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Datasheet for the decision of 21 October 2022

Case Number: T 0084/19 - 3.3.08

Application Number: 11818806.9

Publication Number: 2606152

IPC: C12Q1/68, C12N15/11, A61K48/00, G01N33/68

Language of the proceedings: EN

Title of invention:
Methods for determining the presence or risk of developing facioscapulohumeral dystrophy (FSHD)

Patent Proprietor:
Fred Hutchinson Cancer Research Center
Leiden University Medical Center
University of Rochester

Opponent:
Müller Fottner Steinecke Rechtsanwalts- und Patentanwaltspartnerschaft mbB

Headword:
Methods for determining the presence or risk of developing FSHD/FRED HUTCHINSON CANCER RESEARCH CENTER
LEIDEN UNIVERSITY MEDICAL CENTER
UNIVERSITY OF ROCHESTER

Relevant legal provisions:
EPC Art. 83, 108
EPC R. 6(4), 6(5)
RFees Art. 2, item 11
RPBA Art. 12(4)
RPBA 2020 Art. 13(2)
Art. 2 and 3 Commission Recommendation 2003/361/EC of 6 May 2003

Keyword:
Appeal deemed validly filed - (yes)
Main request - admission (yes), sufficiency of disclosure (no)
Amended auxiliary request 1 after summons - admission/cogent reasons (no)
Auxiliary request 2 - admission (yes), requirements of the EPC met (yes)

Decisions cited:
G 0003/97, G 0004/97, T 0409/91, T 0217/15, T 0494/18, T 1839/18, T 2091/18, T 2920/18, T 0225/19, T 2295/19, T 1151/04, T 1063/06, T 0247/20

Catchword:
Eligibility requirements for paying a reduced appeal fee by an appellant - opponent in case of opposition filed as a straw man (Reasons 1 to 9.2).

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Case Number: T 0084/19 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 21 October 2022

Appellant: (Opponent)	Müller Fottner Steinecke Rechtsanwalts- und Patentanwaltspartnerschaft mbB P.O. Box 11 40 Römerstrasse 16b 52428 Jülich (DE)
Representative:	Jaekel, Robert Witthoff Jaekel Steinecke Patentanwälte PartG mbB Postfach 1140 52412 Jülich (DE)
Respondent: (Patent Proprietor 1)	Fred Hutchinson Cancer Research Center 1100 Fairview Avenue North Seattle, WA 98109 (US)
Respondent: (Patent Proprietor 2)	Leiden University Medical Center Albinusdreef 2 2333 ZA Leiden (NL)
Respondent: (Patent Proprietor 3)	University of Rochester Medical Center 601 Elmwood Avenue Box OTT Rochester, NY 14642 (US)
Representative:	MacLeod, Ian J A Kemp LLP 80 Turnmill Street Gray's Inn London EC1M 5QU (GB)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on**

5 November 2018 concerning maintenance of the European Patent No. 2606152 in amended form.

Composition of the Board:

Chairman	P. Julià
Members:	M. Montrone
	A. Bacchin

Summary of Facts and Submissions

I. The appeal is against the decision of an opposition division to maintain the European patent No. 2 606 152 in amended form. This patent is based on European patent application No. 11818806.9 which has been published as International patent application WO 2012/024535 (the "patent application").

II. With their statement of grounds of appeal, the opponent ("appellant") submitted new documents and raised various objections, including sufficiency of disclosure, against the subject-matter of claim 14 of the request upheld by the opposition division.

III. In reply, the patent proprietor ("respondent") submitted a main request and auxiliary requests 1 and 2. Furthermore, new documents were filed.

IV. The appellant replied to the respondent's submission and the respondent replied thereto. Both parties submitted further arguments and documents. As an auxiliary measure, oral proceedings were requested by both parties.

V. In a communication in preparation of oral proceedings, the parties were informed of the board's provisional, non-binding opinion on the issues of the appeal.

VI. Both parties replied to the communication of the board.

In their reply, the respondent submitted that the appellant's appeal was not deemed to be validly filed. Furthermore, a new auxiliary request 2 was filed and

former auxiliary request 2 was renumbered as auxiliary request 3.

In their reply, the appellant provided arguments in support of a validly filed appeal and informed the board that they would not attend the oral proceedings.

VII. In a further communication, the parties were informed of the board's provisional opinion that the appeal was deemed to be validly filed.

VIII. Oral proceedings were held on 21 October 2022 by videoconference and in the absence of the appellant. During the oral proceedings, the respondent withdrew the main request and made auxiliary request 1 their new main request. Furthermore, the former auxiliary requests 2 and 3 were renumbered as auxiliary requests 1 and 2, respectively.

IX. Claims 14 and 15 of the main request read as follows:

"14. An agent capable of inhibiting or suppressing the level of DUX4-fl expression, for use in a method of treating a mammalian subject suffering from, or at risk for developing, Facioscapulohumeral Dystrophy (FSHD) wherein the agent is capable of increasing chromatin mediated repression, optionally wherein the agent inhibits histone demethylase LSD1 activity, and further optionally wherein the agent is pargyline.

15. An agent capable of inhibiting DUX4-fl mediated transcription activation in a population of cells in a mammalian subject, for use in a method of treating a mammalian subject suffering from, or at risk for developing, Facioscapulohumeral Dystrophy (FSHD) wherein the agent is an agent that interferes with

DUX4-fl binding to one or more DUX4-fl consensus binding sites comprising the sequence "TAAYBBAATCA", wherein the agent comprises a DUX4-S polypeptide, or a nucleic acid molecule encoding DUX4-S polypeptide."

X. Auxiliary requests 1 and 2 were identical to the main request except for the deletion of claim 14 in auxiliary request 1 and the deletion of claims 14 and 15 in auxiliary request 2.

XI. The following documents are referred to in this decision:

D3: van der Maarel S.M. *et al.*, NIH Public Access, Author Manuscript, pages 1 to 12 (published in final edited form as: Trends in Molecular Medicine, 2011, Vol. 17(5), pages 252 to 258;

D8: Metzger E. *et al.*, Nature, 2005, Vol. 437, pages 436 to 439;

D13: Lee M.G. *et al.*, Chemistry & Biology, 2006, Vol. 13, pages 563 to 567;

D14: Sun G. *et al.*, Molecular and Cellular Biology, 2010, Vol. 30, pages 1997 to 2005;

D15: El Mansouri F.E. *et al.*, Arthritis Research & Therapy, 2014, Vol. 16, R113, pages 1 to 15;

D16: Hayward D. and Cole P.A., HHS Public Access, Author manuscript, pages 1 to 16 (published in final edited form as: Methods of Enzymology, 2016, Vol. 573, pages 261 to 278).

XII. The parties' submissions on procedural issues, namely i) whether the appeal is deemed to be validly filed and ii) whether auxiliary request 1 can be admitted into the appeal proceedings, are set forth in the Reasons for the Decision.

XIII. The appellant's written submissions on substantive issues, insofar as relevant to the present decision, may be summarised as follows:

Main request

Sufficiency of disclosure - claim 14

Claim 14 encompassed any agent for use in the treatment of Facioscapulohumeral Dystrophy (FSHD) that inhibited or suppressed the expression level of full-length DUX4 (DUX4-fl) and increased chromatin-mediated repression. Since the agents in claim 14 were not structurally defined, the claim encompassed myriads of potential compounds including remote ones acting through signaling proteins. In particular, due to the use of the term "*optionally*" in claim 14, the agent was not limited to inhibitors of the histone demethylase LSD1 activity, including pargyline.

Thus, claim 14 encompassed as embodiment myriads of potential compounds for use in the treatment of FSHD. These compounds had to increase a chromatin-mediated repression by any possible means and to inhibit or suppress the expression of DUX4-fl to any possible extent. However, the patent application provided no guidance for a skilled person to select such functional compounds that had also to be suitable for the claimed therapeutic application. Absent any rule for selecting agents beyond LSD1 inhibitors, the skilled person had

to resort to trial-and-error experimentation on arbitrarily selected chemical compounds to determine whether or not any of them had all required properties. This required a research programme amounting to undue burden.

XIV. The respondent's submissions on substantive matters, insofar as relevant to the present decision, may be summarised as follows:

Main request

Sufficiency of disclosure - claim 14

The patent's contribution to the art justified the breadth of claim 14. The patent disclosed for the first time that an incomplete developmental silencing of a retrogene array caused FSHD (see paragraph [0230], last sentence). The causative role of the transcription factor DUX4 in this disease was described in Examples 3 to 5, in particular an inappropriate expression of factor DUX4-fl caused by an aberrant chromatin repression and leading to FSHD. This disclosure guided the skilled person in the development of FSHD therapies (see paragraph [0291]). Based on the data disclosed in the patent, it was plausible that FSHD could be treated by increasing chromatin repression which inhibited or suppressed the level of DUX4 gene expression, as shown in Examples 1 to 6 of the patent.

It was known in the art that a chromatin-mediated repression resulted in the inhibition of gene expression (see e.g. document D8, abstract). This meant that the mechanism of action on which the FSHD therapy in claim 14 relied on for inhibiting the expression of the DUX4-fl gene was known to the skilled person at the

relevant date. The patent's contribution to the art was the provision of a new therapeutic use (the treatment of FSHD) mediated through a known mechanism of action (chromatin-mediated repression). Since the mechanism of action was therefore known to achieve the desired therapy set out in claim 14, the situation in this case differed fundamentally from those dealt with in decisions T 1063/06 and T 1151/04.

The skilled person based on the teaching of the patent and taking common general knowledge into account was able to identify agents that caused chromatin repression to achieve the therapeutic effect. Document D8, for example, disclosed that several LSD1 inhibitors were successful in reinstalling a chromatin-mediated repression for inhibiting the gene expression of an androgen-receptor (see page 437, Figure 3, legend, page 438, column 2, second paragraph, and Figure 4c). The suitability of LSD1 inhibitors to mediate chromatin repression was likewise disclosed in documents D15 and D16 (see D15, abstract, and D16, page 5, penultimate paragraph). Although documents D15 and D16 were post-published, they referred to documents that were published prior to the relevant filing date of the patent. Thus, numerous agents for repressing chromatin were known to the skilled person at the relevant filing date of the patent and the patent provided the guidance to allow the skilled person to find in a straightforward manner further agents suitable for the treatment of FSHD.

Although chromatin-mediated repression was a complex process and not every LSD1 inhibitor had a therapeutic effect, this was irrelevant because the patent taught that H3K9 methylation (H3K9me3) played a central role in chromatin repression (see paragraphs [0226] and

[0227]) and the methylation status of H3K9 in chromatin was easily determined (see e.g. documents D8, D13, and D15). The patent therefore provided a straightforward guidance for selecting suitable agents and assays that allowed to test these agents for a therapeutic effect (see Example 6).

Although the genomic context of a target gene affected chromatin repression, this was irrelevant in the present case because the patent taught that by using FSHD muscle cells for testing potential LSD1 inhibitors, the skilled person would have necessarily succeeded in identifying further agents with desired therapeutic properties. The skilled person was therefore not in a trial and error situation. Moreover, there were also no serious doubts about the specificity of pargyline as suitable therapeutic agent. The withdrawal of this agent from the market for the treatment of hypertension had to be seen in perspective, since many agents were available for this therapeutic application. However, as regards FSHD no such agent existed. In such a situation, and due to the severity of FSHD, different standards for using therapeutic agents had to be applied.

XV. The appellant requested that the appeal was deemed to be validly filed. The appellant further requested that the decision under appeal be set aside, and the patent be revoked to the extent of claim 14 as maintained. Furthermore, the appellant requested that auxiliary request 1 (filed as new auxiliary request 2 with the submission dated 7 October 2022) not be admitted into the proceedings, and that documents D18 to D24a and D27 to D29 be admitted into the appeal proceedings.

XVI. The respondent requested that the appeal was not deemed to be validly filed. Further the respondent requested that the appeal be dismissed or, in the alternative, that the patent be maintained on the basis of the main request (filed as auxiliary request 1 in reply to the statement of grounds of appeal), or any of auxiliary requests 1 or 2. The respondent further requested that auxiliary request 1 (filed as new auxiliary request 2 with the submission dated 7 October 2022) be admitted into the proceedings, but not the appellant's documents D18 to D24a, and D27 to D29.

XVII. Since none of the documents filed in appeal proceedings, i.e. documents D18 to D31 were necessary for the board to arrive at a decision, the admissibility of any of these documents into the appeal proceedings needed not to be considered.

Reasons for the Decision

Whether the appeal is deemed to be filed

1. With submissions filed in preparation of the oral proceedings, the respondent objected that the appeal was not deemed to be filed in view of Article 108, second sentence, EPC, due to an apparent lack of entitlement to the reduced appeal fee by the appellant/ opponent, Müller Fottner Steinecke Rechtsanwalts- und Patentanwaltspartnerschaft mbB ("the patent attorney firm"). The conditions for an appellant be entitled to pay a reduced appeal fee were not fulfilled as being set forth in Article 2, item 11, Rules relating to fees (RFees) in conjunction with Rules 6(4) and 6(5) EPC, with reference to the Notice from the EPO dated 18 December 2017 concerning the reduced fee for appeal (OJ EPO 2018, A5; in the following "the EPO Notice")

and the Commission Recommendation 2003/361/EC of 6 May 2003 concerning the definition of micro, small and medium-sized enterprises (in the following "the Commission Recommendation").

1.1 The respondent did not dispute that the appellant in the present proceedings was the patent attorney firm and that, as such, qualified as a small and medium-sized enterprise (SME) within the meaning of Article 2 of the Commission Recommendation.

However it was submitted that in cases in which a notice of opposition, and later an appeal, were filed by a patent attorney firm acting as a straw man opponent, in accordance with established EPO practice, i.e. G 4/97, for the purpose of eligibility to pay a reduced appeal fee, the appellant and the interested party instructing the appellant should be regarded as linked enterprises within the meaning of Article 3(3) of the Commission Recommendation.

In this context, the contractual relationship between the appellant and the interested party instructing the appellant necessarily implied that they were linked enterprises so that the staff headcount and the financial ceilings of both entities should be taken into account in order to assess if the appellant fulfilled the requirements of an SME.

There were strong doubts as to the veracity of the declaration made by the appellant, as it was unlikely that the opposition had been filed by an SME in the light of the invention at stake, particularly the fact that only claim 14, which related to treatments for FSHD, had been opposed. According to the EPO Notice (see paragraphs 10 and 11), in case of doubt, the

appellant carried the burden of proof that the eligibility criteria had been met. In the present case, the appellant failed to provide such proof.

As a consequence the appellant was not entitled to pay a reduced appeal fee and the appeal had to be regarded as not deemed filed.

2. In reply thereto, the appellant referred to decision G 4/97 (see headnote) as allowing that a professional representative acting in his own name on behalf of a client could file an opposition. This was no circumvention of the law by abuse of process. According to the established case law, the burden of proof was on the party alleging that an opposition was inadmissible. In the present case, the respondent's objection was solely based on a speculation, namely that the appellant's client was "*overwhelmingly more likely*" to be a large entity because the objected subject-matter was directed to a medical use claim. However, no evidence was filed to support this speculation and thereby that the appellant was not entitled to a reduced appeal fee. Thus, the appeal was validly filed.

3. The board follows the arguments of the appellant and does not agree with the respondent's assessment for the following reasons:

(a) *The patent attorney firm is the only appellant in the present proceedings*

3.1 The entitlement to pay a reduced appeal fee under the conditions set by Article 2, item 11, RFees and Rule 6(4), (5) EPC must be assessed *vis-à-vis* the entity which has assumed the procedural status of an appellant.

Article 2, item 11, RFees provides that a reduced appeal fee may be paid for an appeal filed by a natural person or an entity referred to in Rule 6, paragraphs 4 and 5, EPC, i.e. *inter alia* small and medium-sized enterprises as defined in the above-mentioned Commission Recommendation. For this purpose appellants must file a declaration that they are a natural person or an entity covered by Rule 6(4) EPC in accordance with point 3 of the EPO Notice.

3.2 Therefore, to assess eligibility for paying a reduced appeal fee, the *status of appellant*, at the time of filing the notice of appeal, is the only relevant question under Article 2, item 11, RFees and Rule 6(4) EPC (see also point 9 of the EPO Notice).

3.3 In the present case, in conformity with the established jurisprudence of the Boards of Appeal set by decisions G 3/97 and G 4/97, the status of appellant is vested in the patent attorney firm. This fact was not disputed by the respondent, who explicitly acknowledged that the appellant was entitled to file an opposition and an appeal, when asked during the oral proceedings before the board.

3.4 As established by the Enlarged Board of Appeal in decisions G 3/97 and G 4/97, it is admissible to file an opposition on behalf of a third party. The status of opponent is a *procedural status*, which is acquired by any person filing an opposition in compliance with the provisions under Article 99 EPC in conjunction with Rule 76 EPC. Accordingly, the opponent is exercising its own right as a member of the public to file an opposition, even if a third party (the "principal") had incited the opponent to file the opposition. In such a

case the opponent cannot be regarded to act on the basis of the principal's personal entitlement. The question whether the opponent's acts accord with the intentions or instructions of the principal is relevant only to the internal relationship between the latter and the opponent, and has no bearing on the opposition proceedings. Accordingly there cannot be another true opponent apart from the formally authorised opponent so that the principal can under no circumstances be treated as a party (cf. G 3/97, Reasons 2.1 and 2.2).

3.5 Without disregarding that this decision properly regards admissibility of an opposition, the board considers that the application of the principles set out in the decisions G 3/97 and G 4/97 has a direct impact on the question of eligibility to pay a reduced appeal fee. Indeed the latter depends in this case on whether a straw man opponent may validly acquire the status of opponent/appellant.

3.6 With regard to the present case the patent attorney firm has validly acquired the procedural status of opponent and no special reasons were raised, nor does the board see any, to regard the filing of the opposition in the present case as a circumvention of the law by abuse of process as referred to in decisions G 3/97 and G 4/97 (see Headnotes 1(b) and 1(c)), i.e. the patent attorney firm is clearly neither acting on behalf of the patent proprietor, nor is it lacking entitlement to act as a European professional representative.

(b) *The patent attorney firm is entitled to pay a reduced appeal fee in accordance with Article 2, item 11, RFees and Rule 6(4) EPC.*

4. The respondent has not disputed that the patent attorney firm fulfils the requirements of a small and medium-sized enterprise as established by Article 2 of the Commission Recommendation.

It however submitted that it was unlikely that the opposition and the related appeal were filed in the interest of said SME itself but, in view of the subject-matter of the patent at issue, it was highly probable that they were filed in the interest of a third/instructing party (the "principal"). Thus, the contractual relationship between the patent attorney firm and the instructing party had to be regarded as that of "linked enterprises" in the sense of Article 3(3)(c) of the Commission Recommendation. Therefore, under these circumstances, the appellant should have provided further evidence proving that the patent attorney firm together with the instructing party were eligible for, and entitled to, pay a reduced appeal fee by the third/instructing party.

5. The board does not find support in the present case for applying the concept of "linked enterprises" according to Article 3(3) of the Commission Recommendation to the situation of an appeal filed by a straw man opponent.

5.1 As explained in Recitals 9 of the Commission Recommendation, for a better understanding of the real economic position of SMEs and to remove from the category groups of enterprises whose economic power may exceed that of genuine SMEs, a distinction should be made between autonomous, partner and linked enterprises.

5.2 However, first, there is no evidence on file to support or show that any of the relationships indicated in

Article 3(3) of the Commission Recommendation, in particular concerning contractual relationships in which an enterprise exercises a dominant influence over another entity, is truly applicable to the contractual relation between the appellant (the patent attorney firm) and the third/instructing party (the "principal") (Article 3(3)(c) of the Commission Recommendation).

5.3 Second, assuming that the internal legal relationship between the opponent and any third/instructing party had a legal significance for external purposes would be at odds with the interpretation of Article 99 and Rule 76 EPC established in the decisions G 3/97 and G 4/97. Under the EPC system, the opponent is the only person who matters in relation to the proprietor and the EPO; a third/instructing party (the "principal"; see G 3/97, Reason 2.1) will under no circumstances be treated as a party of the proceedings before the EPO. As long as the legal system has no objection to the filing of an opposition by the third/instructing party (the "principal") itself, there is also no objection to this party inciting a straw man to file an opposition. This interpretation is in line with the fact that under the EPC the opponent’s motives are of no relevance for the purposes of the opposition procedure (see G 3/97, Reasons 3.2.2 and 3.2.3).

5.4 The respondent's allegation that the third/instructing party (the "principal") cannot be a SME (for which, however, no evidence was provided) has thus no bearing and cannot be taken into account on the issue at stake, namely whether the filing of the present opposition/ appeal by a straw man (the patent attorney firm) constitutes a circumvention of the eligibility criteria to pay a reduced appeal fee.

5.5 Thus, the board sees no reasons to consider that the position of the third/instructing party (the "principal") bears any relevance.

6. Further, having regard to the burden of proof in the context of paying a reduced appeal fee, the board fails to see special reasons for investigating the veracity of the appellant's original (SME) declaration, as requested by the respondent.

6.1 The burden of proving that the eligibility criteria have been met lies in principle on the person claiming entitlement to pay a reduced appeal fee. Appropriate evidence may be requested *in case of doubt* as to the veracity of the (SME) declaration given by an appellant (cf. EPO Notice, point 10).

6.2 In the present case, the appellant made the necessary SME declaration upon filing the appeal and paying the reduced appeal fee. In reaction to the respondent's challenge to the appellant's eligibility for a payment of a reduced appeal fee, the appellant with submissions dated 10 October 2022 referred to decisions G 3/97 and G 4/97 and argued that the respondent’s allegations were lacking any legal bases and were based on pure speculations. The board agrees with the appellant and, considering the overall procedural situation, has no doubts as to the veracity of the appellant’s original SME declaration. Indeed, the respondent did not dispute that the patent attorney firm, the appellant in this case, satisfied the requirements set by the Commission Recommendation for an SME.

6.3 The board would also like to point out that the present case is fundamentally different from those in which a board has required the provision of appropriate

evidence because either no SME declaration (as required by points 3 and 4 of the EPO Notice) was filed when paying a reduced appeal fee (e.g. T 225/19, Reasons 2.7 and 3), or the qualification of the appellant as SME was at dispute (e.g. T 225/19, Reasons 4 and 5). None of these situations apply here.

6.4 Under these circumstances, the board has no doubts that the filing of the opposition and the appeal by the patent attorney firm constitutes no circumvention of the law regarding the entitlement to pay a reduced appeal fee.

(c) *Potential implications*

7. Finally the respondent raised potential implications if an appellant paid a reduced appeal fee without having the burden of providing evidence if the fulfilment of the requirements were challenged.

8. The board however does not consider these potential implications to be relevant.

8.1 As indicated above, in the present case the appellant has discharged the burden of proving that they fulfilled the requirements for a reduced appeal fee (see point 6.2 above). Doubts as to the veracity of the relevant SME declaration must be adequately raised in a convincing manner, which was not done in this case.

8.2 Under the present circumstances, the respondent’s arguments, if followed, would be equal to accept that a person acting on behalf of a third/instructing party (the "principal") is not the true opponent, but rather that either the third/instructing party (the "principal") is the true opponent or that they should

be considered as multiple or a plurality of appellants. The procedural situation of an appellant consisting of a plurality of persons, in which each one must be an entity or a natural person within the meaning of Rule 6(4) EPC (see EPO Notice, point 5), is however distinct from the one of a so-called straw man opponent.

8.3 The respondent's arguments would further imply that the appellant/opponent must reveal the motives for the opposition and/or the identity of the third/instructing party (the "principal"), which is neither the purpose of, nor required by, Article 99 EPC, as indicated and established in the decisions G 3/97 and G 4/97 (see e.g. G 3/97, Reasons 3.2.2 and 3.2.3).

9. Finally, the board cannot follow the respondent’s submissions that decision T 1839/18 availed the argument that companies employing "straw men" to file their oppositions/appeals could abuse the provisions relating to entitlement to pay a reduced appeal fee.

9.1 First, in case T 1839/18 the board was not called upon deciding this question, since in the case at stake the full appeal fee had been paid and no abuse was alleged. Second, the board there merely observed that if opponents under their true guise had no right to the fee reduction, they would run the risk - if found out - of their opposition being deemed not filed for non-payment of the appeal fee, Article 8, RFee with Article 99(1), last sentence, which would rather be to their detriment. However, the board did not identify any circumstances under which it could be concluded that there is an abuse, if the entity which assumed the status of opponent actually did not fulfill the requirements for a reduced appeal fee. Quite to the opposite, it was noted that it is not up to the Boards

of Appeal to "*question the wisdom of decisions made by the Administrative Council in full knowledge and awareness of the established jurisprudence of the Enlarged Board of Appeal. Should the Administrative Council have wished to impose further conditions for taking advantage of paying a reduced fee and in order to avoid abuses, it would no doubt have done so*." (cf. T 1839/18, Reason 2.20). The present board concurs with these considerations and concludes that, under the current law, eligibility requirements to pay a reduced appeal fee must be fulfilled solely with regard to the entity which vests the status of opponent/appellant, with due account being taken of the relevant jurisprudence of the Enlarged Board of Appeal, including that concerning the employment of "straw men".

9.2 As the present board has not been given reasons to doubt that in this case the employment of a straw man was a means of circumventing the law on payment of a reduced appeal fee and since the appellant fulfils the requirements for paying a reduced appeal fee, the board comes to the conclusion that the appeal fee has been paid in the correct amount. As a consequence, the appeal is deemed to be validly filed.

Main request

Admission of the main request into the appeal proceedings

10. The main request was filed by the respondent as auxiliary request 1 in reply to the appellant's statement of grounds of appeal and, at the oral proceedings before the board, the respondent made this auxiliary request their main request. This request is identical to auxiliary request 1 filed on 26 July 2018

in preparation of the oral proceedings before the first instance and it is also identical to the claim request upheld by the opposition division except for the splitting of the product-claim into two independent product-claims, namely claims 14 and 15.

Since the statement of grounds of appeal and the reply thereto were filed before the date of entry into force of the RPBA 2020, the transitional provisions set out in Article 25(2) RPBA 2020 apply and, in the present case, the discretion of the board has to be exercised in accordance with Article 12(4) RPBA 2007.

11. The main request was already filed at the proceedings before the first instance as well as at the onset of the appeal proceedings. All parties, and in particular the appellant, were well aware of the respondent's interest of prosecuting this request. In view of these circumstances, the board admits the main request into the appeal proceedings (Article 12(4) RPBA 2007).

Claim construction - claim 14

12. The main issue concerning substantive matters in this case is sufficiency of disclosure. A construction of the subject-matter of claim 14, i.e. the sole claim objected in these proceedings, is therefore essential.

13. Claim 14 is drafted as a purpose limited medical use claim in accordance with Article 54(5) EPC (see above). It relates to an agent for use in the treatment of a mammalian subject suffering from, or being at risk for developing, Facioscapulohumeral Dystrophy (FSHD), i.e. a specific form of muscle dystrophy (see patent, paragraph [0001]).

13.1 The claim further functionally defines this agent as being capable of inhibiting or suppressing the level of the DUX4-fl expression and of increasing chromatin-mediated repression (see patent, paragraphs [0008] and [0075]). The terms "*inhibiting*", "*suppressing*", and "*increasing*" in claim 14 are not further defined. Thus, these terms comprise any degree of inhibition, suppression, and increase.

13.2 DUX4 is a double homeobox retrogene that encodes a transcription factor (see patent, paragraphs [0001] and [0036], and document D3, page 4, third paragraph). The term "*DUX4-fl*" refers to the full-length DUX4 open reading frame (ORF), while the term "*DUX4-S*" as, for example, used in claim 15 of the main request refers to a short splice variant of DUX4 ORF (see patent, page 5, lines 37 to 40).

13.3 Likewise the term "*chromatin mediated repression*" in claim 14 is not further defined. The term refers to a chromosomal structure that is modified by any means and to such an extent that the level of DUX4-fl expression is inhibited or suppressed, for example, because of a restricted physical access to the promoter region of the DUX4 gene. These chromatin modifications might be located at a specific site (e.g., the DUX4 locus), or at unspecific distant chromosomal regions (e.g., an enhancer), as long as the level of DUX4-fl expression is inhibited or suppressed at any extent.

13.4 Claim 14 further states that "*optionally wherein the agent inhibits histone demethylase LSD1 activity, and further optionally wherein the agent is pargyline*" (emphasis added). For the purpose of claim construction, these features in claim 14 are merely optional and have therefore no bearing on the

definition of the claimed subject-matter and the scope of the claim.

13.5 The agent of claim 14 for use in treating FSHD is therefore not structurally defined but merely functionally defined by its capabilities of increasing chromatin-mediated repression and inhibiting or suppressing the level of DUX4-fl expression. Consequently, claim 14 encompasses *inter alia* as embodiment all chemical compounds for the treatment of FSHD that increase chromatin-mediated repression by any means (such as acetylation, phosphorylation, methylation, etc., see *inter alia*, document D14, page 1997, paragraph bridging columns 1 and 2, and page 2004, column 2, second paragraph) and inhibit or suppress the level of DUX4-fl expression at any extent. The agent of claim 14 is not limited to any compound class, or chemical structure for achieving these results.

Sufficiency of disclosure - claim 14

14. As set out above under claim construction, claim 14 encompasses *inter alia* as embodiment all chemical compounds suitable for use in the treatment of FSHD that increase a chromatin-mediated repression by any means and which, as a result thereof, inhibit the expression of DUX4-fl to any extent. This embodiment will be considered in the following.

15. The respondent submitted that the embodiment under consideration was sufficiently disclosed in the patent application, *inter alia* because the breadth of the claim was justified by the patent application's contribution to the art.

16. The requirement of sufficiency of disclosure of an invention is to ensure that the exclusive right conferred by a patent should be justified by the actual technical contribution to the art (see Case Law of the Boards of Appeal of the EPO, 10th edition 2022, hereinafter "Case Law", II.C.8.1, e.g. decision T 409/91, OJ EPO 1994, 653, Reasons 3.5). A technical contribution to the art requires, however, that the claimed invention can be realised by the skilled person at the effective date of the patent application based on the application as a whole and in consideration of the common general knowledge of the skilled person (see Case Law, II.C.2, II.C.3.1, and II.C.4). In the present case, realisation of claim 14 requires that an agent suitable for the treatment of FSHD that increases chromatin-mediated repression and inhibits DUX4-fl expression is available to the skilled person across substantially the whole breadth of the claim without undue burden (see Case Law, II.C.5.4, II.C.6.7, II.C. 7.1.2, and II.C.7.2).

16.1 The board concurs with the respondent that the patent application discloses in Examples 1 to 5 experimental data showing that the stable and inappropriate expression of DUX4-fl from a permissive 4A chromosome in differentiated muscle cells causes FSHD (see page 35, lines 1 to 6; page 57, lines 6 to 12; page 85, lines 17 and 18; page 91, lines 23 to 25; page 100, lines 1 to 4). Furthermore, the patent application discloses a specific model for FSHD pathophysiology (see page 82, line 31 to page 83, line 19).

16.2 As regards therapies for FSHD, the patent application, in particular Examples 3 and 5 disclose several target genes of the DUX4-fl transcription factor that "*may help guide the development of therapies for FSHD*" (see

inter alia, page 90, line 14 to page 91, line 20; page 100, line 25 to page 101, line 5; Figure 18; and page 103, lines 17 to 21). Furthermore, Example 6 discloses that DUX4 can be a therapeutic target itself. Pargyline is an agent reported to inhibit the activity of LSD1 that demethylates histone 3 at lysine 9 (H3K9) in chromatin. This LSD1 inhibitor suppresses DUX4 mRNA levels in FSHD muscle cells. The patent application concludes in Example 6 from the data disclosed in Figures 22 and 23 that "*agents that increase chromatin mediated repression, such as agents that inhibit LSD1 activity, will be useful to suppress DUX4 and are candidate therapeutic agents for FSHD*" (see page 103, line 24 to page 104, line 20).

16.3 Thus, Example 6 of the patent application provides information on an assay method which can be used for testing candidate therapeutic agents for the treatment of FSHD based on the agent pargyline that increases chromatin mediated repression by inhibiting LSD1 demethylase activity. However, the subject-matter of claim 14 is neither limited to this specific agent nor to agents that increase chromatin repression by LSD1 inhibition. Notwithstanding that, except for pargyline, the patent application provides no information for any other suitable agent that may increase chromatin mediated repression by any other means and inhibit or suppress the level of DUX4-fl expression - at any extent.

17. The respondent argued that the disclosure of pargyline in the patent application provided the skilled person with one way of achieving the desired therapeutic effect. Moreover, several assays were disclosed in the patent application that allowed the skilled person to identify and obtain further agents in a straightforward

manner. Agents having the properties of being LSD1 inhibitors and/or monoamine oxidase inhibitors were known to the skilled person, such as those disclosed in document D8 (see page 438, column 2, second paragraph), and in post-published documents D15 (see abstract), and D16 (see page 5, penultimate paragraph).

17.1 With respect to documents D8, D15 and D16, the board notes that each of these documents discloses solely LSD1 inhibitors, such as pargyline, i.e. the agent exemplified in the patent application. Alternatively siRNA molecules are disclosed which specifically knock-down the expression of specific genes (see document D8, page 437, Figure 3, Legend, and page 438, column 2, second paragraph; document D15, abstract, page 4, column 2, second paragraph; document D16, page 5, fourth paragraph). Thus the agents shown in these documents to increase chromatin mediated repression are those disclosed in the patent application. Accordingly the disclosure of these documents does not go beyond that of the patent application. As a side remark, siRNA molecules likewise disclosed in these documents act directly on mRNA, and hence, do not increase chromatin repression. Therefore such siRNA molecules do not fall within the scope of claim 14.

17.2 Furthermore, documents D15 and D16 are published after the relevant filing date of the patent application. Thus, the question arises whether or not these documents can be accepted at all as being an account of what the skilled person knew at the effective date about agents that increase chromatin repression. In the board's view, however, this question can be left unanswered, since the disclosure of both documents is restricted to LSD1 inhibitors and siRNA (document D15), or to LSD1 inhibitors only (document D16). Other agents

that potentially increase chromatin repression by a mechanism different from inhibiting LSD1 are not disclosed in any of documents D15 and D16 nor, as stated above, in document D8.

17.3 As mentioned likewise above, LSD1 is a specific demethylase that removes repressive methyl residues from histone proteins (H3K9me3). However, claim 14 is not limited to LSD1 inhibitors but encompasses any chemical compound that increases chromatin repression and inhibits or suppresses the level of DUX4-fl expression at any extent. Document D14, for example, discloses that not only methylation but also other histone modifications such as acetylation and phosphorylation have an effect on, and can alter, the chromatin structure and that "*the sum of these modifications may be the ultimate determinant of the chromatin state that regulates gene transcription*" (see page 1997, column 1, second paragraph to column 2, second full paragraph, page 2004, column 2, second paragraph).

17.4 Therefore, the documents on file, in particular documents D8, and D14 to D16 provide evidence that the mechanisms causing an increased chromatin repression are neither straightforward nor simple. Since the repression might be mediated by local and/or global chromatin (histone) modifications such as those referred to above (acetylation/deacetylation, phosphorylation/dephosphorylation, methylation/ demethylation), either through mechanisms that act directly or indirectly on the target gene (see, for example, the role of interleukin-1β in the induction of the microsomal prostaglandin E synthase 1 expression as described in document D15), it remains unpredictable whether or not any agent tested will have an effect on

inhibiting or suppressing the level of DUX4-fl expression.

17.5 The patent application describes a number of assay methods which can be used to identify LSD1 inhibitors other than pargyline that might increase chromatin repression and inhibit/suppress the level of expression of the DUX4-fl gene. However this teaching of the patent application, contrary to the respondent's assertion, provides no guidance for the skilled person which would allow her/him at least an educated guess as to select, for example, a particular chemical structural class to which agents other than LSD1 inhibitors belong, let alone for agents involved in all other chromatin (histone) modifications (see above) across substantially the whole breadth of claim 14.

17.6 In these circumstances, in a search for therapeutic agents falling within substantially the whole breadth of claim 14, the skilled person would have to test a virtually unlimited amount of chemical compounds of various chemical structures. Although a reasonable amount of trial-and-error experimentation may be acceptable to acknowledge that the claimed invention can be carried out without undue burden, this presupposes that sufficient information is available that leads the skilled person directly towards success through the evaluation of initial failures (see Case Law, II.C.6.7).

17.7 In the present case, and based on the evidence on file, the skilled person would need to test all chemical substances affecting directly or indirectly the structure of chromatin (such as phosphorylation, acetylation, and/or methylation levels) without any guarantee that agents would be found that (directly/

indirectly) increase chromatin repression and (directly/indirectly) inhibit or suppress the level of DUX4-fl expression - at any possible extent. Therefore the patent application does not provide the skilled person at the relevant date of the application with any guidance enabling her/him, without undue experimentation, to obtain substantially all of the agents as defined in claim 14. Such a situation is often described in the case law as an invitation to perform a "research programme" and considered to amount to an undue burden (see CLBA, II.C.6.7).

17.8 The board does therefore not agree with the respondent that the present case differs from those cases dealt with in the decisions T 1151/04 (see Reason 3.1.2) and T 1063/06 (see Reason 5.1). Although, contrary to the situation in decision T 1063/06 (see Reason 5.2), the mechanism of action (i.e. chromatin repression) is known in the present case, this mechanism is not limited to a single enzyme but involves many different enzymic reactions that could act unpredictably directly or indirectly on DUX4-fl gene expression. Moreover, the patent application does not disclose any selection rule for agents other than those acting on LSD1 (see above).

18. In view of the above considerations, the board concludes that for the embodiment under consideration of claim 14, and hence the main request, the requirements of Article 83 EPC are not met.

19. In view of this conclusion, the question about the specificity of pargyline can be left unanswered.

20. Furthermore, since the subject-matter of claim 14 has been found by the board not to comply with the requirements of Article 83 EPC on the basis of the

documents already submitted during the first instance proceedings, there is no need to consider any of the new documents filed by the appellant in appeal proceedings in support of their case on insufficiency of disclosure or any of the new documents submitted by the respondent in reply thereto. Consequently, the question of admitting all these new documents into the appeal proceedings can likewise be left unanswered.

Auxiliary request 1 (filed as auxiliary request 2 with the letter dated 7 October 2022)

Admission into the appeal proceedings of auxiliary request 1

21. Auxiliary request 1 was filed with the respondent's letter of 7 October 2022, i.e. after notification of the summons to oral proceedings and after the board had issued the communication under Article 15(1) RPBA 2020. Thus, its admittance depends on whether Article 13(2) RPBA 2020 applies to the present case.

22. The appellant objected to admittance of auxiliary request 1 for lack of compliance with Article 13(2) RPBA 2020. It was submitted that the filing of this auxiliary request was an amendment of the respondent's case within the meaning of Article 13(2) RPBA 2020 and that there was no justification for filing this auxiliary request only two weeks before the oral proceedings. On the contrary, the respondent had reasons to file and should have filed this auxiliary request 1 already with the reply to the statement of grounds of appeal.

23. In support of admittance, the respondent argued that auxiliary request 1 merely consisted in the deletion of claim 14 of the main request and thus it could not be

regarded as an amendment of the party's appeal case, which required a justification by exceptional circumstances (Article 13(2) RPBA 2020). The more so because the deletion of claim 14 removed all objections raised in appeal proceedings. Following the deletion of claim 14 of the main request, the remaining subject-matter did not imply a change of the legal and factual framework of the appeal, and no objections were raised against the subject-matter remaining in appeal proceedings.

24. The board cannot follow the respondent's argumentation.

24.1 With regard to the question of whether a new request filed after the statement of grounds of appeal or the reply thereto constitutes an amendment to the party's appeal case within the meaning of Article 13(2) RPBA 2020, the present board concurs with the line of jurisprudence considering that a new request filed after the statement of grounds of appeal or the reply thereto with a set of claims that is different to that of the previous requests is to be regarded as an "amendment to the party's appeal case", even if the amendment consists only in the deletion of claims and the remaining claims were already part of a request in appeal (see e.g. T 2295/19, Reasons 3.4.4; T 2920/18, Reasons 3.6.4; T 2091/18, Reasons 4.1 and 4.2; T 494/18, Reasons 1.3.2 and 1.4; and T 247/20, Reasons 1.3).

This interpretation follows from a systematic reading of the Rules of Procedure of the Boards of Appeal, according to which the statement of grounds of appeal and the reply thereto must contain a party's complete appeal case (Article 12(3) RPBA 2020). Moreover a party's appeal case should be directed *inter alia* to

the requests on which the decision under appeal was based (Article 12(2) RPBA 2020). Accordingly, all parties' requests have to be expressly specified at the onset of the appeal proceedings. The filing of a new claim request at later stages of the appeal proceedings must be considered an amendment of the party's case, a procedural step that formally changes the factual and legal situation of the appeal proceedings.

24.2 Had the respondent intended to pursue this change, they would have had reasons to file it already in reply to the statement of grounds of appeal, since the subject-matter of auxiliary request 1 had not been attacked by the appellant at that stage of the proceedings. This fact must have been clear also earlier to the respondent, since it was even underlined in the appealed decision, in which the opposition division noted that no objection had been raised against the DUX4-s polypeptide or the encoding nucleic acid disclosed in claim 14(b) of the main request at first instance (cf. appealed decision, point 5.3.1.5), i.e. claim 15 of the main request in appeal proceedings.

The respondent neither provided an explanation for the late filing of auxiliary request 1 nor referred to any circumstances, let alone exceptional ones, that had prevented the respondent from filing auxiliary request 1 at the onset of the appeal proceedings. The board fails also to see any justification for the late filing of this amendment.

25. The board thus decided to exercise its discretion under Article 13(2) RPBA 2020 and not to admit auxiliary request 1 into the appeal proceedings.

Auxiliary request 2 (filed with the reply to the statement of grounds of appeal)

Admission into the appeal proceedings of auxiliary request 2

26. Auxiliary request 2 was originally filed in response to the preliminary opinion of the opposition division and in preparation of the oral proceedings at first instance. Since the opposition division decided to maintain the patent in amended form on the basis of the main request, the admission of *inter alia* auxiliary request 2 into the proceedings was not considered by the opposition division.

27. In reply to the appellant's statement of grounds of appeal, the respondent filed *inter alia* auxiliary request 2. Since the statement of grounds of appeal and the reply thereto were filed before the date of entry into force of the RPBA 2020, the transitional provisions set out in Article 25(2) RPBA 2020 apply and, in the present case, the discretion of the board has to be exercised in accordance with Article 12(4) RPBA 2007.

28. In application of its discretionary power under Article 12(4) RPBA 2007, the board admits auxiliary request 2 into the proceedings. As indicated above, this auxiliary request was already filed at the proceedings before the first instance as well as at the onset of the appeal proceedings. All parties were thus well aware of the respondent's interest of prosecuting this auxiliary request and therefore, had sufficient time and ample opportunity to consider the factual and legal situation arising from this auxiliary request.

Substantive matters

29. Moreover, since no ground of opposition has been raised against the subject-matter of auxiliary request 2, the board concludes that this set of claims complies with the requirements of the EPC.

Order

For these reasons it is decided that:

1. The appeal is deemed to have been validly filed.

2. The decision under appeal is set aside.

3. The case is remitted to the opposition division with the order to maintain the patent on the basis of claims 1 to 13 of auxiliary request 2 filed with the reply to the statement of grounds of appeal and a description to be adapted thereto.

The Registrar: The Chairman:

L. Malécot-Grob P. Julià

Decision electronically authenticated