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Datasheet for the decision of 22 November 2023

Case Number: T 0528/21 - 3.3.04

Application Number: 13809853.8

Publication Number: 2867245

IPC: C07K1/00, C07K16/00, A61K38/17

Language of the proceedings: EN

Title of invention:
Purification of Iduronate-2-sulfatase

Patent Proprietor:
Takeda Pharmaceutical Company Limited

Opponent:
HGF Limited

Headword:
Iduronate-2-sulfatase purification/TAKEDA

Relevant legal provisions:
EPC Art. 54(2), 56
RPBA 2020 Art. 11, 12(4), 12(6), 13(1)

Keyword:
New evidence filed with statement of grounds of appeal - circumstances of appeal case justify admittance (yes)
Late filed evidence - should have been submitted with statement of grounds of appeal
Remittal - (no)
Public availability of Kroean patent document upon registration - (yes)
Inventive step - (no)

Decisions cited:
T 0091/98, T 0314/99, T 1553/06, T 2451/13

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Case Number: T 0528/21 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 22 November 2023

Appellant: (Opponent)	HGF Limited Saviour House 9 St Saviour Gate York YO1 8NQ (GB)
Representative:	HGF HGF Limited 1 City Walk Leeds LS11 9DX (GB)
Respondent: (Patent Proprietor)	Takeda Pharmaceutical Company Limited 1-1, Doshomachi 4-chome Chuo-ku Osaka-shi, Osaka (JP)
Representative:	Carpmaels & Ransford LLP One Southampton Row London WC1B 5HA (GB)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 10 March 2021 concerning maintenance of the European Patent No. 2867245 in amended form**

Composition of the Board:

Chairwoman	M. Pregetter
Members:	O. Lechner
	M. Blasi

Summary of Facts and Submissions

I. The appeal by the opponent (appellant) lies from the opposition division's interlocutory decision that the patent as amended in the form of the main request (comprising the set of claims as filed by letter of 7 November 2019) and the invention to which it related met the requirements of the EPC.

II. The patent was granted on European patent application No. 13 809 853.8, which had been filed as an international application published as WO 2014/005014 (the "application as filed") and claiming priority from US 2012 61/666,733.

III. In its decision, the opposition division held that the main request complied with Rule 80 and Articles 84, 123(2), 87, 54, 56 and 83 EPC.

IV. In its statement of grounds of appeal, the appellant raised objections under Articles 123(2), 87, 54, 56 and 83 EPC. It also submitted new documents D2b and D55 to D60.

V. In reply, the patent proprietor (respondent) maintained the main request as addressed in the decision under appeal and filed sets of claims of two auxiliary requests.

VI. By further letters, the appellant filed new documents D61, D61a, D62 (by letter dated 2 June 2022) and D64 (by letter dated 18 October 2022) and the respondent new document D63 (by letter dated 2 August 2022).

VII. In the course of the written appeal proceedings, following a request submitted by the respondent, a change in the entries pertaining to the person of the respondent was recorded in the European Patent Register in view of a transfer of the patent.

VIII. The parties were summoned to oral proceedings in accordance with their respective requests. In reaction to the board's communication under Article 15(1) RPBA, the respondent submitted a set of claims of auxiliary request 3.

IX. The oral proceedings before the board took place on 22 November 2023.

X. Claim 1 of the main request, identical to claim 1 of auxiliary requests 1 to 3, reads

"1. A composition comprising purified recombinant iduronate-2-sulfatase (I2S) having the amino acid sequence of SEQ ID NO:1, wherein the purified recombinant I2S comprises at least 70% conversion of the cysteine residue corresponding to Cys59 of SEQ ID NO:1 to Cα-formylglycine (FGly), and wherein the purified recombinant I2S contains less than 150 ng/mg Host Cell Protein (HCP)."

XI. Reference is made to the following documents:

D1: WO 2012/177020 A2

D2: Korean Patent No. 10-1158673 (in Korean)

D2a: English translation of parts of document D2 - 4 pages

D2b: corrected English translation of Figures 16 and 17 of document D2 - 2 pages

D3: Declaration of Chiwon Kim, dated 4 June 2019 and including Appendices 1 to 7 (54 pages)

D14: Clarke L. A., Expert Opin. Pharmacother. (2008); 9(2): 311-317

D20: Declaration of Mr D. Nichols before the patent trial and appeal board of the USPTO for Case IPR2016-00258; Patent 9,051,556; dated 11 August 2016

D24: Korean Intellectual Property Office (KIPO), Patent Examination Guidelines, English Edition, December 2017, www.kipo.go.kr - 957 pages

D25: Hoffman K.; Biopharm. (2000), 13(5): 38-45

D26: Zoon K. C.; Points to Consider in the Manufacture and Testing of Monoclonal Antibody Products for Human; U.S. Department of Health and Human Services Food and Drug Administration Center for Biologics Evaluation and Research; 28 February 1997; 50 pages

D27: ICH Harmonised Tripartite Guideline; Specifications: Test Procedures and Acceptance Criteria for Biotechnological/Biological Products; Q6B; Current Step 4 version; dated 10 March 1999; 20 pages

D28: Champion K. et al.; BioProcess Int (2005); September: 52-57

D29: Wang X. et al.; Biotechnol. Bioeng. (2009); 103(3): 446-458

D30: Protein Purification Handbook (2001); 18-1132-29; Edition AC; Amersham Biosciences: 98 pages

D31: Wilson K. et Walker J.(Eds.); Principles and Techniques of Biochemistry and Molecular Biology (2010); 7th Edition; Cambridge University Press; : 760 pages

D32: Cummings L. J. et al; Chapter 24: Protein Chromatography on Hydroxyapatite Columns; Methods in Enzymology (2009), 463: 387-404

D33: Notarial certificate including the original and an English translation of page 3201 of the Patent and Utility Model Examination Guidelines published in March 2012 by the KIPO - 11 pages

D34: Notarial certificate including the original and an English translation of Article 216 of the Korean Patent Act effective from 1 July 2011 - 4 pages

D35: Patent Examination Guidelines, Korean Intellectual Property Office, March 2019, two cover sheets and pages 237 to 238 of the guidelines

D39: Notarial certificate including the "Notice of Decision of Information Disclosure" of 21 July 2020 to a request dated 20 July 2020 (in Korean and its English translation), Receipt No.: 6953163 - 8 pages

D40: Notarial certificate including the "Notice of Decision of Information Disclosure" of 3 July 2020 to a request dated 2 July 2020 (in Korean and its English translation), Receipt No.: 6906061 - 8 pages

D41: Notarial certificate including the "Notice of Decision of Information Disclosure" of 3 July 2020 to a request dated 23 June 2020 (in Korean and its English translation), Receipt No.: 6869974 - 8 pages

D42: Notarial certificate including a copy of the Patent Register of D2 (in Korean and its English translation) - 6 pages

D58: Notarial certificate including the Civil Petition No. 1AA-2107-0070451 filed on 2 July 2021 via the On-line Public Communication Portal Operated by Anti-Corruption & Civil Rights Commission e-People (www.epeople.go.kr) and the reply thereto dated 12 July 2021 (in Korean and its English translation) - 11 pages

D59: Declaration of Jongkook Lee, dated 16 July 2021 including Attachments A to F - 9 pages

D60: Notarial certificate including the "Herald Business Newspaper" article "Green Cross Corporation R&D Workshop "Let's Make a Strong Pharmaceutical Company through Beneficial Cycles of R&D" by Moon-Sool Jo, in Korean and English; Uploaded: May 12, 2012, at 08:13 - 5 pages

D61: Notarial certificate including the Civil Petition No. 1AA-2203-0405366 filed on 14 March 2022 via the On-line Public Communication Portal Operated by Anti-Corruption & Civil Rights Commission e-People (www.epeople.go.kr) and the reply thereto dated 25 March 2022 (in Korean and its English translation) - 12 pages

D61a: Notarial certificate including Articles 41 and 87 of the Korean Patent Act effective from 15 March 2012 in English and Korean - 5 pages

XII. The appellant's arguments, insofar as relevant to the decision, can be summarised as follows:

(a) Admittance of documents D58 to D60 - Article 12(4) and (6) RPBA

The submission of documents D58 to D60 was not an amendment of the case. Public availability of document D2 upon registration of the patent at the Korean Intellectual Property Office (KIPO) had been asserted from the outset of the opposition proceedings. Documents D58 to D60 were highly relevant and served as further evidence to confirm KIPO practice as set out in document D33 (the KIPO Guidelines as in force in 2012) and provided concrete evidence countering the respondent's unsupported allegations that document D2 had not been available to the public before the priority date of the patent in suit. In its decision, the opposition division had relied on document D24, the KIPO Guidelines which applied as of 2017, rather than on document D33. As the English translation of the relevant provisions differed, the opposition division's reliance on document D24 was flawed and demonstrated that the division did not give proper consideration to the correct legal position at the effective date. Documents D58 to D60 were submitted to address this incorrect interpretation that the opposition division applied to the KIPO Guidelines.

(b) Admittance of documents D61 and D61a - Article 13(1) RPBA

Documents D61 and D61a were submitted in response to the respondent's allegation first made in reply to the statement of grounds of appeal that the example provided in document D33 illustrated that public availability upon registration was conditional.

(c) Request for remittal to the opposition division

The opposition division had taken a decision on the issue of public availability of document D2 and the board should therefore review that decision. Documents D58 to D60 merely confirmed the position already argued during the opposition proceedings, i.e. that the public could already have been aware of the existence of document D2 before the priority date of the patent in suit. A remittal was not justified and not required.

(d) Public availability of document D2

The opposition division erred in not accepting D2, a published Korean patent, as state of the art.

The standard to be applied was that of a balance of probabilities because the information relating to patent document D2 was not evidence that had been available only to the appellant.

It was stated in the last paragraph of document D33 that anyone could inspect the documents of the application once the application was registered as a patent. Thus, a mechanism had to be in place for allowing this. Document D41 showed that D2 was amongst the documents available for file inspection. According

to declaration D59, any member of the public could obtain a list of patent applications filed by a particular applicant by entering the applicant code number on the dedicated KIPO website. The applicant code number was provided by KIPO on request. The list of patent applications showed application numbers even before the publication of the patent applications. By clicking on a selected application number whose patent register had been created - status indicated as "allowed" - detailed information on such application including its registration number, i.e. patent number, was displayed. By using the registration number, a copy of the application documents could be requested from the same website and, within several hours, the requested documents including the original specification could be downloaded from the website. By following these steps, which were confirmed by KIPO in document D58 as having been in place in 2012, any member of the public could have obtained a copy of D2 once the patent register was created and, therefore, even before the publication date of the patent, similar to the example provided in D59. As D2 had been registered as a patent, this implied that it had been allowed, as shown by document D42.

The respondent's assertion that "creation" of the patent register could be distinct from "issuance" was hypothetical. As evidenced by document D40, the patent register of D2 was created on 19 June 2012, 08:14:43 hours, and D39 confirmed that third parties knowing the patent number could inspect the application documents and obtain a copy from the point in time when the patent register was issued. As explained in declaration D59, creation of the patent register takes place shortly after the registration date, generally within one business day. As shown with a recent example, by

following the steps set out above on 6 July 2021, copies of the application documents of a Korean patent which had been registered on 1 July 2021 could be downloaded from the KIPO website on the day of the search, and before publication of the respective patent on 8 July 2021.

Competitor-monitoring was a routine process carried out by businesses. Moreover, the broader public had been made aware of Green Cross Corporation, one of the proprietors of patent D2, being involved in the development of Hunterase treatments by document D60 which reports on a Green Cross Corporation R&D workshop during which presentations on successful development of Hunterase as a therapeutic agent for Hunter syndrome were given.

For the question of public availability, the practical possibility of gaining access was sufficient. Actual access was not required. D2 could also not be regarded as hidden. Decision T 1553/06 was concerned with a different situation. Even if the two-stage test set out in that decision were applied, the test would be met. Even if the test were not met, decision T 1553/06 itself acknowledged that the test was not conclusive as to whether or not a document was available to the public. Moreover, for assessing whether a document was available to the public, it was not correct to require a motivation for the skilled person to carry out a search.

(e) Inventive step - claim 1 - Article 56 EPC

Closest prior art

Document D2 represented the closest prior art. Document D1, which had the same disclosure as document D2, was used as translation.

Difference, its technical effect, and objective technical problem

The subject-matter of claim 1 differed from the teaching of document D2 (paragraphs [0057], [0112], [0129], and [0136] of document D2 which corresponded to paragraphs [53], [123], [139] and [146] of document D1), only in that it required a host cell protein (HCP) level of less than 150 ng/mg.

The less than 150 ng/mg HCP feature was not a difference since the HCP level in a drug substance required for marketing approval in the US was <100 ppm (as stated in paragraph [0140] of the patent in suit itself). This was consistent with the disclosure in documents D26 to D29, which each described the likely range of HCPs in biological products reviewed by the FDA as 1 to 100 ppm (i.e. 1 to 100 ng/mg).

The recited level of HCP was not associated with any (unexpected) technical effect other than a final product with fewer impurities, which was inherent to any purification of a composition. No comparative data had been provided comparing this purer drug substance to the one disclosed in document D2.

The objective technical problem was the provision of an alternative I2S composition.

Obviousness

It was obvious and within the skilled person's routine abilities to provide a drug formulation with the lowest possible HCP contamination to increase safety.

The skilled person would have been motivated to apply the I2S purification process described in document D2 with the reasonable expectation that, working within the parameters defined in document D2, the resulting recombinant I2S protein would retain a conversion of greater than 75% of the cysteine residue corresponding to Cys59 (see claim 2). Methods for measuring HCP contamination levels were known in the art (see e.g. document D25, page 39, Table 1).

As acknowledged in the patent in suit (see paragraph [0140]), regulatory authorities in many markets required an HCP concentration of <100 ng/mg (ppm) in a drug substance. Thus, the skilled person was also motivated to vary the parameters described in document D2 to reduce the level of HCP to a level acceptable for regulatory approval.

The teaching of document D2 would lead the skilled person to expect that reducing HCP to the claimed level was achievable at the priority date. Once the physico-chemical properties of a protein were known, the skilled person would have arrived at the claimed composition by routine methods. The detailed purification method described in document D2 provided an obvious way to arrive there, as it comprised cation exchange chromatography, which was known to remove HCP contaminants.

Concerning the HCP contamination levels allowed for drug compositions, further reference was also made to e.g. documents D25, page 38, middle column; page 39, Table 1; page 40, left-hand column, line 18 from the bottom and following lines; D28, page 54, left-hand column, last paragraph and middle column paragraph 1 and D29, page 447, right-hand column, paragraph 1.

Expert declaration D20 explained (see paragraph 7) that the co-expression of formylglycine generating enzyme (FGE) for increasing FGly content in a I2S preparation would be associated with elevated HCP levels. However, alternative methods were known, such as the addition of hydrolysate to a culture medium of CHO cells, which did not require the increase in HCP. The method described in document D2 confirmed that there was no general association between the percentage of FGly conversion and HCP levels, but rather an association that was entirely specific to the production method. The subject-matter of claim 1 was however not limited to a specific production method.

There was no evidence on file to support the respondent's allegation that the use of hydrolysates, as disclosed in document D2, had been associated with elevated HCP levels making the purification of I2S more difficult. As shown in document D14 (see page 312, right-hand column, paragraph 1), it was already known that the purification of I2S required various chromatographic and ultrafiltration steps.

Documents D30 to D32 showed that HCP removal was an entirely routine process for a person skilled in the art.

The additional features introduced by claims 2 to 10 were all obvious forms of the claimed composition or were inherent properties of the claimed compositions as demonstrated by the prior art.

XIII. The respondent's arguments, insofar as relevant to the decision, can be summarised as follows:

(a) Admittance of documents D58 to D60 - Article 12(4) and (6) RPBA

The submission of documents D58 to D60 was an amendment of the appellant's case. The case amendment was complex, and admittance would contravene procedural economy. The opposition division had taken into consideration all the evidence on file and just assessed the relevant parts in the decision under appeal. Documents D58 to D60 could and should have been filed during the opposition proceedings since the public availability of patent document D2 had already been an issue during that phase. Admission of documents D58 to D60 would create a fresh case. Furthermore, the newly filed documents did not address the failings in the appellant's arguments.

(b) Admittance of documents D61 and D61a - Article 13(1) RPBA

The submission of documents D61 and D61a could not be considered as being a direct response to the opposition division's decision. Documents D61 and D61a were filed at an inappropriately late stage in the proceedings, even later than documents D58 to D60. Neither document D61 and D61a, nor any other documents filed, showed beyond reasonable doubt that patent document D2 was

available to the public. Thus, D61 and D61a should not be admitted.

(c) Request for remittal to the opposition division

The purpose of the appeal proceedings was to review the opposition division's decision. However, if the new evidence, including documents D58 to D60, were admitted, this would change the situation. An initial assessment of the new evidence and the associated arguments relating to the asserted public availability of patent document D2 and KIPO's practice should be made by the opposition division. It was unfair to the board to have to consider the evidence and arguments without such prior assessment by the opposition division. The respondent should likewise be given an opportunity to respond in full before two different instances. Thus, if the new evidence were to be admitted, the case should be remitted to the opposition division.

(d) Public availability of document D2

There was no proof beyond reasonable doubt that a member of the public had access to the content of document D2, nor was there evidence that the skilled person could have acquired knowledge or awareness of the existence of document D2. The standard of "beyond reasonable doubt" had to be applied because the evidence regarding the publication of document D2 lay within the appellant's sphere. Evidence relied upon, including documents D58 and D59, originated from Green Cross, owner of patent D2, to which the respondent had no access.

Document D33, last paragraph, relied upon by the appellant, confirmed that registered applications might not always be made available to the public, or at least that the act of making them available might not occur immediately after registration.

There was no clear link between documents D39 and D40. Document D39 stated that inspection of an application was possible "*from the point when the patent register of the patent in question was issued*". Document D40 referred to the point in time when the patent register for D2 was "*created*". No indication had been provided regarding whether creation and issuance of the patent register occurred at the same time. Presumably, an entry was created in the system and at some point that entry was issued to make it available for inspection.

The lag remained ambiguous even in light of documents D58 or D59 because neither indicated the point in time at which documents were "*issued*" or marked as allowed on the KIPO system relative to the time at which the entry was created.

The register entry for document D2 was created four days after the patent was registered. Therefore, it was similarly reasonable to expect that a further period of time elapsed between creation of the register entry and the application being laid open - if it was laid open at all. In order to make a patent document available for download by clicking on an icon, the icon must first have been made clickable. Document D41 did not support the appellant's case since it was assumed therein that a third party had knowledge of the specific patent number in order to search for the patent document. A member of the public had no knowledge of the number.

Even if document D2 had been made available for inspection at some point in time, there was no evidence that it had been made available to the public before the priority date of the patent in suit. Documents D58 and D59 were only general documents that reported a process by which access to an allowed application might generally have been possible. There was no evidence relating to document D2 specifically. The situation was analogous to that underlying decision T 91/98.

Moreover, even if the register had been created and published in good time, this would not have meant that document D2 had been made available to the public. A member of the public would not have been aware of the existence of document D2. The situation was comparable to that underlying decision T 314/99. Furthermore, a keyword search relating to the content of document D2 could not have provided a member of the public with the document. Documents D39, D41 and D58 made it clear that a member of the public could only inspect document D2 by knowing the patent number of the registered application, which required the very elaborate procedure, described in documents D58 and D59, for which the applicant code number had to be known. The criteria established by decision T 1553/06 for the public availability of a disclosure stored on the World Wide Web were not met. At best, document D2 had been theoretically accessible, failing to meet at least the "practical possibility" threshold of decision T 1553/06.

(e) Inventive step - claim 1 - Article 56 EPC

Closest prior art

Even if document D2 were to be considered as having been made available to the public, it did not render the claims obvious because the HCP levels in the I2P preparation of document D2 were unknown. It was not contested that document D1 had the same disclosure as document D2.

Difference, its technical effect, and objective technical problem

The subject-matter of claim 1 differed from the teaching of document D1 (claim 2, paragraphs [53], [123], [139], [146]) only in that it required a host cell protein (HCP) level of less than 150 ng/mg.

The technical effect due to this difference was improved safety while retaining a high FGly content.

The objective technical problem was the provision of an improved I2S composition.

Obviousness

The claimed solution was not obvious in relation to the teaching of document D1 since an increased FGly content necessarily resulted in higher HCP levels in the preparation. The method of document D1 increased the FGly content by adding hydrolysate (see paragraphs [42] and [109]). However, the hydrolysate led to higher cell growth and (host cell) protein expression in general (see document D20, paragraph 7). The skilled person would have considered these elevated HCP concentrations

problematic since the removal of HCP was complex and unpredictable, as disclosed in document D20 (see paragraph 8, page 6). General HCP purification methods were not known. Document D29 (see page 447, paragraph spanning left- and right-hand columns) explained that the level of acceptable HCPs was reviewed on a case-by-case basis by the regulatory authorities, i.e. HCP levels of 1 to 100 ppm (ng/ml) were not always expected (see also document D28, page 54, left-hand column, chapter "Acceptable Levels of Residual HCP").
Given the danger of I2S product loss, the skilled person would have refrained from adding additional purification steps.

Example 3, Table 13 of the patent showed that an I2S product with an HPLC purity of 99.9%, i.e. the same purity level as reported in document D1, was associated with an HCP contamination of 372 ng/mg. Document D20 reported in paragraph 8 that a subpopulation of HCPs almost inevitably co-eluted with the I2S target protein. I2S had an isoelectric point (pI) of 4 to 5 like other lysosomal proteins and it was thus particularly difficult to remove proteins with the same pI. Accordingly, there had been no reasonable expectation of success in achieving the claimed HCP level of less than 150 ng/mg.

The argument that document D1 disclosed a therapeutic composition was not indicative of HCP levels lower than 150 ng/mg given that other compositions with much higher HCP levels had already been administered to patients.
Document D1 did not employ the four-step purification method according to Example 1 of the patent. However, successful HCP removal required the four-step method disclosed in the particular order shown.

Document D14 did not report any issue with purification since it disclosed the I2S preparation elaprase having a lower FGly content of only about 50%. However, the production of a more active I2S preparation comprising 70% FGly required improved HCP removal during purification.

Documents D30 to D32, cited by the appellant to show that the protein purification processes used in the examples of the patent were known and routinely used methods, did not specifically address the reduction of HCP levels and certainly not in the context of the I2S protein or a situation where high FGly levels were achieved along with an increased HCP level in the starting material.

XIV. The parties' requests relevant to the decision were as follows.

(a) The appellant requested that
- the decision under appeal be set aside, and the patent be revoked in its entirety;
- documents D2b, D50, D50a, D51, D55 to D61, D61a, D62 and D64 be admitted; and
- document D63 not be admitted into the appeal proceedings.

(b) The respondent requested that
- the appeal be dismissed, implying that the patent be maintained as amended according to the main request (comprising the set of claims as filed with letter of 7 November 2019), or alternatively;
- the patent be maintained in amended form on the basis of the set of claims of one of auxiliary

requests 1 and 2 (as filed with the reply to the statement of grounds of appeal) or of auxiliary request 3 (as filed with the letter dated 20 October 2023.

The respondent also requested that

- auxiliary request 3 be admitted into the proceedings,
- document D63 be admitted, and
- documents D46 to D52, D2b, D55 to D61, D61a, D62 and D64 not be admitted into the appeal proceedings.

In the event that any of the before-mentioned documents were admitted into the proceedings, remittal of the case to the opposition division for further prosecution was requested.

Reasons for the Decision

Admittance of documents D58 to D61 and D61a

1. Documents D58 to D60 - Article 12(4) and (6) RPBA

1.1 Documents D58 to D60 were filed with the appellant's statement of grounds of appeal. The admittance of these documents and the appellant's related submissions had to be considered on the basis of Article 12(4) to (6) RPBA, applicable in the version of the RPBA which entered into force on 1 January 2020.

1.2 In agreement with the respondent, the board regarded these new items of evidence and the associated submissions, first filed on appeal, as amendments within the meaning of Article 12(4) RPBA and the board

therefore had discretion as to whether or not to admit this amendment.

Document D58 is a civil petition, i.e. an information disclosure request, submitted via the "On-line Public Communication Portal", answered by the Information System Department of KIPO (Korean Intellectual Property Office), concerning the availability of an entire patent specification via the KIPO website in 2012.

Document D59 is a declaration in which a Korean patent attorney who had worked at the KIPO from 2003 to 2013 provided an explanation as to KIPO's procedures for making patent documents available.

Document D60 is a news article published in May 2012 reporting about a R&D workshop held by the company Green Cross Corporation.

1.3 The appellant's justification for filing these new items of evidence was that the opposition division had relied upon document D24, i.e. the English version of the KIPO Patent Examination Guidelines applicable as of 2017, rather than document D33, i.e. the English version in force at the relevant time in 2012, the passage relied upon by the opposition division being different in these two versions. Documents D58 to D60 served as further evidence to confirm that the practice described in KIPO's Patent Examination Guidelines applicable at the relevant point in time meant that document D2 had been available to the public by inspection of application documents upon registration.

1.4 The respondent argued that documents D58 to D60 should have been submitted in the proceedings before the opposition division and should therefore not be

admitted.

1.5 The board agrees with the respondent that these items of evidence and associated submissions added some complexity to the proceedings in that they also needed consideration. However, they did not create a fresh case but stayed within the framework of what had been argued by the appellant in opposition, namely that the disclosure of patent document D2 had been made available to the public upon registration. While these documents could have been filed during opposition proceedings, they specifically addressed the opposition division's conclusions as to the issue of public availability of patent document D2. The division considered the public availability of patent document D2 to be a legal fiction and based this finding first and foremost on the explicit wording of the KIPO Patent Examination Guidelines D24 which, however, had not been applicable at the relevant point in time. The division further considered that a member of the public could not have been aware of the existence of D2 until its date of publication. The board agrees that submission of the additional evidence D59 to D60 can be seen as an appropriate reaction to the decision under appeal.

1.6 In light of the above considerations, the board decided to admit documents D58 to D60 into the proceedings (Article 12(4) and (6) RPBA).

2. Documents D61 and D61a - Article 13(1) RPBA

2.1 Documents D61 and D61a were submitted with the appellant's letter dated 2 June 2022 to counter the respondent's arguments that public availability of patent document D2 upon registration was conditional.

2.2 However, the issue of public availability upon registration being conditional had already been addressed in the decision under appeal. This issue constituted the appellant's justification as to why further evidence was filed on appeal. Accordingly, these two documents addressing that same issue should have been submitted at the latest with the statement of grounds of appeal.

Thus, documents D61 and D61a were not admitted into the proceedings (Article 13(1) RPBA).

Request for remittal to the opposition division

3. The respondent requested a remittal of the case to the opposition division for further prosecution should *inter alia* any of documents D58 to D60 be admitted into the proceedings.

4. Pursuant to Article 11 RPBA a board shall not remit a case to the department whose decision was appealed for further prosecution, unless special reasons present themselves for doing so. Hence, there is no principle that all issues should be assessed by two separate deciding bodies as suggested by the respondent. Instead, remittal needs to be decided on a case-by-case basis. In the present situation, the board saw no special reasons for remitting the case to the opposition division. The parties had been aware, since the beginning of the opposition proceedings, of both
i) the relevance of the teaching in document D2 to the claimed subject-matter; and
ii) the controversy regarding its public availability
and had addressed this in their submissions.

Therefore, the board considered the parties, and the board, to be in a position to deal with the matters on appeal. Remittal would have prolonged the overall duration of the proceedings before the EPO. Consequently the board decided not to remit the case to the opposition division for further prosecution (Article 11 RPBA).

Patent document D2 as state of the art

5. Document D2 is a copy of Korean patent No. 10-1158673. Document D2a is an English translation of the sections of document D2 which differ from those disclosed in document D1 (WO 2012/177020). The bibliographic data on patent document D2 (see document D2a) indicate a date of filing of 8 February 2012, a date of registration of 15 June 2012 and a date of publication of 3 July 2012.

6. The parties were in dispute as to whether the disclosure of patent document D2 had been made available to the public before 29 June 2012, i.e. before the priority date of the patent in suit.

7. The opposition division had decided that the disclosure of patent document D2 was not prior art. It held that the public availability of patent document D2 appeared to be a legal fiction and that members of the public could not have acquired knowledge or awareness of the existence of patent document D2 until its date of publication. The appellant contested these findings.

8. The board is convinced that the disclosure of patent document D2 had been made available to the public prior to the priority date of the patent in suit.

9. The board does not agree with the respondent's view that all the evidence lay in the appellant's sphere and, therefore, a stricter standard of proof should be applied, namely that of beyond reasonable doubt, and not the standard of a balance of probabilities.

9.1 As pointed out by the respondent, there is indeed a certain relationship between the production of evidence and Green Cross Corporation, co-owner of patent D2, in that the petitioner's address on civil petition D58 is shown on patent document D2. However, at issue was the asserted public availability of the disclosure of patent document D2 via the KIPO website. There is no reason to believe that it was impossible for the respondent to obtain information from KIPO which could serve as evidence in the proceedings before the EPO, nor had such an impossibility been put forward by the respondent. The further issue of how the situation would have to be assessed in light of the fact that the appellant in the current proceedings was, in fact, not Green Cross Corporation did not therefore have to be considered by the board.

9.2 Moreover, the respondent's reference to decision T 2451/13 which required a yardstick of "beyond reasonable doubt" is also of no assistance. This decision concerned the prior art status of a commercial brochure which originated from and was published by the opponent and, therefore, all the evidence about the publication had essentially been in the hands of the opponent (see T 2451/13, Reasons 3.2.6).

9.3 Even though the board does not share the respondent's view on the standard of proof, the board considers that what matters is not whether it was more likely than not that the disclosure of patent document D2 had been made

available to the public prior to the priority date. Rather, what matters is whether or not the board is convinced that the disclosure of patent document D2 had indeed been made available before that date. This is the case for the following reasons.

10. It was common ground that the KIPO allowed for the possibility of inspection of documents relating to patent applications filed with the KIPO. However, the parties were in dispute as to whether the disclosure of patent document D2 was made available to the public at all or, at least, in the relevant period, i.e. before 29 June 2012.

11. The respondent submitted in one line of argument that it was not proven that patent document D2 related to an application that had been made available for public inspection and referred to the conditional wording used in the passages of all the versions of the KIPO Patent Examination Guidelines D24, D33 and D35 relied upon by the appellant.

11.1 The board accepts that, as pointed out by the respondent, the versions of the KIPO Patent Examination Guidelines D24, D33 and D35, i.e. irrespective of whether they were applicable in the relevant period of 2012, indicate that not all registered patent applications are made available to the public.

11.2 However, the board considers it proven that patent document D2 was not of a kind which was not "laid open or not published after registration", as mentioned e.g. in the final paragraph of document D33 (and also in the passage on page 238 of document D35) referred to by the respondent. In document D39, the KIPO confirmed that a third party who knew the patent number of "Korean

Patent No. 1158673", i.e. patent document D2, could inspect the application documents and obtain a copy thereof through the KIPO website from the point when the patent register of the patent in question was issued. Such a confirmation could not have been provided by KIPO had patent document D2 or the related application documents not been laid open or not published after registration. Moreover, the respondent had also not provided any evidence for its assertion that the disclosure of patent document D2 was not available for, i.e. excluded from, public inspection.

In this context, the board also sees no inconsistency between documents D39 and D40, both issued by the KIPO, as submitted by the respondent. In the board's view, both documents relate to the same point in time, namely the creation of the patent register of patent document D2. This occurred on 19 June 2012.

11.3 The board does not accept the respondent's further reading of these passages of the KIPO Patent Examination Guidelines to the effect that they would suggest that the act of making registered applications available might not occur immediately following registration. At the same time, however, the board agrees with the respondent that additional steps had to be met in order for the disclosure of patent document D2 to be obtainable by a member of the public. The respondent referred in this context to document D58, in which the KIPO outlined the procedure available in the year 2012 for obtaining a copy of the application documents, including the entire specification. The respondent highlighted that a patent number appearing in the patent application list resulting from a search on the KIPO website would have been identifiable only after the icon "application number" had become

clickable and that this only occurred if the status of the application number had been indicated as "Allowed". Moreover, there could have been waiting lists for icons to become clickable.

11.4 However, as evidenced by document D40, the patent register of patent document D2 had been created on 19 June 2012. As highlighted by the appellant, patent document D2 is a published Korean patent which means that it had been allowed. As submitted in the statement of grounds of appeal with reference to document D42, which is a copy of the patent register of patent document D2, creation of the patent register took place after the applicant had paid the registration fee to the KIPO on receiving a Notice of Allowance for the application.

11.5 The period from the creation of the patent register on 19 June 2012 until 28 June 2012, the latter being the day prior to the priority date of the patent in suit, may be considered short. Nevertheless, the board is convinced that the disclosure of patent document D2 could have been obtained by any member of the public prior to the priority date via the KIPO website.

As shown by declaration D59, copies of the application documents, including the original specification, of another Korean patent were obtained within several hours by performing a search on 6 July 2021 following the procedure set out in document D58. This other patent had been registered on 1 July 2021 and copies of the application documents were obtained before the patent was published on 8 July 2021, i.e. within a few days from the date of registration.

The board acknowledges that the search reported in declaration D59 was performed years after the priority date of the patent in suit. However, the board has no doubt that the disclosure of patent document D2 could have been retrieved by following the same procedure, since the KIPO confirmed in document D58 that this search procedure had also been in place in 2012.

In relation to patent document D2, the respondent referred to a time lag of four days from the date of registration (15 June 2012 as indicated on documents D2 or D42) to the date of creation of the patent register (19 June 2012 as mentioned in document D40). However, even if a similar period was assumed for the occurrence of the earliest point in time at which - from the creation of the patent register - the disclosure of patent document D2 would have been available on the KIPO website, that date would still lie prior to 29 June 2012. In this context, it amounts to mere speculation on the respondent's part that icons on the KIPO website might have not been clickable for a substantial period, or not at all until after 28 June 2012.

The respondent's reference to decision T 91/98 in which the deciding board did not consider the date of availability of a document's information as sufficiently proven is also of no assistance since, in the current case, the evidence to be considered by this board is not comparable and the underlying situation also differs, in particular in that it is a national patent authority which was in charge of making the disclosure of patent document D2 available to the public.

12. In a further line of argument, the respondent argued that, even if the patent register had been created for patent document D2, this did not mean that the disclosure of patent document D2 had been made available to the public. The search procedure set out by the appellant with reference to documents D58 and D59 for accessing the disclosure required knowledge of the applicant code number and the patent number of a registered application in order for a member of the public to be able to request inspection of the documents prior to the publication date of the patent. This process included numerous assumptions such as an awareness of Green Cross Company, a search on the KIPO database for the applicant code number of that company and performance of a search regularly in order to identify patent document D2 in the very short time window between the creation of the patent register and the priority date of the patent in suit. Such a merely theoretical, in contrast to practical, possibility of having access, did not make patent document D2 available to the public within the meaning of Article 54(2) EPC. It was a hidden document.

12.1 The board, however, does not agree that, in view of the procedure to be followed for gaining access to the disclosure of patent document D2, this document should be considered a hidden document or, in other words, not be considered as having been made available to the public because a member of the public only had a theoretical possibility of gaining access. Instead, any member of the public, by following the steps outlined in documents D58 and D59 on the KIPO website, could have gained access to patent document D2. The required applicant code number was obtainable via the KIPO and the required patent number was obtainable on the website when the steps were followed. Document D60

evidences that Green Cross Corporation was known to the public.

12.2 Whether or not there had been motivation for a member of the public to search for the disclosure of patent document D2 or whether a member of the public actually gained access to patent document D2 prior to the priority date of the patent in suit, is of no relevance. In order for the disclosure of patent document D2 to have been made available to the public within the meaning of Article 54(2) EPC, it is sufficient that a member of the public had the possibility of gaining access to the disclosure of patent document D2. That this accessibility was not merely theoretical was demonstrated by the search process which would have led to the retrieval of the disclosure of patent document D2 prior to the priority date of the patent in suit.

12.3 The board considers neither decision T 314/99 nor decision T 1553/06 to be of relevance to the current case.

Decision T 314/99 was concerned with the question of whether the arrival of a diploma thesis in the archive of the library of a university made the diploma thesis available to the public. This was denied by the deciding board since arrival did not mean that the thesis was catalogued or otherwise prepared for the public to acquire knowledge of it because, in the absence of such means of information, the public would remain unaware of its existence.

Decision T 1553/06 was concerned with several documents stored on the web and accessible via a specific URL. None of those documents, however, was a disclosure of a

patent document accessible via the website of a national patent authority. Furthermore, while a two-step test was proposed by the deciding board for assessing whether a document stored on the web and accessible via a specific URL was made available to the public within the meaning of Article 54(2) EPC, the board also acknowledged that the conclusion of whether or not such a document was to be considered as having been made available to the public was the result of the assessment of the circumstances of each individual case (see T 1553/06, Reasons 6.7.3).

13. Therefore, the disclosure of patent document D2 is state of the art within the meaning of Article 54(2) EPC, irrespective of the validity of the priority of the patent in suit.

Main request

Inventive step - claim 1 - Article 56 EPC

Document D2 as closest prior art

14. It was common ground between the parties that the relevant disclosures of document D2 (in the Korean language) could be obtained by referring to document D1 (in the English language). Hence, the references in the following to document D1 are representative of equivalent disclosures in document D2.

15. Document D1 discloses a composition for treating Hunter syndrome, comprising as an active ingredient an I2S having the amino acid sequence of SEQ ID NO: 1 of the patent in suit, wherein a cysteine residue at position 59 in the I2S amino acid sequence is converted into

FGly at a molar ratio of 75% or higher (see claims 1 and 2). Starting at paragraph [110], document D1 describes the purification of I2S. Paragraph [123] of document D1 discloses that cation exchange chromatography (CEX) was conducted to obtain I2S showing high activity (a high content of FGly) with a high content of sialic acid and to remove other impurities, i.e. product-related impurity in the form of aggregated I2S and processed I2S or process-related impurity in the form of HCP.

Difference, its technical effect, and the objective technical problem

16. The subject-matter of claim 1 differs from the disclosure in document D1 in that it specifies that the I2S composition contains less than 150 ng/mg Host Cell Protein (HCP).

17. The technical effect is a composition with a low HCP level of less than 150 ng/mg HCP content, which is linked to improved product safety (see e.g. document D28, page 54, paragraph bridging the left and middle columns).

18. The objective technical problem is the provision of an I2S composition with improved safety.

Obviousness

19. It was common knowledge to the skilled person that patient safety requires that contaminants such as HCP be eliminated or reduced to the lowest practical levels to prevent problems such as adverse immune reactions (see document D25, p 38, middle column, paragraph 1) and that most biotechnology products reviewed by the

FDA contain ELISA-based host cell protein levels of 1 to 100 ng/mg (see document D28, page 54, middle column, paragraph 1; D29, page 447, right-hand column, paragraph 1).

Based on this knowledge, the skilled person was motivated to bring the host cell proteins (HCPs) levels in the I2S preparation intended for therapeutic use, as described in document D1, to levels within the ranges approved by the regulatory authorities for other therapeutic proteins.

20. Document D1 provides clear guidance on how to remove impurities such as HCPs, suggesting that using CEX during the intermediate purification phase of a protocol involving four chromatographic steps is effective for reducing impurities in an I2S preparation with a high FGly content (see D1, paragraphs [122] and [123]).

Moreover, purification of I2S using various chromatographic and ultrafiltration processes was already part of the common general knowledge (see document D14, page 312, right-hand column, paragraph 1).

21. It was also within the skilled person's common general knowledge that purity can be achieved by adding or repeating steps, especially for purification of therapeutic proteins, as taught e.g. in document D30 (see page 7, last seven lines; page 18, paragraph 3).

It was also known, e.g. from document D30, page 35, paragraph 1, that separation of the target protein from most bulk impurities, such as other proteins etc., should take place in the intermediate purification

phase. This phase occurs between the capture phase (which aims to isolate, concentrate, and stabilise the target product) and the polishing phase (which aims to achieve high purity). This approach was, in fact, implemented in the purification protocol described in document D1.

22. The board considers that, having regard to the common general knowledge of the skilled person in the field and the teaching in document D1, the skilled person, faced with the above-mentioned problem, would have arrived at an I2S composition with at least 70% FGly conversion and less than 150 ng/mg HCP by applying routine measures.

Thus, the subject-matter of claim 1 does not involve an inventive step within the meaning of Article 56 EPC.

Auxiliary requests 1 to 3

Inventive step - claim 1 - Article 56 EPC

23. The wording of claim 1 of the main request and of claim 1 of each of auxiliary requests 1 to 3 is identical. Consequently, the same inventive step considerations as provided for the main request apply to auxiliary requests 1 to 3. The subject-matter of the auxiliary requests therefore also lacks an inventive step within the meaning of 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 Chairwoman:

I. Aperribay M. Pregetter

Decision electronically authenticated