Photo: North Dakota State University

Intellectual property in plant breeding

Patented Outgrowths

After six months of standstill, the European Patent Office no longer patents the native traits of plants. The political struggle between traditional breeders and the agrochemical industry over our future crops will continue anyway. *Lab Times* author Florian Fisch tries to clarify the confusion.

Barely recognised by the public, Benoît Battistelli, the President of the European Patent Office (EPO) in Munich, made a remarkable announcement on 24th November 2016: Decisions on the patentability of plants resulting from selecting native traits will be suspended until a discord with the European Commission is solved. The dead end was reached after the European Commission published a notice explaining its view on the plant patent issue earlier that month. For seven months after the EPO's decision, nobody got European patents on plants validated, nor could competitors or NGOs attack the validity of the applications. On 29th June 2017, the Administrative Council of the EPO decided to scrap the native trait patents altogether.

The circumstances of this turmoil are of course very complicated – or, for anyone not accustomed to patent law, a matter of judicial hairsplitting. But at the core of the disagreement between the EPO and the European Commission lies a much more tangible and fundamental dispute between large agrochemical companies and small scale traditional breeders.

EPO's contradictory decisions

"Syngenta and consorts are trying to find marketable non-GM-plants whereas the traditional breeders would like to expel patent law from plant breeding altogether", says Herbert Zech, Professor of Life Sciences Law and Intellectual Property Law at the University of Basel, Switzerland. And poor EPO just got stuck in between the frontlines.

But the EPO is not just the victim: Between 2010 and 2015, the judges of its Enlarged Board of Appeal and in this function the guardians of the European Patent Convention issued two landmark decisions that were contradictory – at least in the eyes of non-specialists. The first decision restricted the patentability of marker-assisted breeding, SMART-breeding or precision breeding, and left the agrochemical industry in disarray.

The second, opening the route up again, shocked NGOs and small scale breeders. This spurred a lot of activity in European politics. Taken together, both decisions made the work of intellectual property law professors more interesting but left European patent litigation in paralysis.

European patents left in paralysis

"A patent is a contract between inventor and the public, where the inventor discloses the invention to the public domain in return for a limited monopoly". This explanation, offered by a law firm, is typical. Everything is supposed to be simple: the invented method has to be new (meaning unpublished), inventive (as judged by experts in the field) and marketable (meaning physically possible). This works rather well for a new molecule that kills pests, for example.

A traditional plant breeder, however, is not well served by these rules. His method of production is not technical, which means not repeatable. Crossing two plants a second time will yield a completely new set of individuals, compared to the first time. The breeder can describe perfectly well how to castrate flowers and fertilise them with another variety. But the result of the crossing is influenced by a lot of randomness during meiosis that the breeder cannot control. It is not possible to give instructions that any expert in the field can follow to produce the same plant.

Traditional breeding isn't repeatable…

This is why countries have established another protection system: plant variety protection. The conditions for getting this kind of intellectual property awarded are the presence of a variety that is distinct from others, uniform in its characteristics and stable over many generations. So

Photo: EPO

A remarkable announcement by Benoît Battistelli, President of the European Patent Office…

breeders need not know how the new variety was created, but they must have put the obtained variety to the test – a kind of product certification. This is usually performed by an organisation close to the Ministry of Agriculture, while "ordinary" patents are normally evaluated by an office around the Ministry of Economy.

… biotechnology changed this

These two separate systems, patent and plant variety protection, made perfect sense in an age where breeding and engineering were two worlds apart.

"The rise of biotechnology has opened breeding for patentabilty", says law professor Zech. By transferring a gene from one organism to another, bioengineers can repeatedly reproduce specific traits in any variety of their liking. For example, Monsanto and BASF can transfer the gene for the cold shock protein B from *Bacillus subtilis* in any maize variety with the same result for every successful transfer. As a result, the companies got their patent without challenge (EP2602325).

The boundary between the two systems seems to be clearly drawn in article 53b of the European Patent Convention,

European patents shall not be granted in respect of plant or animal varieties or essentially biological processes for the production of plants or animals.

The rapid progress in plant breeding technology blurs this separation more and more. Lawyers are beginning to quarrel about every part of the article. "This is exactly where the difficulty started because nobody ever defined if the exclusion of an essentially biological process also applies to the products of such processes", says Heli Pihlajamaa, Director of Patent Law at the EPO.

So the judges of the EPO's Enlarged Board of Appeal had to deliberate on the question. Unfortunately, their answer caused more confusion than clarification.

The right, "not to be patented"

The efficacy and side effects of the patent system in general are criticised far and wide. But when living organisms are touched, the resistance gets more principled. "No patents on seeds!", is the slogan and the name of a coalition of NGOs that is active on the European level. Members range from the militant Greenpeace to the more pragmatic Public Eye, from the development organisation Swissaid to groups opposing genetic technologies like Genewatch UK. The strongest opponents stem from the organic farming movement and Mother Nature activists. They fight what they see as the objectification of plants. The "Rheinauer Theses on the Rights of Plants", for example, an obscure document written by Swiss activists drawn from academia and farming, is surprisingly influential. According to this document, plants have, " the right not to be patented".

Plants are not inventions. No plant owes its existence to human intervention alone. Patents on plants should therefore be rejected not only for socio-economic reasons, but also for the plant's own sake.

This mindset can be found in the Swiss constitution, requiring that the Confederation, "shall take account of the dignity of living beings." This article even caught the attention of the Ig Nobel Committee that awarded its Peace Prize to the Federal Ethics Committee on Non-Human Biotechnology and all citizens of Switzerland for, "adopting the legal principle that plants have dignity."

In Europe, it's different

The "No patents on seeds!" coalition claims that farmers are "hunted" for patent infringements by agrochemical companies. Activists often refer to the case of Percy Schmeiser, a Canadian farmer who was sued by Monsanto for having evaded licence fee payments. The activists usually do not mention that Schmeiser admitted having actively selected genetically-modified herbicide-resistant rapeseed on his field and that the situation in Europe is different, as it is not the farmers but the breeders who have to pay the fees.

The more pragmatic resistance comes from the many small scale breeders. They are more or less unified in Europe in the view that patents hinder innovation. Patented traits are excluded from the breeders privilege, a sort of an open source innovation system. So while protected plant varieties are freely available for further breeding, patented traits belong the title holder irrespective of the plant variety they happen to be crossed into.

François Meienberg, former campaigner for Public Eye, one of the leading organisations behind "No Patents on Seeds!" finds the burden too heavy for them to bear:, "Small and medium sized breeding companies cannot afford a law department to challenge patent claims and defend themselves in court. A system that demands that much effort is simply not suitable to increase innovation in a system that worked fine until today."

Companies suing each other

Interestingly, the patents causing the staying of proceedings at the EPO were not contested by NGOs but by competitor companies. The plant breeding giants Syngenta from Switzerland and Limagrain from France opposed what was famously known as the broccoli patent and the Anglo-Dutch food producer Unilever litigated against the infamous tomato patent.

The broccoli patent, or more precisely the, "Method for selective increase of the anticarcinogenic glucosinolates in brassica species" (EP1069819) was invented by plant geneticist Richard Mithen, then at the John Innes Centre in Norwich, UK, ▶▶

Timeline: 1973 to 2017

European Plant Patents

1973
European Patent Convention is signed by 16 countries.

1998
European Council adopts the Biopatent Directive in order to harmonise European rules.

2000
European Patent Convention is revised.

9th December 2010
Enlarged Board of Appeal of the EPO rules against the patentability of conventional breeding even when marker-assisted (decisons G 1/08 Tomato I and G2/07 Broccoli I).

25th March 2015
Enlarged Board of Appeal of the EPO rules in favour of the patentability of plants even when resulting from conventional breeding (G2/12 Tomato II and G2/13 Broccoli II).

8th November 2016
European Commission issues a notice on the interpretation of the Biopatent Directive against the patentability of plants, resulting form marker-assisted breeding.

24th November 2016
EPO stays all proceedings on native trait patents.

29th June 2017
The Administrative Council of the EPO amends rules as to exclude the patentability of native trait patents.

Crazy tomato (possibly genetically engineered)

and his PhD student Kathy Faulkner. They sold their patent to the technology management company Plant Bioscience in Norwich who, together with Monsanto, has marketed the broccoli variety Beneforté in the USA and the UK since 2010. Whether or not Beneforté really does protect against cancer is not a condition for getting a patent.

According to law professor Zech, Syngenta and Limagrain opposed this patent in 2003 to obtain clarity on whether this type of patent is valid or not.

18 claims against the wrinkled tomato

In a similar case in 2008, Unilever contested the tomato patent named "Method for breeding tomatoes having reduced water content and product of the method" (EP1211926) that is held by the Israel Ministry of Agriculture. It was invented by research scientist Arthur Schaffner at the Ministry's own Agricultural Research Organisation. It is also known as wrinkled tomato patent and describes a plant that produces dried or predried fruit directly on the stem.

The broccoli patent consists of 18 claims. Typical for patents, many of them sound identical but describe a minute addition to the previous claims. In summary they specify how to cross and select a wild species and a breeding line of *Brassica oleracea* with the aim of gleaning high levels of two known groups of anticarcinogens: 4-methylsulfinylbutyl glucosinolates and 3-methylsulfinylpropyl glucosinolates. These are known to induce phase II drug metabolising enzymes in human cells and thereby counteract chemical carcinogens (claims 1 to 3). Certain RFLP markers and DNA-probes are used to quickly select the right lines (claims 4, 5, 6 and 12).

The rest of the 18 claims say that the patent really covers both molecular families and that it not only includes the broccoli plant, but also its seeds, its inflorescence and its cells, having 10 to 100 micromoles of dry weight of the required molecules in them.

The broccoli patent is a typical case for marker-assisted breeding, which is something that any modern breeder, even organic breeders, do routinely nowadays. The plant might have been invented by traditional breeders and obtained plant variety protection, yet neither the inventors from academia nor the patent holder companies are really breeders.

The tomato patent is even less technical: A *Lycopersicum esculentum* plant is crossed with another *Lycopersicum* species and selected so that the tomato fruits start dehydrating after ripening. There is no genetics involved. Just crossing, collecting, growing, pollinating, collecting, growing, analysing by judging the wrinkling of the fruits... The total number of claims: 16.

Broccoli and tomatoes in court

On 9th December 2010, the EPO's Enlarged Board of Appeal decided on both patent disputes at once as the questions were the same. The verdicts were later baptised as "Broccoli I" (G 2/07) and "Tomato I" (G 1/08). To reach their verdicts, the judges had to decide whether the claims of the patents were based on "essentially biological processes", according to the famous article 53b of the European Patent Convention.

The Enlarged Board decided that the patents could not be granted as,

[...] a process for the production of plants which is based on sexual crossing of whole genomes and the subsequent selection of plants [...] remains excluded from patentability [...].

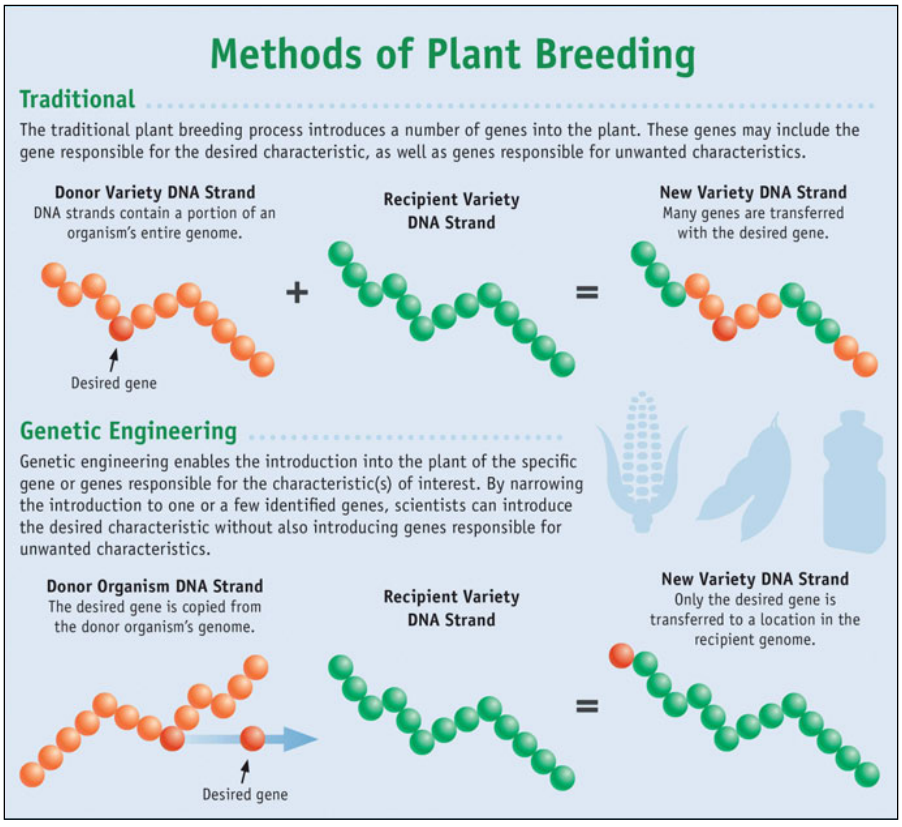
They denied patentability even though the crossing and selecting of traditional breeding are arguably technical steps. The use of genetic markers even more so. The judges even noted that,

"leaving tomatoes on the vine past ripening and determining by looking at them which ones are sufficiently wrinkled for the purpose of enabling or assisting selection of the suitable plants is a technical step [...]".

Just as,

"[...] leaving [chemical] substances in a vessel for a certain time in order that a desired reaction takes place is a technical measure [...]".

But all the technology in the world does not alter the fact that the actual creation of new plants still happens through pure sexual reproduction.



FDA graphic by Michael J. Ermarth

Variety protection vs. patent

Two Systems Struggle for Authority

Plant variety protection

▶ *Protection of:* Reproductive material

▶ *Condition:* Distinctiveness, uniformity, stability

▶ *Responsible institution:* Usually close to the Ministry of Agriculture

▶ *Relevant treaty:* European Patent Convention, guarded by the European Patent Organisation (EPO)

▶ *Special provisions:* Breeders exemption requests no licence fees for continued innovation, except for essentially derived varieties with only minor modifications. Farmers' privilege allows farmers in some countries for some types of plants to freely or cheaply reuse seed from their own production.

▶ *Repository:* There are national registers for all tradable varieties.

Patent

▶ *Protection of:* Inventions susceptible to industrial application

▶ *Condition:* Novelty (not published), inventive step (in the eye of experts in the field), industrial application

▶ *Responsible institution:* Usually at the Ministry of Economy

▶ *Relevant organisation:* Convention of the International Union for the Protection of New Varieties of Plants (UPOV)

▶ *Special provisions:* Breeders must check for themselves whether they are infringing a patent. But judges may force patent holders to hand out compulsory licenses at set fees.

▶ *Repository:* All international patents are freely available and searchable at virtually all patent offices including the EPO.

So for the EPO, the process of traditional breeding, however technically-assisted, cannot be protected by patents. And neither can processes be protected by plant variety protection. This route is open only to the plant varieties themselves. In consequence, modern breeding processes will have no protection. Only when the plant production itself is technical is the practice patentable.

No protection for modern breeding

"The verdict of the EPO was surprising. The agrochemical companies feared what would happen to classic GM plant patents", says Herbert Zech from the University of Basel. On a continent deeply opposed to genetic engineering, this was bad news for those technology firms. For the small and medium sized breeders and NGOs this was a victory – albeit not fought for by themselves.

The losing companies did not rest. They reformulated their claims and appealed the case. On 25th March 2015, the Enlarged Board of Aappeal issued another pair of decisions known as "Broccoli II" (G 2/13) and "Tomato II" (G 2/12). In contrast to the first double decision five years earlier and to the horror of small breeders, NGOs and many European politicians, the judges ruled that the two patents are now valid.

What happened? The judges took a purely legal stance and avoided straying into economic or social terrain. Plant varieties and essentially biological processes are excluded from patentability, according to article 53b of the convention. But fruits, seeds, leaves, stems, roots and for that matter whole plants are not varieties but products. And even if the plants are produced by crossing and selecting, clearly an essentially biological process as judged just a year before, the products themselves are still patentable.

A fascinating u-turn

So, no company can protect the breeding process or the variety, but it can certainly describe a tomato that wrinkles on the vine or a broccoli that contains high content of anticancer glucosinolates. In the words of the judges,

"Broadening the scope of the process exclusion to the extent that it included also the products obtained by essentially biological processes for the production of plants would introduce an inconsistency in the system of the European Patent Convention, as plants and plant material other than plant varieties are generally eligible for patent protection."

"This was a huge decision", says Zech, "The breeding process cannot be patented but results of the process can." In- ▶▶

Photo: Seminis

A wild broccoli variety with the ability to produce high levels of a certain phytonutrient, glucoraphanin, was cross-pollinated with commercial broccoli, resulting in a new variety of an allegedly healthier "Super Broccoli" (photo) which contains higher levels of glucoraphanin, too.

stead of "huge" one could also say "absurd", "surreal" or "detached". So after this second ruling, the business model of agrochemical companies was saved.

The legislator disagrees

The Netherlands and Germany were not happy about the decision. Citizens of both countries are very sceptical about genetically-modified plants and both countries have strong breeding industries that rely on traditional methods. The Netherlands and Germany also amended their national laws to specifically exclude product patents based on crossing and selecting – although without any real implication, as patentability is defined by the same multilateral agreement as the European Patent Convention.

Thus, when The Netherlands held the Presidency of the Council of the European Union (where all the heads of state and ministers are united) in the first half of 2016, they pushed the topic and made the European Commission (where all the EU bureaucrats are) check its biotech directive. Although the EPO is not part of the EU, it has integrated the EU biotech directive as an aid to interpreting the European Patent Convention. Both the rulings of the Enlarged Court of Appeal of the EPO made explicit reference to the directive.

The problem with this directive is that it was issued in 1998, when genetically modified plants were just appearing in the real world of agriculture. So it is very hard to find out today what the politicians and bureaucrats really wanted to say at the time.

The judges of the EPO were arguing that the biotech directive, "does not support a broad reading of the exclusion under article 53b", meaning that it was not destined to refuse the plant product patents but really only patents on the process of breeding. Whatever this distinction might mean in the real world.

Were the EPO judges wrong?

The European Comission issued a notice on 8th November 2016, seven months later, where it argued that the judges were wrong,

"The Commission takes the view that the EU legislator's intention when adopting [the biotech directive] was to exclude from patentability products (plants/animals and plant/animal parts) that are obtained by means of essentially biological processes."

This notice does not have direct legal implication, as it is up to the EPO and its Enlarged Board of Appeal to interpret the rules, even if they come from other sources.

Nevertheless, the president of the EPO took the decision to halt all processes on native trait patents until the member states of the organisation take a decision on how to move on. Or as the Director of Patent Law, Heli Pihlajamaa, says, "We always stay if there is a question about the correct interpretation of regulations concerning the European Patent Law – this is good administrative practice." As of 29th June 2017, the Administrative Council of the EPO accepted the view of the European Commission and amended the rules so as to explicitly exclude simple plants with fruits, seeds, leaves, stems and roots. So it reads article 53b as any other person would do.

Swiss law professor and IP expert, Herbert Zech, thinks that, "the rapid advance of technology puts economic strain on smaller breeders".

Photo: TU Berlin/ Philipp Arnoldt

Huge legal diversity

As if the two intellectual property systems for plants weren't complex enough, there is the additional level of international agreements. Neither the EU nor the EPO have a unified patent system. The EPO merely decides whether patents are granted, the courts of the member states decide whether they are upheld. Sometimes patents are valid in some countries but not in others. It is even common practice that companies try to "destroy" granted patents in order to be "free to operate" as patent specialists use to say.

On a global level, even the differences between the USA and Europe are huge. In the USA, for example, plant varieties can be patented. And there are various international agreements and organisations. The UN World Intellectual Property Organization (WIPO) and the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) fight for authority. The WIPO, having a special focus on sharing access and benefit, and TRIPS, being part of the big overarching free trade agreement. And it does not stop there. There is another organisation independent of the UN regulating plant variety protection: The International Union for the Protection of New Varieties of Plants (UPOV).

Plant property rights: a battleground

Despite everyone's assurance that it's all about fostering innovation, plant property right has become a political battleground. And it's not just the small, traditional breeders, who focus on whole varieties, against the technological agrochemical giants that want to protect single traits. It is also those who embrace new technologies, against the ones, who fear their negative effects. For example, Amadeus Zschunke, director of the Swiss biodynamic (organic as well as an-

Some statistics...

EPO Patents in Numbers

- ▶ **38** member states of the EPO in 2016.
- ▶ **160,000** patents were applied for at the EPO in 2016.
- ▶ **60%** of the applied patents (96,000) were granted by the EPO in 2016.
- ▶ **4%** of applied patents (5700) were in the field of biotechnology. Equally as many were on pharmaceuticals. Most granted patents belong to medical technology (12,000).
- ▶ **300** patent applications (0.2%) per year concern GM-plants.
- ▶ **70** patent applications (0.05%) per year describe non-GM-plants.

Sources:
www.epo.org/news-issues/issues/biotechnology-patents.html;
http://documents.epo.org/projects/babylon/eponet.nsf/0/5D3BD1BD120859A9C12580D4005AD126/$File/Applications_by_field_of_technology_2007-2016_en.xlsx;
http://documents.epo.org/projects/babylon/eponet.nsf/0/5D3BD1BD120859A9C12580D4005AD126/$File/Granted_patents_by_technology_field_2007-2016_en.xlsx

Genetic changes in barley genomes aim at reducing unpalatable flavours in beer.

throposophical) breeding company Sativa Rheinau, says, "Without the European system, genetically-modified maize, rapeseed and sugar beets would have been cultivated in Europe long time ago – irrespective of the wishes of the consumers."

The way out of the trenches is far from clear. In most European countries there are ways to get compulsory licences. The difficulty for plant breeders is to find out, whether there is a patented trait in a certain plant. The PINTO database of the European Seed Association, although not exhaustive, can help in this direction. The burden of checking everything out lies with the current innovator. The past innovator has no duty to cooperate with his fellow plant breeders.

Amadeus Zschunke from the Swiss biodynamic breeding company, Sativa Rheinau: "Without the European system, genetically-modified plants would have been cultivated in Europe long time ago – irrespective of the wishes of the consumers."

Even the agrochemical companies acknowledge that the patent system has to become more open. Michael Kock, head of intellectual property at Syngenta, says, "The intellectual property system is outdated. We need to get away from exclusivity and move towards access and benefit sharing." He advertises an international licensing platform (*www.ilp-vegetable.org*), where participants agree to make their patents available for a fair price set by an independent expert committee. But the system is based on a private initiative, which can be revoked at any time. Monsanto, for example, does not take part. So something along the lines of compulsory licensing would be necessary for a satisfying solution.

Despite throwing SMART-breeding out of patents, the dispute over the patentability of plants will not be over soon. The changes were made to the rules of the EPO, not the patent convention itself. Still, in the absence of another absurd verdict, genome editing with CRISPR/Cas9 remains patentable. As well as mutation breeding, induced by chemicals or radiation.

The next bone of contention

For example, the two patents of Carlsberg and Heineken protect barley genomes, chemically mutagenised with sodium azide (NaN_3). In both cases, the genetic changes aim at reducing unpalatable flavours in beer. For example, one of two lipoxygenase genes (LOX-1 and LOX-2) is responsible for the production of the precursors of trans-2-nonenal, a compound that makes beer smell old. The knock down is achieved by introducing premature stop codons (EP2384110, "Barley with reduced lipoxygenase activity and beverage prepared therefrom").

The other knocks down the methionine S-methyltransferase (MMT) by inactivating a splicing site to produce a truncated version of the enzyme. Thus, it produces less of a precursor that breaks down to dimethyl sulfide, known to smell like cabbage. Breweries try to get rid of this compound by cooking the wort for a long time. So the patented barley could also reduce the energy consumption of brewing (P2373154 "Barley and malt-derived beverages with low dimethyl sulfide level").

Such changes introduced into plant genomes by mutagenesis are clearly technical and can be described by referring to the respective gene sequences. So this is considered to be more like classical genetic engineering, but probably more acceptable to the public, as these changes could clearly arise through natural processes as well. This is why Michael Kock remains sceptical that the patent dispute is now over, "The definition of patentability will remain difficult and unclear", says Kock. "So we need solutions, which support an open use of patents."

Photo: Syngenta

Syngenta's Michael Kock thinks that, "the intellectual property system is outdated".

Open use of patents is needed

Technological advances will continue to put the system under increasing pressure. Breeders will have to find a way to keep pace. Law professor Herbert Zech sees this as the origin of all the trouble. So his analysis differs from that of most NGOs, "I don't think that the concentration of plant breeding at agrochemical companies is caused by patents. It is rather the rapid advance of technology that puts economic strain on smaller breeders." Florian Fisch

Novel and inventive but...

Not Patentable!

If you have a new (unpublished), inventive (in the eye of experts) and applicable idea, you can publicly disclose how it works in exchange for a 20 to 25 year monopoly guaranteed by the state. Except if the invention is …

- ▶ a discovery, a scientific theory or a mathematical method
- ▶ an aesthetic creation
- ▶ a rule for performing a mental act, playing games or doing business
- ▶ a computer programme
- ▶ a presentation
- ▶ contrary to "ordre public" or morality
- ▶ a surgical or therapeutic procedure on the human or animal body
- ▶ a diagnostic method in human or veterinary medicine
- ▶ a plant or animal variety
- ▶ an essentially biological process for the production of plants or animals

Sources: European Patent Convention Articles 52 and 53 (www.epo.org/law-practice/legal-texts/html/epc/2016/e/ar52.html; www.epo.org/law-practice/legal-texts/html/epc/2016/e/ar53.html)