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**Datasheet for the decision
of 24 January 2019**

Case Number: T 0857/14 - 3.3.01

Application Number: 00947934.6

Publication Number: 1190260

IPC: G01N33/86

Language of the proceedings: EN

Title of invention:

DETECTION OF VON-WILLEBRAND FACTOR (VWF) ACTIVITY

Patent Proprietor:

K.U. LEUVEN RESEARCH & DEVELOPMENT

Opponent:

Siemens Healthcare Diagnostics Products GmbH

Headword:

Detection of von-Willebrand factor/K.U. LEUVEN

Relevant legal provisions:

EPC Art. 100(c), 56
RPBA Art. 12(4)

Keyword:

Grounds for opposition - added subject-matter (yes)

Inventive step - (no)

Late-filed request - request could have been filed in first instance proceedings (no); admitted (yes)

Decisions cited:

Catchword:



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Case Number: T 0857/14 - 3.3.01

D E C I S I O N
of Technical Board of Appeal 3.3.01
of 24 January 2019

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Decision under appeal: **Interlocutory decision of the Opposition
Division of the European Patent Office posted on
10 February 2014 concerning maintenance of the
European Patent No. 1190260 in amended form**

Composition of the Board:

Chairman L. Bühler
Members: T. Sommerfeld
J. Molina de Alba

Summary of Facts and Submissions

I. European patent No. 1190260 is based on application No. 00947934.6, which was filed as international application and published as WO 01/02853. The patent is entitled "Detection of von-Willebrand factor (vWF) activity" and was granted with 36 claims.

Claim 1 as granted reads as follows:

"1. A method for detecting von-Willebrand disease (vWD) comprising the steps of:

a) detecting von-Willebrand Factor (vWF) activity in a sample comprising a soluble form or portion of glycoprotein Ib(α) (GPIb(α)) and ristocetin or a fragment thereof or botrocetin capable of inducing binding of vWF to GPIb(α),

b) determining the amount of vWF-antigen in said sample,

c) determining the ratio between vWF-activity and vWF-antigen for said sample,

d) comparing the under (c) obtained ratio to the range of ratios established as normal range."

II. Opposition was filed against the granted patent, the opponent requesting revocation of the patent in its entirety on the grounds of lack of inventive step (Article 56 EPC and Article 100(a) EPC), lack of sufficiency of disclosure (Article 100(b) EPC) and added subject-matter (Article 100(c) EPC).

III. The documents cited during the proceedings before the opposition division and the board of appeal include the following:

- D1 Veyradier A et al., Int. J. Clin. Lab. Res. 1998, 28: 201-210
- D2 Hoylaerts MF et al., Biochem. J. 1995, 306: 453-463
- D4 Murata M et al., J. Biol. Chem. 1991, 266(23): 15474-15480
- D5 Eller T, Hämostaseologie 1994, 7: 534-540
- D9 Murdock PJ et al., Thromb. Haemost. 1997, 78: 1272-1277
- D14 López JA, Blood Coagul. Fibrin. 1994, 5: 97-119
- D15 Second Declaration of Dr. Hans Deckmyn
- D15-O WO 92/16225

IV. By an interlocutory decision announced at the oral proceedings, the opposition division decided that the patent could be maintained in amended form on the basis of the third auxiliary request filed during the oral proceedings (Articles 101(3)(a) EPC).

The opposition division considered that the claim sets according to the main request (claims as granted) and to the first and second auxiliary requests added subject-matter contrary to Article 123(2) EPC.

V. Both the patent proprietor and the opponent lodged an appeal against that decision.

With its statement of grounds of appeal, the appellant-patent proprietor requested that the patent be maintained as granted (main request), or, alternatively, according to the first to sixth auxiliary requests, all filed with the grounds of appeal.

With its statement of grounds of appeal, the appellant-opponent requested that the decision be set aside and the patent revoked in its entirety.

- VI. Both appellants replied to each other's statement of grounds of appeal. With its reply, the appellant-patent proprietor submitted new auxiliary requests 1 to 13 to replace the previous auxiliary requests on file.
- VII. Summons for oral proceedings before the board were issued. In a subsequent communication, the board provided its preliminary opinion on some issues.
- VIII. The appellant-patent proprietor replied by letter dated 26 November 2018 and submitted a new auxiliary request 7 to replace the auxiliary request 7 on file.
- IX. During the oral proceedings, the appellant-patent proprietor withdrew auxiliary requests 1 to 4, 6, 8, 9 and 11 to 13. At the end of oral proceedings the chairman announced the board's decision.

The **main request** consists of the claims as granted.

Auxiliary request 5 is identical to the auxiliary request which was considered allowable by the opposition division (then third auxiliary request). Claim 1 of auxiliary request 5 differs from claim 1 of the main request in that the following amendments have been made:

"1. A method for ~~detecting~~ discriminating between von-Willebrand disease (vWD) type 1 and type 2, the method comprising the steps of:
..."

Claim 1 of **auxiliary request 7** differs from claim 1 of auxiliary request 5 in that step (a) has been amended as follows:

"1. ...

a) detecting von-Willebrand Factor (vWF) activity in a blood, serum or plasma sample comprising assaying said sample in the presence of a soluble form or portion of recombinant glycoprotein 1b(α) (rGP1b(α))... capable of inducing binding of vWF to rGP1b(α), ..."

Claim 1 of **auxiliary request 10** differs from claim 1 of auxiliary request 5 in that the following features have been inserted:

"1. ...

a) detecting von-Willebrand Factor (vWF) activity in a sample comprising assaying said sample in the presence of a soluble form or portion...

...

wherein either said GP1b(α) is bound to a solid support by a specifically reacting anti-GP1b(α) antibody or a complex of vWF and GP1b(α) is bound to a solid support by a specifically reacting anti-GP1b(α) antibody."

- X. The appellant-patent proprietor's arguments, in so far as they are relevant to the present decision, may be summarised as follows:

Main request - Article 100(c) EPC

The method steps of claim 1 were disclosed in originally filed claim 23 (combined with originally filed claim 1). As to the claim preamble, the skilled person would understand that the application as filed disclosed a method of detection of von Willebrand

disease (vWD). Both steps (a) and (b) of the claimed method, directed to the measurement of von Willebrand factor (vWF) activity or antigen, respectively, were useful for classification of the vWD but of course also for detection of the disease; the last two steps allowed further classification. Hence, the method allowed the determination of whether the patient had the disease or not and was therefore suitable for diagnosis. This was also apparent from page 5, third paragraph; page 11, line 25 to page 12, line 4; page 2 (step (b)). The application explicitly taught on page 23, last paragraph, that the test of the invention could be used to diagnose vWD.

Auxiliary request 10 - admission

This request was filed with the reply to the opponent's grounds of appeal. Since the nature of the amendments was simple and it would have been immediately apparent which grounds of opposition were addressed and how, they could not have come as a surprise to the opponent. In fact, the amendment corresponded to what was stated as the preferred embodiment on page 8, paragraph 2, of the application. Because the opposition division had accepted that there was no need for restricting the claims further, filing this request had not been necessary before. As to the argument that the amendment raised clarity issues, this was not open to discussion since these features were already in the granted claims (4, 6, 7 and 8).

Auxiliary requests 5, 7 and 10 - Article 56 EPC

D1 was the closest prior art. It reviewed a number of assays, including the vWF ristocetin cofactor activity on page 203, last paragraph; in the last sentence of

this passage, it acknowledged problems with the assay, but it was apparent from page 204, first paragraph, that the solution to these problems was to perform the assay more carefully. Moreover, D1 also disclosed the collagen binding assay, which was a non-platelet-based alternative assay. D2, which was a mechanistic study that would not necessarily be combined with a clinical study such as D1, did not lead to the invention because it did not even hint or mention that its test could be useful in the context of vWD. Moreover, D2 used GP1b complex, not GP1b(α), and, in view of D14, it would not be expected that GP1b(α) would be equally functional. The suggestion that soluble GP1b(α) could also include the whole GP1b complex was not derivable from page 6 of the application, which made clear that only GP1b(α) subunits could be joint together. As to D4, it had been questioned in D15 that the soluble fragment of GP1b(α) could bind as described in D4.

The use of recombinant GP1b(α) as claimed in auxiliary request 7 further addressed the problem of assay variability. This was also shown in the application in Example 4, which demonstrated the reliability, repeatability and accuracy of the assay using recombinant protein (page 26, lines 15 ff). Contrary to GP1b(α) purified from natural sources (as was GP1b in D2), the recombinant protein was not variable in any way. The use of recombinant GP1b(α) was not disclosed in any assay of the art. D15-0 suggested the use of such a recombinant GP1b(α) fragment but did not back up this suggestion with tests, contrary to the patent, which also showed a correlation with the methods of the prior art (Example 3 and Figure 1; Example 4 and Figures 2a to d). Figures 5 and 6 showed that it worked in patients as well.

Regarding auxiliary request 10, although it was common general knowledge to bind antibodies to solid supports, a suggestion to bind GP1b(α) to the solid support via an antibody was nowhere in the prior art. This feature, however, allowed the assay to perform reliably, and was in fact required for the assay to work, as shown in D15. The skilled person trying to adopt D2's assay would not get a functioning assay and would have no pointer from the prior art on how to modify the assay so that it would work, let alone to use GP1b(α) antibodies. This was disclosed as the preferred embodiment in the application and was also exemplified in the examples, which demonstrated that it worked well.

- XI. The appellant-opponent's arguments, in so far as they are relevant to the present decision, may be summarised as follows:

Main request - Article 100(c) EPC

Granted claim 1 was directed to the detection of any form of vWD using any possible sample, by a method comprising four steps, including step (a), which was the measurement of vWF activity according to the method of the invention. This new assay for measuring vWF activity was in fact the core of the application as filed, as apparent from the originally filed claims. The application as filed did not clearly disclose that the method of the invention was indeed meant to diagnose vWD, nor was there an indication that the discriminating method could detect all vWD forms. As to page 23, this was part of Example 3, wherein the vWF activity was assayed in samples from patients known to have vWD; this example could not be generalised and was

not sufficient to broaden the diagnostic use as in the claim.

Auxiliary request 10 - admission

Claim 1 comprised two amendments in relation to claim 1 of auxiliary request 5, and there was no substantiation of the amendments, neither in the statement of the grounds of appeal nor in the reply. Only after the preliminary opinion did the patent proprietor provide an explanation of which grounds of opposition were addressed by the amendments. The amendments, which came from the description, raised new issues which had not been discussed before, in particular under Articles 123(2) and 84 EPC.

Auxiliary requests 5, 7 and 10 - Article 56 EPC

D1, a review about the different procedures to detect vWD, was the closest prior art. It disclosed different vWF activity tests, including the ristocetin cofactor activity test, which measured platelet agglutination in response to vWF. The difference was that step (a) of the claimed method made use of soluble GPIb(α) instead of platelet-bound GPIb(α). Although not shown in the application, it could be considered plausible that there was an improvement. The problem was thus the provision of an improved method for measurement of vWF activity. It was known at the priority date that the use of platelet-based assays was problematic: D2 (page 457, right column, third sentence of section "Specificity of ristocetin..."); D5 (page 538, middle column, lines 10 to 14); D9 (page 1272, left column, penultimate sentence and right column, last sentence before section "Materials and Methods"). There was thus motivation to provide alternative assays without

platelets. D2 disclosed a test making use of purified GP1b which was attached to a support and taught that its test had the advantage over the platelet-based tests in that it avoided unspecific reactions between ristocetin/botrocetin and other platelet proteins. Therefore, the skilled person would have recognised these advantages and would have combined the teaching of D2 with that of D1 to arrive at the claimed invention. The definition of soluble GP1b(α) in the application also encompassed the larger GP1b complex of D2, as was apparent from page 5, last paragraph, and page 6, last paragraph. Moreover, D4 taught that binding of GP1b(α) subunit was identical to binding to whole GP1b (page 15479, left column, second paragraph; abstract, first three sentences).

The application as filed did not disclose any advantage of using recombinant GP1b(α), as claimed in auxiliary request 7. Page 5, last paragraph to page 6 first and second paragraphs, disclosed many alternatives as to how GP1b(α) could be provided, and did not disclose any technical effect associated with this feature. Example 4, which was only one example with specific components (such as ELISA, binding antibody, GP1b(α) fragment), did not compare recombinant GP1b(α) with other sources. Nor was there any indication that any advantages would be linked to the use of the recombinant protein. The use of recombinant GP1b(α) was known in the prior art, also in an assay to detect vWF: D15-0, page 7, third paragraph.

Regarding auxiliary request 10, it was common general knowledge to attach antigens or other molecules to solid support either directly or with specific antibodies; accordingly, this was an equally suitable alternative from among others. Use of such anti-GP1b(α)

antibodies was in fact described in the application as filed as being one among other alternatives (page 7, last paragraph to page 8, second paragraph). There was no demonstration in the application as filed that this was an improvement over the prior art.

- XII. The appellant-patent proprietor requested that the decision under appeal be set aside and that the patent be maintained as granted (main request), or, alternatively, that the opponent's appeal be dismissed (auxiliary request 5 filed with the letter of 27 October 2014), or, alternatively, that the patent be maintained on the basis of the claims of auxiliary request 7 filed with the letter dated 26 November 2018, or, alternatively, of auxiliary request 10 filed with the letter dated 27 October 2014.

The appellant-opponent requested that the decision under appeal be set aside and that European patent No. 1190260 be revoked.

Reasons for the Decision

1. The appeals are admissible.
2. Main request (claims as granted): added subject-matter
 - 2.1 Claim 1 is directed to a method for detecting von-Willebrand disease (vWD) comprising steps (a) to (d) as defined in the claim (for the complete wording of the claim, see section I above).
 - 2.2 None of the originally filed claims was directed to a method for detecting von-Willebrand disease. The independent method claims of the application as filed

were directed to a method for detecting von-Willebrand factor (vWF) activity (claim 1) and a method for the discrimination between von-Willebrand disease (vWD) type 1 and type 2 (claim 23). Further independent claims were directed to uses (claims 24 to 28) and kits (claim 29). A method comprising steps (a) to (d) as claimed in granted claim 1 (with the exception of the alternative "botrocetin") is disclosed in originally filed claim 23 when read in combination with originally filed claim 1; however said method is, as mentioned above, for the discrimination between von Willebrand disease type 1 and type 2. Hence, none of the originally filed claims can provide any basis for a method with the purpose as claimed in granted claim 1.

2.3 The appellant-patent proprietor argued that it was clear from the whole application as filed that the method of the invention was directed to the detection of vWD; moreover, the claimed method included steps, such as steps (a) and (b), that were suitable not only for the classification of vWD but also for its detection. The following passages of the application as filed were indicated as basis for granted claim 1: pages 4 to 5; page 5, lines 12 to 19; page 3, lines 20 to 21; page 2, lines 26 to 30; page 11, line 25 to page 12, line 4; page 23, first sentence of last paragraph.

2.3.1 Except for the passage on pages 11 and 12, none of the indicated passages discloses a method with the steps as claimed; they either relate to the methods of the prior art or refer generally to an "assay system of the invention", without further defining the assay, or, being part of an example (page 23, see below), they refer to a specific assay which is encompassed in step (a) of the claim.

2.3.2 The passage on page 2 cited by the appellant-proprietor is part of the paragraph of lines 23 to 30, which discusses the prior art and states that "no single test is sufficiently robust to permit detection of all vWD variants" (lines 23 to 24). It then goes on to discuss the vWF:Ag assay (which corresponds to step (b) of the claimed method) and its shortcomings, concluding that it "will help detect all type 3, most type 1 and only some type 2 vWD patients". On the basis of this passage, the appellant-patent proprietor argued that, because the claimed method encompasses even additional steps involving detecting vWF activity (step (a)) and determining the ratio between vWF activity and vWF antigen (step (c)), it is certainly capable of detecting all three types of vWD. The board notes that, while this might be true, the passage itself still does not provide a clear and unambiguous disclosure of a method of diagnosis of vWD comprising the four steps as claimed.

2.3.3 Similarly, it is also not apparent how the passage on page 5, lines 12 to 19, should constitute any basis for granted claim 1. This passage refers to the "assay system of the present invention" but does not further define it by reference to the steps of granted claim 1. In fact, from the whole of the application, and also from page 5, lines 12 and 13, it is apparent that the assay of the invention relates to a method for detecting von Willebrand factor (vWF) activity, i.e. the assay of step (a) of granted claim 1; it does not include the further steps of the claimed method. Regarding the passage on page 5, second paragraph, stating that "The technical problem underlying the present invention was to provide improved means for a more reproducible and more precise test for von-Willebrand factor with a low inter- and intra-assay

variability", it is noted that this statement does not refer to diagnosis of vWD but rather to a "test for von-Willebrand factor". Again, this passage concerns step (a) of the claimed method only.

2.3.4 Likewise, the first sentence of the last paragraph of page 23 of the application as filed cannot provide any basis either. Although it indeed refers to diagnosis of vWD, it is in the context of a very specific embodiment of step (a) as claimed, namely the ELISA assay described in Example 3, as is clearly stated in the indicated sentence: "These data show that the ristocetin induced binding of vWF to GPIb, which is routinely tested in a platelet agglutination assay, can be reproducibly studied in an ELISA setup and that this test can be used to diagnose patients with vWD". Again, this passage does not refer to a method with the four steps as claimed.

2.3.5 Finally, the passage bridging page 11 (last paragraph) and page 12 (first paragraph) discloses a method with steps (a) to (d) as claimed, but again (as originally filed claim 23) it is in the context of a method for the discrimination between von Willebrand disease (vWD) type 1 and type 2 and not of a method for detection of vWD.

2.4 Granted claim 1 thus comprises added subject-matter and therefore the main request is not allowable for lack of compliance with Article 100(c) EPC.

3. Auxiliary request 5

3.1 This request is identical to the set of claims considered allowable by the opposition division. The purpose of the method has been amended in line with

originally filed claim 23, and hence the objection for added subject-matter discussed above in relation to the main request no longer applies.

Inventive step

3.2 The present patent is directed to "a method for detecting von-Willebrand factor (vWF) activity comprising assaying a sample in the presence of a soluble form or portion of glycoprotein Ib(α) (GPIb(α)) and ristocetin, or a functionally equivalent substance" (paragraph [0001]). A number of prior-art assays are discussed in paragraph [0003], in particular measurement of the vWF:Ag, which "provides good information on the absolute level of vWF present but no information on the quality of the vWF", and measurement of vWF activity by the vWF:ristocetin cofactor assay and the vWF:collagen binding assay. According to paragraph [0004], the current tests for von-Willebrand's disease are based on measurements of bleeding time, vWF antigen and vWF ristocetin cofactor activity (employing platelet aggregating activity in the presence of ristocetin). However, platelet-based assays have shortcomings, such as relatively poor sensitivity and reproducibility. The technical problem underlying the present invention is thus described as being "to provide improved means for a more reproducible and more precise test for von-Willebrand factor with a low inter- and intra-assay variability" (paragraph [0005]).

3.3 The presently claimed subject-matter corresponds to a particular embodiment of the invention, disclosed e.g. in paragraph [0025] of the patent, which makes use of the vWF activity detection method of the invention for discriminating between von Willebrand disease (vWD)

types 1 and 2. This discriminatory method is based on the fact that type 1 vWD patients are characterised by a normal ratio of vWF:RiCof (vWF activity) to vWF:Ag (vWF antigen), whereas in type 2 patients this ratio is below the reference or normal range; a reduction of vWF:RiCof activity is, accordingly, typical for type 2 patients (paragraph [0026]).

- 3.4 Document D1, which also discloses methods for the discrimination between vWD types, including types 1 and 2, is the closest prior art. According to the opposition division's decision, and not disputed by the parties, the difference to the claimed subject-matter is that the platelet-dependent vWF:RiCof-assay of D1 is replaced by an assay format using a soluble form or portion of GPIb(α), which is capable of binding to vWF. Although not demonstrated experimentally, the board considers that it is plausible in theory that the assay of the invention is more reproducible and more precise, with a low inter- and intra-assay variability, than the prior-art platelet-dependent vWF:RiCof-assays as stated in the patent in paragraph [0005]. The technical problem can thus be formulated as the provision of an improved method for discrimination between vWD types 1 and 2. The solution is the method as claimed, and the board is satisfied that the solution solves the technical problem.
- 3.5 It next has to be assessed whether the claimed solution involves an inventive step.
- 3.6 D1 discusses the (platelet-dependent) vWF ristocetin cofactor activity test and concludes that it is a "sensitive test, but its main limit is a poor interlaboratory reproducibility" (page 203, right column, last sentence). The lack of reproducibility and

precision of platelet-based assays was also known from other prior-art documents (D2, page 457, right column, third sentence of the section "Specificity of ristocetin..."; D5, page 538, middle column, lines 10 to 14; D9, page 1272, left column, penultimate sentence, and right column, last sentence before section "Materials and Methods"). Hence, the skilled person would be motivated to investigate ways to improve the reproducibility and precision of the vWF ristocetin cofactor activity test and would be prompted to provide alternative assays that were not dependent on the use of platelets. Such an assay is described in document D2 in the form of an ELISA test which makes use of a soluble form of GPIb (purified GPIb), i.e. a GPIb which is not on a platelet surface but rather bound to the solid phase of a microtiter plate (page 454, section "Studies of interaction between vWF and GPIb"). D2 teaches that its assay can be used to measure the vWF activity in a sample (page 456, section "Botrocetin-mediated vWF binding to GPIb", first sentence), with advantages over agglutination studies using platelets (page 457, section "Specificity of ristocetin-mediated vWF binding to GPIb", third sentence).

- 3.7 By combining the teachings of D1 and D2, the skilled person, motivated to provide an improved method to discriminate between vWD types 1 and 2, would thus have considered to replace the method of measurement of vWF activity used in D1 by a method making use of soluble GPIb (i.e. GPIb which is not attached to platelets). The board considers that, although D2 discloses the use of the whole GPIb complex rather than of the GPIb(α) subunit as in the method of the invention, such a further distinguishing feature does not contribute per se to inventive step because it was well known in the

prior art (as acknowledged in the application on page 3, lines 8 to 10) that the GP1b binding site for vWF resided in the GP1b(α) subunit. The skilled person would thus have arrived at the claimed subject-matter without inventive skill.

3.8 The appellant-patent proprietor essentially argued that the skilled person would not have considered using the method of D2 in the context of the claimed subject-matter because D2's method was merely an *in vitro* kinetics study with no clinical application, which did not use GP1b(α) but rather GP1b (a complex of at least four polypeptides). Being that the interaction of vWF with the glycoprotein 1b-IX complex (GP1b-IX), which includes two GP1b(α) subunits, two GP1b(β) subunits, two GPIX subunits and one GPV subunit (D14), is central to important processes in haemostasis and thrombosis *in vivo*, the skilled person would not expect that a GP1b(α) alone or a portion thereof would interact with vWF in the same manner as the GP1b-IX complex or even the purified GP1b complex of D2. Moreover, D2 did not assay patient samples but rather examined binding of known concentrations of purified vWF to the purified GP1b complex, and there was no evidence that the concentrations of vWF used in D2 were relevant to levels of normal or defective vWF found in patient samples containing a mixture of proteins.

3.9 The board notes that, since it was known that the interaction between vWF and GP1b occurred via the GP1b(α) subunit (see above), the skilled person would have a reasonable expectation that an assay using said GP1b(α) subunit would allow vWF activity to be tested. In fact, the prior art had already demonstrated that binding of a GP1b(α) subunit fragment comprising the binding site for vWF was identical to the binding of

the whole GP1b molecule (D4, page 15479, left column, second paragraph; abstract, first three sentences). Although the appellant-patent proprietor argued that D15 showed that the assay format of D4 could not have worked, the board notes that not only is D15 not part of the prior art, it neither raises doubts that an assay with the GP1b(α) subunit could work: rather it indicates that given formats (as regards attachment to the support) are needed to make the assay work.

- 3.10 As to the testing of patient samples, again it is noted that the present claim does not specify which samples are to be used, and indeed this could include purified samples. Obviously, since the method is for discriminating between different types of vWD, it is apparent that the samples must be obtained from patients, but there is no reason to exclude that such samples may be pre-treated, e.g. to remove eventually interfering components. On the other hand, there is no reason to doubt that the method of D2 could work with patient samples as well. In fact, it is not apparent from the patent's examples that any particular measures had to be taken when using patient plasma samples. Finally, the method of D2 provides proof of concept that soluble GP1b can be used to determine vWF ristocetin activity in a platelet-free assay; in this context, the vWF concentrations which were used in the purified samples of D2 do not play a role.
- 3.11 Claim 1 of auxiliary request 5 is thus considered to lack inventive step. Hence, auxiliary request 5 is not allowable for lack of compliance with Article 56 EPC.

4. Auxiliary request 7

4.1 Auxiliary request 7 was submitted with the letter dated 26 November 2018, sent in reply to the communication of the board of appeal setting out its preliminary opinion on some issues. This request merely differs from the previous auxiliary request 7, which had been submitted with the letter of reply to the opponent's statement of grounds of appeal, in that claim 32 has been deleted as reaction to an objection raised by the board in the above-mentioned communication. The appellant-opponent had no objections to the admission of this request and neither has the board.

Inventive step

4.2 Claim 1 of auxiliary request 7 essentially differs from claim 1 of auxiliary request 5 in that step (a) has been amended to specify that the samples should be blood, serum or plasma samples, and that the test comprised assaying said sample in the presence of a soluble form, or portion thereof, of recombinant GP1b(α) (for the exact wording, see section IX above). The appellant-patent proprietor relied solely on the latter amendment, namely the use of recombinant GP1b(α), for the discussion of inventive step.

4.3 The board fails to see how the restriction to recombinant GP1b(α) can contribute to inventive step. Production of proteins in recombinant systems was routinely available to the skilled person at the priority date of the patent, and the skilled person, motivated to produce a standardised assay, would certainly consider using recombinant GP1b(α). The patent did not disclose any advantage linked to using recombinant GP1b(α), this being one of many possible alternative ways of providing GP1b(α) which were contemplated on page 5, last paragraph, to page 6,

first and second paragraphs of the application as filed. Moreover, use of a recombinant GP1b(α) in an assay to detect vWF had been already disclosed in the prior art (D15-O, page 7, third paragraph).

4.4 The appellant-patent proprietor essentially argued that this feature further addressed the problem of assay variability since, contrary to GP1b(α) purified from natural sources (as was GP1b in D2), the recombinant protein would not be variable. The examples of the patent, in particular Example 4, provided evidence for the reliability, repeatability and accuracy of the assay using the recombinant protein (page 26, lines 15 ff). As to D15-O, this document suggested the use of recombinant GP1b(α) but did not provide any evidence that it indeed worked, contrary to the patent which extensively demonstrated that the assay worked and correlated with the methods of the prior art (examples and figures).

4.5 The board agrees that it is plausible in theory, although not demonstrated in the patent, that the use of recombinant GP1b(α) instead of GP1b(α) purified from natural sources may contribute to more reproducibility and less variability of the test assay. However, such advantages would be expected from the prior art, and hence the skilled person, seeking to optimise the assay, would certainly consider using recombinant GP1b(α) and would be able to use it and test it without the need for inventive skill. As to D15-O, this document only serves as evidence that, already before the priority date of the patent, the skilled person would have considered the use of recombinant GP1b(α) in an assay for detecting vWF. Whether D15-O has indeed performed such an assay is irrelevant in this context.

4.6 Claim 1 of auxiliary request 7 is considered to lack inventive step. Hence, auxiliary request 7 is not allowable for lack of compliance with Article 56 EPC.

5. Auxiliary request 10

5.1 Admission

5.1.1 Auxiliary request 10 was submitted with the letter dated 27 October 2014, filed as reply to the opponent's statement of grounds of appeal. Pursuant to Article 12(4) RPBA, the boards of appeal have the discretion to admit requests which could have been presented in the proceedings before the examining or opposition division. When exercising their discretion, the boards take into account the circumstances of the particular case and the arguments put forward by the parties.

5.1.2 The board is convinced by the arguments of the appellant-patent proprietor that there had been no reason to file such a request during the first-instance proceedings because the opposition division had not given indications that further amendments, other than those made to the then third auxiliary request (corresponding to present auxiliary request 5), were required. Hence, the submission of this request only at the appeal stage is not procedurally objectionable.

5.1.3 The appellant-opponent further argued that the appellant-patent proprietor, when submitting this request, had not provided any explanation concerning how it was to address outstanding objections, such a substantiation having been given only in a latter letter filed in reply to the board's communication. The board however notes that, as argued by the appellant-patent proprietor, the nature of the amendments was

such that it would have been immediately apparent to the appellant-opponent which objections were addressed and how.

5.1.4 A further argument from the appellant-opponent was that the amendments were such that they raised problems under Articles 123(2) and 84 EPC. The board is not convinced, however, by this argument and notes that the language of the claim is very similar to the language of granted claims 4, 6, 7 and 8 so that any possible issues under Articles 123(2) and 84 EPC are either not of such a nature as to prevent further examination or not even open to discussion.

5.1.5 Accordingly, the board decided to exercise its discretion pursuant to Article 12(4) RPBA to admit this request into the proceedings.

5.2 Inventive step

5.2.1 Claim 1 of auxiliary request 10 essentially differs from claim 1 of auxiliary request 7 in that step (a) is no longer restricted to the use of recombinant GP1b(α) and has been amended to specify that GP1b(α) or a complex of vWF and GP1b(α) are bound to a solid support by an anti-GP1b(α) antibody (for the exact wording, see section IX above).

5.2.2 The board fails to see how the amendment inserted into claim 1 of auxiliary request 10 can contribute to inventive step. The binding of molecules to a solid support, either directly or via a specific antibody, is commonly used in the context of assays like the one of claim 1, step (a). In the application as filed, the use of anti-GP1b(α) antibodies for this purpose was disclosed as being one among other equally suitable

alternatives (page 7, last paragraph to page 8, first paragraph) and there was no evidence at all for an improvement achieved by this particular feature. Hence, the board comes to the conclusion that the skilled person would arrive at the claimed subject-matter without the need for inventive skill.

- 5.2.3 The appellant-patent proprietor essentially argued that, although it was common general knowledge to bind antibodies to solid supports, there was no suggestion anywhere in the prior art to bind GP1b(α) to a solid support via a specific antibody. It was this particular feature, which was disclosed as part of the preferred embodiment in the patent, that allowed the assay to perform reliably and in fact to work, as had been shown in D15. When attempting to adopt D2's assay, the skilled person would have failed and, without the knowledge of the patent, would have had no pointer to how to change the assay so that it would work.
- 5.2.4 The board notes that D2 had already used an assay format wherein the GP1b molecule was attached to the solid support and there would have been no reason for the skilled person not to try the routine procedure of attaching the GP1b(α) to a solid support, either by a specific antibody or by any other alternative procedure as known from the prior art and discussed in the patent application (*supra*). It would be well within the routine work of the skilled person to test different configurations and select those that worked or performed better. Moreover, whether such a configuration as claimed worked better than other configurations, as alleged on the basis of D15, has not been shown or suggested in the patent but only much later, D15 being a post-published declaration.

5.2.5 Claim 1 of auxiliary request 10 also lacks inventive step. Accordingly, auxiliary request 10 is not allowable for lack of compliance with Article 56 EPC.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The patent is revoked.

The Registrar:

The Chairman:



M. Schalow

L. Bühler

Decision electronically authenticated