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**Datasheet for the decision  
of 24 June 2014**

**Case Number:** T 0111/10 - 3.3.02

**Application Number:** 97909428.1

**Publication Number:** 0934531

**IPC:** G01N33/68, G01N33/569,  
C12Q1/68, A61K31/70

**Language of the proceedings:** EN

**Title of invention:**  
DIAGNOSIS OF SPONGIFORM ENCEPHALOPATHY

**Patent Proprietor:**  
D-Gen Limited

**Opponent:**  
Prionics AG

**Headword:**  
Diagnosis of spongiform encephalopathy/D-GEN

**Relevant legal provisions:**  
EPC Art. 123(2), 114(2), 56  
RPBA Art. 13

**Keyword:**  
Main request - added subject-matter (yes)  
Auxiliary request 1 - late-filed and not clearly allowable  
Auxiliary request 2 - reformatio in peius  
Auxiliary request 3 - inventive step (yes)

**Decisions cited:**  
G 0001/99, T 1979/11, G 0009/91, G 0009/92

**Catchword:**

Prohibition of reformatio in peius: see reasons 4.3



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Case Number: T 0111/10 - 3.3.02

**D E C I S I O N**  
**of Technical Board of Appeal 3.3.02**  
**of 24 June 2014**

**Appellant:** Prionics AG  
(Opponent) Wagistrasse 27a  
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**Representative:** Meissner, Bolte & Partner GbR  
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**Respondent:** D-Gen Limited  
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**Representative:** Potter Clarkson LLP  
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**Decision under appeal:** **Interlocutory decision of the Opposition  
Division of the European Patent Office posted on  
23 November 2009 concerning maintenance of the  
European Patent No. 0934531 in amended form.**

**Composition of the Board:**

**Chairman** U. Oswald  
**Members:** T. Sommerfeld  
R. Cramer

## Summary of Facts and Submissions

- I. European patent No. 934 531, based on European patent application No. 97909428.1, which was filed as an international patent application published as WO 1998/016834, was granted with 15 claims.

Claim 1 as granted read as follows:

"1. A method of typing a sample of a prion or spongiform encephalopathy disease the method comprising comparing and identifying similar physiochemical properties of the sample with a standard sample of known PrP<sup>Sc</sup> type, wherein the physiochemical properties are the sizes and ratios of distinct PrP<sup>Sc</sup> glycoforms."

Independent claim 10 as granted read as follows:

"10. A method for identifying infection in an animal and/or tissue of bovine spongiform encephalopathy the method comprising providing a prion protein from an animal and/or tissue sample and identifying that said prion protein can be **characterized by** having three distinct bands on an electrophoresis gel following proteinase K digestion, the bands comprising i) a band of highest molecular weight in the greatest proportion, ii) a band of lowest molecular weight in the lowest proportion, and iii) a band with a molecular weight between i and ii and of a proportion between i and ii, and **characterized by** having substantially similar glycoform proportions as bovine spongiform encephalopathy."

- II. Opposition was filed against the granted patent, the opponent requesting revocation of the patent to the extent of granted claims 1 to 13, on the grounds of

lack of novelty and inventive step (Articles 54(2) and 56 EPC in combination with Article 100(a) EPC).

- III. During the proceedings before the opposition division, the patent proprietor requested that the opposition be rejected and the patent maintained as granted (main request) or alternatively according to the first, second or third auxiliary request filed with letter of 17 March 2008.
- IV. The documents cited during the proceedings before the opposition division and the board of appeal include the following:
- D1 Kascsak et al. 1986, J. Virol. 59(3), 676-683
  - D2 Oberdieck et al. 1994, Arch. Virol. 136, 99-110
  - D4 Beekes et al. 1995, J. Gen. Virol. 76, 2567-2576
  - D5 Foster et al. 1993, Veterinary Record 133, 339-341
- V. By an interlocutory decision pronounced at oral proceedings on 20 May 2008 and posted on 23 November 2009, the opposition division decided that the patent be maintained in amended form on the basis of the third auxiliary request filed with letter of 17 March 2008 (Articles 101(3)(a) and 106(2) EPC).
- The opposition division considered that claim 1 according to the main request (claims as granted) and to the first and second auxiliary requests lacked novelty over D1, while the claims of the third auxiliary request were both novel and inventive.
- VI. The opponent (hereinafter appellant) lodged an appeal against that decision, requesting that the decision be set aside and the patent revoked in its entirety. With the statement of the grounds of appeal, the appellant

argued that claims 1 and 10 as maintained by the opposition division lacked an inventive step.

- VII. The patent proprietor (hereinafter respondent) filed a response to the appellants' grounds of appeal, requesting that the appeal be dismissed and the patent be maintained in the form upheld by the opposition division (main request) or, alternatively, according to auxiliary requests 1 to 12 filed with the letter of reply. The respondent further requested oral proceedings as an auxiliary measure.
- VIII. Summons for oral proceedings before the board were issued, scheduling oral proceedings for 24 June 2014.

As an annex to the summons to oral proceedings, the board issued a communication pursuant to Article 15(1) RPBA, summarising the situation and expressing a detailed preliminary opinion concerning Articles 123(2) and 84 EPC in respect of the amendments made to the granted claims.

- IX. With letter dated 23 May 2014, the respondent submitted a new main request (corresponding to the claims as maintained by the opposition division), auxiliary request 1 (corresponding to the claims as granted) and auxiliary request 2 (corresponding to auxiliary request 6 as filed with the reply to the grounds of appeal) to replace the requests on file.
- X. Oral proceedings before the board took place on 24 June 2014 as scheduled.

During the oral proceedings, the respondent filed a further claim request as first auxiliary request, and requested that the previous first and second auxiliary

requests (filed with letter of 23 May 2014) be renumbered as second and third auxiliary requests, respectively.

Claim 1 of the **main request** (claims as maintained by the opposition division) differs from granted claim 1 as follows (insertions underlined, deletions struck through):

"1. A method of typing a sample of ~~a prion or~~ bovine spongiform encephalopathy or Creutzfeld-Jakob disease the method comprising comparing and identifying similar physiochemical properties of the sample with a standard sample of known PrP<sup>Sc</sup> type, wherein the physiochemical properties are the sizes and ratios of distinct PrP<sup>Sc</sup> glycoforms."

Claim 1 of the **first auxiliary request** differs from granted claim 1 as follows:

"1. A method of identifying ~~typing~~ a sample of ~~a prion or~~ bovine spongiform encephalopathy or typing a sample of Creutzfeld-Jakob disease the method comprising comparing and identifying similar physiochemical properties of the sample with a standard sample of known PrP<sup>Sc</sup> type, wherein the physiochemical properties are the sizes and ratios of distinct PrP<sup>Sc</sup> glycoforms."

The **second auxiliary request** consists of the claims as granted.

In the **third auxiliary request**, granted claims 1 to 9 as granted have been deleted, claim 1 being identical to granted claim 10.

XI. The appellant's submissions, in so far as relevant to the present decision, may be summarised as follows:

*Main request - added subject-matter*

A method for typing bovine spongiform encephalopathy (BSE) had no basis in the application as filed. In contrast to Creutzfeld-Jakob disease (CJD), for which the application identified types 1, 2, 3, 4 and 5, there were no different types identified for BSE. The passage on page 11, lines 12 to 15 was not supported by any data and referred only to transmission of BSE to wild-type mice, in contrast to CJD which occurred in humans.

*First auxiliary request - admissibility*

This request did not *prima facie* comply with Articles 123(2) and (3), 54(2) and 56 EPC. There was no basis for a method of identifying BSE with the particular combination of features as claimed (Article 123(2) EPC). Identifying BSE was broader in scope than typing BSE (Article 123(3) EPC), even considering the scope of the granted claims as a whole.

*Second auxiliary request - admissibility*

This request should not be admitted because it violated the principle of prohibition of *reformatio in peius*. G 1/99 related to an exceptional case; exceptions however should be interpreted very narrowly. T 1979/11 was a different situation in that the proprietor of the patent had had no possibility to file an appeal, since its main request had been allowed. In the present case, however, the patent proprietor could have appealed and returned to the main request.



*Third auxiliary request - inventive step*

Either D1 or D4 could be considered the closest prior art. D4's abstract disclosed a method for routine diagnosis of BSE and CJD; page 2569, left column, second paragraph taught that Western blot was used for determining BSE and page 2569, right column, penultimate line referred to a "characteristic 3-band pattern". Prompted by the disclosure of D1 or D4, the skilled person would look into D2 to find the characteristic 3-band pattern for BSE of D2's figure 2 (C1 lane). Document D5 was not relevant for the third auxiliary request, because the claims were directed to identifying infection rather than to typing of prion diseases.

- XII. The respondent's arguments, in so far as relevant for the present decision, may be summarised as follows:

*Main request - added subject-matter*

A basis for the amendments could be found in the following passages of the application as filed: paragraph bridging pages 8 and 9; page 10, lines 5 to 26; page 11, lines 12 to 15; page 12, section "Discussion"; page 26, lines 23 to 26.

According to the application, typing of BSE did not require identification of different groups of BSE; instead, it meant identifying a prion disease as being BSE and not another prion disease.

Page 11, lines 12 to 15 comprised an explicit disclosure for the combination of BSE and assessing sizes of the glycoforms.

*First auxiliary request - admissibility*

This claim request was submitted as a direct response to a new line of argumentation by the appellant, which had only been put forward at oral proceedings. Moreover it addressed the objections under Articles 123(2) and 84 EPC put forward by both the board and the appellant. For Article 123(3) EPC, the patent as a whole had to be considered: granted claim 10 was also directed to a method for identifying BSE and thus there was no broadening of scope. As regarded Article 123(2) EPC, a basis could be found on page 1, first paragraph. If claim 1 of the main request was considered not to fulfil Article 123(2) EPC due to the appellant's interpretation of "typing", then claim 1 of this request necessarily complied with Article 123(2) EPC.

*Second auxiliary request - admissibility*

This request had been submitted as a direct response to objections raised by the board. There was no violation of the prohibition of *reformatio in peius*, because the present case fell within the exceptions foreseen by decision G 1/99 (headnote), as confirmed by T 1979/11. Whether or not the proprietor could have appealed was not relevant for the criteria in G 1/99 or T 1979/11; the only criteria were whether the patent was incorrectly maintained by the opposition division and the patent would otherwise have to be revoked (G 1/99, headnote).

*Third auxiliary request - inventive step*

The claimed method was explicitly directed to detecting whether there was a BSE infection rather than a prion infection in general. There was no motivation to

combine D4 or D1 with D2 because the purpose of D2 was not to identify types of prion diseases. Instead, D2's purpose was to look for antibodies to distinguish normal and pathological prion isoforms (page 108, final paragraph under "Discussion"); page 106, penultimate paragraph stated that proteinase K treatment was not needed if appropriate antisera were used. Moreover, D2 did not recognise any significance for the particular band pattern. The reference to a "characteristic 3-band pattern" in D4 (page 2569) was only in relation to the immunoblot of figure 1b; figure 7 on the other hand did not show any characteristic 3-band pattern. The claimed method was a very important development, as highlighted by D5 (page 340 under "Discussion"), because it allowed to identify BSE even when it had crossed the species barrier.

XIII. The appellant (opponent) requested that the decision under appeal be set aside and that the European patent No. 0934 531 be revoked to the extent to which it was opposed.

The respondent (patent proprietor) requested that the appeal be dismissed (main request) or alternatively that the decision under appeal be set aside and the patent be maintained in amended form according to auxiliary request 1 filed during the oral proceedings or auxiliary requests 2 or 3 filed with the letter of 23 May 2014.

## **Reasons for the Decision**

1. The appeal is admissible.

2. Main request: Article 123(2) EPC

2.1 The present opposition did not cite Article 100(c) EPC as a ground of opposition. However, as confirmed by the Enlarged Board of Appeal in its decision G 9/91 (OJ 1993, 408, reasons 19), in case of amendments of the claims or other parts of a patent in the course of opposition or appeal proceedings, such amendments are to be fully examined as to their compatibility with the requirements of the EPC.

2.2 The main request corresponds to the claims as maintained by the opposition division, and differs from the claims as granted in that "a prion or spongiform encephalopathy disease" has been replaced by "bovine spongiform encephalopathy or Creutzfeldt-Jakob disease" in claim 1. As basis for the amendments in relation to the granted claims, the respondent indicated a number of passages in the description, *inter alia* Figures 4, 5a, 5b and 8a, as well as page 10, lines 5 to 26; page 11, lines 12 to 15; page 12, section "Discussion"; page 26, lines 23 to 26.

2.3 The board comes to the conclusion that there is no basis in the application as filed for the combination of features "typing a sample of bovine spongiform encephalopathy" and "comparing and identifying similar (...) sizes (...) of distinct PrP<sup>Sc</sup> glycoforms". Of the above-mentioned passages, the only passage wherein glycoform size is mentioned in the context of bovine spongiform encephalopathy (BSE) is the passage on page 11, lines 12 to 15. This passage however is in the very specific context of transmission of BSE to wild-type mice, wherein the band sizes of PrP were shifted to a lower molecular mass as compared to type 2 Creutzfeldt-Jakob disease (CJD) transmissions. There is

no disclosure in the application as filed allowing to generalise this disclosure to the claimed subject-matter. In addition, although the application discloses typing of a prion disease in the sense of identifying whether said prion disease is CJD 1, 2, etc. or BSE, it does not disclose typing of a BSE disease, which would imply identifying different types of BSE disease.

2.4 Accordingly, claim 1 of the main request does not comply with the requirements of Article 123(2) EPC.

3. First auxiliary request: Admissibility

3.1 This request was only submitted during oral proceedings before the board. Hence its admission is at the board's discretion (Article 114(2) EPC), governed by the principles laid down in Article 13 RPBA.

3.2 The board notes that, despite the fact that the appellant's arguments under Article 123(2) EPC were only presented at oral proceedings, the same objection - albeit with a slightly different argumentation - had already been raised by the board in writing. Hence, the respondent had already had an opportunity to address it (Article 12(1)(c) RPBA). Moreover, this late-filed request not only *prima facie* fails to overcome the deficiencies of the main request under Article 123(2) EPC (*supra*) but also introduces amendments which raise new issues under Article 123(2) EPC. Indeed, it is not readily apparent where any basis is to be found for a method for identifying BSE which comprises the combination of features as claimed.

3.3 As such, the first auxiliary request is *prima facie* not allowable under Article 123(2) EPC and the board thus

exercises its discretion under Article 13 RPBA not to admit it into the proceedings.

4. Second auxiliary request: Admissibility

4.1 This request - which consists of the set of claims as granted - was submitted during the written proceedings as a response to the objections under Articles 123(2) and 84 EPC raised in the board's communication sent under Article 15(1) RPBA.

4.2 This set of claims is broader in scope than the set of claims as maintained by the opposition division (present main request). Allowing such a claim set would thus put the opponent and sole appellant in a worse situation than if it had not filed an appeal, contrary to the principles of prohibition of *reformatio in peius* summarised by the Enlarged Board of Appeal in G 9/92 (OJ 1994, 875; headnote II). It follows that such a claim set can only be admitted in exceptional circumstances and following the principles developed in G 1/99 (OJ EPO 2001, 381).

G 1/99, headnote and point 15 of the reasons, states that, where the patent as maintained in amended form would otherwise have to be revoked as a direct consequence of an inadmissible amendment held allowable by the opposition division, the non-appealing patent proprietor/respondent has three possibilities for amendments: the first of these possibilities consists of the addition of further limiting features to the claim, while the last of these possibilities consists of deleting the inadmissible amendment maintained by the opposition division, within the limits of Article 123(3) EPC.

4.3 The board observes that the exceptional possibilities for amendment foreseen by G 1/99 (*supra*) only apply if the patent would otherwise have to be revoked, i.e. provided that, in view of the prohibition of *reformatio in peius*, the patent proprietor did not have any other possibility of amendment which would allow rescue of even part of the opposed patent. In the present case however such a possibility existed: the respondent could have simply deleted the alternative "bovine spongiform encephalopathy" from claim 1. Although this would have resulted in a restriction of scope, it cannot be considered unduly or inequitable for a patent proprietor who, having not appealed, cannot from the outset expect to get more than what was already maintained by the opposition division. It is clear from G 1/99 (see point 15 of the reasons) that the principle of *reformatio in peius* has to be respected by the boards of appeal and that any exception to this principle should be construed narrowly.

4.4 As regards the respondent's arguments based on decision T 1979/11 of 28 June 2013 it is noted that in the underlying case an amendment restricting rather than broadening the scope was apparently not available. Moreover, the broadening of scope was a reaction by the respondent/patentee to an objection by the appellant/opponent which had been raised for the first time in the statement of the grounds of appeal; the board in T 1979/11 thus concluded that it would not be equitable to allow the appellant/opponent to present a new attack and at the same time to deprive the proprietor/respondent of a means of defence (reasons 2.1). In the present case, however, there has been no new attack from the appellant but rather an objection raised by the board and then also taken up by the appellant.

4.5 The second auxiliary request is thus not admitted into the proceedings.

5. Third auxiliary request

5.1 Admissibility

The third auxiliary request was filed in due time as sixth auxiliary request with the respondent's reply to the grounds of appeal (Article 12(1)(b) and (2) RPBA), and then re-filed as second auxiliary request with the respondent's reply to the board's communication (Article 12(1)(c) RPBA) and finally re-numbered at oral proceedings. It is furthermore considered as a *bona fide* attempt to overcome the objections on file. The appellant has made no objections to the admission of this request into the appeal proceedings; the board also has none. The third auxiliary request is thus admitted into the proceedings.

5.2 Articles 123(2), 84, 83 and 54 EPC

All claims of this request are identical to granted claims and thus Article 84 EPC is not open for discussion. Moreover, since the patent proprietor (respondent) has not agreed to the introduction of fresh grounds of opposition, Articles 123(2) and 83 EPC, which were not invoked as grounds of opposition, are not open for discussion either (G 9/91 *supra*, reasons 18). Lastly, no novelty objection has been raised against these claims and the board too is satisfied that the claimed subject-matter is novel.

5.3 Inventive step



- 5.3.1 The claimed subject-matter is directed to methods of diagnosing BSE, which involve immunoblotting of prion (PrP)-containing samples, previously treated with proteinase K. Identification of a specific pattern of abundance of PrP glycoforms - with decreasing band intensity from the higher to the lower molecular weight glycoforms - makes it possible to distinguish BSE from other prion diseases, even in cases of BSE transmission to other species. As pointed out by the respondent, such a method is of relevance for epidemiological studies, overcoming difficulties described in the prior art (D5, page 340, right column, first four lines of "Discussion").
- 5.3.2 Documents D1 and D4 were considered by both parties as equally suitable starting points for the discussion of inventive step. Both documents disclose Western blotting of PrP-containing samples as a method of diagnosis for prion diseases. However, document D1 is concerned with establishing Western blot profiles for different scrapie strains (i.e. typing of scrapie), while D4 is directed at diagnosing prion diseases in general, including BSE (see abstract). And although many of D4's experimental procedures involve scrapie samples, Figure 7 of D4 is specifically directed to detection of BSE. Hence, document D4 which is directed to the same purpose as claim 1 of the third auxiliary request - namely identification of BSE infection - is the closest prior art.
- 5.3.3 D4 discloses Western blot mapping of disease-specific amyloid in various animal species and humans with transmissible spongiform encephalopathies (TSE), see title. The method involves treatment of the samples with proteinase K, followed by SDS-disc PAGE

(electrophoresis) and then immunoblotting (page 2569, left column, second and third paragraphs). D4 further discloses that "in the immunoblot, (...), a characteristic three-band pattern in the molecular mass range 20-30 kDa can be clearly visualized" (page 2569, right column, last sentence). The difference to claim 1 is thus that a specific pattern of band intensities for BSE is not disclosed, as, in fact, D4 does not analyse differences in band intensities at all.

5.3.4 The technical problem can thus be formulated as the provision of a method for identification of infection with BSE, and the solution is the method as claimed. In view of the examples of the patent, the board is satisfied that the problem has been plausibly solved.

5.3.5 The board acknowledges that document D4 clearly teaches immunoblotting of proteinase K-treated samples as suitable for the routine diagnosis of TSE in non-experimental hosts such as sheep, cows or humans, and discusses the advantages of the method (page 2574, left column, third full paragraph). The skilled person is thus prompted by D4 to use this method for the diagnosis of TSE disease in general. By using this method, the skilled person would identify the typical three-band pattern, which is characteristic for TSE (D4, page 2569, right column, last sentence; D2, page 103, lines 9 to 12). However, there is no hint in D4 that the analysis of band intensities for the different-sized glycoforms may allow to distinguish different prion diseases, let alone that the identification of a specific 3-band pattern with decreasing intensity from the higher to the lower molecular-weight band, as in claim 1, makes it possible to distinguish BSE from other prion diseases.

- 5.3.6 The only document on file which provides a disclosure of the claimed band pattern in a sample of BSE is document D2: in figure 2 (a photograph of an immunoblot for PrP<sup>Sc</sup>), such a band pattern is apparent - by simple visual inspection - on lane C1. However, there is no recognition in D2 that this band pattern, which is not further analysed or discussed in D2, is a specific band pattern for BSE which can be used to distinguish this TSE disease from other TSE diseases. Indeed, D2 is not at all concerned with the identification of band patterns for prion diseases but instead aims at providing antisera which recognise PrP<sup>Sc</sup> - preferably even in the absence of a step of proteinase K treatment (D2, page 106, penultimate paragraph). The skilled person would also not be in a position to conclude, solely on the basis of D2, that such a band pattern, seen once for a sample of BSE, was reproducible and of any significance at all. Hence, even if the skilled person, seeking to develop a method for detecting BSE infection, considered the combination of D4 with D2 - which is questionable - he would not arrive at the solution to the problem.
- 5.3.7 Similarly, the solution is also not obvious when starting from D1. Although D1 recognises that different Western blot profiles may correspond to infection with different scrapie strains, it does not teach or suggest that Western blot profiles may also distinguish prion diseases of different origins. Again, combination with D2 would not lead to the claimed solution.
- 5.3.8 Claim 1 of the third auxiliary request thus involves an inventive step. The same applies to dependent claims 2 to 4.

5.3.9 Claims 5 and 6 are identical to granted claims 14 and 15 which were not part of the extent to which the patent was opposed as defined by opponent's statement under Rule 76(2)(c) EPC. This subject-matter is therefore not the subject of the opposition proceedings and consequently also not of the present appeal proceedings.

## Order

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

1. The decision under appeal is set aside.
2. The case is remitted to the department of first instance with the order to maintain the patent in amended form on the basis of auxiliary request 3, filed as auxiliary request 2 with the letter of 23 May 2014, and a description to be adapted thereto.

The Registrar:

The Chairman:



N. Maslin

U. Oswald

Decision electronically authenticated