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Datasheet for the decision of 10 February 2025

Case Number: T 0250/23 - 3.3.09

Application Number: 12758652.7

Publication Number: 2753187

IPC: A23L33/135, A23L2/52, A61K35/74, A61P3/04, A61P3/06, A23K10/16

Language of the proceedings: EN

Title of invention:
METHOD FOR PREVENTING AND/OR TREATING INSULIN RESISTANCE

Patent Proprietor:
Caelus Pharmaceuticals B.V.
Stichting Amsterdam UMC

Opponent:
Strawman Limited

Headword:
Insulin resistance/CAELUS

Relevant legal provisions:
EPC Art. 100(c), 123(3), 84, 83, 54, 56
RPBA 2020 Art. 12(4)

Keyword:
Grounds for opposition - extension of subject-matter (yes)
Auxiliary request 1 - allowable

Decisions cited:
T 1868/16

Europäisches Patentamt
European Patent Office
Office européen des brevets

Beschwerdekammern

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Case Number: T 0250/23 - 3.3.09

D E C I S I O N
of Technical Board of Appeal 3.3.09
of 10 February 2025

Appellant: (Patent Proprietor 1)	Caelus Pharmaceuticals B.V. 50, Rondweg 3474 KG Zegveld (NL)
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Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 29 November 2022 concerning maintenance of the European Patent No. 2753187 in amended form.**

Composition of the Board:

Chairman	A. Haderlein
Members:	F. Rinaldi
	A. Jimenez

Summary of Facts and Submissions

I. This decision concerns the appeals filed by the patent proprietors and by the opponent against the opposition division's interlocutory decision.

II. With the notice of opposition the opponent requested that the patent be revoked under Article 100(a) (lack of novelty and of inventive step), (b) and (c) EPC.

III. The documents submitted during the opposition proceedings include:

D1: WO 2011/043654 A1

D2: R.B. Canani *et al.*, "Potential beneficial effects of butyrate in intestinal and extraintestinal diseases", World Journal of Gastroenterology, 17(12), March 2011, 1519-28

D3: R. Muños-Tamayo *et al.*, "Kinetic modelling of lactate utilization and butyrate production by key human colonic bacterial species", FEMS Microbiology Ecology, 76, 2011, 615-24

D4: US 2007/0258953 A1

D6: Y. Sanz *et al.*, "Insights into the roles of gut microbes in obesity", Interdisciplinary Perspectives on Infectious Diseases, Article ID 829101, 2008

D7: WO 2010/108865 Al

D26: P.A. Gilijamse *et al.*, "Treatment with *Anaerobutyricum soehngenii*: a pilot study of safety and dose–response effects on glucose metabolism in human subjects with metabolic

syndrome", npj Biofilms and Microbiomes, 6:16, 2020

D27: Declaration by A. Goodman (filed by the opponent)

D38: Declaration by W. de Vos (filed by the patent proprietors)

D39: Email from R. Pukall of DSMZ dated 11 September 2020

D40: A. Belenguer *et al.*, "Two routes of metabolic cross-feeding between *Bifidobacterium adolescentis* and butyrate-producing anaerobes from the human gut", Applied and Environmental Microbiology, 72(5), May 2006, 3593-9

IV. In the decision under appeal, the opposition division concluded, among other things, that the ground for opposition of Article 100(c) EPC prejudiced maintenance of the patent as granted (main request) and that the invention set out in auxiliary request 1 was insufficiently disclosed.

V. On appeal, the patent proprietors maintained the main request (i.e. that the patent be maintained as granted) and filed a total of 53 auxiliary requests. Auxiliary requests 1 to 47, which had been presented during the opposition proceedings, were filed with the statement setting out the grounds of appeal, as were the following documents, among other citations:

D49: C. Ramirez-Farias *et al.*, "Effect of inulin on the human gut microbiota: stimulation of *Bifidobacterium adolescentis* and *Faecalibacterium prausnitzii*", British Journal of Nutrition, 101, 2009, 541-50

D50: C. Engels *et al.*, "The common gut microbe *Eubacterium hallii* also contributes to

intestinal propionate formation", Frontiers in Microbiology, 7, May 2016, Article 713, 1-12

VI. Relevant to this decision is the wording of claim 1 of the patent as granted and of claim 1 of auxiliary request 1.

Claim 1 of the patent as granted reads as follows:

"*Eubacterium hallii* or relatives having at least 98% sequence identity with the 16S rRNA sequence of *Eubacterium hallii*, and/or *Alcaligenes faecalis* or relatives having at least 98% sequence identity with the 16S rRNA sequence of *Alcaligenes faecalis*, for use in preventing and/or treating insulin resistance and/or insulin resistance-related complications selected from metabolic syndrome, dyslipidemia, type 2 diabetes mellitus, and insulin resistance in endocrine diseases such as in obese subjects with type 1 diabetes mellitus, Cushing's disease and lipodystrophy syndromes".

Claim 1 of auxiliary request 1 differs from claim 1 of the main request in that the terms "or relatives having at least 98% sequence identity with the 16S rRNA sequence of *Eubacterium hallii*," and "or relatives having at least 98% sequence identity with the 16S rRNA sequence of *Alcaligenes faecalis*," have been deleted.

VII. The patent proprietors' arguments on appeal are summarised as follows.

- The amendment in claim 1 of the main request was allowable. With regard to the application as filed and D1, to which reference was made, the term "et rel." denoted relatives identified by having at

least 98% sequence identity with *Eubacterium hallii* and *Alcaligenes faecalis*. The list of bacteria in Table 3 of D1 showed examples and was not meant to be static.

- The invention was sufficiently disclosed. No serious doubts supported by verifiable facts had been presented by the opponent. Example 1 provided data which supported the claimed invention. Example 3 confirmed the results for *Eubacterium hallii*. The micro-organism DSM 17630 had been deposited with the Institute DSMZ and was publicly available.
- The subject-matter of claim 1 was novel over the disclosure of D6.
- D2 was not the closest prior art. Even if the skilled person started from this document, the subject-matter of claim 1 involved an inventive step. The skilled person would not have arrived at the subject-matter claimed, which requires *Eubacterium hallii* and *Alcaligenes faecalis*.

VIII. The opponent's arguments on appeal are summarised as follows.

- The amendment in claim 1 of the main request was not allowable. The wording in D1 was not a general statement that all relatives had a 98% sequence identity. Deleting the relatives from claim 1 (as done in some auxiliary requests) led to objections under Articles 123(3) and 84 EPC.
- The invention was insufficiently disclosed. The data in Examples 1 and 3 of the patent did not show that the effect was credible. It had not been shown that *Eubacterium hallii* and *Alcaligenes faecalis* were suitable for treating insulin resistance. The

deposit of DSM 17630 did not meet the requirement of sufficiency of disclosure.

- The subject-matter of claim 1 lacked novelty in view of the implicit disclosure of D6.
- The subject-matter of claim 1 did not involve an inventive step starting from the closest prior art D2. The skilled person would have looked for suitable butyrate-producing bacterial species and would have arrived at *Eubacterium hallii* in view of the teaching of either D3 or D4.
- Several documents, including D38 to D40, D49 and D50, should not be considered on appeal.

IX. Final requests

The patent proprietors requested that the decision under appeal be set aside and that the patent be maintained as granted (main request), or alternatively on the basis of any one of auxiliary requests 1 to 47, filed with the statement setting out the grounds of appeal, or auxiliary requests 48 to 53, filed with the reply to the opponent's statement setting out the grounds of appeal.

The opponent requested that the decision under appeal be set aside and that the patent be revoked.

Reasons for the Decision

1. Patent

The patent is directed to *Eubacterium hallii* and/or *Alcaligenes faecalis* bacteria for use in preventing or treating insulin resistance or insulin resistance-related complications. Optionally the bacteria are used in a pharmaceutical, food or feed composition.

2. *Admittance of documents*

2.1 The opponent argued that several documents that the patent proprietors filed during the opposition proceedings (including documents D38 to D40) and on appeal (D49 and D50) should not be considered in the proceedings.

2.2 Document D38

2.2.1 The opposition division exercised its discretion to admit D38 (Declaration of W. de Vos, filed by the patent proprietor) into the proceedings.

2.2.2 Submissions can be held inadmissible on appeal only on the basis of Article 114(2) EPC and Articles 12(4), 12(6) and 13 RPBA. Document D38 was admitted into the first-instance proceedings and was addressed in the impugned decision. Hence according to Article 12(2) RPBA it forms part of the appeal proceedings. In addition, the opposition division exercised its discretion under Article 114(2) EPC by applying the correct criteria and there is no indication that this has been done in an unreasonable way.

2.2.3 In more detail, the opposition division decided to admit D38 during the oral proceedings. It did so after having heard the parties on admittance of both D38 and D27. The latter document is a declaration filed by the opponent after opposition had been lodged. The patent proprietors had objected to the admittance of D27 during the opposition proceedings. D38 was filed shortly after, and in reply to the declaration D27.

2.2.4 In the decision under appeal, the opposition division noted that D38 was filed before the point in time set under Rule 116(1) EPC and that "the declarations in D27 and D38 are considered *prima facie* potentially highly relevant for the outcome of the procedure".

2.2.5 Thus the opposition division considered and decided on the admittance of D27 and D38 jointly. Manifestly, in its view, both documents further elucidated matter relevant to the outcome of the case. It follows from this that the opposition division had exercised its discretion on admittance of D38 correctly, taking into account the right principles (*prima facie* relevance) and in a reasonable way.

2.2.6 To conclude, there are no reasons to exclude D38 from the appeal proceedings.

2.3 Documents D39, D40, D49 and D50

2.3.1 The patent proprietors filed documents D39 and D40 (during the opposition proceedings) and D49 and D50 (on appeal). All these documents were filed to demonstrate that the *Eubacterium hallii* strain DSM 17630 (also referred to as L2-7) would have been publicly available at the patent's filing date, and also since then.

2.3.2 The opponent's allegation that the strain DSM 17630 would not have been publicly available was raised after it filed its notice of opposition. It is not apparent from the minutes of the oral proceedings that this aspect was discussed before the opposition division. Similarly, the admittance of documents D39 and D40 (as opposed to document D38) was not discussed either.

2.3.3 In their statement setting out the grounds of appeal, the patent proprietors explained that they had not been able to argue on sufficiency of disclosure of the strain DSM 17630. The conclusion that the strain was regarded as insufficiently disclosed was only mentioned in the impugned decision.

2.3.4 Although D39 and D40 were filed well before the point in time set under Rule 116(1) EPC and support the patent proprietors' position, they were not discussed by the opposition division (be it as to admittance or as to their substance). It follows from this that the opposition division might not have correctly assessed the relevant aspects with regard to the objection raised against the public availability of DSM 17630 and the evidence that the patent proprietors provided.

2.3.5 Under these circumstances, no reason can be seen to disregard these documents on appeal.

2.3.6 As regards D49 and D50, it is plain to see that these documents were filed in direct reaction to the decision under appeal. These documents were filed to rectify the error in the decision identified by the patent proprietors.

2.3.7 To conclude, documents D39, D40, D49 and D50 are to be considered in the proceedings (Article 12(4) RPBA).

3. *Article 100(c) EPC*

3.1 The opposition division concluded that claim 1 involved added subject-matter due to the feature "98% sequence identity with the 16S rRNA sequence". This feature had been added to claim 1 during the examination proceedings.

3.2 As regards the micro-organisms to be used according to the application as filed, the parties agree that:

- there was no literal basis for this amendment in the application as filed
- the application as filed referred to "*Eubacterium hallii* et rel." and "*Alcaligenes faecalis* et rel."
- for the definition of the term "et rel.", page 3 of the application as filed referred to Table 3, column headed "level 3", of the international patent application D1, which was incorporated by reference in the disclosure of the application as filed.

3.3 To be allowable under the EPC, an amendment has to be directly and unambiguously derivable for the skilled person from the application as filed. The same criteria must apply all the more so when the amendment is based on a document which is incorporated by reference in the application as filed.

3.4 There is a body of case law decisions, such as T 689/90, in which tests were developed for assessing whether an amendment based on an incorporation by reference is allowable. In the current case, it is not

necessary to run such a test. Whether the amendment in question is allowable can be determined by applying the "gold standard" (G 2/10).

3.5 The passage of the application as filed on page 3 that refers to D1 (i.e. WO 2011/043654 A1) reads:

"*The addition 'et rel.' behind the genus-like group name (level 2 group name) stands for "et relatives", indicating all relatives of this phylogenetic group, i.e., those indicated in Table 3 of WO 2011/043654 (which is herein incorporated by reference), in the column headed 'level 3'. This information, including the indicated 16S rRNA gene sequences, can be used to develop specific PCR primers or LCR probes to detect the one or more members of these groups. In some literature the addition "et rel." is replaced by "-like" to indicate the fact that the group includes more than one related species. However, this is a rather ambiguous designation and hence all terms with 'et rel.' are clearly defined in Table 3 of WO 2011/043654*".

3.6 Table 3 of D1 encompasses a long list of micro-organisms that spans pages 35 to 61. According to the header of Table 3, level 1 corresponds to the phylum or the *Clostridium* cluster; level 2 includes groups of sequences with 90% or more sequence similarity; and level 3

"*represents unique phylotypes that were defined as species for cultivated microorganisms, or representatives of each monophyletic group with ≥ 98% sequence identity for clones corresponding to uncultured microorganisms (herein identified as 'relatives' or 'et rel.'*)"

On page 52 of Table 3, below the column reading "level 3", six bacteria belonging to *Eubacterium hallii* et rel. are listed, and on page 58 three bacteria belonging to *Alcaligenes faecalis* et rel.

3.7 On the face of it, the relatives intended to be covered by the expression "et rel." in the application as filed are those that are listed in Table 3 of D1, under the header "level 3".

3.8 The patent proprietors argued that the skilled person would understand that the bacteria in Table 3, level 3 merely constitute a list of examples. The number of known relatives increased with time as further relatives were identified. This was derivable from page 3 of the application as filed and several sections of D1, in particular the header of Table 3 (see above, point 3.6) and passages bridging pages 18 and 19 and pages 22 and 23. All these sections of D1 made reference to 16S rRNA sequences. In the light of this, the skilled person would have used the entries in level 3 of Table 3 as a catalogue of 16S rRNA sequences and they would have identified relatives having at least 98% sequence identity with the 16S rRNA sequence.

3.9 However, the header on Table 3 of D1 refers to two specific alternatives of micro-organisms listed at level 3: those defined as species or representatives of each monophyletic group with ≥ 98% sequence identity for clones corresponding to uncultured micro-organisms. This disclosure is not a general statement that explicitly encompasses all relatives having 98% sequence identity, and in particular new relatives. There is no direct and unambiguous disclosure to this effect in Table 3, level 3 of D1.

3.10 Accordingly, the feature added to claim 1 as granted does not produce the same result in terms of the set of micro-organisms that the skilled person would arrive at by reading the definition of "et rel." on page 3 of the application as filed in combination with the referenced section of D1. It follows from this that the amendment is not allowable.

3.11 To conclude, the ground for opposition under Article 100(c) EPC prejudices maintenance of the patent as granted.

4. *Auxiliary request 1 - Articles 123(3) and 84 EPC*

4.1 In claim 1 of this request, the restriction to 98% sequence identity with the 16S rRNA sequence of both micro-organisms was deleted.

4.2 The opponent considered that this deletion led to an extension of the protection conferred. This was contrary to the requirement of Article 123(3) EPC. The amendment also added unclear matter to the claim.

4.3 The opponent's arguments are not convincing. Claim 1 as granted refers to *Eubacterium hallii* or specified relatives. They are presented as alternatives in the granted claims. Each alternative has its own technical meaning. Deleting one alternative does not extend the protection conferred by the claim of the other alternative remaining in the claims. The same applies to *Alcaligenes faecalis* or its relatives.

4.4 The opponent's interpretation according to which the term "*Eubacterium hallii*" when used alone encompassed anything having 97% sequence identity has no basis in

the patent specification. Rather, it appears to be based on the opponent's understanding of claim 1, as set out in the technical expert's declaration D27.

4.5 For the sake of argument only, the following is added. If the skilled person were to understand that the term "*Eubacterium hallii*" encompassed anything having 97% sequence identity, then this understanding would also have been the skilled person's understanding when reading claim 1 as granted. A consequence of this understanding would be that the relatives would constitute a restricted, i.e. preferred, alternative of *Eubacterium hallii*, namely one where a higher sequence identity of 98% is required. It follows from this that, even with such an interpretation of claim 1, the amendment does not generate extended protection.

4.6 As is manifest from what is stated above, the deletion of one alternative from a claim as granted cannot add any lack of clarity to the subject-matter remaining in the claim. Any alleged lack of clarity associated with that subject-matter must have been inherent in the claims as granted and therefore is not open to an objection under Article 84 EPC.

4.7 To conclude, the amendment in claim 1 does not contravene the requirements of Articles 123(3) or 84 EPC.

5. *Auxiliary request 1 - sufficiency of disclosure*

5.1 The opposition division concluded that the invention was insufficiently disclosed for *Alcaligenes faecalis* and for the *Eubacterium hallii* strain L2-7 (DSM 17630). The reasons were as follows.

- Example 1 of the patent demonstrated a correlation of increases in the *Eubacterium hallii* and *Alcaligenes faecalis* with the allogenic faecal transplant, but the results observed could equally be caused by one or more of the other changes observed.
- While Example 3 showed a causality between oral administration of *Eubacterium hallii* to mice and a normalisation of insulin sensitivity, no such causality data were provided for *Alcaligenes faecalis*. Therefore the invention was not enabled for *Alcaligenes faecalis*.
- As for the strain DSM 17630, the deposit was not made in accordance with the conditions of the Budapest Treaty. It had not been shown that the strain was freely available to the public without restriction.

5.2 On appeal, the opponent agreed with this assessment. In addition, it contested that the patent proprietors were "in possession of the invention and able to solve the problem" when the application was filed. The opponent maintained that, in line with T 1868/16, mere verbal statements were not enough. The patent application had to provide some information, such as experimental tests showing that the claimed compound had a direct effect on a metabolic mechanism specifically involved in the disease. The patent's Examples 1 and 3 did not demonstrate the therapeutic effect set out in claim 1.

5.3 The objections set out in the decision under appeal and raised by the opponent are not convincing. The reasons are as follows.

5.4 Claim 1 of the application as filed makes it clear that the invention at the date of filing was (and has always

been since then) directed to *Eubacterium hallii* and *Alcaligenes faecalis* for use in preventing or treating insulin resistance or insulin resistance-related complications.

5.5 Example 1 of the patent sets out a credible explanation, supported by extensive experimental evidence, why the inventors arrived at their conclusion. The experiments involved transplanting diluted faecal samples into the duodenal tube of obese patients. One group received diluted stool samples from lean donors (allogenic group), the other group (control or autologous group) their own diluted stools. In the allogenic group, a marked improvement in peripheral insulin sensitivity was observed. No significant change was observed in the control group. The change in jejunal mucosal microbiota following faecal transplant was also monitored. Seven bacteria significantly associated with the difference between the allogenic and control groups were detected (Table 1).

5.6 A conclusion presented in Example 1 is that an association was found between small intestinal concentrations of *Eubacterium hallii* and *Alcaligenes faecalis* and the improvement in insulin sensitivity in the allogenic group.

5.7 Example 3 concerns a separate test carried out on mice. Oral supplementation of *Eubacterium hallii* to the small intestine was demonstrated to have an effect on normalisation of insulin resistance. This experiment further supports the conclusions that were drawn based on the change in jejunal mucosal microbiota observed in Example 1. Although no further experiments are disclosed in the patent for *Alcaligenes faecalis* (e.g. no oral supplementation experiments on mice), there is

no apparent reason why the conclusions drawn from Example 1 would not also apply to *Alcaligenes faecalis*.

5.8 As an intermediate conclusion, in view of the results in Examples 1 and 3, it is credible on the basis of the application as filed alone that the invention claimed can be carried out and that the effects set out in claim 1 are achieved.

5.9 In this respect, the current case hand is markedly different from the case underlying T 1868/16, in which no data were provided and reference was made to ongoing trials. According to the cited decision, a possible way to demonstrate that the invention was sufficiently disclosed involved "*sufficient evidence or at least a technically plausible concept that allowed the skilled person to conclude that the claimed compound is suitable for the claimed therapeutic use*" (Reasons, 4.7). In the current case, the evidence given in Examples 1 and 3 of the patent in suit meets this requirement.

5.10 The opponent reviewed the results in Example 1 and Table 1 and argued with reference to declaration D27 that the effects disclosed were more likely to be caused by the decreased level of *E. coli* in the allogenic group. It also referred to a possible difference of jejunal levels and faecal levels of micro-organisms in healthy and in obese individuals. Furthermore, the opponent objected that the patent did not disclose whether the individuals that exhibited an increase in small intestinal *Eubacterium hallii* were the same individuals that exhibited an improvement in insulin sensitivity.

5.10.1 However, presenting an alternative mechanism does not invalidate the disclosure made in the patent. The relevant question is whether the invention set out in the patent was sufficiently disclosed at the time of its filing. The board has no doubt that the skilled person would have been able to carry out the invention as disclosed in the application as filed. The same applies to the invention in the patent in suit. For completeness, that the invention disclosed in the application as filed does indeed work was confirmed with *Eubacterium hallii* strain L2-7 by the scientific publication D26, published in 2020.

5.10.2 Similarly, the argument that other conclusions might be drawn from the data in Example 1 and Table 1 of the patent does in itself not invalidate the conclusions discussed in the patent. It may well be that the data in Example 1 are not complete. For instance, no indication is given of all the bacteria screened. Example 1 also does not explicitly disclose that the individuals that exhibited an increase in small intestinal *Eubacterium hallii* were the same individuals that exhibited an improvement in insulin sensitivity. However, the data that has been presented in Example 1 is in itself consistent, sufficiently detailed and credible.

5.10.3 It is also observed that the conclusions that the opponent considered more likely could have been the starting point for presenting its own (experimental) data. No such data were filed. In this respect, the opponent has not presented serious doubts substantiated by verifiable facts. Instead, it made only its own allegations based on the factual data given in the patent.

5.10.4 As regards the decrease in *E. coli* in the small intestines of the allogenic group highlighted by the opponent, this could have been caused by secretion of antagonistic compounds. As explained in declaration D38, *Eubacterium hallii* is known to produce such a compound.

5.11 With regard to the opposition division's assessment that the *Eubacterium hallii* strain DSM 17630 was not publicly available because it was not deposited as per the Budapest Treaty, the following is observed.

5.11.1 In its decision, the opposition division referred to Guidelines F-III 6.2 and to the Notice from the European Patent Office dated 7 July 2010 concerning inventions which involve the use of or concern biological material.

5.11.2 The most relevant passage in the Guidelines for a micro-organism deposited well before the filing date of the patent, as DSM 17630 was, reads as follows:

"*The biological material may be ... a standard preserved strain, or other biological material which the division knows to have been preserved in a recognised depositary institution and to be available to the public without restriction ... In any of these cases no further action is called for*."

5.11.3 The Leibniz Institute DSMZ, with which DSM 17630 was deposited, is an international depositary authority under Article 7 of the Budapest Treaty. This has been so throughout the life of the patent in suit (see for example Official Journal of the EPO, 4/2011, page 317, and 2024, A53, page 20).

5.11.4 As the patent proprietors correctly submitted, one of the core tasks of DSMZ is to acquire, maintain and distribute all bacterial type strains. This organisation is the only institution in Germany with a mandate of running the public strain collection.

5.11.5 By the email D39, DSMZ confirmed that the strain was publicly available. The strain can currently be ordered from DSMZ. Documents D40, D49 and D50 show that this strain was used by various research teams.

5.11.6 Conversely, the opponent has not provided a single piece of evidence for its allegation that the strain was not publicly available.

5.11.7 Thus there is no reason to consider the strain not publicly available or that it might not have been available throughout the life of the patent.

5.12 To conclude, the invention disclosed in the claims of auxiliary request 1 meets the requirement set out in Article 83 EPC.

6. *Auxiliary request 1 - novelty*

6.1 The opposition division concluded that the subject-matter of claim 1 was novel over D6.

6.2 The opponent argued that the opposition division had erred. In its view, if D6 taught that commensal bacteria probiotics downregulated pro-inflammatory pathways, and the mechanism of action was via butyrate, which was able to treat insulin resistance, then the use of *Eubacterium hallii*, a butyrate producer, to treat insulin resistance had to be considered disclosed in D6.

6.3 However, the consistent view in the Boards of Appeal is that for an invention to lack novelty its subject-matter must be clearly and directly derivable from the prior art (Case Law of the Boards of Appeal of the EPO, 10th edition, 2022, Chapter I.C.4, second paragraph). This board subscribes to this view.

6.4 As regards D6, it is uncontested that this document does not explicitly disclose the use of *Eubacterium hallii* in preventing or treating insulin resistance. Instead, this bacterium is described as a butyrate-producing bacterium in the context of energy metabolism. The only specific activity of butyrate-producing bacteria referred to in this document is that they are related to higher gut metabolic activity leading to overweight. In conclusion, there is not even an implicit disclosure concerning insulin resistance in D6.

6.5 Therefore the subject-matter of claim 1 is novel over D6 (Article 54 EPC).

7. *Auxiliary request 1 - inventive step*

7.1 It is in dispute whether the subject-matter of claim 1 involves an inventive step.

7.2 Closest prior art and distinguishing features

7.2.1 The parties exchanged elaborate arguments on the choice of the closest prior art. For the opponent the closest prior art was D2. Instead, the patent proprietors suggested several other documents, with D7 being preferred.

7.2.2 In the specific circumstances of this case, throughout the opposition and appeal proceedings the opponent consistently used one single document as the starting point for assessing inventive step, namely D2. Thus the opponent regards D2 as the closest prior art. In line with this, the opposition division considered D2 as the starting point for assessing inventive step.

7.2.3 Therefore, for the purpose of reviewing the opposition division's decision, D2 has to be used as the starting point for assessing inventive step. In this respect, the patent proprietors' considerations of what they consider the closest prior art (in order to argue that an inventive step is to be acknowledged) are not relevant.

7.2.4 D2 is a scientific publication which addresses a wide range of beneficial effects on human health that butyrate has. In the paragraph headed "Obesity and insulin resistance" D2 discloses, based on a referenced publication, that dietary supplementation with butyrate can prevent and treat diet-induced obesity and insulin resistance in mouse models. The conclusion presented is that butyrate may have a potential application in the prevention and treatment of metabolic syndrome in humans.

7.2.5 The patent proprietors contested that the invention's mechanism of action involved or required butyrate. Nevertheless, inventive step has to be assessed in the light of the prior art available at the date of filing. In the following, an inventive-step analysis is carried out based on the teaching of D2 that calls for butyrate as the active component.

7.2.6 The opponent argued that throughout its disclosure D2 mentioned butyrate-producing bacteria. Therefore it considered that D2 disclosed the use of butyrate-producing bacteria for use in preventing and/or treating insulin resistance.

7.2.7 However, the paragraph in D2 that specifically mentions insulin resistance is restricted to oral administration of butyrate as such. How far the active substance to be administered can be modified is a question to address under obviousness.

7.2.8 To conclude, the difference of claim 1 from D2 is that *Eubacterium hallii* and *Alcaligenes faecalis* are used for preventing or treating insulin resistance.

7.3 Problem to be solved

7.3.1 According to the patent proprietors, the problem solved was to improve prevention and/or treatment strategies for insulin resistance and/or insulin resistance-related complications. Instead, for the opponent the problem was to provide a probiotic-based composition as an alternative for the delivery of butyrate to treat or prevent insulin resistance.

7.3.2 The problem identified by the opponent encompasses pointers towards the solution because it explicitly states that the solution starting from D2 has to be probiotic-based.

7.3.3 On this basis alone, the problem formulated by the opponent has to be rejected.

7.3.4 The formulation of the problem suggested by the patent proprietors refers to an improvement. However, in view

of the following considerations, it is not required to take into account the more ambitious problem proposed by the patent proprietors.

7.3.5 It follows from this that the problem to be solved is to provide prevention or treatment of insulin resistance and/or insulin resistance-related complications.

7.4 Non-obviousness

7.4.1 As its title indicates, D2 is a review of effects of butyrate in intestinal and extra-intestinal diseases. Among other things, D2 discloses aspects that influence the butyrate production in the intestine, such as the lumen pH. Ways to administer butyrate are also discussed. It is suggested to administer butyrate orally, although butyrate has poor palatability and is therefore difficult to administer to children. Furthermore, probiotics may be used to modulate the intestinal flora.

7.4.2 Starting from the closest prior art, the skilled person would have had to decide not to administer a palatable formula of butyrate. Then, they would have had to choose not to modulate the intestinal flora (e.g. by modifying the lumen pH) but to administer butyrate-producing bacteria. Finally, they would have had not to select the specific butyrate-producing bacteria mentioned in D2 - which are stated to represent the most important groups of butyrate producers in the human intestine - but to look for other butyrate-producing bacteria.

7.4.3 In summary, D2 itself does not mention the use of micro-organisms for managing insulin resistance, and

the only micro-organisms mentioned in D2 are not the ones of claim 1. The skilled person would have had no motivation to turn to D3 or D4, which mention *Eubacterium hallii* among other bacteria. To do all this starting from the closest prior art is considered to encompass more than routine measures.

7.4.4 The same line of argument applies for the second micro-organism of claim 1, *Alcaligenes faecalis*.

7.5 To conclude, the subject-matter of claim 1 involves an inventive step (Article 56 EPC). The same applies to the remaining claims of auxiliary request 1.

8. *Adaptation of the description*

8.1 During the oral proceedings before the board, the patent proprietors filed replacement paragraphs [0001] to [0031] of a description adapted to auxiliary request 1. The remaining paragraphs of the patent's description remained unaltered.

8.2 The opponent raised no objection with regard to the adapted paragraphs of the patent's description. The board has no reason to differ.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the opposition division with the order to maintain the patent in the following version:

Description:
- Paragraphs 1 to 31 received during oral proceedings before the board on 10 February 2025
- Paragraphs 32 to 55 of the patent specification.

Claims:
- Nos. 1 to 14 of auxiliary request 1 as filed with the statement setting out the grounds of appeal.

The Registrar: The Chairman:

K. Götz-Wein A. Haderlein

Decision electronically authenticated