

**Internal distribution code:**

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

**Datasheet for the decision  
of 24 January 2017**

**Case Number:** T 2323/11 - 3.3.04

**Application Number:** 05796045.2

**Publication Number:** 1794305

**IPC:** C12N15/82, C12N15/55

**Language of the proceedings:** EN

**Title of invention:**

Recombination cassettes and methods for sequence excision in plants

**Applicant:**

BASF Plant Science GmbH

**Headword:**

Sequence excision/BASF

**Relevant legal provisions:**

EPC Art. 53(b)

**Keyword:**

"Main request and auxiliary request 1 - essentially biological process for the production of plants (yes)"

"Remittal (yes)"

**Decisions cited:**

G 0002/07, G 0001/08

**Catchword:**



**Beschwerdekammern**  
**Boards of Appeal**  
**Chambres de recours**

European Patent Office  
D-80298 MUNICH  
GERMANY  
Tel. +49 (0) 89 2399-0  
Fax +49 (0) 89 2399-4465

Case Number: T 2323/11 - 3.3.04

**D E C I S I O N**  
**of Technical Board of Appeal 3.3.04**  
**of 24 January 2017**

**Appellant:** BASF Plant Science GmbH  
(Applicant) 67056 Ludwigshafen (DE)

**Representative:** Oltmanns, Heiko  
Herzog Fiesser & Partner Patentanwälte  
PartG mbB  
Dudenstrasse 46  
68167 Mannheim (DE)

**Decision under appeal:** **Decision of the Examining Division of the European Patent Office posted on 9 June 2011 refusing European patent application No. 05796045.2 pursuant to Article 97(2) EPC.**

**Composition of the Board:**

**Chairwoman** G. Alt  
**Members:** B. Claes  
L. Bühler

## Summary of Facts and Submissions

- I. The appeal was lodged by the applicant (hereinafter "appellant") against the decision of the examining division to refuse European patent application 05796045.2 having the title "*Recombination cassettes and methods for sequence excision in plants*". The application was published as international application WO 2006/032426.
- II. The decision under appeal dealt with a main request and an auxiliary request 1. Claim 1 of both requests was identical and read:
- "1. A method for producing a transgenic plant comprising:
- i) crossing a first transgenic plant comprising in its genome a DNA construct comprising
    - a1) at least one recognition sequence of at least 10 base pairs for the site directed induction of DNA double-strand breaks by a sequence specific DNA-endonuclease and
    - b1) a nucleic acid sequence to be excised, wherein said elements a1) and b1) and optionally further elements are flanked by homology sequences A and A', having sufficient length and sufficient homology in order to ensure homologous recombination between A and A' and having an orientation which - upon recombination between A and A' - will lead to an excision of said elements a1) and b1), and
    - c1) at least one additional sequence conferring to said plant an agronomically valuable trait, wherein said sequence is not localized between the homology sequences A and A' and would not be

excised from the genome upon recombination  
between A and A'

with a second transgenic plant comprising in its genome  
an expression cassette comprising

- a2) the parsley ubiquitin promoter, and operably  
linked thereto
- b2) a nucleic acid sequence coding for a sequence  
specific DNA-endonuclease having a sequence  
specificity for said recognition sequence a1),

ii) generating descendants (F1) following this  
crossing, and - **optionally - sexually or asexually  
generating further-descendants, and**

iii) isolating descendants which have undergone  
recombination between the homology sequences A and A'  
and which do not comprise in their genome said elements  
a1) and b1) but comprise sequence c1)." (emphasis added  
by the board).

III. In the decision under appeal the examining division  
held that the subject-matter of claim 1 of both  
requests constituted an essentially biological process  
for the production of plants which was excluded from  
patentability by virtue of Article 53(b) EPC. In an  
*obiter dictum* the examining division held further that  
the subject-matter of claim 1 of both requests also  
lacked inventive step (Article 56 EPC).

IV. With the statement of grounds of appeal the appellant  
submitted a new main request and three auxiliary  
requests. Claim 1 of the main request and of the 1st  
auxiliary request were identical to claim 1 pending  
before the examining division but for the deletion of  
the feature "- optionally - sexually or asexually  
generating further-descendants, and" (see section II,

where this feature was emphasised by the board). The 2nd and 3rd auxiliary requests comprised no process claims for the production of plants.

- V. When the board summoned the appellant to oral proceedings, it also informed it *inter alia* of its preliminary opinion that the subject-matter of claim 1 of both the main request and the 1st auxiliary request was excluded from patentability pursuant to Article 53(b) EPC.
- VI. In preparation for the oral proceedings the appellant submitted further arguments.
- VII. At the oral proceedings the the appellant was heard on the pertinent issues. At the end of the oral proceedings the Chairwoman announced the decision of the board.
- VIII. The appellant's arguments as relevant for the present decision can be summarised as follows:

*Main request and 1st auxiliary request - claim 1 - essentially biological process for the production of plants*

The excision of the target gene in accordance with the method of claim 1 constituted an "additional step of technical nature" as referred to in Headnote 3 of decision G 2/07 of the Enlarged Board of Appeal which took place "within the steps of sexually crossing and selecting". This step modified "a trait in the genome of the plant produced", *i.e.* the loss of the target gene, and this modification was not "the result of the mixing of the genes of the plants chosen for sexual crossing".

The "mixing of the genes of the plants chosen for sexual crossing" could only refer to the *meiotic* mixing of the genes of the gametes of parental plants when fusing to form a zygote (see 3rd paragraph in point 6.4.2.3 of the decision where the Enlarged Board of Appeal referred to a resulting trait as determined by meiosis). The "result of the mixing of the genes" referred to the genomic make-up of the zygote and only encompassed such traits as present in the zygote, *i.e.* the direct result of the mixing.

The excision of a gene according to the present invention, *i.e.* the modification of a trait, was meiosis-independent and occurred in mitotic stages *after* the formation of the zygote when the sequence-specific DNA endonuclease was expressed, and thus after mixing of the genes. The genomic make-up of the plant produced by the method of the invention differed from the genomic make-up of the zygote. Consequently, the modification of the trait according to the method of the present invention was not "the result of the mixing of the genes". Therefore, the method of claim 1 fulfilled the criteria laid down in Headnote 3 of decision G 2/07 and was not excluded from patentability.

The examples disclosed that the plant produced by the cross of the two parental transgenic plants was a chimeric plant which contained both cells which comprised the target gene in their genome and cells which had the target gene excised (see Figure 34 of the application). The trait (excision) was thus not the result of the mixing of the genes of the parent plants in the sense of decision G 2/07 and was not determined by the underlying natural phenomenon of meiosis.

The modified trait of the plants of the present invention could not be found in either of the parent plants. In addition, the excised target gene was irrecoverably lost in the generated progeny and impossible to retrieve by further crossings. Both these characteristics differentiated the claimed process from conventional breeding methods in which Mendel's laws applied and in which suitable back-crosses made it possible to retrieve lost features resulting from the mixing of the genomes of the parent plants.

- IX. The appellant requested that the decision under appeal be set aside and that a patent be granted on the basis of the main request or, alternatively, of one of the 1st to 3rd auxiliary requests, all filed with the statement setting out the grounds of appeal.

### **Reasons for the Decision**

1. The appeal is admissible.

*Main request and 1st auxiliary request - claim 1*

*The invention described in the application*

2. Genetic engineering of plants by transformation typically involves the introduction of a gene of interest ("trait gene") and a marker gene (e.g. a selectable marker such as an antibiotic or herbicide resistance gene) into the genome of the plant. The marker sequence allows identification and selection of desired plant cells during the transformation process, but typically lacks any function after the transformation was successful. However, their presence in the genome of the resulting organisms influences the



acceptance of such plants as food products among consumers (see application as published page 1, lines 9 to 20).

3. The present invention concerns the removal of unwanted sequences, e.g. such marker sequences, from the genome of transgenic plants which comprise an introduced gene for an agronomically valuable trait. The claimed method concerns the sexual crossing of two distinct transgenic parent plants. The first transgenic parent plant contains, besides sequences of interest conferring a particular trait on the plant, an undesired gene sequence in its genome ("target gene"). The second transgenic parent plant comprises a transgene encoding a particular sequence-specific DNA endonuclease which, when expressed in a cell which comprises the "target gene" in its genome, irreversibly excises this target gene from the genome. From such crosses, descending plants can be isolated which lack the marker sequences in their genome.
  
4. Independent claim 1 is accordingly directed to **a method for producing a transgenic plant by** i) **crossing a first transgenic plant** (comprising in its genome a "trait gene" of interest and a "target gene", e.g. an undesired marker gene) **with a second transgenic plant** (comprising in its genome the gene for a particular sequence-specific DNA endonuclease); **generating descendants (F1)** and iii) **isolating descendants** which do not comprise the target gene in their genome.

*Essentially biological process for the production of plants  
(Article 53(b) EPC)*

5. Article 53(b) EPC provides that "European patents shall not be granted in respect of (b) ... essentially biological processes for the production of plants ...; this provision shall not apply to microbiological processes ...".
6. In the consolidated decisions G 2/07 and G 1/08 (OJ EPO 2012, 130 and 206) the Enlarged Board of Appeal specified that (emphasis added by the board) "[a] *non-microbiological process for the production of plants which contains or consists of the steps of **sexually crossing the whole genome of plants and of subsequently selecting plants*** [was] *in principle excluded from patentability as being "essentially biological" within the meaning of Article 53(b) EPC*" (see decision G 2/07 and G 1/08, *supra*, Headnote, answer 1; emphasis added by the board).
7. In the decision under appeal the examining division held that the subject-matter of claim 1 pending before it was a method as held excluded from patentability pursuant to Article 53(b) EPC by the Enlarged Board. Claim 1 of the main request and the 1st auxiliary request before the board is identical to the claim 1 pending before the examining division but for the deletion of an optional feature (see section IV) which was not of relevance for the substantiation of the decision. Accordingly, the examining division's judgement applies to claim 1 of the main request and the 1st auxiliary request.

8. Claim 1 is directed to those steps in the production process of a transgenic plant which involve the crossing of two particular plants and the generation of first generation descendants (F1) thereof and the isolation and selection of those descendants which have lost the unwanted sequences in their genome (see section II and point 4). Accordingly, the board considers that Article 53(b) EPC and decisions G 2/07 and G 1/08, *supra*, of the Enlarged Board of Appeal are pertinent for assessing the patentability of the subject-matter of claim 1 as it consists of a non-microbiological process for the production of plants which contains or consists of the steps of sexually crossing the whole genome of plants and of subsequently selecting plants.
  
9. In the reasons for its decisions G 2/07 and G 1/08, *supra*, the Enlarged Board considered that, under Article 53(b) EPC, excluded "*processes were characterised by the fact that the **traits** of the plants resulting from the crossing **were determined by the underlying natural phenomenon of meiosis. This phenomenon determined the genetic make-up of the plants produced, and the breeding result was achieved by the breeder's selection of plants having the desired traits***" (see decisions G 2/07 and G 1/08, *supra*, point 6.4.2.3 of the reasons; the full paragraph on page 199; emphasis added by the board).
  
10. The appellant has argued that, in the claimed method, the step of the excision of the target gene was *not* the result of meiosis and the mixing of the parental genes, but that this process step took place at mitotic stages after the mixing of the genes and the formation of the zygote. The appellant therefore considered that the claimed method was rather a process as considered by

the Enlarged Board in the Headnote, answer 3 of its decisions G 2/07 and G 1/08, *supra*, namely: "[i]f, however, such a process contains **within** the steps of sexually crossing and selecting an **additional step of a technical nature**, which step by itself **introduces a trait into the genome or modifies a trait in the genome** of the plant produced, so that the introduction or modification of that trait is **not the result of the mixing of the genes** of the plants chosen for sexual crossing, then the process is not excluded from patentability under Article 53(b) EPC" (emphasis added by the board).

11. The board concurs with the appellant that the factual excision of the target gene in the context of the claimed process occurs after the zygote has been formed. The board notes, however, that in the context of the claimed invention the step of the excision of the target gene in the genome of the progeny of the two particular parent plants can only occur if the zygote generated upon crossing the parent plants combines the features of i) the presence of the target gene (from the first parent plant) and ii) the presence of the transgene encoding a particular sequence-specific DNA endonuclease (from the second parent plant; see point 3). The presence (or absence) of these features in the genomes of the respective gametes which fuse to generate the desired zygote, and thus the plant resulting from the crossing, is determined by meiosis upon the production of these gametes.
  
12. The board considers therefore that the trait of the excision of the target gene is the result of the crossing of the parent plants and is determined by the underlying natural phenomenon of meiosis, as the latter determines the genetic make-up of the plants produced.

13. The board thus concludes that the claimed method is a method as held to be excluded from patentability by virtue of Article 53(b) EPC by the Enlarged Board of Appeal in the context of Headnote, answer 1 of decisions G 2/07 and G1/08, *supra* (see point 10 above).
  
14. In view of the above finding the board can also not concur with the appellant's argument that, in the context of the claimed method, the excision of the target gene was an *"additional step of a technical nature which step by itself introduces a trait into the genome or modifies a trait in the genome of the plant produced, so that the introduction or modification of that trait is not the result of the mixing of the genes of the plants chosen for sexual crossing"*, i.e. a step held by the Enlarged Board in its decisions G 2/07 and G 1/08, *supra*, to render an excluded method for the production of plants as not excluded from patentability under Article 53(b) EPC (see point 11). Indeed, since the introduction or modification of the trait in the genome of the produced plant, in the present case, constitutes the result of the mixing of the genes of the plants chosen for the sexual crossing, the escape gate provided by the Enlarged Board in Headnote, answer 3 of its decisions G 2/07 and G 1/08, *supra*, does not apply.
  
15. Lastly, the appellant has argued that, in contrast to conventional breeding methods which followed Mendel's laws, in the method as claimed the feature resulting from the cross was not present in either of the parent plants and that the excised gene was irrevocably lost for further generations. The board notes however, that also in conventional breeding methods, traits in the resulting progeny are not necessarily identifiable or present as such in the respective parent plants. Indeed

new features in the progeny may well be the result of crossing and selection and therefore the mixing of the genes. Furthermore, as with the result of conventional breeding methods, suitable back-crossing with the first parent in the context of the claimed invention may well reinstate the undesired target gene in the genome of the plants resulting from the claimed method. The board is accordingly of the opinion that these arguments fail to distinguish the claimed subject-matter from the processes referred to by the Enlarged Board of Appeal in the Headnote, Answer 1, of decisions G 2/07 and G 1/08, *supra*.

16. Hence, in view of the above considerations the board judges that the method as subject-matter of claim 1 is excluded from patentability by virtue of Article 53(b) EPC.

*2nd and 3rd auxiliary requests - remittal of the case to the examining division for further prosecution*

17. As compared to the main request and the 1st auxiliary request, the 2nd and 3rd auxiliary requests are restricted to product and use claims and comprise no process claims for the production of plants (see section IV). The decision under appeal is silent on the patentability of the subject-matter claimed in the 2nd and 3rd auxiliary requests.
18. Pursuant to Article 111(1) EPC, following the examination as to the allowability of the appeal, the board shall decide on the appeal and, in this respect, it may either exercise any power within the competence of the department which was responsible for the decision appealed or remit the case to that department for further prosecution.

19. The board considers that a case like the present one, in which amendments have been proposed by the appellant which limit the requests to subject-matter on which the examining division has not expressed an opinion or issued a decision, gives rise to fresh issues which require further examination in relation to both the formal and substantive requirements of the EPC. The board considers it appropriate in these circumstances that the further examination should be carried out by the examining division, also to provide the appellant the opportunity to have its case considered without the loss of an instance.
  
20. Under the circumstances the board therefore considers it appropriate to exercise its discretion under Article 111(1) EPC to remit the case to the examining division for further prosecution.

**Order**

**For these reasons it is decided that:**

1. The decision under appeal is set aside.
2. The case is remitted to the examining division for further prosecution.

The Registrar:

The Chairwoman:



P. Cremona

G. Alt

Decision electronically authenticated