Reasons for opposition against European Patent EP 2 966 992 B1

Title: HIGH TEMPERATURE GERMINATING LETTUCE SEEDS
Application number**:** 14712250.1
Patent holder: Rijk Zwaan Zaadteelt en Zaadhandel B.V.
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Opponents:

“No Patents on Seeds!”

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The opposition is filed against the patent as a whole. Revocation of the whole patent and, if necessary, a public hearing of the opposition is requested.

Some grounds for opposition, selected from the text of opposition as filed

a) The patent violates Article 53 (b) EPC because the patent claims plants and plant varieties are derived from essentially biological processes.

b) The patent is not inventive and therefore in contradiction to the requirements of Article 56 EPC.

c) The so-called invention is not disclosed sufficiently and cannot therefore be carried out without undue burden.

1. The content of the patent as claimed and its ‘inventiveness’

1.1. The content of the patent as claimed:
The patent claims a broad range of lettuce plant seeds, the plants, harvest and propagation material; the seeds are capable of germinating at elevated temperatures. Such seeds are supposedly important for future breeding under ongoing climate change. Therefore, the patent claims can impact important areas of food security. More specifically, the patent can block access to biological diversity needed by breeders to produce improved varieties. As stated in the patent:

> “[0008] Improving the capability of lettuce seeds to germinate at a high temperature may also enlarge the total acreage for lettuce cultivation. Areas of the world with relatively warm winters are unsuitable for lettuce cultivation, since the germination capabilities of current lettuce varieties are insufficient to overcome thermo-inhibition under such high temperatures.
> [0009] In a more global context, rising temperatures due to global warming may have a considerable impact on soil temperature. As such, high temperatures, and the resulting increase in soil temperatures, is considered a significant environmental stress that may limit worldwide crop productivity in the near future.”

According to the description in the patent, all lettuce seeds, lettuce plants, their offspring and suitable propagating materials with the described characteristics, regardless of whether the plants originated from conventional breeding (such as conventional mutagenesis) or genetic engineering (including genome editing), are claimed:

> “[0044] It is understood that a parent plant that provides the mutation of the invention is not necessarily a plant grown directly from the deposited seeds. The parent can also be a progeny plant from the seed, or a progeny plant from seeds that are identified to have (or to have acquired) the trait of the invention by other means.
> [0045] In one embodiment, the invention relates to lettuce plants that carry the trait of the invention and that have acquired the said trait by introduction of the genetic information that is responsible for the trait from a suitable source, either by conventional breeding, or genetic modification, in particular by cis-genesis or trans-genesis. Cis-genesis is genetic modification of plants with a natural gene, encoding an (agricultural) trait from the crop plant itself or from a sexually compatible donor plant.”
>
> “[0077] A method for the production of a Lactuca sativa L. plant having the mutation, which when homozygously present provides the seed in an unprimed state with the capability to germinate at a high temperature, may comprise using a method for genetic modification to introgress the said trait into the Lactuca sativa L. plant. Genetic modification comprises transgenic modification or transgenesis, using a gene from a non-crossable species or a synthetic gene, and cisgenic modification or cisgenesis, using a natural gene, coding for an (agricultural) trait, from the crop plant itself or from a sexually compatible donor plant.”

All offspring of following generations of all groups of lettuce with the described characteristics are claimed:

> “[0036] The lettuce plant into which the trait of the invention can be introduced can for example be, a lettuce plant from any one of the types of cultivated lettuce from the following group: iceberg or crisphead, butterhead, romaine or cos, green leaf, red leaf, lollo, oakleaf, curly, incised leaf, multileaf, cutting, stem, Batavia, and Latin lettuce.”

In claim 1, seed with the described characteristics is claimed, insofar as it is not derived from "essentially biological processes":

> “A seed lot of the species Lactuca sativa L. wherein the seeds belonging to the seed lot comprise a mutation, which when homozygously present, provides the seeds in an unprimed state with the capability to germinate at a high temperature (…) wherein said mutation is present in seeds of which a representative sample has been deposited (…) and wherein the seeds belonging to the seed lot are not exclusively obtained by an essentially biological process.”

The wording of claim 5 is similar:

> “A lettuce plant of the species Lactuca sativa L. carrying a mutation, which when homozygously present in a seed, provides the seed in an unprimed state with the capability to germinate at a high temperature, as defined in any one of the claims 1-3, and wherein the plant is not exclusively obtained by an essentially biological process.”

<u>1.2. The technical character of the ‘invention’</u>

In view of the broad scope of claims and their potential impact on future plant breeding as well as in regard to Articles 53 (b), 56 and 83, it is important to characterise the ‘inventiveness’ of the patent in more detail.

The examples cited in the patent show that the lettuce plants are derived from conventional, non-technical methods ("essentially biological" methods). For this purpose, thousands of lettuce seeds were exposed to non-specific stress factors (chemical substances) which are known to increase the natural, spontaneous rate of mutation (mutagenesis breeding). The resulting changes are not targeted and not due to a specific technical intervention:

> „[0095] Seeds of the wild type lettuce varieties Apache, Sensaï, Troubadour, and Yorvik (…) were treated with EMS (…) [0096] Approximately 1500 treated seeds per variety per EMS dose were germinated and the resulting plants were grown in a greenhouse in The Netherlands (...) to produce seeds. [0097] Following maturation, M2 seeds were harvested and bulked in one pool per variety per treatment. The resulting eight pools of M2 seeds were used as starting material to identify the individual M2 seeds containing high temperature germination alleles.“

The plants were selected on the basis of their phenotypic characteristics and produced by crossing and selection:

> „[0101] Any seeds that germinated at the given temperatures were grown into plants. These plants were self-fertilised to produce M3 seed. The M3 seeds were again germinated at 34°C under continuous dark conditions, to confirm the presence of high temperature germination alleles.“

In addition, the plants are characterised by describing genetic linkage groups. The gene location is described, but not a specific functional DNA sequence:

> „[0093] In deposits NCIMB 41915, NCIMB 41916, NCIMB 41917, NCIMB 41918, NCIMB 41919, NCIMB 41922, and NCIMB 41926, the mutation providing the seeds in an unprimed state with the capability to germinate at a high temperature, is located on linkage group 3, between markers HTG-1 (SEQ ID NO: 1) and HTG-2 (SEQ ID NO: 2). In NCIMB 41923 the mutation is located between markers HTG-3 (SEQ ID NO: 3) and HTG-4 (SEQ ID NO: 4).“

If the plants are crossed further with other varieties, again it is only the desired plants that are selected from the phenotype. The marker genes related to the linkage groups do not play any role within this process. Also the term homozygosity is only used to describe the desired phenotype:

> „[0110] A lettuce plant of the invention was crossed with a wild type (WT) lettuce plant of the incised leaf type, which does not carry the trait of the invention.
> [0112] (…) In approximately another quarter of the F3 seed lots, nearly 100% of the seeds tested germinated, which indicated that the mutation was present in the corresponding F2 mother plant in a homozygous state. In approximately half of the F3 seed lots, approximately 25% of the seeds tested germinated, indicating that the mutation was present in the corresponding F2 mother plant in a heterozygous state. The segregation of the F3 seed lots corresponds to a monogenic recessive inheritance of the trait of the invention. An F3 plant was then grown from an F3 seed lot which had the mutation homozygously present in the corresponding F2 mother plant. This F3 plant was used for further crossing to transfer the trait of the invention to other lettuce plants.“

<u>1.3. Summary: claims as granted and their scope in comparison to ‘inventiveness’</u>

The disclosed technical teachings of the patent are not in accordance with the granted claims: without the exact indication of the DNA sequence of the functional genes, genetic engineering methods cannot be used. Thus, with the information given in the patent, it is not possible to breed the described plants with methods other than conventional breeding ("essentially biological processes"). Without precise information about the DNA sequence, it is also not possible to verify the actual homozygosity of the plants, which is considered essential to establish the desired characteristics.

The only method disclosed in the patent is the breeding of plants starting from a broad range of genetic diversity (derived from random mutations) based on crossing and selection to grow suitable "homozygous" plants. Clearly, this process cannot be considered genetic engineering, which would allow targeted intervention in the genetic material. It is evident that, according to the categories established in patent law, the process as described has to be regarded as "essentially biological".

Therefore, the technical information provided in the patent is in contradiction to the substance of claims 1 and 5 (on which the other claims depend) in which seeds and plants are claimed that are not derived from "essentially biological processes". Such plants cannot be produced with the technical information as disclosed in the patent.

Consequently, the patent does not specify any technical features that would allow reliable achievement of specific results. The plants can only be derived from crossing and selecting, starting from a broad range of genetic diversity. The process is not based on any technical invention. This conclusion is also evident from the wording of the patent:

> „[0039] In the absence of molecular markers, or in the event that recombination has occurred between the molecular markers and the mutation and these are not predicative any longer, equivalence of mutations may still be determined by an allelism test. To perform an allelism test, material that is homozygous for the known mutation, a so-called tester plant, is crossed with material that is homozygous for the mutation to be tested. This latter plant is referred to as the donor plant. The donor plant to be tested should be or should be made homozygous for the mutation to be tested. The skilled person knows how to obtain or produce a plant that is homozygous for the mutation to be tested. Seeds of at least twenty F3 seed lots arising from the F2 of the cross between a donor plant and a tester plant are germinated in the dark and at temperatures of at least 31.8°C. When approximately 100% of the seeds tested from all aforementioned F3 seed lots germinate, then the phenotype related to the mutation is observed, and the mutation of the donor plant and the tester plant have been proven to be equivalent or the same.“

The influence of any supposed mutations on the described phenotype cannot be determined because no DNA sequence is provided with a pre-determined function. It is unclear how genetics and phenotypic traits are related to each other. However, it is already known from existing publications, that several gene sequences are associated with high temperature germination (Schwember & Bradford, 2010, Argyris et al., 2011, Argyris et al., 2008, Yoong et al., 2016). In fact, available literature shows that the germination of lettuce seed is a quantitative trait (Schwember & Bradford, 2010, Argyris et al., 2011, Argyris et al., 2008, Yoong et al., 2016). Therefore, it is to be assumed that a significant proportion of the described properties depends on the genetic background of the respective varieties. Similar features have also been found in the model plant Arabidopsis (Tamura et al., 2006) and naturally occurring "primitive" lettuce plants (Yoong et al., 2016).

Whether and to what extent further specific genetic conditions are responsible for the expression of the desired characteristic in the deposited samples cannot be determined. In the patent it just states that:

> „[0040] In the event that more than one gene is responsible for a certain trait, and an allelism

> test is done to determine equivalence, the skilled person doing the test has to make sure that all relevant genes are present homozygously in order for the test to work properly.“

In summary, no technical invention is disclosed in the patent that would enable reliable and predictable production of lettuce seeds with the desired characteristics. Whosoever wants to breed lettuce with the desired characteristics will only be offered a "representative sample". It has to be understood from the patent description that, even within this sample as deposited, only some, but not all seeds are supposed show the desired characteristics and gene combinations.

In consequence, the patent lacks any technical invention. Rather, the patent is based on a trivial, "essentially biological process" which is neither patentable as a process nor in terms of the results obtained. This fact is also relevant with regard to Articles 56 and 83 of the EPC.

The patent is a typical example of how certain companies try to circumvent existing prohibitions through specific loopholes, i.e., by referring to conventional, non-targeted methods of mutagenesis. But these methods are neither inventive, technical nor targeted. Rather, such methods, like all conventional "essentially biological" methods, rely on a wide array of genetic diversity or phenotypic traits, which are processed by crossing and selection.

Patents on the breeding of plants and animals that are based on crossing and selection, starting from a broad range of genetic diversity, are clearly a violation of the prohibition of Article 53 (b) and are ‘essentially non-technical’. In addition, such patents hinder, restrict or block the access to and use of biodiversity, which is necessary for future breeding, especially crucial in times of climate change.

2. Specific legal arguments in regard to Article 53 (b)

Conventional breeding has to be understood as non-technical traditional methods of producing plants and animals based on crossing and selection, without using technologies to bypass natural biological mechanisms governing gene regulation, reproduction and inheritance. Based on this understanding of conventional breeding as ‘essentially biological’, there are some fundamental differences in comparison to genetic engineering that are highly relevant for the interpretation of Article 53 b, EPC.

<u>2.1 Clear and comprehensive definition of ‘essentially biological processes for breeding’</u>

Essentially, conventional breeding is <u>always</u> based on a wide range of genetic and biological diversity found in natural populations, as well as in previously bred plant and animal varieties and breeds. In addition, new mutations happen continually and can, for example, be triggered in plants by exposure to sunlight. Not all of these mutations are beneficial. Crossing and selection are, therefore, crucial to breeding plants with desirable traits with optimal combinations of genetic information.

Other additional techniques can be used to increase genetic diversity e.g. by exposing the seeds to specific chemicals to increase the natural rate of mutation. This process is known as mutagenesis, which, in a first step, <u>enhances genetic diversity through known biological mechanisms</u>. The plant genome reacts to external stress factors and the desired traits are established in the following steps of crossing and selection.

This process of conventional mutagenesis has been used in plant breeding for many decades and is still widely applied. Experts estimate that there are already thousands of varieties grown based on random mutation. Until now, all these varieties could be used freely to produce the next generations of plants and varieties. However, patents can severely hamper or block access to these plants for other breeders. In many varieties, patents might well accumulate with every further step in crossing. This could seriously disadvantage small to medium size breeders, as well as damage overall innovation and diversity in plant breeding.

In order to differentiate this process from technical methods of genetic engineering, it is important to understand that, taken as a whole, the results of mutagenesis are not totally random. They are governed by various biological mechanisms of evolution, inheritance and gene regulation which, for example, can change some specific genome locations more frequently than others, and preserve specific traits in species over long periods of time. As a result, breeding through mutagenesis can generate greater genetic diversity, but the desired traits are not brought about by direct technical intervention. Plants and animals with the desired traits are the result of cross breeding and selection of particular plants or animals that are chosen from a whole range of biodiversity. This process is time-consuming and requires careful choice by breeders.

Genetic engineering on the other hand uses direct technical and targeted intervention to establish new traits. These technical interventions bypass natural biological mechanisms governed by evolution, inheritance and gene regulation, and are much faster than conventional breeding. For example, additional gene sequences can be directly inserted into the genome. Genetic engineering intervenes directly in the genome, and therefore the resulting plants and animals can be very different to those from conventional breeding. This is a fundamental difference between genetic engineering and ‘essentially biological processes’ for breeding.

In the context of the EPC, methods used in conventional mutagenesis can be clearly distinguished from technology used in genetic engineering: genetic engineering can be used to directly establish new traits in plants. Mutagenesis, on the other hand, is a first step in the selection and crossing process that simply increases genetic diversity. As is the case with all conventional breeding processes, crossing and selection play an essential and central part in the subsequent choice of the desired traits.

According to the decisions of the Enlarged Board of Appeal G2/07 and G1/08, the application of simple technical tools, does not turn an ‘essentially biological process’ into a technical, patentable invention:

> *“Such a process does not escape the exclusion of Article 53(b) EPC merely because it contains, as a further step or as part of any of the steps of crossing and selection, a step of a technical nature which serves to enable or assist the performance of the steps of sexually crossing the whole genomes of plants or of subsequently selecting plants.”*

Only a technical intervention which directly introduces a new trait would be eligible for patent protection:

> *“If, 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”.*

This reasoning is also in accordance with the current test guidelines for patents (part G, Chapter II, point 5.4):

> *"Thus transgenic plants and technically induced mutants are patentable, while the products*

of conventional breeding are not."

"Genetic engineering techniques applied to plants which techniques differ profoundly from conventional breeding techniques as they work primarily through the purposeful insertion and/or modification of one or more genes in a plant, are patentable."

Moreover, the EU Commission in its statement on corresponding articles in Directive 98/44/EC of the European Parliament and of the Council on the legal protection of biotechnological inventions of 6 November 2016 follows the same reasoning:

“The trigger point for ensuring the patentability of either a plant or an animal is the technical process, such as for instance the insertion of a gene into a genome. Essentially biological processes are not of a technical nature and therefore, according to the position taken by the legislator, they cannot be covered by a patent.”

Indeed, EU Directive 98/44/EC, in recitals 1, 2, 52 and 53, as well as in Article 16, explicitly refers to the term ‘genetic engineering’. In addition, recitals 9 and 10 refer to ‘biotechnology’. This wording – as well as the negotiating history of the Directive – clearly shows that patents should only be granted on modern biotechnology and genetic engineering processes and products, and should not be extended to conventional breeding by the backdoor.

2.2 Clarification of the legal details in regard to a systematic interpretation of the current EPC

According to the EU Commission statement, products derived from ‘essentially biological processes’ are not patentable:

“the Commission takes the view that the EU legislator’s intention when adopting Directive 98/44 /EC was to exclude from patentability products (plants/animals and plant/animal parts) that are obtained by means of essentially biological processes.”

This interpretation of current patent law in regard to the prohibition of patents on plants and animals derived from conventional breeding was also adopted by all the governments of the EU member states in a decision taken in February 2017.[1] Corresponding prohibitions are also part of national legislation in several of the contracting states of the EPO such as Germany, the Netherlands, France, Austria and Portugal. Finally, in June 2017, the Administrative Council of the EPO, made a decision on amending the Implementing Regulations of the EPC with the new Rule 28 (2).

Further, according to the text of the resolution from 2012, the EU Parliament

“Calls on the EPO also to exclude from patenting products derived from conventional breeding and all conventional breeding methods, including SMART breeding (precision breeding) and breeding material used for conventional breeding;(...)”.[2]

However, in December 2018, the Technical Board of Appeal of the EPO came to the conclusion that Rule 28 (2) is in conflict with the EPC and could therefore not be applied in subsequent decision making. In this decision, the Technical Board of Appeal overlooked the fact that even without the new Rule 28 (2), the prohibitions set out in Article 53 (b) are binding for plants and animals derived from ‘essentially biological processes’. There are several reasons for this, one of which is the legal logic of the patent system: if the patentability of processes alone is prohibited, but patents on plants and animals are allowed, then prohibitions on the patenting of processes would be ineffective. This point of view is expressed in another decision of the Technical Board of Appeal of the EPO. In its

1 www.consilium.europa.eu/en/meetings/compet/2017/02/20-21/
2 www.europarl.europa.eu/sides/getDoc.do?pubRef=-//EP//TEXT+TA+P7-TA-2012-0202+0+DOC+XML+V0//EN

decision T1242/06[3] from 31 of May 2012 it states:

> *"The board still has to address the further argument that, (…) it would be wrong to the claimed subject-matter to be patented, since this would render the exclusion of essentially biological processes for the production of plants completely ineffective, thereby frustrating the legislative purpose behind the process exclusion in Article 53(b) EPC. (Nr. 40)*
>
> *Disregarding the process exclusion in the examination of product claims altogether would have the general consequence that for many plant breeding inventions patent applicants and proprietors could easily overcome the process exclusion of Article 53(b) EPC by relying on product claims providing a broad protection which encompasses that which would have been provided by an excluded process claim (...). (Nr. 47)"*

Especially relevant in this context is the systematic legal interpretation of the prohibition of patents on 'essentially biological processes': Article 53 (b) EPC for the most part excludes 'essentially biological processes' for the production of plants and animals from patentability. However, an exception set out in the second sentence of Art 53 (b) EPC states that "microbiological processes or the products thereof" are patentable.

The EPC accepts thereby that a process for breeding plants or animals should be excluded from patentability. A patent covering a process provides the patent holder with protection for process. Furthermore, a patented process covers all products manufactured with the process. Conversely, a patent covering a product only affords the patent holder protection for the product. Therefore, a patent on a process with its inherent derivate product protection is definitively 'more' than a simple claim on a product.

From this it follows that if Article 53 (b) EPC excludes a process for the breeding of plants and animals from patentability, then this encompasses product protection for products manufactured with this process. To then grant a patent on a product which was derived from the process and which is excluded from patentability according Article 53 (b) EPC, undermines the intention of the legislator and provides protection for something that would have been already within the scope of the (excluded) patent on the process, which, according to Article 53 (b) EPC, cannot be granted.

The legislator was aware of this and framed the following legal provisions accordingly: the exception explicitly allows that, on the one hand, microbiological processes themselves, and, on the other hand, the products obtained with the help of these processes are patentable. If the legislator had been of the opinion that the products were invariably not encompassed by Art 53 (b), then it would not have been necessary to add the products in Sentence 2 of Art. 53 b. However, this precise exception shows that, according to the intention of the legislator, the (wider) process claim, as opposed to simply the product claim, encompasses the product that has been (excluded from patentability) manufactured using the process.

Therefore, a claim on plants and animals directed at a plant or animal derived from 'essentially biological processes', cannot be granted due to the already effective prohibition in Article 53 (b) EPC. This would in effect mean placing something under protection that was already contained in the prohibited process claim set out in Art. 53 b EPC - and if this product was clearly within the scope of the (excluded) process claim, it cannot be re-protected by a patent granted solely on the product.

It is widely known that the Enlarged Board of Appeal came to other conclusions in its decisions

3 www.epo.org/law-practice/case-law-appeals/pdf/t061242ex2.pdf

G2/12 and G3/12. However, there is a legal error in the systematic EPA interpretation of patent law: the EPA solely and separately dealt with the ‘systematic interpretation’ (G2/12 grounds for decision VII No. 2) of Sentence 1 in Article 53 (b) EPC thereby taking Article 53 (a) and 53 (c) EPC into account. However, the Enlarged Board ignored the direct context of Sentence 2 in Art 53 (b) EPC and does not answer the question of how this sentence is to be interpreted within the legal context as an exception to Sentence 1, Article 53 (b), EPC. It should also be noted that Article 53 (c) EPC was only adopted after Article 52 (4) EPC 1973 was adopted in Art. 53 in which exceptions were defined as ‘non-commercial’ and therefore only to a limited extent useful for systematic interpretation.

Thus, if Sentence 2 of Article 53 (b), EPC is taken into account for the interpretation of Sentence 1 in Article 53 (b), the decision G2/12 is not sustainable and cannot be applied in future decisions.

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