BL O/422/12

26th October 2012

PATENTS ACT 1977

APPLICANT Lanzhou Veterinary Research Institute *et al*

ISSUE Whether patent application GB0916723.0 complies with sections 1(1)(b) & 14(5)(b)

HEARING OFFICER C L Davies

DECISION

Introduction

1 International patent application PCT/CN2008/000126 entitled "A method for preparing antigens of foot and mouth disease virus" was filed in the name of Lanzhou Veterinary Research Institute *et al* (the "Applicant") on 17/01/08 (Priority Date: 23/03/07). The international patent application was published by WIPO as WO2008/116368 on 02/10/08, entered the UK national phase as GB0916723.0 and was re-published as GB2463783A on 31/03/10.

2 During the course of substantive examination and despite several rounds of correspondence, the Applicant has been unable to convince the Examiner that the application was inventive over the prior art.

3 The matter subsequently came before me to decide at a hearing held on 27th June 2012. The Applicant was represented by Mr David Brown assisted by Ms Catherine Williamson (Haseltine Lake LLP). Dr Patrick Purcell, Senior Patent Examiner at the IPO, also attended.

4 The Examiner set out in a pre-hearing report dated 13th June 2012, the outstanding issue of inventive step, according to the Windsurfing/Pozzoli approach. Prior to the hearing, the Applicant filed "skeleton arguments" dated 20th June 2012, which addressed the Examiner's objections raised in the report of 23rd March 2012, together with five sets of claims (one Main Request plus 4 Alternative Requests) and further documents to support their arguments.

5 Given the imminent compliance date, at the hearing, the Hearing Officer asked Mr Brown to file a further F52 and fee to extend the compliance date to 23rd July 2012. This was subsequently done.

The Invention

6 The invention relates to a method for expressing antigens of foot and mouth disease virus (FMDV) in insect *in vivo* by using recombinant baculovirus and seeks to provide a recombinant vaccine for combatting foot and mouth disease in cloven-hoofed animals, specifically bovines, which is an improvement over traditional foot and mouth disease (FMD) vaccines. It is purported that the method as described in this invention produces FMDV antigens safely and highly effectively by a baculovirus expression system, namely the silkworm baculovirus (eukaryotic) expression system, and thus provides means of addressing short-comings such as high cost of production, short period of immunity, and security issues around escape of the virus during preparation of the vaccine leading overall to a FMD vaccine with higher security and efficacy.

The claims

7 As stated earlier, the Applicant filed with their skeleton arguments, multiple sets of claims for consideration at the hearing: a "Main Request" plus 4 further alternative requests labelled 1st Alternative Request, 2nd Alternative Request, 3rd Alternative Request and 4th Alternative Request. To avoid any doubts/confusion over which claim set was under discussion at the hearing, the Hearing Officer asked Mr Brown to select a set for main consideration. Mr Brown opted to focus on the "1st Alternative Request" but requested that the Hearing Officer be mindful of the additional requests should she be minded to refuse the claims of the 1st Alternative Request.

8 The 1st Alternative Request reads as follows:

Claim 1:

A method for preparing immunogenic antigens of foot-and-mouth disease (FMD) virus, wherein the immunogenic antigens are protective in that after one immunisation they illicit an immune response in a bovine that protects four or five out of five bovines against foot-and-mouth disease for 10 consecutive days after challenge by intradermal tongue inoculation of homological foot-and-mouth disease virus with 10,000BID$_{50}$ potency, which comprises:

cloning the nucleotide sequences shown in SEQ ID NO:1; SEQ ID NO:3 or SEQ ID NO:5 respectively into baculovirus carrier vector to construct the recombinant transfer vector, wherein the baculovirus carrier vector is pVL1393, the said recombinant transfer vector is pVL1393 (P1-2A3C), pVL1393 (ORF) or pVL1393 (VP1);

transfecting parental baculovirus with the said transfer vector to perform DNA recombination to obtain recombinant baculovirus; wherein the baculovirus is BmNPV-ZJ8;

infecting the insect hosts with the said recombinant baculovirus; wherein the insect hosts is silkworm larvae or pupae (Bombyx mori);

culturing the infected insect hosts for the expression of antigens of foot-and-mouth disease virus whereby 5 days after infection, SEQ ID NO:1; SEQ ID NO:3 or SEQ ID NO:5 antigens are expressed at a level respectively more than 100 times, more than 10 times or more than 100 times higher than antigen expression obtained by conventional FMD viral vaccine, as measured by optical density; and

collecting and purifying the expressed foot-and-mouth disease virus antigens so expressed; wherein the antigens are for use in immunising animals against FMD to obtain the said protective response.

Claim 2:

The method of claim 1, wherein the recombinant baculovirus is selected from:

(1) recombinant silkworm nuclear polyhedrosis virus rBmNPV (ORF), deposited as CGMCC Accession No. 1980;

(2) recombinant silkworm nuclear polyhedrosis virus rBmNPV (P1-2A3C), deposited as CGMCC Accession No. 1979;

(3) recombinant silkworm nuclear polyhedrosis virus rBmNPV (VP1), deposited as CGMCC Accession No. 1975.

Issue to be decided

9 The issue to be decided is whether the claims satisfy section 1(1)(b) of the Patents Act 1977 (the "Act"), i.e. whether they comprise an inventive step. The examiner also indirectly raised the issue of clarity under 14(5)(b) which I will also consider.

The Law

10 The law regarding inventive step is found in sections 1 and 3 of the Act. The relevant parts read as follows:

Patentable Inventions

1.-(1) A patent may be granted only for an invention in respect of which the following conditions are satisfied, that is to say –
(a) ...
(b) it involves an inventive step;
(c) ...
and references in this Act to a patentable invention shall be construed accordingly.

11 Section 3 defines what is meant by 'inventive step'.

Inventive Step

3. An invention shall be taken to involve an inventive step if it is not

obvious to a person skilled in the art, having regard to any matter which forms part of the state of the art by virtue only of section 2(2) above (and disregarding section 2(3) above).

12 I do not propose to quote sections 2(2) and 2(3) here, but it follows from these that the state of the art comprises all matter which has at any time before the priority date of the application been made available to the public, whether in the UK or elsewhere.

13 The correct test for determining inventive step is the structured approach found in *Windsurfing International Inc. v Tabur Marine (Great Britain) Ltd, [1985] RPC 59* as reformulated by Jacob LJ in *Pozzoli SPA v BDMO SA [2007] EWCA Civ 588* (see paragraph 23 of the Court of Appeal's judgment). The four steps of the test are now:

(1)(a) Identify the notional "person skilled in the art"

(1)(b) Identify the relevant common general knowledge of that person;

(2) Identify the inventive concept of the claim in question or if that cannot readily be done, construe it;

(3) Identify what, if any, differences exist between the matter cited as forming part of the "state of the art" and the inventive concept of the claim or the claim as construed;

(4) Viewed without any knowledge of the alleged invention as claimed, do those differences constitute steps which would have been obvious to the person skilled in the art or do they require any degree of invention?

14 It was agreed at the hearing that the structured approach for determining inventive step should be followed but the Hearing Officer observed that in the correspondence between the Examiner and the Applicant, the structured approach had only been adopted by the Examiner in the pre-hearing report. Mr Brown had indeed acknowledged in the opening paragraphs of his skeleton arguments that the arguments therein were addressing the Examiner's report dated 23rd March 2012 and that he was content to adopt the Windsurfing/Pozzoli approach at the hearing. Mr Brown agreed to file written submissions ("submissions") detailing the Applicant's inventive step arguments adopting the Windsurfing/Pozzoli approach as put forward at the hearing, and these were subsequently filed on 6th July 2012.

Applying the Windsurfing/Pozzoli test

Step 1(a): Identify the notional "person skilled in the art"

15 The Applicant agrees essentially with the Examiner's assessment of the "person skilled in the art" as expressed in the Examiner's pre-hearing report which, for completeness, I have repeated below:

"The person skilled in the art is considered to be a team comprising

molecular biologists having knowledge of baculovirus expression systems and those with expertise in recombinant vaccine production and administration".

16 At the hearing and quoting from the Applicant's submission, I agree with the Applicant's further emphasis that "knowledge of baculovirus expression systems and recombinant vaccine production is only a **small** part of the skilled person's total knowledge and does not encompass the skilled person's total knowledge". I agree also with the Applicant's further assertions set out as (a) to (c) on page 2 lines 17-25 of their submission.

17 I confirm therefore that I am content with the assessment of the skilled person as identified by the Examiner and as further clarified by the Applicant.

Step 1(b): Identify the relevant common general knowledge of that person

18 The Applicant agrees essentially with the Examiner's statement in the pre-hearing report that *"the common general knowledge of this skilled person is considered to include advantages of the baculoviral expression system (ie. those provided at pages 1-2 of the description of the present application)".*

19 In their submission however, the Applicant maintains their previous point (made above under step 1(a)) that "knowledge of the baculoviral expression system is only a **part** of the skilled person's total knowledge and is not limited to this."

20 In their submission at page 2, line 34 to page 4, line 5, the Applicant made further observations about the skilled person and their level of knowledge which I have considered carefully and accept to be relevant.

Step 2: Identify the inventive concept of the claim in question or if that cannot readily be done, construe it:

21 The Applicant disagrees however with the Examiner's assessment of the inventive concept of the claims. In the pre-hearing report, the Examiner identified the inventive concept as: *"A method for preparing an immunogenic foot-and-mouth disease virus (FMDV) antigen in an <u>in vivo</u> baculovirus expression system".*

22 At the hearing, the Applicant strongly disagreed that the inventive concept is at the "high generic level" as assessed by the Examiner: the level of generality of this statement is much too high, maintaining that Claim 1 is clearly defined in much more detail than the Examiner's statement suggests, with Claim 1 being specifically defined by the **steps of the method** described in Claim 1, the outcome of performing these specific steps, and also by the outcome of the use of the antigens produced by the method in a vaccination.

23 The Applicant considers the inventive concept to be what is set out in the finer details of the claim, and at the hearing (confirmed in their submission) asserted the following as "a fair assessment of the inventive concept", with the following particular features of Claim 1 being intimately linked to the particular method

steps defined in Claim 1:

> *- after **one** immunisation;*
>
> *- they [the FMD] antibodies elicit an immune response in a **bovine** that **protects four or five out of five bovines** against foot-and-mouth disease for 10 consecutive days after challenge by intradermal tongue inoculation of homological foot-and-mouth disease virus with 10,000 BID_{50} potency;*
>
> *- the antigens are prepared by culturing live silkworms with the specific recombinant baculovirus **BmNPV-ZJ8** transfected using the specific carrier vector **pVL1393** to introduce the heterologous DNA of SEQ ID NO:1, SEQ ID NO:3 or SEQ ID NO:5;*
>
> *- the culturing being done to a high expression level whereby 5 days after infection [of silkworm insect hosts] SEQ ID NO:1, SEQ ID NO:3 or SEQ ID NO:5 **antigens are expressed at a level respectively more than 100 times, more than 10 times or more than 100 times higher** than antigen expression obtained by conventional FMD viral vaccine, as measured by optical density;*
>
> *- the antigens are **for use** [ie. are effective and intended for use] in immunising animals against FMD to obtain the **said** protective response [ie. the 4-5 out of 5 protection after only one immunisation].*

24 Having given careful thought to the arguments made by Mr Brown at the hearing and indeed careful consideration to the submission, skeleton arguments and the Examiner's pre-hearing report, I have come to the view that at this stage of the proceedings, the Examiner's broad/high level approach in identifying the inventive concept is not appropriate and in doing so, has missed out aspects present in Claim 1 which are subtly important and which must be given due consideration when assessing inventiveness.

25 In the pre-hearing report and the Official report of 23rd March 2012, the Examiner maintained that Claim 1 in the Main and subsequent further Alternative Requests are characterised by a result to be achieved: that the antigens produced by the method are "immunogenic" and are "protective", amounts to no more than a result to be achieved and that expression of the FMDV antigens by the claimed method would result in expression "… *whereby 5 days after infection, SEQ ID NO:1; SEQ ID NO:3 or SEQ ID NO:5 antigens are expressed at a level respectively more than 100 times, more than 10 times or more than 100 times higher than antigen expression obtained by conventional FMD viral vaccine, as measured by optical density;"* is again a result to be achieved.

26 As requested by Mr Brown, I have given careful consideration as to whether or not the "level of protective effect/immune response" and the "level of expression" features in Claim 1 provide limitations.

27 From the Applicant's arguments and papers on file, it is clear that the fact antigens produced by the method of the present invention are protective in that they elicit an immune response in bovines which have only been immunised

once, is a key part of the invention and I am therefore prepared to accept that the "level of the protective effect/immune response" is limiting on the claim, and thus give proper weight to it.

28 I also appreciate from arguments presented that clear advantages are shown by using the silkworm insect hosts for expression of antigens of FMD virus, I nevertheless maintain the Examiner's view that the "level of expression" feature in Claim 1 amounts to definition by result which renders the scope of the claim unclear with regard to section 14(5)(b) and is therefore not limiting on the claim.

29 In my view, the inventive concept is a more detailed version of the Examiner's assessment, giving weight to "immune response" which the Applicant asserted at the hearing and in their submission and also taking into consideration the specific recombinant baculoviruses specified in claim 2, to replace the "definition by result" feature in claim 1:

"A method for preparing an immunogenic foot-and-mouth disease virus (FMDV) antigen in an in vivo baculovirus expression system where:

*- after **one** immunisation;*

*- they [the FMD] antibodies elicit an immune response in a **bovine** that **protects four or five out of five bovines** against foot-and-mouth disease for 10 consecutive days after challenge by intradermal tongue inoculation of homological foot-and-mouth disease virus with 10,000 BID_{50} potency;*

*- the antigens are prepared by culturing live silkworms with the specific recombinant baculovirus selected from rBmNPV (ORF), deposited as CGMCC Accession No. 1980; rBmNPV (P1-2A3C), deposited as CGMCC Accession No. 1979; rBmNPV (P1-2A3C), deposited as CGMCC Accession No. 1979; rBmNPV (VP1), deposited as CGMCC Accession No. 1975, transfected using the specific carrier vector **pVL1393** to introduce the heterologous DNA of SEQ ID NO:1, SEQ ID NO:3 or SEQ ID NO:5; the recombinant transfer vector for each respectively being pVL1393 (P1-2A3C), pVL1393 (ORF) or pVL1393 (VP1);*

*- the antigens are **for use** [ie. are effective and intended for use] in immunising bovines against FMD to obtain the **said** protective response [ie. the 4-5 out of 5 protection after only one immunisation].*

Step 3: Identify what, if any, differences exist between the matter cited as forming part of the "state of the art" and the inventive concept of the claim or the claim as construed

30 Having found the inventive concept to be narrower than that defined by the Examiner, the differences between the prior art and the claimed method are more than identified by the Examiner, ie. that the antigens produced by the claimed method are stated to be immunogenic and protective in that they elicit an immune response in a bovine that protects 4 or 5 out of 5 bovines against FMDV after one challenge.

31 I have given careful consideration to the detailed observations regarding the differences between the cited 13 prior art documents and the claimed invention which the Applicant provided in their skeleton arguments and also the observations and updated novelty table relating to Claim 1 of the 1st Alternative Request provided in their submission. I am grateful to Mr Brown for taking me through the prior art documents and identifying the differences at the hearing. I accept the differences identified by the Applicant.

Step 4: **Viewed without any knowledge of the alleged invention as claimed, do those differences constitute steps which would have been obvious to the person skilled in the art or do they require any degree of invention?**

32 The Applicant points out in paragraph 2, page 5 of their skeleton argument that since "each item of prior art needs to be so radically modified, in so many ways that are quite different as between one item and another, that it is just impossible to fairly conclude, without foreknowledge of the invention and the work underlying the present application, that it was obvious to pick and choose features from the prior art and recombine them to arrive straight at the invention, somehow fully formed. This would require "mosaicing" of bits and pieces of the prior art references, of a kind that the case law has consistently ruled inadmissible over many years, and on a scale that is clearly impossible to see as being obvious".

33 The Applicant also asserts at paragraph 5, page 5 of the same document that **all** of the prior art is deficient in that it would not lead obviously to the presently claimed invention, with each of the cited prior art documents differing from the presently claimed invention in at least one important feature, for example the nucleotide sequence used, expression system or method of vaccination. The Applicant asserts further at paragraph 6, page 5 that none of the cited prior art could be obviously combined to lead to the present invention.

Advantages of the current invention

34 In the pre-hearing report, the Examiner maintained that the presently claimed method does not provide immunogenic FMDV antigens that show any advantage over any of the vaccine preparations detailed in prior art documents (ix) – (xiii) (also denoted (a)-(e) in the official report dated 23rd March 2012 and also in the Applicant's skeleton).

35 At the hearing, Mr Brown discussed in detail the advantages of the present invention as compared with the above mentioned prior art which, to all intents and purposes, the subtleties might not be fully apparent from the description. He described the invention as a "sweet spot" in the art, requiring the method steps to be closely adhered to in order to achieve the advantages of the invention, namely: level of protection obtained for bovines after only a single immunization; the high level of expression of the FMDV antigens, using baculovirus-silkworm expression system, produced by the method.

36 I am persuaded by the Applicant's arguments: in light of what has been before me, I agree with the Applicant that there are too many variables and steps that the notionally skilled person would have to take into consideration in order to

arrive at the claimed invention.

37 In my view therefore, I find that the invention of Claim 1 demonstrates an inventive step over the prior art. However, I am not satisfied that this claim is clearly defined in accordance with section 14(5)(b) because the "level of expression" feature constitutes definition by result.

Auxiliary Requests & possible amendment

38 At Mr Brown's request, I have also given consideration to the Auxiliary Requests filed with the skeleton prior to the hearing.

39 In my view, there is an acceptable set of claims which the Applicant can rely on, namely the 2nd Alternative Request. The 2nd Alternative Request consists only of 1 independent claim – which is silent in respect of the "level of expression" feature- but in my view overcomes the definition by result (clarity) objection present in the 1st Alternative Request, instead, specifying recombinant baculovirus selections which, when the invention is worked, should deliver the high expression levels.

40 Further amendment of the 2nd Alternative Claim 1 will be necessary to replace "animals" (penultimate line) with "bovines" and also amendment of the description to bring it into line with the claim.

Conclusion

41 Whilst I find that Claim 1 of the 1st Alternative Request complies with s(1)(1)(b) of the Act insofar as it comprises an inventive step, I nevertheless find that this claim does not comply with s 14(5)(b) insofar since it lacks clarity (ie. it is characterised in terms of a result to be achieved in respect of the "level of expression" feature).

42 As indicated above, I believe there is a possible amendment which, if undertaken, should allow this application to proceed to grant.

43 Therefore, I give the Applicant an opportunity to amend the current application as indicated above and to formally file claim 1 as set out in the 2nd Alternative Request filed with the Applicant's skeleton on 20th June 2012.

44 As things stand, I note the compliance period (as extended) expires on 23rd September 2012. Therefore I order as follows:

(i) If the Applicant requests a discretionary extension to extend the compliance period to 23rd November 2012 by filing F52, appropriate fee and files amendments to address the outstanding clarity objections no later than 23rd November 2012, the application will be remitted to the examiner for processing;

(ii) If the Applicant does not request a discretionary extension to extend the compliance period further, the application will subsequently be treated as having been refused for non-compliance with section 14(5)(b).

Appeal

45 Under the Practice Direction to Part 52 of the Civil Procedure Rules, any appeal must be lodged within 28 days.

C L Davies
Deputy Director acting for the Comptroller