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Appeal No. T0420/19-3.3.04
European Patent No. 2373154
European Patent Application 09771493.5
Title: Barley and malt-derived beverages with low dimethyl sulfide level
Patent proprietor: Carlsberg Breweries A/S and Heineken Supply Chain B.V.
Opponent: Dr. Christoph Then
Our ref.: P1600EP00

In response to the Summons to oral proceedings dated 26 March 2021, the proprietors hereby file the following written submissions.

Presence and language at oral proceedings

In accordance with the instructions for oral proceedings by videoconference via Zoom detailed information on the persons attending the oral proceedings is enclosed in a separate document.

The representatives of the patent proprietors intend to use the English language during the oral proceedings. In the event another party intends to use another language than English, a translation into English is hereby requested.

Main request

Proprietor respectfully requests that the European patent is maintained as granted.

Auxiliary requests

In the event that the patent cannot be maintained as granted, proprietor requests that the patent is maintained in amended form based on one of the auxiliary requests 1 to 16:

Auxiliary request 1	Filed as auxiliary request 1 with the Grounds of Appeal on 17 April 2019

Auxiliary request 2	Filed as auxiliary request 2 with the Grounds of Appeal on 17 April 2019
Auxiliary request 3	Attached hereto
Auxiliary request 4	Filed as auxiliary request 3 with the Grounds of Appeal on 17 April 2019
Auxiliary request 5	Filed as auxiliary request 4 with the Grounds of Appeal on 17 April 2019
Auxiliary request 6	Filed as auxiliary request 5 with the Grounds of Appeal on 17 April 2019
Auxiliary request 7	Attached hereto
Auxiliary request 8	Filed as auxiliary request 6 with the Grounds of Appeal on 17 April 2019
Auxiliary request 9	Filed as auxiliary request 7 with the Grounds of Appeal on 17 April 2019
Auxiliary request 10	Filed as auxiliary request 8 with the Grounds of Appeal on 17 April 2019
Auxiliary request 11	Filed as auxiliary request 9 with the Grounds of Appeal on 17 April 2019
Auxiliary request 12	Filed as auxiliary request 10 with the Grounds of Appeal on 17 April 2019
Auxiliary request 13	Filed as auxiliary request 11 with the Reply to the Grounds of Appeal on 4 September 2019
Auxiliary request 14	Attached hereto
Auxiliary request 15	Attached hereto
Auxiliary request 16	Attached hereto

3rd Auxiliary Request

Claims

Compared to the claims of the patent as granted, the claims of the 3rd auxiliary request have been amended as follows:

Claim 6 has been amended to specify that the mutation in the gene encoding MMT is a G→A mutation of base no. 3076 of SEQ ID NO:3. Basis for the amendment can e.g. be found in original claims 17.

Claims 8 to 9 have been deleted.
Granted claim 11 (now claim 9) was dependent on claims 6 to 9, and in the amended claim, the wording of former claim 6 has been introduced.

New claim 10 corresponds to granted claim 11 as dependent on granted claims 7 and 8 restricted to one of the mutations cited in granted claim 8. Basis for claim 10 can be found in original claims 27, 13 and 17.

Granted claim 13 (now claim 12) was dependent on claims 6 to 9, and in the amended claim, the wording of former claim 6 has been introduced.

New claim 13 corresponds to granted claim 13 as dependent on granted claims 7 and 8 restricted to one of the mutations cited in granted claim 8. Basis for claim 13 can be found in original claims 34, 13 and 17.

Granted claim 14 was dependent on claims 6 to 9, and in the amended claim the wording of former claim 6 has been introduced.

New claim 15 corresponds to granted claim 14 as dependent on granted claims 7 and 8 restricted to one of the mutations cited in granted claim 8. Basis for claim 15 can be found in original claims 43, 44, 13 and 17.

Granted claim 15 (now claim 16) was dependent on claims 6 to 9, and in the amended claim the wording of former claim 6 has been introduced.

New claim 17 corresponds to granted claim 15 as dependent on granted claims 7 and 8 restricted to one of the mutations cited in granted claim 8. Basis for claim 17 can be found in original claims 51, 22, 13 and 17.

As indicated herein above all amendments to the claims were contained in the application as originally filed and the amended claims thus comply with Art. 123(2) EPC.

7th Auxiliary Request

Compared to the claims of the patent as granted, the claims of the 7th auxiliary request have been amended as follows:

Claim 1 has been amended to specify that the mutation in the gene encoding MMT is a G→A mutation of base no. 3076 of SEQ ID NO:3 or a G-A mutation of base no. 1462 of SEQ ID NO:16. Basis for the amendment can e.g. be found in original claims 17, 18 and 24 of the application as filed.

Claim 6 has also been amended to specify that the mutation in the gene encoding MMT is a G→A mutation of base no. 3076 of SEQ ID NO:3 or a G-A mutation of base no. 1462 of SEQ ID NO:16. Basis for the amendment can e.g. be found in original claims 17 and 18 of the application as filed.

Granted claims 8 to 9 have been deleted.

As indicated herein above all amendments to the claims were contained in the application as originally filed and the amended claims thus comply with Art. 123(2) EPC.

14th Auxiliary Request

Claims

Compared to the claims of the patent as granted, the claims of the 14th auxiliary request have been amended as follows:

Granted claims 6 to 10 have been deleted.

Granted claim 11 (now claim 6) was dependent on now deleted claims 6 to 9, and accordingly, the wording of former claim 6 has been introduced to granted claim 11 (now claim 6).

New claim 7 corresponds to granted claim 11 as dependent on granted claim 8.

Granted claim 13 (now claim 9) was dependent on now deleted claims 6 to 9, and accordingly, the wording of former claim 6 has been introduced to granted claim 13 (now claim 9).

New claim 10 corresponds to granted claim 13 as dependent on granted claim 8.

Granted claim 14 (now claim 11) was dependent on now deleted claims 6 to 9, and accordingly, the wording of former claim 6 has been introduced to granted claim 14 (now claim 11).

New claim 12 corresponds to granted claim 14 as dependent on granted claim 8.

Granted claim 15 (now claim 13) was dependent on now deleted claims 6 to 9, and accordingly, the wording of former claim 6 has been introduced to granted claim 15 (now claim 13).

New claim 14 corresponds to granted claim 15 as dependent on granted claim 8.

Granted claim 16 has been deleted.

Granted claims 17 to 19 (now claims 15 to 17, respectively) were dependent on now deleted claim 16, which inter alia was dependent on claim 6. Accordingly, the wording of granted claims 6 and 16 has been introduced into granted claims 17 to 19 (now claims 15 to 17, respectively).

As indicated herein above all amendments to the claims were contained in the application as originally filed and the amended claims thus comply with Art. 123(2) EPC.

15th Auxiliary Request

Compared to the claims of the patent as granted, the claims of the 15th auxiliary request have been amended as follows:

Claim 1 has been amended to specify that the mutation in the gene encoding MMT is a G→A mutation of base no. 3076 of SEQ ID NO:3. Basis for the amendment can e.g. be found in original claims 17 and 24 of the application as filed.

Granted claims 6 to 10 have been deleted.

Granted claim 11 (now claim 6) was dependent on now deleted claims 6 to 9, and accordingly, the wording of former claim 6 has been introduced to granted claim 11 (now claim 6). Furthermore, it has been specified that the mutation in the gene encoding MMT is a G→A mutation of base no. 3076 of SEQ ID NO:3. Basis for the amendment can be found in original claims 17 and 27 of the application as filed.

Granted claim 13 (now claim 8) was dependent on now deleted claims 6 to 9, and accordingly, the wording of former claim 6 has been introduced to granted claim 13 (now claim 9). Furthermore, it has been specified that the mutation in the gene encoding MMT is a G→A mutation of base no. 3076 of SEQ ID NO:3. Basis for the amendment can be found in original claims 17 and 34 of the application as filed.

Granted claim 14 (now claim 9) was dependent on now deleted claims 6 to 9, and accordingly, the wording of former claim 6 has been introduced to granted claim 14 (now claim 9). Furthermore, it has been specified that the mutation in the gene encoding MMT is a G→A mutation of base no. 3076 of SEQ ID NO:3. Basis for the amendment can be found in original claims 17, 43 and 44 of the application as filed.

Granted claim 15 (now claim 10) was dependent on now deleted claims 6 to 9, and accordingly, the wording of former claim 6 has been introduced to granted claim 15 (now claim 13). Furthermore, it has been specified that the mutation in the gene encoding MMT is a G→A mutation of base no. 3076 of SEQ ID NO:3. Basis for the amendment can be found in original claims 17 and 51 of the application as filed.

Granted claim 16 has been deleted.

Granted claims 17 to 19 (now claims 11 to 13, respectively) were dependent on now deleted claim 16, which inter alia was dependent on claim 6. Accordingly, the wording of granted claims 6 and 16 has been introduced into granted claims 17 to 19 (now claims 11 to 13, respectively). Furthermore, it has been specified that the mutation in the gene encoding MMT is a G→A mutation of base no. 3076 of SEQ ID NO:3. Basis for the amendment can be found in original claims 17 and 54 of the application as filed.

As indicated herein above all amendments to the claims were contained in the application as originally filed and the amended claims thus comply with Art. 123(2) EPC.

16th Auxiliary Request

Compared to the claims of the patent as granted, the claims of 16th auxiliary request have been amended as follows:

Claim 1 has been amended to specify that the mutation in the gene encoding MMT is a G→A mutation of base no. 3076 of SEQ ID NO:3. Basis for the amendment can e.g. be found in original claims 17 and 24 of the application as filed.

Granted claims 6 to 13 have been deleted.

Granted claim 14 (now claim 6) was dependent on now deleted claims 6 to 9, and accordingly, the wording of former claim 6 has been introduced to granted claim 14 (now claim 9). Furthermore, it has been specified that the mutation in the gene encoding MMT is a G→A mutation of base no. 3076 of SEQ ID NO:3. Basis for the amendment can be found in original claims 17 and 43 of the application as filed.

Granted claim 15 to 18 have been deleted.

Granted claim 19 (now claim 7) were dependent on now deleted claim 16, which inter alia was dependent on claim 6. Accordingly, the wording of granted claims 6 and 16 has been introduced into granted claim 19 (now claim 7). Furthermore, it has been specified that the mutation in the gene encoding MMT is a G→A mutation of base no. 3076 of SEQ ID NO:3. Basis for the amendment can be found in original claims 17 and 54 of the application as filed.

As indicated herein above all amendments to the claims were contained in the application as originally filed and the amended claims thus comply with Art. 123(2) EPC.

Exceptions to patentability

As outlined in the Grounds of Appeal filed 17 April 2019, patent proprietors are of the opinion that the plants of the present invention have not been exclusively obtained by means of an essentially biological process. As such they are not excluded from patentability.

Even if this were to be the case, patent proprietors agree with the Board of Appeal that the plants of the patent are not excluded from patentability based on decision G3/19 of the Enlarged Board of Appeal.

Sufficiency of Disclosure

Patent proprietors submit that the invention is sufficiently disclosed and in this regard make reference to the Grounds of Appeal of 17 April 2019.

Inventive step

Closest prior art

In the communication of the Board of Appeal pursuant to Art. 15(1) of the Rules of Procedure, the Board has indicated that their preliminary view is that the closest prior art vis-à-vis claim 6 is D1.

Patent proprietors do not agree that D1 is the closest prior art, neither to claim 6 nor in relation to any of the other claims. According to established case law of the Boards of Appeal, the closest prior art for assessing inventive step is normally a prior art document disclosing subject-matter conceived for the same purpose or aiming at the same objective as the claimed invention and having the most relevant technical features in common (see p. 178 last paragraph to p. 179 first paragraph in Case Law of the Boards of Appeal of the European Patent Office, 2019).

On p. 180 in section 3.2 the Case Law of the Boards of Appeal of the European Patent Office, 2019 states that:

> *According to established case law, a central consideration in selecting the closest prior art is that it must be directed to the same purpose or effect as the invention, otherwise it cannot lead the skilled person in an obvious way to the claimed invention.*

According to the "Summary of the Invention", the invention relates to beverages having very low levels of DMS or even no DMS at all, which are prepared from barley malt (see [0013] of the patent). Based on said low levels or absence of DMS, the beverages have remarkable flavor properties (see [0015] of the patent). The invention further provides barley or malt kernels with defects that specifically block formation of the DMS precursor. Notably, the barley of the invention might be exploited as a raw material in effective industrial applications such as in the production of such beverages (see [0016] of the patent).

In other words, the overall invention relates to beverages having very low levels of DMS or even no DMS as all as well as to methods and materials for production thereof. The barley plant claimed in claim 6 to 10 need to be evaluated based on the overall purpose of the invention and not merely on its specific mutation.

D1 relates to inactivation of the Methionine S-Methyltranferase (MMT) gene to investigate the SMM cycle in plant sulfur metabolism (see e.g. the title, first sentence of the introduction and page 1809 2nd col., 2nd paragraph). Figure 1 of D1 illustrates that MMT catalyses synthesis of S-methyl-Met (SMM), which can be converted to Met. D1 discloses transgenic mutants of Arabidopsis and maize, carrying insertions of large DNA fragments into the *mmt* gene. These Arabidopsis and maize plants have reduced levels of SMM. D1 takes interest in SMM in order to investigate its role in controlling depletion of free met, and concludes that "these data indicate that the SMM cycle contributes to regulation of Ado-Met levels rather than preventing depletion of free Met".

D1 does not relate to beverage production and is totally silent with respect to the challenge of DMS in beverages related to conversion of plant based SMM.

Accordingly, D1 is neither conceived for the same purpose nor aiming at the same objective as the claimed invention. In conclusion, the skilled person could not reasonably be expected to use a reference on basic plant research in relation to plant sulphur metabolism as a starting point for reducing DMS in a beverage.

In contrast, D2 teaches that DMS is a troublesome flavour in beer and teaches a process for producing wort and/or beer with reduced amounts of DMS.

Thus, D2 is conceived for the same purpose or aiming at the same objective as the claimed invention. It is thus submitted that D2 constitutes the closest prior art, even in relation to claims directed to barley plants.

Specifically, the patent clearly describes that the aim or purpose of the barley plants of claim 6 is useful as raw material in the product of beer having a low level of DMS-specific taste (see [0016]-[0017] of the patent).

Therefore, D2 also constitutes the closest prior art to claim 6.

In the preliminary opinion, the Board of Appeal has not raised any objections in relation to independent claims 1, 11, 13, 14 and 15. Patent proprietors agrees that these claims are inventive. As outlined in detail above, D2 constitutes the closest prior art and reference is made to the Grounds of Appeal of 17 April 2019 explaining in detail why the claims of the patent are inventive over D2 even if combined with D1. The claims of the auxiliary requests are inventive for similar reasons. Reference is also made to the discussion of claim 6 presented below. The arguments presented in relation to claim 6 are – at least partly - also relevant vis-à-vis the other claims.

Main Request – claim 6 – D2 as closest prior art

As outlined above, patent proprietors consider D2 to constitute the closest prior art.

D2 teaches that DMS is a troublesome flavour in beer, which is produced by the conversion of SMM ([0038]). D2 teaches a process for producing beer and/or wort with reduced amounts of DMS from barley malt ([0019]). The process of D2 is based on the addition of specific enzymes to a mash, which is then processed. In terms of barley plants, D2 does not provide much guidance. Specifically, paragraph [0037] of D2 describes that focus has been put on barley varieties with low levels of precursors of T2N (another off-flavour in beer) and paragraph [0083] discloses certain properties of barley malt used for the Examples of the patent. Apart from this, D2 is completely silent with regard to the properties of the barley.

The difference between D2 and claim 6 is that claim 6 relates to a barley plant carrying a mutation in the gene encoding MMT.

The technical effect of the difference is that beverages prepared from said barley plant have reduced off-flavours due to reduced amounts of DMS. More specifically, beverages prepared from barley plants of the invention have a level of DMS below 20 ppb, whereas beverages prepared from ordinary barley plants as described in D2 have DMS levels above 20 ppb.

Thus, the objective technical problem can be seen as provision of a barley plant useful for production of beverages having reduced off-flavours due to reduced amounts of DMS.

The objective technical problem is solved by the invention as disclosed in the patent. In this regard reference is made to Examples 1, 5, 6, 7 and accompanying figure 5, as well as to the Grounds of Appeal filed 17 April 2019.

Starting from D2 the skilled person would have found no guidance on how to solve the technical problem. As noted above D2 nowhere describes or even hints at a certain barley plant being useful for production of beverages with low DMS levels. D2 is also completely silent in regard to the MMT gene.

It is questionable whether the skilled person setting out to solve above-mentioned technical problem would have consulted D1, because D1 relates to a different technical field. Thus, as explained above D1 focuses on investigating the role of SMM in controlling depletion of free Met in Arabidopsis and Maize. Arabidopsis cannot be used for producing beer and the use of maize in beer production is very limited and significantly different to the use of barley. Thus, maize is only used in beer production in non-germinated form as a source of starch. SMM is produced in germinating barley kernels (see [0005] of the patent). The limited amount of non-germinated maize used in beer production does not contribute significantly to SMM. The skilled person had no reason to look in a document relating to plants, which are not used for malt production to find solutions to a problem that arises during germination of barley. Furthermore, the type of mutations in the plants described in D1 are not useful for producing food within the EU. The Arabidopsis plant carries a transgenic T-DNA insert and transgenic plants cannot readily be approved in EU. The maize plant carries a *Mu* transposon, which may change its position within the genome and thus is inherently unstable.

Even if the skilled person had consulted D1, the skilled person would not have arrived at the invention for several reasons.

First of all, D1 nowhere describes DMS or DMS levels in the plants or in extracts of the plants. Whereas SMM may be a precursor of DMS, the cited prior art nowhere teaches that DMS is exclusively produced from SMM. The skilled person could not reasonably predict the levels of DMS in an extract or beverage prepared from one of the *mmt* mutant plants described in D1. In addition, it should be noted that D1 only discloses the SMM levels in the leaves of the plants and not in the kernels. As explained in [0005] of the patent SMM is produced in the barley kernel during germination. Based on D1 it is not known if the described mutations of MMT would have affected the SMM levels in germinated seed of Arabidopsis or maize.

More importantly, as is well-known to the skilled person, one plant is different from another plant. Accordingly, the mere fact that an *mmt* mutant in maize is viable and has low SMM levels in the leaves does not provide any evidence that a similar mutant in barley will have low SMM levels in the germinated kernel. For example, D1 states that it was known that Arabidopsis and maize each had one *mmt* gene (p. 1809, right column, lines 11-12). However, the skilled person did not know at the time of the invention whether the same was true in barley, or whether barley contains more than one *mmt* gene. The skilled person reading D1 would also not have known whether Arabidopsis and maize contain an additional activity compensating for loss of MMT activity that helps the *mmt* mutant Arabidopsis and maize plants to remain viable.

Plants in general are well known to have high levels of gene duplication and redundancy. This is also the case in barley, as shown in Khursheed et al. (1988) (filed with the Grounds of Appeal), where the authors state that: "The analysis of α-amylase gene regulation is complicated by the fact that there are multiple genes located in two different chromosomal loci."

In the particular case of barley MMT, Pimenta et al., (1998)(filed with the Grounds of Appeal) hypothesised that an MMT isoenzyme is likely to exist in barley (p. 437, right column, lines 3-5), and thus, that more than one gene may produce MMT activity in barley.

Accordingly, based on all the above, the skilled person would have no reason to consider that the teaching of D1 of the properties of a mutation in *mmt* in Arabidopsis and maize would apply to barley. In addition, the skilled person still would not have reason to try and apply the teaching of D1 to barley, as D1 also fails to suggest that it could be feasible or even desirable to further reduce the DMS levels as compared to D2.

Thus, claim 6 is inventive over the teaching of D2 – even if combined with the teaching of D1.

Main Request – claim 6 – D1 as closest prior art

In the in event that the Board of Appeal should maintain that D1 is closest prior art vis-à-vis claim 6, claim 6 is never-the-less inventive.

Following the problem-solution approach once the closest prior art has been identified, the next step is formulation of the objective technical problem. In accordance with the Guidelines for Examination at the EPO G-VII 5, the objective technical problem is identified by studying the patent, the closest prior art and the distinguishing feature(s) between the claimed invention and the closest prior art, identifying the technical effect resulting from the distinguishing features, and then formulating the technical problem.

This approach has also been endorsed by the Boards of Appeal. Thus, p. 190 last paragraph in the Case Law of the Boards of Appeal of the European Patent Office, 2019 states that:

> *"In T 1019/99 the board stated that the correct procedure for formulating the problem is to choose a problem based on the technical effect of exactly those features distinguishing the claim from the prior art that is as specific as possible without containing elements or pointers to the solution (see also T 1557/07, T 1192/09)."*
> *[our underlining]*

As described above D1 describes *mmt* mutants of Arabidopsis and maize having reduced levels of SMM. The document further describes that SMM contributes to regulation of the Ado-Met levels.

The distinguishing feature between D1 and the invention of claim 6 is that claim 6 relates to a barley plant having a total loss of MMT function.

As described in the patent, the technical effect of this difference is that the plant is useful for preparation of beer or other barley based beverages having a low level of DMS-specific taste (see [0016] of the patent).

Accordingly, the objective technical problem solved by the invention of claim 6 is the provision of a plant useful for preparation of beverages having reduced off-flavours, and in particular reduced amounts of DMS.

The Board of Appeal has identified another technical problem, namely the provision of a null mutant MMT plant of a different species. In doing so, the Board has completely disregarded the technical effect obtained by the difference between the prior art and the invention, which the patent clearly describes as the plants being useful for preparation of beer or other barley based beverages having a low level of DMS-specific taste.

The objective technical problem identified by the Board of Appeal in the preliminary opinion is not even a technical problem. According to established case law (e.g. T 939/92) the skilled person is assumed not to act out of idle curiosity but rather with a specific technical problem in mind. Providing a null mutant MMT plant of another species is not an attempt to solve a specific technical problem, but only satisfies the idle curiosity. It follows that this cannot be an objective technical problem.

As noted above, both the Guidelines for examination at the EPO as well as the established case law of the Boards of Appeals clearly stipulates that the procedure for formulating the technical problem is to choose a problem based on the technical effect of the features distinguishing the claim from the prior art.

Furthermore, it is important to formulate the technical problem in a manner so that it does not contain pointers to the solution or partially anticipate the solution. In the regard the Case Law of the Boards of Appeal of the European Patent Office, 2019 on p. 190 in the first paragraph of section 4.3.1 states that

> *"According to the established case law, the technical problem addressed by an invention has to be formulated in such a way that it does not contain pointers to the solution or*

partially anticipate the solution, since including part of a solution offered by an invention in the statement of the problem necessarily results in an ex post facto view being taken of inventive step when the state of the art was assessed in terms of that problem (see e.g. T 229/85, OJ 1987, 237; T 99/85, OJ 1987, 413; T 289/91, OJ 1994, 649; T 422/93, OJ 1997, 24; T 986/96; T 799/02; T 2049/11; T 2461/11).
[our underlining]

By formulating the technical problem as the provision of a null mutant MMT plant of a different species, the Board of Appeal has included part of the solution offered by the invention in the statement of the technical problem, which is not permissible.

Thus, the patent proprietors submits that the objective technical problem must be formulated based on the technical effect offered by the distinguishing features, while avoiding pointers to the solution provided by the invention.

Nothing in the patent indicates that the purpose of the patent or the technical effect obtained by the patent is the provision of another null mutant plant of a different species. In contrast, the patent clearly describes that the invention relates to barley based beverages with low levels of DMS, and methods and materials for producing such beverages (see e.g. Summary of the invention paragraphs [0013]-[0017]. The technical effect of the distinguishing features between D1 and the invention is thus that the plant of the invention is useful for preparation of beer or other barley based beverages having a low level of DMS-specific taste.

Accordingly, it is submitted that the objective technical problem solved by the invention of claim 6 is the provision of a plant useful for preparation of beverages having reduced off flavours, and in particular reduced amounts of DMS.

Based on the teaching of D1, the skilled person could not have solved the technical problem. D1 is completely silent with regard to off flavours, let alone the level of DMS in food or beverages. D1 does not even disclose DMS levels in a simple extract prepared from the plants disclosed therein.

Even if the skilled person had considered to prepare a null mutant *mmt* barley plant based on the teaching of D1, the skilled person would have had absolutely no reasonable expectation that such a barley plant in fact would solve the technical problem.

First of all D1 is completely silent with regard to DMS. Whereas SMM may be a precursor of DMS, the cited prior art nowhere teaches that DMS is exclusively produced from SMM. Thus, the skilled person did not known whether reducing SMM levels would lead to a similar reduction of DMS.

In addition, D1 only discloses the SMM levels in the leaves of the plants and not in the kernels. As explained in [0005] of the patent SMM is produced in the barley kernel during germination. Based on D1

it is not known if the described mutations of MMT would have affected the SMM levels in germinated seed of Arabidopsis or maize.

Furthermore, as outlined in detail above, plants in general are well known to have high levels of gene duplication and redundancy, and in the particular case of barley MMT, others (Pimenta et al., 1998) had hypothesised that an MMT isoenzyme is likely to exist. Thus, the skilled person had no reasonable expectation that preparing a null mutation in *mmt* in barley would in fact lead to low DMS levels in beverages prepared from such barley.

Turning to D2 would not have helped, since D2 also does not describe any effects of mutations in MMT.

Even if we accepted the Board of Appeal's objective technical problem, namely the provision of a null mutant *mmt* plant of a different species, the solution, a barley null *mmt* mutant is by no means obvious.

First and foremost, the methods of D1 rely on screening libraries of pre-existing Arabidopsis/maize mutant libraries generated using either T-DNA insertion technology or transposon technology. For Arabidopsis, a library of 60,480 lines was screened (page 1813, right column, Arabidopsis mutant isolation), for maize a library of 42,000 F1 maize plants were screened (page 1814, left column, top). In both cases a PCR based screening method was employed. At the priority date of the present patent in 2008 similar libraries were not readily available for barley, and generation of such libraries in barley was by no means a trivial task. No large scale methods for insertion of T-DNA was available, and the Mu element used for preparation of the maize library is a maize transposon. Furthermore, neither the genomic sequence of barley, nor the sequence encoding MMT in barley was known, as illustrated in example 8 of the Patent.

Starting from D1, the skilled person seeking to find a null *mmt* mutant from another plant species, would have turned the attention to plant species for which similar mutational libraries existed and where the genomic sequence was available.

Furthermore, and as demonstrated in the patent and described in detail above, the null *mmt* barley mutant surprisingly results in barley that can be used to produce beer with less off flavours. In addition, reduced energy input is required for producing beer from the barley plants of the invention since it is no longer necessary to treat the malt or wort at temperatures above 70°C (see paragraph [0011], [0012] and [0016] item iii) and iv). These results could not have been predicted from D1 even if D2 were taken into consideration.

It is thus concluded that claim 6 as granted is inventive over the disclosure of D1.

Auxiliary requests 1, 2 and 11 – claim 6

Claim 6 of auxiliary requests 1, 2 and 11 are inventive for similar reasons as the main request.

Auxiliary request 4 – claim 6 – D2 as closest prior art

As outlined above, patent proprietors consider D2 to constitute the closest prior art. D2 is summarized above under the discussion of the main request.

The difference between D2 and claim 6 is that claim 6 relates to a barley plant carrying a mutation in the gene encoding MMT, wherein the mutation results in a gene encoding a truncated form of MMT comprising at the most the 288 N-terminal amino acid residues of SEQ ID NO: 6.

The technical effect of the difference is that beverages prepared from said barley plant have reduced off-flavors due to reduced amounts of DMS. More specifically, beverages prepared from barley plants of the invention have a level of DMS below 20 ppb and a level of SMM below 20 ppb, whereas beverages prepared from ordinary barley plants as described in D2 DMS levels above 20 ppb.

Thus, the objective technical problem can be seen as provision of a barley plant useful for production of beverages having reduced off-flavours, and in particular reduced amounts of DMS.

The objective technical problem is solved by the invention as disclosed in the patent. In this regard, reference is made to Examples 1, 5, 6, 7 and accompanying figure 5, as well as to the Grounds of Appeal filed 17 April 2019.

Starting from D2 the skilled person would have found no guidance on how to solve the technical problem. As noted above D2 nowhere describes or even hints at certain barley plant being useful for production of beverages with low DMS levels. D2 is also completely silent with regard to MMT.

As noted above it is questionable whether the skilled person would have consulted D1. However, even if the skilled person had consulted D1, the skilled person would not have arrived at the invention essentially for the reasons outlined above.

Thus, claim 6 is inventive over the teaching of D2 – even if combined with the teaching of D1.

<u>Auxiliary request 4 – claim 6 – D1 as closest prior art</u>
In the in event that the Board of Appeal should maintain that D1 is closest prior art vis-à-vis claim 6, claim 6 is never-the-less inventive.

As explained above in relation to the main request, the objective technical problem is chosen based on the technical effect of the features distinguishing the claim from the prior art.

As described above D1 describes *mmt* mutants of Arabidopsis and maize having reduced levels of SMM. The document further describes that the SMM contributes to regulation of the Ado-Met levels.

The distinguishing feature between D1 and the invention of claim 6 is that claim 6 relates to a barley plant having a total loss of MMT function, wherein the mutation results in a gene encoding a truncated form of MMT comprising at the most the 288 N-terminal amino acid residues of SEQ ID NO: 6.

As described in the patent, the technical effect of this difference is that the plant is useful for preparation of beer or other barley based beverages having a low level of DMS-specific taste (see [0016] of the patent).

Accordingly, the objective technical problem solved by the invention of claim 6 is the provision of a plant useful for preparation of beverages having reduced off flavours, in particular reduced levels of DMS.

Based on the teaching of D1, the skilled person could not have solved the technical problem. D1 is completely silent with regard to the level of DMS in beverages. D1 does not even disclose DMS levels in a simple extract prepared from the plants disclosed therein.

Even if the skilled person had considered to prepare a null mutant MMT barley plant based on the teaching of D1, the skilled person would have had absolutely no reasonable expectation that such a barley plant in fact would solve the technical problem for the reasons described in detail in relation to the main request.

Turning to D2 would not have helped, since D2 also does not describe any effects of mutations in MMT. In can thus be concluded that even based on D1 as closest prior

It is thus concluded that claim 6 of the 4th auxiliary request is inventive over the disclosure of D1.

Auxiliary requests 5, 6 and 12 – claim 6

The claims of auxiliary requests 5, 6 and 12 are inventive for similar reasons as auxiliary request 3.

Auxiliary requests 3 and 8 – claim 6 – D2 as closest prior art

As outlined above, patent proprietors consider D2 to constitute the closest prior art. D2 is summarized above under the discussion of the main request.

The difference between D2 and claim 6 is that claim 6 relates to a barley plant carrying a G→A mutation of base no. 3076 of SEQ ID NO:3 in the gene encoding MMT.

The technical effect of the difference is that beverages prepared from said barley plant have reduced off-flavours due to reduced amounts of DMS.

Thus, the objective technical problem can be seen as provision of a barley plant useful for production of beverages having reduced off-flavours, in particular reduced amounts of DMS.

The objective technical problem is solved by the invention as disclosed in the patent. In this regard reference is made to Examples 1, 4, 5, 6, 7, 9 and accompanying figure 5, as well as to the Grounds of Appeal filed 17 April 2019.

Starting from D2 the skilled person would have found no guidance on how to solve the technical problem. As noted above D2 nowhere describes or even hints at certain barley plant being useful for production of beverages with low DMS levels. D2 is also completely silent in regard to the MMT gene or any mutations therein.

As outlined above it is questionable whether the skilled person setting out to solve above-mentioned technical problem would have consulted D1, however even if doing so the skilled person would not have arrived at the invention for several reasons.

One plant is different from another plant and as outlined in detail above in relation to the main request, based on the teaching of D1 the skilled person could have no reasonable expectation that a null mutation of the MMT gene in barley would have a similar phenotype as the mutations in Arabidopsis and maize disclosed by D1. Further, the skilled person could not reasonably predict the levels of DMS in an extract or beverage prepared from such plants.

Furthermore, D1 nowhere discloses or suggest a G→A mutation of base no. 3076 of SEQ ID NO:3 in the gene encoding MMT. In fact, D1 is silent with regard to any single nucleotide mutations, and nowhere does D1 teach a single nucleotide mutation in a splice site.

Thus, the Arabidopsis *mmt* mutant described by D1 has an insertion of a T-DNA located close to the 3' end of intron 7. D1 states that "*an insertion at this point is expected to stop formation of a competent enzyme, given the large size of the T-DNA*" (see p. 1809, 2nd col., first paragraph of the results section). The maize *mmt* mutant described by D1 has a Mu element inserted after the codon specifying amino acid 989.

When consulting D1, the skilled person would not have been led in the direction of a single nucleotide mutation, let alone a single nucleotide mutation in a splice site. In particular, the skilled person would not have been led to either a G→A mutation of base no. 3076.

This is even more the case as the prior art does not disclose the genomic sequence of the *mmt* gene of barley. Furthermore, as described in paragraph [0008] of the patent no useful methods for site-directed mutagenesis in barley were available at the filing date of the patent.

Importantly, the skilled person would not have been able to prepare the claimed barley plant based on the disclosure of D1. As noted above, at the filing date of the patent no useful methods for site-directed mutagenesis in barley were available, and D1 does not provide any screening methods useful for identifying single nucleotide substitutions. The screening methods described by D1 are PCR based methods that rely on random insertion of heterogeneous DNA, such as T-DNA or the Mu element.

Insertion of such heterogeneous DNA within a specific known genomic DNA sequence can be detected by PCR screening. However, such screening methods are not capable of identifying single nucleotide substitutions, and certainly not in an unknown genomic sequence.

Thus, even if the skilled person had set out to prepare a barley plant carrying a mutation in the *mmt* gene, the skilled person could not have arrived at the claimed mutation based on the teaching of D1.

As described in the patent in Example 2, barley plants carrying a G→A mutation of base no. 3076 were identified by a method involving a first step of random mutagenesis followed by a rapid high-throughput screening procedure developed by the inventors for detection of barley grains lacking MMT activity (Example 2 in the patent). Development of the screening procedure was not trivial as demonstrated by the lack of success of a different screening method (see Approach 2 of Example 2). The technical effect of this mutation, namely a reduction in DMS content and a reduction in off flavour of the resulting beer was unexpected.

According to the case law of the Boards of Appeal, any specific mutation with a desired technical effect generated by random mutagenesis indeed constitutes an inventive contribution to the art. Thus, in paragraph 17 the decision T737/96 states that the isolation of specific mutant strains with specific properties, albeit achieved by conventional mutagenesis techniques, never-the-less constitutes a contribution to the art which deserves patent protection, because random mutagenesis techniques contain elements of surprise which justify the recognition of an inventive step.

In conclusion, the skilled person reading D1 would not have arrived at the claimed mutation. Accordingly, even if combining the teaching of D2 with the teaching of D1, the skilled person would not have arrived at the claimed invention.

Claim 6 and claims dependent thereon are thus inventive over the disclosure of D2 combined with the disclosure of D1.

<u>Auxiliary requests 3 and 8– claim 6 – D1 as closest prior art</u>

In the in event that the Board of Appeal should maintain that D1 is closest prior art vis-à-vis claim 6, claim 6 is never-the-less inventive.

As explained above in relation to the main request, the objective technical problem is chosen based on the technical effect of the features distinguishing the claim from the prior art.

As described above D1 describes *mmt* mutants of Arabidopsis and maize having reduced levels of SMM. The document further describes that the SMM contributes to regulation of the Ado-Met levels.

The distinguishing feature between D1 and the invention of claim 6 is that claim 6 relates to a barley plant having a total loss of MMT function, wherein the barley plant carries a G→A mutation of base no. 3076 of SEQ ID NO:3 in the gene encoding MMT.

As described in the patent, the technical effect of this difference is that the plant is useful for preparation of beer or other barley based beverages having a low level of DMS-specific taste (see [0016] of the patent).

Accordingly, the objective technical problem solved by the invention of claim 6 is the provision of a plant useful for preparation of beverages having reduced off-flavors, in particular reduced amounts of DMS.

Based on the teaching of D1, the skilled person seeking to solve aforementioned technical problem could not have arrived at the claimed invention.

First of all D1 is completely silent with regard to the level of DMS in beverages. D1 does not even disclose DMS levels in a simple extract prepared from the plants disclosed therein. Even if the skilled person had considered to prepare a null mutant MMT barley plant based on the teaching of D1, the skilled person would have had absolutely no reasonable expectation that such a barley plant in fact would solve the technical problem for the reasons described in detail in relation to the main request.

Furthermore, the skilled person would not have arrived at a barley plant carrying a G→A mutation of base no. 3076 of SEQ ID NO:3 in the gene encoding MMT. D1 nowhere discloses or suggest such a mutation. In fact, D1 is silent with regard to any single nucleotide mutations, and nowhere does D1 teach a single nucleotide mutation in a splice site.

Thus, the Arabidopsis *mmt* mutant described by D1 has an insertion of a T-DNA located close to the 3' end of intron 7. D1 states that "*an insertion at this point is expected to stop formation of a competent enzyme, given the large size of the T-DNA*" (see p. 1809, 2nd col., first paragraph of the results section). The maize *mmt* mutant described by D1 has a Mu element inserted after the codon specifying amino acid 989. Thus, in contrast to the mutation of the invention, both of the mutations disclosed by D1 are insertions of large DNA sequences.

When consulting D1, the skilled person would not have been lead in the direction of a single nucleotide mutation, let alone a single nucleotide mutation in a splice site. In particular, the skilled person would not have been lead to a G→A mutation of base no. 3076.

This is even more the case as the prior art does not disclose the genomic sequence of the *mmt* gene of barley. Furthermore, as described in paragraph [0008] of the patent no useful methods for site-directed mutagenesis in barley were available at the filing date of the patent.

Importantly, the skilled person would not have been able to prepare the claimed barley plant based on the disclosure of D1. As noted above, at the filing date of the patent no useful methods for site-directed

mutagenesis in barley were available, and D1 does not provide any screening methods useful for identifying single nucleotide substitutions. The methods of D1 are based on the availability of pre-generated libraries. As noted above such libraries were not available for barley at the priority date. Furthermore, the screening methods described by D1 are PCR based methods that rely on random insertion of heterogeneous DNA, such as T-DNA or the Mu element. Insertion of such heterogeneous DNA within a specific genomic DNA sequence can be detected by PCR, provided that genomic sequence information is available. At the priority date the genomic sequence of barley was not available. In addition, such PCR based screening methods are not capable of identifying single nucleotide substitutions.

Thus, even if the skilled person had set out to prepare a barley plant carrying a mutation in the *mmt* gene, the skilled person could not have arrived at the claimed mutation using the screening methods taught by D1.

As described in the patent in Example 2, a barley plant carrying a G→A mutation of base no. 3076 was identified by a method involving a first step of random mutagenesis followed by a rapid high-throughput screening procedure developed by the inventors for detection of barley grains lacking MMT activity. Development of the screening procedure was not trivial as demonstrated by the lack of success of a different screening method (see Approach 2 of Example 2). The technical effect of this mutation, namely a reduction in DMS content and a reduction in off flavour of the resulting beer was unexpected.

According to the case law of the Boards of Appeal, any specific mutation with a desired technical effect generated by random mutagenesis indeed constitutes an inventive contribution to the art. Thus, in paragraph 17 the decision T737/96 states that the isolation of specific mutant strains with specific properties, albeit achieved by conventional mutagenesis techniques, never-the-less constitutes a contribution to the art which deserves patent protection, because random mutagenesis techniques contain elements of surprise which justify the recognition of an inventive step.

The Board of Appeal appears to be of the opinion that the claimed invention is an arbitrary selection from a range of equally obvious alternatives. Patent proprietors disagree. First of all, the claimed barley plant in fact solves the technical problem. It is thus not an arbitrary selection, but a selection of barley plant useful for preparation of beverages with reduced off-flavorus, in particular beer or other barley based beverages having a low level of DMS-specific taste. Furthermore, the skilled person had no reasonable expectation that a barley plant carrying a G→A mutation of base no. 3076 would in fact solve the technical problem. Finally, the skilled person could not have arrived at the claimed mutation based on the disclosure of D1. D1 gives no guidance on the identification of single nucleotide mutations, because the methods of D1 relies on detection of insertion of a large transgene insert or a transposable element, the Mu element.

Turning to D2 would not have helped, since D2 also does not describe any effects of mutations in MMT.

It is thus concluded that claim 6 of the 6th auxiliary request is inventive over the disclosure of D1.

Auxiliary request 7

Claim 6 of auxiliary request 7 relates to barley plants carrying a G→A mutation of base no. 3076 of SEQ ID NO:3 or a G-A mutation of base no. 1462 of SEQ ID NO:16. Similar considerations re inventive step apply to both of these mutations.

Thus, the claims of auxiliary request 7 are inventive for the same reasons as outlined above.

Auxiliary requests 9, 10 and 13

The claims of auxiliary requests 9, 10 and 13 are inventive for similar reasons as auxiliary requests 3 and 8.

Auxiliary requests 14 to 16

Auxiliary requests 14 to 16 lack claim 6 and dependent claims, and thus the claims of these requests are inventive over D2 and D1.

Yours sincerely
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