

Internal distribution code:

- (A) [-] Publication in OJ
- (B) [-] To Chairmen and Members
- (C) [-] To Chairmen
- (D) [X] No distribution

**Datasheet for the decision
of 14 January 2025**

Case Number: T 2546/22 - 3.3.04

Application Number: 06828912.3

Publication Number: 1957655

IPC: C12N15/82

Language of the proceedings: EN

Title of invention:
Disease resistant plants

Patent Proprietor:
Enza Zaden Beheer B.V.

Opponents:
Rijk Zwaan Zaadteelt en Zaadhandel B.V.
Pop Vriend Research B.V.
Nunhems B.V.

Headword:
Lettuce/ENZA

Relevant legal provisions:
EPC Art. 100 (b), 83

Keyword:

Sufficiency of disclosure (no) - patent as granted - undue burden

Decisions cited:

G 0009/92, T 0226/85, R 0015/11, R 0004/17

Catchword:



Beschwerdekammern

Boards of Appeal

Chambres de recours

Boards of Appeal of the
European Patent Office
Richard-Reitzner-Allee 8
85540 Haar
GERMANY
Tel. +49 (0)89 2399-0

Case Number: T 2546/22 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 14 January 2025

Appellant: Enza Zaden Beheer B.V.
(Patent Proprietor) Haling 1E
1602 DB Enkhuizen (NL)

Representative: Höpfner, Sebastian
ZSP
Patentanwälte PartG mbB
Hansastraße 32
80686 München (DE)

Respondent I: Rijk Zwaan Zaadteelt en Zaadhandel B.V.
(Opponent 1) Burgemeester Crezeelaan 40
2678 KX De Lier (NL)

Representative: Krohn, Mascha Dorothea
Rijk Zwaan
Zaadteelt en Zaadhandel B.V.
Burgemeester Crezéelaan 40
2678 ZG De Lier (NL)

Respondent II: Pop Vriend Research B.V.
(Opponent 2) P.O. Box 5
Middenweg 52
1619 ZG Andijk (NL)

Representative: Brantsandpatents bv
Pauline Van Pottelsberghelaan 24
9051 Ghent (BE)

Respondent III: Nunhems B.V.
(Opponent 3) Napoleonsweg 152
6038 AB Nunhem (NL)

Representative: BASF IP Association
BASF SE
GBI - Z078
67056 Ludwigshafen (DE)

Decision under appeal: **Interlocutory decision of the Opposition
Division of the European Patent Office posted on
5 October 2022 concerning maintenance of the
European Patent No. 1957655 in amended form.**

Composition of the Board:

Chairman A. Chakravarty
Members: D. Luis Alves
L. Bühler

Summary of Facts and Submissions

I. European patent EP 1 957 655, entitled "*Disease resistant plants*", was granted on European patent application No. 06 828 912.3, filed as an international application published as WO 2007/051626.

II. Claims 1 and 4 of the patent as granted read:

"1. Plant, which is resistant to a pathogen, wherein the plant and the pathogen are selected from *Bremia lactucae* on lettuce, *Peronospora farinosa* on spinach, *Pseudoperonospora cubensis* on members of the Cucurbitaceae family, *Pseudoperonospora cubensis* on cucumber, *Peronospora destructor* on onion, *Hyaloperonospora parasitica* on cabbage, *Plasmopara viticola* on grape, *Phytophthora infestans* on tomato and potato, and *Phytophthora sojae* on soybean; said plant has an increased *in planta* homoserine level as compared to said plant that is not resistant to the said pathogen; and said plant has a mutation in its homoserine kinase gene that lowers the homoserine kinase activity of the encoded enzyme."

"4. Plant as claimed in claim 1 or claim 2, wherein the gene is the homoserine kinase gene of *Lactuca sativa* having the nucleotide sequence and amino acid sequence as shown in Fig. 10."

III. Three parties filed oppositions against the patent, invoking the grounds for opposition under Article 100(a) EPC, Articles 53(c), 57, 54 and 56 EPC, as well as the grounds for opposition under Article 100(b) and (c) EPC.

- IV. In the decision under appeal, the opposition division decided that, account being taken of the amendments in the form of auxiliary request 1, the patent and the invention to which it related met the requirements of the EPC. As regards the patent as granted, the opposition division held *inter alia* that the patent did not disclose the invention as defined in the claims in a manner sufficiently clear and complete for it to be carried out by a skilled person (Articles 100(b) and 83 EPC).
- V. The patent proprietor (appellant) filed an appeal against that decision.
- Opponent 1 also filed an appeal but subsequently withdrew it with letter dated 6 February 2023. Opponents 1 to and 3 are therefore respondents I to III to the patent proprietor's appeal.
- VI. Respondent III filed a reply to the appeal. Respondents I and II did not make any substantive submissions in appeal proceedings.
- VII. The board appointed oral proceedings and, in a communication pursuant to Article 15(1) RPBA, informed the parties of its preliminary opinion on the appeal case.
- VIII. Oral proceedings were held in attendance of the appellant. The respondents had informed the board that they would not be attending the oral proceedings. At the end of the oral proceedings the Chair announced the board's decision.
- IX. The following documents are referred to in this decision:

D41: Appendix A: "Silencing of homoserine kinase (DMR1) in lettuce variety Pinokkio" - Experimental report submitted during examination proceedings.

D45c: "Lettuce DMR1 Enza data November 2017" - Experimental report submitted by the patent proprietor during opposition proceedings.

D57: "Experimental Evidence", 10 pages, filed by opponent 3 during opposition proceedings.

D58: Declaration of Dr Posthuma, filed by the patent proprietor during opposition proceedings.

D59: Declaration by Dr. Zeilmaker, including Exhibits A to D, filed by the patent proprietor during opposition proceedings.

D60: "Experimental Evidence", 5 pages, filed by opponent 3 during opposition proceedings.

X. The appellant's arguments, relevant to the decision, may be summarised as follows:

Main request (patent as granted)

Claim construction

Claim 1 was directed to a plant "resistant to a pathogen". This wording did not require 100% resistance, as explained in the patent at paragraph [0042], referring to a level of resistance, paragraph [0066], referring to increased resistance and paragraph [0037], referring to a sufficient accumulation of homoserine.

Disclosure of the invention (Articles 100(b) and 83 EPC)

The opposition division's finding of lack of sufficient disclosure for the claimed invention was wrong. The claimed plants were sufficiently disclosed in the patent. Document D59, a declaration filed by the appellant, stated "*A single screening step would already be sufficient, namely to screen whether a dmrl1-mutated plant is resistant against the pathogen. The resistance can easily be scored visually by examining the conidiophore formation...*" (see page 4, first paragraph).

Although there was no example of a mutant lettuce plant with pathogen resistance in the patent, absolute proof of reproducibility of an invention was not required and some trial and error was admissible (see Case Law of the Boards of Appeal of the EPO, 8th edn., II.C.5.6).

Documents D57 and D60, filed by the opponents during opposition proceedings, did not serve to substantiate serious doubts, as required for a successful objection of lack of sufficient disclosure because the experimental reports they contained did not prove that there was no possible mutation of the homoserine kinase (HSK) gene in lettuce, which resulted in increased resistance to *Bremia lactucae*.

Furthermore, the experiments described in documents D57 and D60 did not include a pre-screen for mutant lettuce plants exhibiting increased homoserine levels. An increased *in planta* homoserine level was however a requirement of claim 1. Thus, the mutants which according to documents D57 and D60 allegedly did not

exhibit increased pathogen resistance, were not encompassed by claim 1.

Moreover, the experiments reported in documents D57 and D60 did not test for pathogen resistance in lettuce plants carrying the same mutations that had been identified in *Arabidopsis* plants, i.e. at the positions of *dmr1-1* to *dmr1-5* of the HSK gene. Instead the opponents had used lettuce plants having mutations elsewhere in the HSK gene. Therefore, it could not be concluded from these experiments that, when following the teaching in the patent about the mutations in *Arabidopsis*, pathogen-resistant lettuce plants could not be obtained.

As regards document D60, Table 1 showed mutations in lettuce plants that had no impact on the homoserine levels. These plants could not serve to show that claimed invention was not sufficiently disclosed because the mutants tested did not fall under claim 1, which required increased *in planta* homoserine levels. The mutant W260Stop, which produced a truncated HSK protein, was not tested for homoserine levels. Thus, this mutant was not part of the subject-matter of claim 1 either. In fact, there was a single mutant lettuce plant in Table 1 which exhibited a detectable level of homoserine, but the level was merely 0.22 nmole/mg fresh weight and thus below the lowest level taught in the patent as necessary to achieve resistance to pathogens (see Table 1 of the patent). Therefore, this mutant could not serve as evidence to show that accumulation of homoserine did not lead to increased pathogen resistance.

In fact, the relationship between an increased pathogen resistance and increased homoserine levels was shown in document D58.

The experimental report in document D57 also had several shortcomings: of the 41 lettuce plants having mutations in the HSK gene (gene as identified in Figure 10 of the patent), only three were tested for pathogen resistance (see page 6, second paragraph, and Table 4); double mutants were not tested; heterozygous mutants were not screened for their homoserine levels. As for the only mutant exhibiting an increased homoserine, the level was 0.38 nmole/mg fresh weight (see Table 3), which was also below that taught in the patent. Therefore, this report could not serve as evidence to show that lettuce plants with pathogen resistance could not be obtained with the teaching in the patent.

The patent provided three methods for identifying orthologues of the *Arabidopsis* HSK gene (see paragraphs [0055], [0057] and [0058]). Therefore, the skilled person was taught how to identify further HSK genes for the plant of interest. The skilled person would screen mutants for their homoserine levels and pathogen resistance, as taught in the patent (see paragraph [0037]).

The patent already provided an indication that lettuce might have two HSK genes: see the wording in paragraph [0049], when referring to *Arabidopsis*, in contrast to the wording in paragraph [0028] "*in most other species tested sofar, HSK appears to be encoded by a single gene*".

In fact, in the experimental report D57 it was admitted that both lettuce HSK genes can contribute to the homoserine levels (see page 8, first paragraph). Indeed, this document showed that it had been possible to identify two orthologue HSK genes in lettuce by following the teaching in the patent. Therefore, it was possible for the skilled person to identify suitable mutant lettuce plants.

Lettuce mutants according to the claims had been identified: document D57 identified a heterozygous mutant with an increased homoserine level, as required by claim 1, and improved resistance to *Bremia lactucae* (see mutant E238K in Table 4 and the value 50% in one of the columns); it additionally provided a further HSK mutant lettuce plant with partial resistance to *Bremia lactucae* (R245K, heterozygous) and one resistant mutant (R245K, homozygous); document D60 showed multiple lettuce mutants with increased resistance (see Table 2, all but one mutant showing values for disease symptoms below those for the wild type).

XI. Respondent III's arguments submitted in writing, relevant to the decision, may be summarised as follows:

The patent did not disclose any lettuce plants falling within the claim. It only identified *Arabidopsis* plants with mutations in the HSK gene. The mechanism underlying the pathogen resistance identified in *Arabidopsis*, involving HSK activity, could not be extrapolated to other species. Therefore the claimed invention was not sufficiently disclosed. The assumption that lettuce HSK protein of Figure 10 of the patent played the same role in lettuce as the HSK in *Arabidopsis*, was incorrect. Document D60 showed that none of the tested lettuce plants having mutations in

the HSK protein shown in Figure 10 of the patent exhibited increased resistance to *Bremia lactucae* (see Table 2). In particular, a mutant resulting in a truncation of about 30% of the HSK protein did not lead to pathogen resistance. In contrast, a truncation in a different HSK gene in lettuce did have an impact on the homoserine level (see document D45c). This HSK gene was however not identified in the patent. In conclusion, it was already an undue burden for the skilled person to identify the correct gene that needed to be mutated in lettuce.

An additional reason why it could not be assumed that the effect of a specific point mutation in the HSK gene in *Arabidopsis* would be the same in a different plant species was that some of the amino acids substituted in the *Arabidopsis* mutants *dmr1-1* to *dmr1-5* were not conserved across species - compare *dmr1-2* in lettuce and *Arabidopsis*.

To date no mutation in lettuce had been identified in the HSK gene depicted in Figure 10 of the patent which had an effect on pathogen resistance. However, such an embodiment was specifically defined in claim 4 as granted.

The patent did not provide guidance on how to identify a mutation in lettuce HSK having the desired effect. The experimental reports in documents D57 and D60 provided evidence that it was an undue burden to identify HSK mutants in lettuce with the desired pathogen resistance. Moreover, the patent failed to identify the *in planta* homoserine level required for pathogen resistance. Document D60 showed that even a mutation which led to increased homoserine levels, comparable to those reported in the patent as suitable

for *Arabidopsis*, did not result in increased resistance to *Bremia lactucae* in the mutant lettuce plants (see document D60, mutant having 0.380 nmol/mg fresh weight).

XII. The appellant requested that the decision under appeal be set aside and the patent be maintained as granted, alternatively, that the patent be maintained in amended form on the basis of the claims of auxiliary request 1 held allowable by the opposition division.

XIII. Respondent III requested that the appeal be dismissed.

Reasons for the Decision

The appeal case

1. The appeal of the patent proprietor is directed against the decision of the opposition division that the patent as granted (main request) was not allowable. Since the patent proprietor is the sole appellant, the allowability of the auxiliary request held allowable by the opposition division cannot be examined (G 9/92, OJ EPO 1994, 875, headnote 1).

Main request (patent as granted)

Disclosure of the invention (Articles 100(b) and 83 EPC)

2. Claim 1 is directed to a plant resistant to a pathogen, and includes lettuce plants resistant to *Bremia lactucae*. The plant is further defined by having (i) "an increased *in planta* homoserine level" compared to non-resistant plants and (ii) "a mutation in its homoserine kinase [HSK] gene that lowers the homoserine

kinase activity of the encoded enzyme". Claim 4 is directed to a lettuce plant where the mutation is in the HSK gene as depicted in Figure 10 of the patent.

3. The opposition division *inter alia* held that the patent did not sufficiently disclose these claimed embodiments relating to lettuce plants.
4. The patent identifies five mutants of *Arabidopsis* with increased pathogen resistance (*dmr1-1* to *dmr1-5*, see example 1). It reports that the responsible mutations are located in the HSK gene. These mutant plants exhibited increased homoserine levels (see example 2). In a separate experiment it was shown that, when seedlings of *Arabidopsis* were infiltrated with homoserine, they exhibited increased pathogen resistance (see example 3). HSK orthologues in other species were identified (see example 4). Further *Arabidopsis* mutants were generated by RNAi gene silencing (see example 5) and random mutagenesis was described (see example 6). The amino acid and nucleic acid sequence of an HSK gene in lettuce is provided in Figure 10.
5. It was common ground that the patent does not identify any mutant lettuce plants with increased homoserine levels or increased resistance to *Bremia lactucae*.
6. The appellant provided several lines of argument as to why the opposition division was mistaken to consider that the claimed invention was not sufficiently disclosed when it came to lettuce plants. In one line of argument, the appellant submitted that the declaration D59 confirmed the reproducibility of the invention since it stated that a single screening step

could identify pathogen-resistant mutant lettuce plants.

7. However, despite this statement in declaration D59, as set out below the appellant failed to identify a single mutant lettuce as defined in claim 4.
8. The respondents provided experimental reports included in documents D57 and D60. The appellant contested that the evidence provided by the respondents was sufficient to substantiate serious doubts that the claimed invention could be carried out by the skilled person.
9. The board is of the view that the respondents have indeed substantiated serious doubts to this effect. Documents D57 and D60 taken together not only provide multiple examples of lettuce HSK mutants which lack pathogen resistance but also provide a rationale explaining this.
 - 9.1 Document D57 describes that two HSK genes were identified in lettuce (see page 1, second paragraph): one which was designated Lsa0250090.1, and is almost identical to the HSK identified in Figure 10 of the patent (in the following "HSK gene 090" or "HSK gene according to the patent"), and another which was designated Lsa035142.1 (in the following "HSK gene 142").

Two populations comprising randomly mutated lettuce plant material were screened to identify lettuce plants having a mutation in the HSK gene which resulted in an amino acid substitution. These were further screened with a predictive model for mutations leading to reduced HSK activity of the encoded protein (see page 1, last paragraph and page 3, fourth and fifth

paragraphs). These plants were then grown and tested for homoserine levels and for resistance to *Bremia lactucae* (see page 1, last paragraph).

Table 3 shows the results for the homoserine levels and Table 4 shows those for the pathogen resistance, presented as scores for two parameters - the "% surface area showing sporulation" and the "intensity [or severity] of the sporulation". As concerns mutations in the HSK gene 090, 41 mutants were identified, and 14 were selected based on the predicted effect of the mutation on the enzyme activity. The presence of the mutation could be confirmed in the seeds, except in three of the mutants (see "Results" on page 6). Table 3 lists the 14 mutants with mutations in the HSK gene 090, as well as five mutants with mutations in the HSK gene 142, along with the measured homoserine levels. The paragraph immediately below Table 3 confirms that 10 mutants having an amino acid substitution in the HSK gene according to the patent (HSK gene 090) were tested for their homoserine levels. None had detectable homoserine levels.

- 9.2 Thus, the appellant's argument that the mutants had not been screened for their homoserine levels is not compatible with what is reported in this document. The appellant further argued that only three mutants had been tested for pathogen resistance and this raised the question of whether non-resistant mutants had purposively been selected for testing. However, this argument cannot call the conclusions drawn in the report in document D57 into question, for the following reasons: The patent teaches that increased pathogen resistance is due to increased homoserine levels, which results from mutations in the enzyme which reduce or eliminate its activity.

It follows that, when screening for *Bremia* resistant mutants, it is possible to either test them directly for resistance or to perform a pre-screen for homoserine levels. The pre-screen for homoserine levels is also in line with the teaching of the patent on paragraphs [0036] and [0037]. Thus, Tables 3 and 4 in document D57 are entirely consistent with this teaching because the testing for homoserine levels already revealed that none of the mutants showed increased homoserine levels, as required by the claims. It was therefore not necessary to test them all for pathogen resistance.

- 9.3 The board therefore concludes that the experiments reported in document D57 are a fair attempt at reproducing the invention and convincingly call its reproducibility into question. The appellant's argument that document D58 shows a correlation between increased homoserine levels and pathogen resistance is not challenged. However, that correlation is not the basis for the respondents' objection.
- 9.4 Document D60 provides a rationale for the failure, reported in document D57, to obtain mutants with increased homoserine levels and increased pathogen resistance. It identifies lettuce mutants with increased homoserine levels and increased resistance but in which a different HSK gene is mutated - the HSK gene 142 (see Tables 1 and 2).
- 9.5 It can be seen from Table 1 that none of the mutations in the gene identified in the patent resulted in homoserine levels above the detection limit, including a plant having a mutation resulting in a truncation of about 30% of the HSK protein (see Table 1, where the

first 14 rows represent mutations in the HSK gene according to the patent, and the last two rows represent mutations in the HSK gene 142; see mutant "W260Stop"). It is reported that, in contrast, such a truncation in the HSK gene 142 was detrimental to plant growth. In other words, it affected the homoserine levels. The document suggests that only the enzymatic activity of the HSK gene 142 product limits the homoserine kinase activity in lettuce and that the product of HSK gene according to the patent cannot compensate for that loss in enzyme activity (see D60, page 4, fourth paragraph, first and last sentences). The board has seen no evidence that casts doubt on the findings reported in document D60.

- 9.6 The board also notes that the lettuce mutants in document D60 are not identical to those identified and tested in document D57, and are thus additional examples of mutants which did not result in the features required by claim 4.
- 9.7 The board concludes from the foregoing that documents D57 and D60 not only raise serious doubts that the patent teaches the skilled person how to obtain, without undue burden, lettuce plants as defined in claim 4 of the patent, but even demonstrate that such lettuce plants cannot be obtained on the basis of the information in the patent. Therefore, lack of sufficiency has been established well beyond the required standard.
10. The appellant's counter arguments did not persuade the board.
11. According to the appellant, pathogen resistant mutant lettuce plants were identified in documents D57, D60

and D45c. However, the board notes that in all these mutants, the mutation was not in the gene identified in the patent, Figure 10, but instead in the HSK gene 142 (as regards documents D57 and D60, see points 9.1 and 9.4 above). This was not disputed by the appellant.

12. The appellant further referred to a pathogen resistant mutant identified in document D41. However, as noted by respondent III and by the board in its communication pursuant to Article 15(1) RPBA, that document does not provide information regarding the gene that was mutated, so that it cannot serve as evidence of a lettuce plant carrying a mutated version of the HSK gene in Figure 10 of the patent. Also this was not disputed by the appellant.
13. The board concludes that neither the patent nor the experimental reports submitted by the parties identify a lettuce plant carrying a mutation in the HSK gene shown in Figure 10 of the patent, that exhibits either increased homoserine levels or increased pathogen resistance.
14. However, a lettuce plant with a mutation in the HSK gene in Figure 10 of the patent is an embodiment specifically claimed in claim 4 of the patent as granted. Consequently, the line of argument that the patent provided the skilled person with a pointer to the possible existence of a second HSK gene in lettuce cannot assist as regards this claimed embodiment.
15. The above notwithstanding, the board does not agree with the appellant's argument that paragraphs [0028] and [0049] of the patent already indicate that lettuce might have two HSK genes. Firstly, paragraph [0049] is a positive statement that in *Arabidopsis*, HSK is

encoded by a single gene. An exception is not even hinted at, let alone pointed out. Secondly, paragraph [0028] lists plant species that have one single HSK, and states that "*[i]n most other plant species tested so far, HSK appears to be encoded by a single gene*". Again, this is an affirmative statement confirming that, as a rule, only a single gene is involved in the expression of HSK. In the board's view the reader is not led to believe that any of the plant species covered by the invention would be an exception to this. The list of exceptions to the general rule, in this same paragraph - potato, tobacco and poplar, further reinforces the reader's understanding that unless an exception is identified, the relevant species has a single HSK gene. Furthermore, the wording of claim 1 is "said plant has a mutation in its homoserine kinase gene" (underlining by the board). Also this wording indicates that there is a single HSK gene for each species listed.

16. In one line of argument, the appellant submitted that the wording "resistant to a pathogen" in claim 1 did not require 100% resistance to the pathogen. This was relevant in the context of the experimental reports submitted by the opponents as documents D57 and D60. The appellant's argument is that these documents show mutants according to claim 1, i.e. plants for which a mutation in the HSK gene resulted in increased homoserine levels and some increase in pathogen resistance. The appellant referred specifically to document D57, Table 4, mutants R245K (homozygous), R245K (heterozygous) and (E238K (heterozygous), as well as to document D60, Table 2.

- 16.1 As regards document D57, the mutants in question are not relevant for claim 4, as explained above (see point 11.).
- 16.2 As regards document D60, Table 2 shows the results obtained for mutant lettuce plants exposed to the relevant pathogen *Bremia lactucae*. They are presented in two forms: the values measured for the parameters designated "% leaf surface showing sporulation" and "Intensity of sporulation on leaf surface"; and the conclusion as "S" for susceptible to the pathogen and "R" for resistant to it. It can be observed that only the resistant control is classified as "R". It is noted that the wild type "Wendel" in row 1 represents the reference for establishing an increase in resistance to pathogen. Further, the last two rows in the table are not relevant for the present issue because they represent mutations in the other HSK gene. According to the appellant, all but one mutant exhibited a decrease in one of the disease parameters. However, from a comparison of Tables 1 and 2, it is apparent that the "Wendel" mutants shown in Table 2 and Table 1 are the same, and that none of them had a homoserine level above the detection limit (see last column in Table 1). Thus, the mutants referred to by the appellant did not exhibit increased homoserine levels as required by claims 1 and 4. In conclusion, irrespective of the values shown for pathogen resistance in Table 2, this document does not serve to show that plants according to claim 4 could be obtained.
17. The appellant further contested the suitability of the experiments reported in documents D57 and D60 to demonstrate that it was an undue burden to identify mutants according to claim 4, on the basis that they did not follow the teaching in the patent to generate

mutations corresponding to those in the pathogen resistant *Arabidopsis* mutants *dmr1-1* to *dmr1-5*.

- 17.1 The board notes that the claims are not restricted to five specific mutants. This notwithstanding, the board is of the view that the respondents followed the teaching in the patent when generating mutants by routine random mutagenesis techniques (compare example 6 of the patent with document D57, ESM mutagenesis). The respondents cannot be required to limit themselves to specific techniques of introducing point mutations.
- 17.2 Moreover, as noted by respondent III, the mutated amino acids in *Arabidopsis* mutants *dmr1-1* to *dmr1-5* are not conserved across all crops (see Figure 1 of the patent). The board also notes that this issue is in any case addressed in document D60, as follows: "*Notably, 3 different mutants comprising a mutation in the direct vicinity of the M241 mutation in the Arabidopsis At2g17265gene (CERVINO_M-972H2 having an P250L mutation; and WENDEL_M-1138H2 and WENDEL-14-033 having an V248I mutation) and 3 different mutants comprising a mutation in the direct vicinity of the A267V mutation in the Arabidopsis At2g17265gene (CERVINO_M-657H1 having an A265T mutation; WENDEL_M-1297H2 having a V269M mutation; and WENDEL M-697H2 having a D276N mutation) were analyzed, wherein both Arabidopsis mutations were reported in the opposed patent to lead to an increased in planta homoserine level and pathogen resistance...*".
- 17.3 The board concludes that the mutations corresponding to positions 265 and 269 in the lettuce HSK protein, which according to document D60 are in direct vicinity of mutation *dmr1-1* in *Arabidopsis* HSK in the patent, are

very pertinent to the issue raised by the appellant (for the location of the mutations in *Arabidopsis* see also the sequence alignment in Figure 1 of the patent). These mutations however did not result in increased homoserine levels or pathogen resistance (see Table 1 of document D60). No further arguments were presented in this context to be considered by the board.

18. In yet a further argument, the appellant submitted that the respondents had not shown that there was no possible mutant lettuce plant, comprising a mutation in the HSK gene depicted in Figure 10 of the patent, which exhibited increased pathogen resistance.
19. However, the opponents cannot be required to demonstrate the non-existence of a mutant lettuce plant with the claimed characteristics, since any experimental evidence, such as that provided in documents D57 and D60, would be open to the criticism that the experiments were not exhaustive in that they did not cover all possible mutations. In such a situation, only the affirmative, i.e. the existence of a mutant plant as claimed, can be proven (for which the burden is on whom asserts), not the negative. This is referred to in the case law as the principle that a negative is not to be proven (*negativa non sunt probanda*; see R15/11, R4/17).
20. The opponents can only be expected to try to repeat specific examples or to prepare other embodiments of the subject-matter claimed following the instructions of the patent. These instructions, possibly together with common general knowledge, should lead necessarily and directly towards success through the evaluation of initial failures or through an acceptable statistical expectation rate in case of random experiments (see

T 226/85, OJ 1988, 336, and decisions following it). The board is convinced that in the present case the respondents have provided persuasive evidence in support of the failure to identify mutant plants according to claim 4. They prepared several examples following the teaching in the patent and routine techniques in the technical field of the patent, and gave also a rationale for their failure to identify mutant plants according to claim 4. This evidence was not successfully refuted by the appellant. The alleged examples of mutants according to the invention were not relevant to the invention as defined in claim 4.

21. In view of the above considerations the board concludes that the ground for opposition under Article 100(b) EPC prejudices the maintenance of the patent as granted.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar:

The Chairman:



A. Wille

A. Chakravarty

Decision electronically authenticated