COUNCIL REGULATION (EEC) No 1768/92

IN THE MATTER OF Application No SPC/GB93/172 for a Supplementary Protection Certificate in the name of Centocor, Inc

DECISION

Application No SPC/GB93/172 for a Supplementary Protection Certificate in the name of Centocor, Inc was lodged on 4 November 1993 with the United Kingdom Patent Office as the competent industrial property office, pursuant to Articles 7(2) and 9(1) of Council Regulation (EEC) No 1768/92 ("the Regulation").

In accordance with rule 3(2) of the Patents (Supplementary Protection Certificate for Medicinal Products) Rules 1992, the application in suit was made on Form SP1. This identified:

- the product for which protection was sought as "Centoxin (HA-1A Monoclonal Antibody";

- the basic patent protecting the product as EP(UK)160670, entitled "Monoclonal Antibodies against Endotoxin of Gram-Negative Bacteria" and granted on 12 May 1993; and

- the first authorization in accordance with Directive 65/65/EEC or Directive 81/851/EEC to place the product on the market in the United Kingdom as No 8563/0010 dated 14 May 1991.

No earlier authorisation to place the product on the market in the Community was identified on Form SP1.

The claims (for GB) of the basic patent EP-0160670 read (emphasis added in italics):

"1. Product comprising (a) an anti-microbial agent and (b) an endotoxin core - or lipid A - specific mammalian monoclonal antibody *as a combined preparation* for use in treating or preventing gram-negative bacterial infection or endotoxin shock resulting therefrom.

2. Product according to claim 1, whereas said infection or endotoxin shock is derived from any of Escherichia, Salmonella, Klebsiella, Pseudomoanas and Serratia".

In Part 1 of the Schedule to Product Licence No 8563/0010,

- paragraph 1 states the name of the product to which the licence relates as "Centoxin (HA-1A Human Monoclonal Antibody) 100 mg/200 ml";

- paragraph 4 states the active constituent of this product to be "HA-1A Human IgM 0.5% w/v";

- paragraph 5 headed "Clinical Indications and Route of Administration" states (emphasis added in italics):

> "Centoxin is indicated for the treatment of patients with the sepsis syndrome and a presumptive diagnosis of Gram-negative bacteraemia, especially those with septic shock. *Centoxin should be given in hospital, along with the appropriate antibiotics and supportive therapy*, as soon as Gram-negative sepsis is clinically suspected. Centoxin should be given once and is not intended for repeated use.
>
> Centoxin is administered as an intravenous infusion over a period of 15 to 30 minutes."

- paragraph 8 identifies the other constituents of the product as sodium dihydrogen phosphate monohydrate, disodium phosphate dihydrate, sodium chloride, human serum albumin and water for injections in bulk.

In their agents' letter dated 3 November 1993 which accompanied the applications the applicants stated:

> "It is respectfully submitted that the schedules to the Authorisation clearly identify the products in question as protected by the basic patent.
>
> Please note for example the reference to administration along with appropriate antibiotics in paragraph 5 of Part 1 of the Schedule to the Product Licence."

In an official letter dated 18 January 1994, the examiner reported that:

> "Notwithstanding the comments in the second and third paragraphs of your agents letter dated 3 November 1993, it appears that the product for which protection is sought, and which has received authorisation to be placed on the market in the UK, is not protected by the basic patent as required by Article 3(a).
>
> Thus, a "product" is defined by Article 1(b) as "the active ingredient or combination of active ingredients of a medicinal product": having regard to paragraphs 4 and 8 of Schedule 1 of Product Licence No 8563/0010, the product in this case would therefore appear to be the antibody alone. However the claims of the patent are directed to a combined preparation of an antibody and an anti-micorbial agent and do not therefore appear to protect an antibody per se.
>
> It does not appear appropriate in the present case to regard the product as a combination of active ingredients. Paragraph 5 of Schedule 1 Product Licence to which you refer suggests that the anti-microbial agent is administered separately from the antibody, and does not form part of either the product as defined by Article 1(b) or the medicinal product as defined by Article 1(a)."

The examiner also reported that:

"The definition of the product at item 4 of Form SP1 is in any case unsatisfactory for the following reasons:

(i) "Centoxin" would appear to be a trade name and is therefore indicative of the origin, rather than the content or composition, of the product;

(ii) This term in any case appears to relate to a medicinal product as defined in Article 1(a), rather than a product as in Article 1(b);

(iii) "HA-1A Human Monoclonal Antibody" does not accord with the identification of the active ingredient in the UK Product Licence. This appears to be restricted to the IgM form of the antibody (see Schedule, Part 1, paragraphs 1 and 4);

(iv) "HA-1A", although used in both Form SP1 and the Product Licence, is not clear in meaning and does not appear in the specification of the basic patent."

Articles 1 and 3 read:

" ARTICLE 1

Definitions

For the purpose of this Regulation:

(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;

(c) 'basic patent' means a patent which protects a product as defined in (b) as such, a process to obtain a product or an application of a product, and which is designated by its holder for the purpose of the procedure for grant of a certificate;

(d) 'certificate' means the supplementary protection certificate.

ARTICLE 3

Conditions for obtaining a certificate

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 of that application;

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

(b) a valid authorization to place the product on the market as a medicinal product has been granted in accordance with Directive 65/65/EEC or Directive 81/851/EEC, as appropriate;

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

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

At an interview with the examiner on 29 April 1994, the agent acting for the applicants proposed that the product should be defined as:

> "Human monoclonal antibody of the IgM isotype which binds specifically to the lipid A domain of endotoxin"

and argued that, pursuant to Article 1(c) of the Regulation, the basic patent EP(UK) 0160670 protected either "an application of a product" or (having regard to section 60(2) of the Patents Act 1977) "a product as such". The agent did not seek to argue that the basic patent protected "a process to obtain a product".

In support of his argument, the agent submitted copies of documents relating to proceedings before the European Patent Office in which the present claims of the basic patent EP(UK) 0160670 were settled prior to the grant of the patent. These documents included a product launch, hospital guidelines and a series of case studies relating to "Centoxin".

The agent also drew the attention of the examiner to the Decision T09/81 of the EPO Technical Board of Appeal dated 25 January 1983 in Asta-Werke, concerning the protection of combined preparations of known therapeutic agents.

However in a further official letter dated 24 June 1994 the examiner maintained that the basic patent EP(UK) 0160670 did not protect either an "application of a product" or "a product as such" where the product for which protection is sought was the antibody alone.

The examiner stated:

> "..... it is not apparent that the claims of the basic patent, which are directed to "a combined preparation [of an anti-microbial agent and an antibody] for use in treating ....", can be regarded as protecting the separate administration of two separate products (one containing the antibody, the other containing the anti-microbial agent), and hence as an "application of" the antibody.

The decision of the EPO Board of Appeal (T09/81) in Asta-Werke does not appear to assist your argument. In this case, it appears that claim 1 (as submitted in the proceedings) to a product comprising two specified components "as a combined preparation for simultaneous, separate or sequential use in cytostatic therapy" (see p373) was allowed because it provided a new combination with a surprising valuable property (see ll 2-3 p375). However, the claim 1 had to be regarded as limited to the joint use of the products since the individual components of the product had known therapeutic applications (see p376).

In Asta-Werke it was expressly stated in both claim 1 and the description that the two products could be administered separately. This is not so in the case of the basic patent, in which (i) the claims make no reference to separate administration and (ii) the relevant description is limited to ll 24-25 p7 and ll 36-37 p7 which merely state that the two components "are given in conjunction" and "administered ..... along with [each other]".

and

"..... even if it could be established there are circumstances in which the supply of the antibody would fall within the provisions of section 60(2), it does not appear to follow from this that the antibody "as such" is protected by the basic patent EP(UK) 0160670."

A hearing was arranged for further consideration of the matter, but was cancelled at the request of the applicants.

A further official letter was accordingly issued on 17 January 1995. This stated:

"Following cancellation of the hearing set for 16 December 1994, the matters raised in the Official Letter dated 24 June 1994 remain outstanding.

Subject therefore to any comments within the period for reply specified above, the Office will reject the application in accordance with Article 10(2) for failure to meet the condition laid down in Article 3(a)."

and set a period of one month for reply.

Articles 10(2) and 10(3) of the Regulation read:

"2. The authority referred to in Article 9(1) shall, subject to paragraph 3, reject the application for a certificate if the application or the product to which it relates does not meet the conditions laid down in this Regulation.

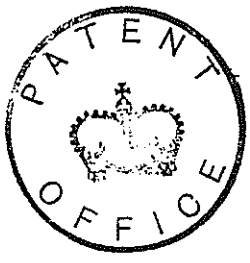
3. Where the application for a certificate does not meet the conditions laid down in Article 8, the authority referred to in Article 9(1) shall ask the applicant to rectify the irregularity, or to settle the fee, within a stated time."

No response has been received to this letter.

Having considered the matter, I am satisfied that, for the reasons stated by the examiner in the official letter dated 24 June 1994, the basic patent does not protect either an antibody as such or an application of an antibody. Accordingly, the application is hereby rejected pursuant to Article 10(2) of the Regulation for failure to meet the condition laid down in Article 3(a).

The period within which an appeal may be lodged with the Patents Court is six weeks from the date below.

Dated this 3 day of May 1995



L LEWIS
Principal Examiner, acting for the Comptroller

THE PATENT OFFICE