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# D E C I S I O N
# of 4 March 2004

**Case Number:** W 0012/03 - 3.3.8

**Application Number:** PCT/EP 02/03575

**Publication Number:** WO 02/81712

**IPC:** C12N 15/70

**Language of the proceedings:** EN

**Title of invention:**
Artificial chromosomes comprising EHV sequences

**Applicant:**
Boehringer Ingelheim Vetmedica GmbH

**Opponent:**
-

**Headword:**
EHV-BAC/BOEHRINGER

**Relevant legal provisions:**
PCT Art. 17.3(a)
PCT R. 13.1, 13.2, 40.1, 40.2(c), 40.2(e), 40.3

**Keyword:**
"Lack of unity a posteriori (no)"
"Refund of the additional search fees (yes)"

**Decisions cited:**
W 0008/91, W 0006/97, G 0001/89

**Catchword:**
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**Case Number:** W 0012/03 - 3.3.8

# D E C I S I O N
**of the Technical Board of Appeal 3.3.8**
**of 4 March 2004**

**Applicant:** Boehringer Ingelheim Vetmedica GmbH
D-55216 Ingelheim am Rhein (DE)

**Representative:** T. Klein
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**Decision under appeal:** **Protest according to Rule 40.2(c) of the Patent Cooperation Treaty made by the applicants against the invitation (payment of additional fees) of the European Patent Office (International Searching Authority) dated 16 October 2002 .**

**Composition of the Board:**

**Chairman:** L. Galligani
**Members:** T. J. H. Mennessier
M. B. Günzel

## Summary of Facts and Submissions

I. International patent application PCT/EP 02/03575 (published as WO-A-02/81712) was filed on 30 March 2002 with twenty eight claims:

**Claims 1 to 6** read as follows:

"1. Bacterial artificial chromosome vector characterized in that it comprises essentially the entire genome of an EHV strain."

"2. Artificial chromosome vector according to claim 1, characterized in that the EHV is EHV-1."

"3. Artificial chromosome vector according to claim 1 or 2, characterized in that the EHV is EHV-4."

"4. Artificial chromosome vector according to any one of claim 1 to 3, characterized in that the EHV strain is RacH."

"5. Artificial chromosome vector according to claim 4, chracterized [sic] in that it is the vector with the accession No. ECACC 01032704."

"6. Artificial chromosome vector according to any one of claim 1 to 5, characterized in that the EHV strain is lacking the glycoprotein gB."

Each of **claims 7 to 16** concerned a bacterial artificial chromosome vector (BAC vector) according to the preceding claims characterised in that the equine

herpesvirus (EHV) strain lacked one or more given glycoproteins.

**Claims 17 to 19** read:

"17. Artificial chromosome vector according to any one of claims 1 to 16, characterized in that the artificial chromosome as [sic] deposited under accession number Q4297 at the ECACC."

"18. Polynucleotide encoding an an [sic] artificial chromosome vector or EHV contained therein according to any one of claims 1 to 17."

"19. Use of an artificial chromosome vector or a polynucleotide according to any one of claims 1 to 18 for the generation of infectious EHV."

**Claims 20 to 23** related to methods for the cloning and/or generation of an EHV (replicating: see claim 20, attenuated: see claims 21 and 22; or virulent: see claim 23) relying on a modification by molecular biology techniques of a BAC vector as defined in any one of claims 1 to 17. **Claim 24** was directed to an EHV obtainable by a method according to any one of claims 20 to 23.

**Claims 25 and 26** were directed to a pharmaceutical composition respectively comprising a polynucleotide according to claim 18 and an EHV according to claim 24.

**Claims 27 and 28** related to the use in the manufacture of a vaccine of a polynucleotide according to claim 18 and of an EHV according to claim 24, respectively.

II. On 16 October 2002, the European Patent Office, acting as an International Searching Authority (ISA), invited the applicants to pay within a time limit of thirty days seven additional search fees pursuant to Article 17(3)(a), Rule 40.1 and 40.3 PCT and issued, as an annex to the invitation, a communication relating to the results of the partial international search carried out on the invention first mentioned in claims 1 and 18 to 28 (all partially).

III. The invitation to pay additional search fees stated the eight "multiple inventions" to which the application was found to relate, namely:

"Invention 1: claims 1, 18-28 (all partially)

Bacterial artificial chromosome vector comprising the genome of an Equine Herpesvirus (EHV). Polynucleotides encoding said vector and its use to generate infectious EHV. Methods to generate a replicating, attenuated or virulent EHV. EHV obtainable according to said methods. Pharmaceutical composition comprising said polynucleotides or EHV, and their use in the manufacture of a vaccine."

"Invention 2: claims 1, 2, 18-28 (all partially)

Bacterial artificial chromosome vector comprising the genome of EHV type 1 (EHV-1). Polynucleotides encoding said vector and its use to generate infectious EHV. Methods to generate a replicating, attenuated or virulent EHV. EHV

obtainable according to said methods.
Pharmaceutical composition comprising said polynucleotides or EHV, and their use in the manufacture of a vaccine."

"Invention 3: claims 1, 3 (partially), 18-28 (all partially)

Bacterial artificial chromosome vector comprising the genome of EHV type 4 (EHV-4).
Polynucleotides encoding said vector and its use to generate infectious EHV. Methods to generate a replicating, attenuated or virulent EHV. EHV obtainable according to said methods.
Pharmaceutical composition comprising said polynucleotides or EHV, and their use in the manufacture of a vaccine."

"Invention 4: claims 1, 2, 4 (partially), 18-28 (all partially)

Bacterial artificial chromosome vector comprising the genome of EHV-1, strain RacH.
Polynucleotides encoding said vector and its use to generate infectious EHV. Methods to generate a replicating, attenuated or virulent EHV. EHV obtainable according to said methods.
Pharmaceutical composition comprising said polynucleotides or EHV, and their use in the manufacture of a vaccine."

"Invention 5: claims 1, 6-28 (all partially)

As Invention 1, but lacking one or more of the following glycoproteins: gB, gC, gD, gE, gG, gH, gI, gJ, gK, gL, gM, gp1, gp2."

"Invention 6: claims 1, 2, 6-28 (all partially)

As Invention 2, but lacking one or more of the following glycoproteins: gB, gC, gD, gE, gG, gH, gI, gJ, gK, gL, gM, gp1, gp2."

"Invention 7: claims 1, 3 (partially), 6-28 (all partially)

As Invention 3, but lacking one or more of the following glycoproteins: gB, gC, gD, gE, gG, gH, gI, gJ, gK, gL, gM, gp1, gp2."

"Invention 8: claims 1, 2, 4 (partially), 6-28 (all partially)

As Invention 4, but lacking one or more of the following glycoproteins: gB, gC, gD, gE, gG, gH, gI, gJ, gK, gL, gM, gp1, gp2."

**Claim 5** was not mentioned with respect to any of those inventions.

Whereas in the application a unique glycoprotein gp1/2 was referred to (see page 2, lines 2 to 9 and claim 16), in the invitation two separate glycoproteins gp1 and gp2 were referred to.

IV. The reasons for the non-unity finding were indicated as being essentially that the common concept linking the different groups of inventions together, said concept being "that they all [related] to the genome of an EHV cloned as a BAC", could not be regarded as the single general inventive concept referred to in Rule 13.2 EPC because it did not involve an inventive step.

The reasoning was as follows. As illustrated, eg in "*Alistair McGregor and Mark R. Schleiss, Mol. Genet. Metab., Vol. 72, 2001, Pages 8 to 14*" (referred to thereafter as document D1) the cloning of herpesviruses as BACs was an established technique, and its advantages were well known in the art. Furthermore, the genome of many herpesviruses had been successfully cloned. EHV serotypes 1 to 5 and many strains of EHV-1 including strain RacH were known in the art. Glycoproteins gB, gC, gD, gE, gG, gH, gI, gJ, gK, gL, gM, gp1 and gp2 as well as herpesvirus genomes cloned as BACs and lacking one of those glycoproteins were also known (as illustrated in "*Daniel Schumacher et al., J. Virol., Vol. 74, No. 23, December 2000, Pages 11088 to 11098*" (referred to thereafter as document D2)). All these features did not seem to provide any special effect over the prior art, nor did their combination. Since no special technical feature within the meaning of Rule 13.2 PCT could be identified to provide a linking concept encompassing the various inventions, the said eight separate groups of inventions were to be distinguished.

V. On 14 November 2002, the applicants paid seven additional search fees under protest pursuant to Rule 40.2(c) PCT and provided a reasoned statement to

the effect of establishing that the international application complied with the requirement of unity of invention.

The applicants stated that the ISA had not provided any proper reasoning, because it had failed to define the technical problem solved by the invention, although for the assessment of an *a posteriori* lack of unity of invention to be based on a lack of inventive step determining whether there was a single general inventive concept required an assessment of the content of the different subject-matter claimed on the basis of the problem and its solution (W 6/97 of 18 September 1997). The applicants also complained that document D1 on which the ISA had essentially made reference to was a document classified in category A and, therefore, could not support on its own an objection to lack of inventive step. Moreover, in conflict with decision W 8/91 of 26 February 1992, the ISA had failed to explicitly explain the reasons why claims **dependent** on claim 1 had been objected on the ground of lack of unity. Also for that reason the payment of seven additional search fees was unjustified. Moreover, account had not been taken of decision G 1/89 (OJ EPO 1991, 155) according to which objections to an *a posteriori* lack of unity should only be raised in clear cases.

The applicants submitted that the technical problem solved by the invention was the provision of means for the production of equine herpesviruses with defined specificities, the solution thereto relying on the cloning of the genome of equine herpesviruses in BAC-vector. Surprisingly and advantageously, such EHV-BACs

allowed the specific inactivation of glycoproteins and were appropriate for medical treatment of horses and embryos thereof (*in utero* treatment).

Document D1 which had been correctly classified by the ISA as a A-document represented only state of the art without any relevance; in particular equine herpesviruses were not referred to therein. As regards document D2, the other document cited in the invitation to pay additional search fees, it related not to EHVs but to a Marek's disease virus strain.

As referred to on page 4 of the application, in order to achieve the successful preparation of EHV-BAC vectors the applicants had to overcome difficulties (referred to on page 4, lines 25 and 26 of the application) which were not predicted in the state of the art. The exercise of inventive skill had been necessary to overcome those difficulties.

VI. On 17 March 2003, the ISA transmitted the International Search Report, which had been established for the whole set of claims.

VII. On the same date, the ISA communicated to the applicants the results of its review under Rule 40.2(e) PCT and ordered the refund of three of the seven additional search fees as "*after performing the additional search, the search officer [had] found that it did not request a major effort for inventions 6-8 over inventions 1-5*". However, the presence of eight separate groups of inventions and, consequently, the need for the payment of the already paid other four additional search fees was confirmed. The technical

problem to be solved was seen as being the provision of specific EHV vaccines and document D2 was considered to represent the closest state of the art.

Document D2 stated that "*because one-step deletion of an essential MDV-1 gene in E. coli was possible, the system was shown to be of advantage for analysis of essential and nonessential MDV-1 genes and may serve as a tool for production of biologically safe modified live virus and/or DNA vaccines*".

It was considered that the skilled person in search of a specific vaccine for another member of the alphaherpesviridae subfamily of the herpesviridae family, namely EHV, would have turned to document D2 and used the method described therein. The same incentive was said to be found also in " *Wolfram Brune et al, TIG, Vol. 16, No. 6, June 2000, Pages 254 to 259* (referred to thereafter as document D3).

Since cloning of an EHV genome as a BAC was not considered to involve an inventive step, two groups of inventions were to be distinguished:

- the genome of an EHV strain cloned as a BAC and related inventions (see **group (1)** of inventions; section III, *supra*); and

- the genome of an EHV strain cloned as a BAC, having a glycoprotein deleted, alone or in combination with one or more of the others and related inventions (see **group (5)** of inventions; section III, *supra*).

Since different serotypes of EHV were known, four additional inventions were to be distinguished:

- the genome of an EHV strain cloned as a BAC, where EHV was EHV-1 and related inventions (see **group (2)** of inventions; section III, *supra*);

- the genome of an EHV strain cloned as a BAC, where EHV was EHV-4 and related inventions (see **group (3)** of inventions; section III, *supra*);

- the genome of an EHV strain cloned as a BAC, where EHV was EHV-1, further having a glycoprotein deleted, alone or in combination with one or more of the others and related inventions (see **group (6)** of inventions; section III, *supra*); and

- the genome of an EHV strain cloned as a BAC, where EHV was EHV-4, further having a glycoprotein deleted, alone or in combination with one or more of the others and related inventions (see **group (7)** of inventions; see section III, *supra*).

Finally, since different strains of EHV-1 serotype, including strain RacH, were known, two additional inventions were to be distinguished:

- the genome of an EHV strain cloned as a BAC, where EHV was EHV-1 strain RacH and related inventions (see **group (4)** of inventions; see section III, *supra*);

– the genome of an EHV strain cloned as a BAC, where EHV was EHV-1 strain RacH, further having a glycoprotein deleted, alone or in combination with one or more of the others and related inventions (see **group (8)** of inventions; see section III, *supra*).

The applicants were invited to pay within one month the protest fee.

VIII. The protest fee was paid by the applicants on 15 April 2003.

## Reasons for the Decision

1. The protest is admissible.

2. The essence of the objection to lack of *a posteriori* unity of invention by the ISA is that, because prior art document D2 discloses a BAC vector comprising the entire genome of a Marek's disease virus (a member of the alphaherpesviridae subfamily of herpesviridae) and also a mutant BAC clone with deletion of the gene for glycoprotein B, the skilled person in search of a specific vaccine for another member of the alphaherpesviridae subfamily, namely EHV, would have cloned an EHV genome as a BAC. Thus, as this involves no inventive step, no general inventive concept links the different groups of inventions, a number of serotypes and strains of EHV being known in the art. In the ISA's view the same conclusion is derivable in the light of documents D1 and D3.

3. The reasoning to be applied, when assessing whether, in a group of inventions claimed in one and the same international application, the inventions are so linked as to form a single general inventive concept as referred to in Rule 13.1 PCT, has to rely on the provision as set forth in Rule 13.2 PCT, according to which, **there shall be a technical relationship among those inventions involving one or more of the same or corresponding "special technical features"**, ie those features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

4. In the present case, the claims directed to bacterial artificial chromosome vectors can be arranged into two main groups of embodiments: the first is that of the claims relating to BAC vectors comprising the **entire** genome of an EHV strain (see claim 1, which refers generally to an EHV strain, and dependent claims 2 to 5, which refer to specific EHV embodiments). The second group of embodiments is that of the claims relating to BAC vectors comprising the genome of an EHV strain lacking one or more given glycoproteins (see claims 1 to 16), a feature which according to the description (see page 3, lines 16 to 24 and page 11, lines 7 to 20) derives from **the deletion of one or more of the corresponding genes encoding a glycoprotein**. All the remaining claims refer essentially back to either one of these two groups of embodiments(see section I, *supra*).

5. A first question to be answered is **whether there exists between these two groups of embodiments of the invention a technical relationship involving one or**

**more of the same or corresponding technical features that define a contribution which each of the claimed embodiments of the invention, considered as a whole, makes over the prior art**.

6. The prior art to be taken into consideration is represented by documents D1, D2 and D3, the only documents cited by the ISA in support of its reasoning. Document D3 is a review which acknowledges (see page 255) that the strategy of cloning an entire viral genome as a BAC has been adopted for four herpesviruses, namely the **Epstein-Barr virus**, **human simplex virus**, **pseudorabies virus** and **human cytomegalovirus**. D1 is a further review which provides (see Table 1 on page 12) a list of the seven herpesvirus genomes known to the authors as having successfully been cloned as bacterial artificial chromosomes in E. coli, said list comprising, in addition to the four viruses referred to in document D3, three further viruses, namely the **mouse cytomegalovirus**, **murine gammaherpesvirus 68** and **guinea pig cytomegalovirus**. Document D2 describes the cloning of the complete genome of one strain of **Marek's disease virus**, which is also a herpesvirus of the alphaherpesviridae subfamily.

7. None of the three documents makes reference to equine herpesviruses. Thus, there is no novelty objection which could have opened the way to an *a posteriori* lack of unity.

8. All the claimed embodiments of the invention rely on vectors the generation of which primarily relies on the application of BAC technology to equine herpesviruses which gives rise to BAC vectors comprising the entire

genome of an EHV strain, from which subsequently one or more genes encoding a glycoprotein can be deleted. As there was no prior art disclosure of the application of such technology to equine herpesviruses (see point 7, *supra*) it can be said that this has been contributed to the art for the first time by the present application. This constitutes the single general concept of the invention. Whether or not such contribution has any inventive merit is something which should be assessed during the further substantive examination of the case. Fact is that the application of BAC technology to EHV establishes a technical relationship among the various embodiments within the concept and, thus, may be seen as "the special technical feature" which links all of them together in the sense of Rule 13.2 PCT.

9. For the foregoing reasons, the embodiments of the invention to which the 28 claims are directed are to be regarded as being linked to each other within a single general inventive concept as required in Rule 13.1 PCT Therefore, the invitation to pay seven additional search fees, three of them having been later reimbursed, was not justified.

**Order**

**For these reasons it is decided that:**

1. Refund of the four additional search fees is ordered.

2. The protest fee shall be refunded.

The Registrar: The Chairman:

A. Wolinski L. Galligani