EC.

82 I draw support for this view from the comments provided by the MHRA and quoted by the examiner in his official letter dated 7 October 2010, i.e.

> *"The Medicines and Healthcare products Regulatory Agency (MHRA) is the competent authority for medicines and medical devices regulation in the UK. It is the MHRA's view that the medicines Directive (2001/83/EC) provides a clear definition of a medicinal product and clearly sets out the requirements for a marketing authorisation for such a product. Where a medical device incorporates a drug substance with action ancillary to that of the device, then that product is still a medical device (regulated in accordance with Directive 93/42/EC) and not a medicinal product. It is also MHRA's view that European Guidance and the relevant Directives, in particular Article 2(2) of the medicines Directive, are clear that there are no products which might be considered both medicinal products and medical devices since, in cases of doubt that Article says that the provisions of that Directive shall apply.*

[23] See for example recitals to Directive 93/42/EEC and. Articles 1(3), 1(4), 1(4a) and 1(5)(c) of Directive 93/42/EEC as discussed above.

In accordance with directive 93/42/EC the MHRA, as a medicines competent authority, does carry out an evaluation, on request, on behalf of a Notified Body where a medicinal substance is to be incorporated into a medical device. Following its evaluation the MHRA issues an opinion on the quality, safety and clinical benefit/risk profile of the incorporation of that substance into the device. That opinion, provided to the Notified Body, does not constitute a marketing authorisation and is not based on a full assessment of the quality, safety and efficacy of the medicinal substance component or of the medical device in its entirety. It is the responsibility of the Notified Body to take account of that opinion in deciding whether to issue its certification."

83 The MHRA is the competent body responsible for dealing with the approvals of both medicinal products and medical devices in the UK. In the context of the latter, it is responsible for designating notified bodies in the UK. I am aware that the MHRA provides guidance and assistance to help users and applicants understand when the Medical Devices Directive applies and when the Medicinal Products Directive applies[24]. Such information is available via its website and through direct contact. The applicant would be aware that such knowledge and assistance is available and that the MHRA is a competent body for the purposes of both codes in the UK and would be available to provide an opinion in just the same way as the Irish Medicines Board and the AFSSAPS[25] in France. None of the MHRA guidance was referred to directly in the correspondence between the applicant and the examiner. However, when this illustrative example is set alongside the fact that the MHRA has a role in dealing with approvals under both codes, it is appropriate for the MHRA to express a view, albeit a general one, on whether or not an opinion on a medical device as part of the conformity assessment procedure is equivalent to an assessment of a medicinal product. While I accept that the MHRA were not directly involved in the particulars of the cases at issue and I note the applicants' comments to this effect, I do consider that the MHRA view on how the two codes for approval of medical devices and medicinal products work is relevant.

84 As noted already, the European Commission has provided Guidance on how to decide when a medical device that incorporates a medicinal product is authorised as a medicinal product and when it is authorised as a medical device. This guidance although it is not legally binding does represent the considered view of experts in the fields of regulatory affairs brought together by the European Commission for this purpose[11,12,17]. Thus I consider that it is very helpful in pointing to how the system for authorising devices is supposed to work. MEDDEV 2.1/3 rev 2, dated July 2001 is the one that has most relevance for the applications in suit[26]. In relation to those cases which fall at the borderline, this guidance indicates, in its introduction, that:

"The determination of the borderline between the Medical Devices Directive 93/42/EEC (MDD) (..), the Active Implantable Medical Device Directive

[24] See MHRA explanation "How we regulate devices" which provides relevant guidance and contact details at http://www.mhra.gov.uk/Howweregulate/Devices/index.htm.

[25] Agence Française de Sécurité Sanitaire des Produits de Santé, AFSSAPS.

[26] See, in particular, the explanation and discussion in the following sections - Introduction (A.1), General Principles (A.2), Medical Devices incorporating a medicinal substance with ancillary action (A.5), and The Consultation Process for Devices incorporating a medicinal substance having ancillary action (B & B.1-B.4).

90/385/EEC (AIMD) (..) and the Medicinal Products Directive 65/65/EEC (MPD) including related directives, was one of the issues discussed at some length during the legislative procedure on the MDD. Therefore, in the MDD several provisions to establish the demarcation between both legal regimes have been laid down. It was recognised that the subject needs to be further explained and illustrated by practical guidance and examples".

It then does on, in the discussion of the general principles, to point out that:

"As a general rule a relevant product is regulated either by the MDD or by the MPD. The authorization or conformity assessment procedure to be followed prior to placing a given product on the market will therefore be governed either by the MDD/AIMD or by the MPD. Normally the procedures of both directives do not apply cumulatively. For defined features, however, some cross-references are made within one regime to specific provisions of the other regime (see Article 1(4) in conjunction with Annex I, section 7.4 MDD; Article 1(3) MDD).

And, having considered the definitions of medical devices and medicinal products under both directives, the guideline indicates that the assessment of the means by which the product carries out its function is important. The guideline indicates that:

"Medical devices may be assisted in their function by pharmacological, immunological or metabolic means, but as soon as these means are not any more ancillary with respect to the principal purpose of a product, the product becomes a medicinal product. The claims made for a product, in accordance with its method of action may, in this context, represent an important factor for its classification as medical device or medicinal product."

I consider that this illustrates and further makes clear that, once, one has determined which of the approval mechanisms applies – that for a device or that for a medicinal product - this sets the overall context or approach within which all and any subsequent considerations must be made. If approved as a device, any subsequent discussion about whether or not the conformity assessment procedure for the device involves a step that is equivalent to an assessment of a medicinal product under Directive 2001/83/EC, has to be considered in the framework of what is the overall purpose of the conformity assessment procedure under the Medical Devices Directive. As I have stated above, it is to allow devices to be freely marked and sold in the EU which have all been verified to show that they perform as the manufacturer claims and do not pose a risk to those using the devices for its intended purpose.

Relevance of class of device under Directive 93/42/EEC

85 The two devices at issue in this case meet the requirement of Article 1(4) of Directive 93/42/EC and, as already noted, are classified as Class III medical devices. Such devices require the highest degree of assessment and authorisation under Directive 93/42/EC because they are considered to pose the highest risk to the human body in use. As such, assessment and authorisation has to occur prior to these devices being placed on the market. As mentioned above, the devices in the current application have been subjected to the conformity assessment procedure described in Article 11(1)(a), i.e. the EC Declaration of Conformity (full quality assurance system) as described in Annex II of Directive 93/42/EEC.

86 According to Annex II (see second paragraph of Section 4.3), the notified body, TUV, who is responsible for carrying out the assessment of the full quality assurance procedure, must consult with a competent body from one of the member states who is designated for the purposes of Directive 65/65/EEC (now Directive 2001/83/EC) in all situations where the medical device incorporates a medicinal product. The notified body is then required to consider the views expressed by the competent body when making its decision whether or not the device, as a whole, meets all the requirements under Annex 1 of Directive 93/42/EEC. If this decision is favourable, the notified body can issue a Declaration of Conformity to the manufacturer who can then arrange to have the CE mark affixed to the device (and the relevant labelling).

87 The purpose of this consultation with the competent body is to answer the requirements of Annex 1, Section 7.4. According to this section, "*the safety, quality and usefulness of the substance must be verified, taking account of the intended purpose of the device by analogy with the appropriate methods specified in Directive 75/318/EEC* [i.e., Directive 2001/83/EC][9]". I note in particular here that the competent body is consulted for its views on the safety, quality and usefulness of the substance and that this is in the context of the intended purpose of the device.

88 In deciding which approval process or directive applies to a product that lies on the border between medicinal products and medical devices, the regulator has to make a decision, taking account of the manufacturer's intended purpose for the product, the way it is presented, and the method by which the principal mode of action is achieved. In the case of a medical device, the principal mode of action is usually by physical means (such as mechanical action, physical barrier, replacement of, or support to, organs or body functions). Medical devices *can* be assisted in their function by pharmacological, immunological or metabolic means but <u>not</u> if this is their principal mode of action. Thus, where a product achieves its principal intended action by pharmacological, immunological or metabolic means, it is a medicinal product

89 The approval for a device is based on an examination of different means and for a different purpose than the approval for a medicinal product. The approval of a medicinal product is based on the fact that a medicinal product achieves its principal action by different means to the device. The clinical trials (or investigations) carried out in relation to approvals for a medicinal product are focussed on determining how the medicinal product achieves as its principal intended action according to the definition in Article 1(2) of Directive 2001/83/EC and which are necessary to produce the summary of product characteristics (SmPC) for the marketing authorisation. Clinical investigations that are carried out as part of the approval process for a medical device are focused on determining - does the medical device work as is claimed by the manufacturer and, in its normal use, does it have any risks that outweigh its benefits – as referred to, for example, in Sections 1-6 and Section 7, Annex 1 of Directive 93/42/EEC?

90 While I note the applicants arguments that an assessment of the substance by a competent body (consulted via the notified body) is made in line with Directive 2001/83/EC, this opinion is given only in relation to a substance that has an action ancillary to that of the device and only in relation to how it interacts with the elements of the devices in the course of its normal conditions of use and its intended purpose. As a consequence, the clinical evaluation carried out on a device is based on an

assessment of how the device works as a whole. The assessment of the medicinal substance incorporated in the device which assists the device to achieve its purpose in an ancillary manner by pharmacological, immunological or metabolic means, is a part of this overall assessment. While tests will have to be carried out using examples of the medical devices and the associated substance, these tests are designed and carried out to meet the requirements of the medical devices directive based on what is the intended purpose of the device. The notified body dealing with the approval process for the device is required to consult with the competent body to assess the substance incorporated into the device. This consultation is based on data provided by the notified body which in turn is the data provided by the manufacturer regarding the conditions of use and intended purpose of the device.

91 I acknowledge, that class III devices will require the greatest degree of investigation under Directive 93/42/EC and so, of all the different classes of devices, class III devices will require the collection of data prior to putting the device on the market and will usually require clinical investigations as distinct from a review of existing data or an assessment of the literature which can be used in other circumstances. However, while acknowledging this, I still do not consider that this is the same as the assessment required for a medicinal product under Directive 2001/83/EC directly where the medical product in questions exercises its principal intended action by pharmacological, immunological or metabolic means.

'Usefulness' v 'Efficacy'

92 I consider that the assessment of the safety, quality and usefulness of a device is NOT the same as the assessment of quality, safety and efficacy on a medicinal product. I consider that determining the usefulness of a device is not equivalent to determining the efficacy of a medicinal product. The former is focused on making sure that exposure to the physical elements of the device does not cause any problems for the user and that there are no unintended side effects arising from the normal use of the device. As Article 3 of the Medical Devices Directive makes clear the devices must meet the essential requirements laid down in the directive "taking account of the intended purpose of the devices concerned".

93 To me this is an overall question of degree. I do not consider that the acceptance by a notified body of an opinion from a competent body in relation to the assessment of a substance incorporated into a device under Directive 93/452/EEC is the same or can be considered to be equivalent to the authorisation granted under Directive 2001/83/EC by a competent body. I do not consider that the requirements to carry out the assessment "*by analogy with appropriate methods specified under Directive 75/318/EC* (now Directive 2001/83/EC*)"* is the same as carrying out the assessment of a medicinal product in accordance with Directive 2001/83/EC where its principal action is by pharmacological, immunological or metabolic means and is not ancillary. Article 3(b) of the SPC regulation makes clear that a valid authorisation is one that is granted "*in accordance with Directive 2001/83/EC*". While the overall approach or framework that the competent body may use in both cases is based on their experience of dealing with medicinal products, the assessment carried out for each is for a different objective and each assesses performance in a different way under the two systems.

Experience in other jurisdictions & previous practice at the IPO

94 The applicant has made reference to two SPCs that were granted in the UK on the basis of the approval of the products they relate to under the medical devices directive, Directive 93/42/EC. These SPCs relate to Hylan A and Hylan B respectively and are based on patent EP(UK) 0320164 B. They were granted in the UK in 1998, although they did not enter into force until 2008 and they expired in 2010.

95 The applicant also refers to a decision from the Netherlands's court in 2004 which overturned the refusal of the Netherlands Patent Office to grant an SPC to the same product. The examiner has made reference to the case from the German courts that also concerns the same product. But in this case the German court upheld (in 2010) the decision of the German Patent and Trademark Office to refuse the SPC application. Although an appeal was allowed from this decision, this was not pursued by the applicant.

96 In considering the translations of the decisions available to me (unofficial translations provided via one of the parties involved in these cases) the key question is does this approval step involve an investigation in relation to the device that is in accordance with Directive 65/65/EEC and has this been verified and confirmed by an appropriate competent body. The NL court found that the Netherlands Patent Office did not verify that the procedure for approving the device did meet this requirement. Thus the court found that the Patent Office had not made its decision in the correct manner and referred the case back to it for a decision.

97 The applicant has also referred a second case from the German court in 2010 where the applicant was successful in gaining an SPC on the basis an approval that was issued under the active implantable medicinal devices directive (AIMDD), Directive 90/385/EEC. This directive also refers (see Article 1(4)) to the need for an assessment by analogy with the procedures laid down in Directives 2001/83/EC in the situation "*Where a device incorporates, as an integral part, a substance which, if used separately, may be considered to be a medicinal product within the meaning of Article 1 of Directive 65/65/EEC and which is liable to act upon the body with action ancillary to that of the device, that device must be assessed and authorized in accordance with this Directive.*" In this case, the court considered that the advance in science and technology justified the definition of medicinal product under Directive 2001/83/EC being extended to cover radioactive materials and that they were satisfied that the assessment by analogy with Directive 2001/83/EC required under the AIMDD was sufficient for the approval obtained under the process in Directive 90/385/EC to be considered to be equivalent to an authorisation under Directive 2001/83/EC and so the requirement under Article 3(b) of the SPC regulation was met and an SPC could be granted.

98 As I have explained above, I do not find this argument persuasive. I do not consider that the opinion provided by a competent authority under the Medicinal Products directive is equivalent to an authorisation for a medicinal product issued by a competent authority under the Medicinal Products Directive.

99 Also, I do not find the fact that two SPCs were granted by the UK Intellectual Property Office 16 years ago based on approvals under Directive 93/42/EC to be

persuasive. As noted above these products were also the subject of litigation in the courts in Netherlands and in Germany and a consensus view was not achieved regarding whether SPCs had been validly granted in this case. The situation under which I am considering the present cases is very different to that that existed in 1998. Based on my analysis of the facts of this case and the applicable legislation and the material on file, I have come to the conclusion outlined below.

Conclusion

100 Taking all of the above into account, I do not consider that EC Design Certificate No. G7 02 05 16178 063, dated 31 May 2002, issued for medical device "*INTERCEPT (Amotosalen Photochemical Treatment) System for Platelets*" under Article 11(1)(a) of the Medical Devices Directive (Directive 93/42/EEC, as amended) for a medical device that meets the criteria of Article 1(4) of this directive and which includes an opinion from a competent body of member state, as designated under the medicinal Products Directive, Directive 65/65/EEC [now Directive 2001/83/EC], as part of its successful fulfilment of the essential requirements under Article 3 and Annex I of Directive 93/42/EEC, can be deemed to meet the requirement under Article 3(b) of the SPC Regulation (Regulation EC 1768/92) that a valid authorisation to place the product applied for, i.e., "*Platelet preparation obtainable by addition, and subsequent photoactivation, of amotosalen or its salt, to a suspension of platelets in plasma"* on the market as a medicinal product has been granted in accordance with Directive 2001/83/EC.

101 Similarly, I do not consider that EC Design Certificate No. G7 06 09 60562 004, dated 21 November 2006, issued for medical device "*INTERCEPT (Amotosalen Photochemical Treatment) System for Plasma*" under Article 11(1)(a) of the Medical Devices Directive, Directive 93/42/EEC, as amended, for a medical device that meets the criteria of Article 1(4) of this directive and which includes an opinion from a competent body of member state, as designated under the medicinal Products Directive, Directive 65/65/EEC [now Directive 2001/83/EC], as part of its successful fulfilment of the essential requirements under Article 3 and Annex I of Directive 93/42/EEC, can be deemed to meet the requirement under Article 3(b) of the SPC Regulation (Regulation EC 1768/92) that a valid authorisation to place the product applied for, i.e. "*Plasma preparation obtainable by addition to plasma, and photoactivation, of amotosalen or its salt"*, on the market as a medicinal product has been granted in accordance with Directive 2001/83/EC.

102 As a consequence, applications SPC/GB/07/043 and SPC/GB/07/044 do not meet the requirements laid down in the SPC regulation and are rejected under Article 10(2).

103 Furthermore, as the product for which an SPC has been applied in each case has not been subject to an administrative authorisation procedure as laid down in Directive 2001/83/EC, I conclude that the product is not eligible under Article 2 of the SPC regulation to be the subject of an SPC certificate.

104 I also consider that the product definitions that have been applied for in relation to SPG/GB/07/043 and SPC/GB/07/044 are not appropriate ones in terms of identifying

the product for which an SPC may be granted. The product definition proposed by the applicant in the course of the processing of this case, while it correctly identifies a product for which an SPC might be granted, there is not a valid authorisation for a medicinal product upon which such an SPC can be delivered.

Appeal

105 Any appeal must be lodged within 28 days

Dr L Cullen
Deputy Director, acting for the Comptroller