CHAPTER 6

NOVELTY

An invention is eligible for a patent only if it is novel in the light of the prior art. Novelty is determined based on certain circumstances that would negate the novelty of the invention. Circumstances like knowledge; use, publication, patent, sale, suppression and concealment have the potential of destroying novelty of an invention. Novelty of an invention is decided based on a single prior art reference. This requirement plays a very important role in ensuring that only worthy inventions that push the limits of science and technology enter into the patent domain.

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Section 102 of Title 35 provides the list of non-exhaustive circumstances that negate the novelty of an invention[254].[255] The novelty requirement overlaps with the subject matter requirement in USA. As most biotech inventions are related to naturally existing products, determination of their novelty overlaps with the products of nature exclusion under the subject matter requirement[256]. While subject matter checks whether the product in question has a hand of man that would make it naturally existing, the novelty requirement goes a step ahead and checks if the non naturally existing product is new and different from the existing products.

Section 102(g) - Prior Conception

Anticipation under section 102 based on prior conception is one of the circumstances under novelty that as been subject of litigation when it comes to gene related inventions. Section 102(g) states that a person shall be entitled to a patent unless "before the applicant's invention thereof the invention was made in this country by another who had not abandoned, suppressed, or

[254] 35 USC Sec. 102.
[255] For more details see Chapter 1.
[256] Courtney J. Miller, Patent Law and Human Genomics, 26 CAP. U. L. REV. 893, 911 (1997).

concealed it[257]. It relates to prior inventorship by another in USA and retains the rules governing the determination of priority of invention[258]. The section further provides that In determining priority of an invention there shall be considered not only the respective dates of conception and reduction to practice of the invention, but also the reasonable diligence of one who was first to conceive and last to reduce to practice, from a time prior to conception by the other[259]. As per the section the inventor who conceives of the invention first and is diligent in reducing it to practice gets priority for patentability.

Conception is defined as the formation in the mind of the inventor, of a definite and permanent idea of the complete and operative invention, as it is to be applied in practice[260]. Actual reduction of a conceived invention to practice requires the claimed invention to work for its intended purpose[261]. There is said to be a constructive reduction to practice when a patent application on the claimed invention is filed at the patent office[262]. Courts have laid down different standards for determining conception, diligence and reduction to practice of gene related inventions.

Hybritech v. Monoclonal [263].

The case relates to a patent owned by Hybritech concerning immunometric assays using monoclonal antibodies. Hybritech sued Monoclonal on March 2, 1984, for damages and an injunction alleging that the manufacture and sale of Monoclonal's diagnostic kits infringed its patent and Monoclonal counter claimed that the patent is invalid due to anticipation by prior conception of the

[257] 35 USC Sec. 102(g).
[258] Kimberly-Clark Corp. v. Johnson & Johnson, 745 F.2d 1437, 1444, 223 USPQ 603, 606 (Fed.Cir.1984) (quoting P.J. Federico, Commentary on the New Patent Act, 35 USCA page 1, at 19 (1954)).
[259] 35 USC Sec. 102(g).
[260] Coleman v. Dines, 754 F.2d 353, 359, 224 USPQ 857, 862 (Fed.Cir.1985).
[261] Great Northern Corp. v. Davis Core & Pad Co., 782 F.2d 159, 165, 228 USPQ 356, 358, (Fed.Cir.1986).
[262] Weil v. Fritz, 572 F.2d 856, 865 n. 16, 196 USPQ 600, 608 n. 16 (CCPA 1978).
[263] Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367 (C.A.Fed. (Cal.),1986).

invention by another person[264]. The district court held that the claimed subject matter of the patent was neither conceived nor actually reduced to practice before May 1980, and was anticipated under § 102(g) by the actual reduction to practice of the invention by doctors Uotila and Ruoslahti at the La Jolla Cancer Research Foundation (LJCRF) as early as November of 1979 and by the actual reduction to practice of the invention by Drs. Oi and Herzenberg (Oi/Herzenberg work) at the Stanford University Laboratory as early as July 1978, later published in December of 1979[265]. Based on the evidence, the Federal Circuit held that Hybritech's inventors conceived the invention before any one else and that the patent is not invalid because of prior conception[266].

The court started its analysis by citing Hybritech's scientist, Dr. David's January 1979 notebook describing in detail, a nylon apparatus that undoubtedly could be used for performing a sandwich assay using monoclonal antibodies and also describing the procedure for detecting an antibody "(a-x)" to an antigen "(x)" complete with diagrams and text, which were illuminated by Dr. David at trial[267]. The notebook was signed by Dr. David on January 4, 1979, and witnessed and signed on January 30 of the same year by Dr. Curry, the first cell biologist hired at Hybritech to set up the hybridoma production program[268]. The court stated that Dr. David testified about the success of the experiment involving a monoclonal sandwich assay with the hepatitis antigen and that was corroborated by the notebooks[269]. Finally, the court pointed out that the record shows that the claimed affinity limitation "of at least about 10 8 liters/mole" was determined and appreciated during the course of the development of the claimed subject matter.

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[264] Id.
[265] Id. at 1369.
[266] Id.
[267] Id. at 1370.
[268] Id.
[269] Id. at 1371.

Based on the information in notebooks, the court stated that the laboratory notebooks, alone, are enough to show that the invention was conceived before May 1980[270]. It further stated that the fact that some of the notebooks were not witnessed until a few months to one year after their writing does not make them incredible or necessarily of little corroborative value[271]. Moreover, it went on to say that labnote books combined with testimonies indicate conception, of the formation in the minds of the inventors of a definite and permanent idea of the complete and operative invention as it was thereafter applied in practice[272].

The court then considered both prior art references. It stated that LJCRF is not prior art because Hybritech conceived before it and was diligent in reducing the invention to practice from January 1979 to the patent application filing date of August 4, 1980[273]. Further, the court went on to state that the Work of Oi/Herzenberg is Not the Claimed Invention because their work does not anticipate every element in the invention and is therefore not prior art[274]. In the light of its analysis, the court concluded that Hybritech's immunometrix assays were not anticipated by prior art based on prior conception.

Hybritech v. Monoclonal, illustrates the value of lab notebooks in proving prior conception and diligence in reducing the invention to practice. It further points out that the prior art, which seeks to negate novelty of an invention should contain all elements and limitations of the invention.

[270] Id.
[271] Id.
[272] Id.
[273] Id. at 1372.
[274] Id.

Amgen v. Chugai[275].

This case is considered to be the most important case relating to novelty of genes and related inventions as it has laid down clear guidelines for determining priority in conception of gene based inventions. Amgen, owner of patent for DNA sequences encoding Erythropoietin (EPO) brought suit against Genetics Institute and Chugai Pharmaceuticals collectively called 'Chugai', owner of patent for method for purification of EPO and EPO compositions, claiming patent infringement, and seeking declaration that Chugai's patent was invalid or, in the alternative, that Amgen did not infringe claims of the patent, and declaration that Chugai's future activities in the production and sale of EPO would infringe Amgen's patent[276]. Chugai counterclaimed, alleging patent infringement and seeking declaratory judgment that Amgen's patent was invalid and not infringed[277]. One of the patent invalidity contention raised by Chugai was that Amgen's patent is invalid because of prior conception of the invention by Dr. Frisch of Genetics Institute.

The court stated that in some instances, an inventor cannot establish a conception until he has reduced the invention to practice through a successful experiment and that is the situation in this case[278]. The court reasoned that the though Fritsch had a complete mental conception of a purified and isolated DNA sequence encoding EPO and a method for its preparation, in which the precise identity of the sequence is envisioned, or in terms of other characteristics sufficient to distinguish it from other genes, all he had was an objective to make an invention which he could not then adequately describe or define[279]. As the structure of the DNA sequence encoding human EPO was unknown until 1983, when the gene was cloned by Lin of Amgen and as Frisch

[275] Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd., 927 F.2d 1200 (C.A.Fed. (Mass.),1991).
[276] Id. at 1204.
[277] Id.
[278] Id. at 1203.
[279] Id.

was unaware of it until 1984, the court stated that Frisch has not conceived it before Lyn.

The court went on to state that a gene is a chemical compound, albeit a complex one, and it is well established in US law that conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials, and to describe how to obtain it[280]. As per the court, conception does not occur unless one has a mental picture of the structure of the chemical, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it[281]. The court pointed out that it is not sufficient to define it solely by its principal biological property, e.g., encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property would not amount to conception[282]. The court held that when an inventor is unable to envision the detailed constitution of a gene so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, i.e., until after the gene has been isolated[283].

Based on the aforementioned concept, the court stated that though Fritsch had a goal of obtaining the isolated EPO gene, whatever its identity, and even had an idea of a possible method of obtaining it, he did not conceive a purified and isolated DNA sequence encoding EPO and a viable method for obtaining it until after Lin and therefore, did not conceive it before Lyn[284]. The court further said that conception of a generalized approach for screening a DNA library that might be used to identify and clone the EPO gene of then unknown constitution is not conception of a "purified and isolated DNA sequence" encoding human

[280] Id. at 1206.
[281] Id.
[282] Id. at 1207.
[283] Id.
[284] id. at 1206.

EPO[285]. It is not "a definite and permanent idea of the complete and operative invention." It further stated that Fritsch's conception of a process had to be sufficiently specific that one skilled in the relevant art would succeed in cloning the EPO gene and he clearly did not have that conception because he did not know the structure of EPO or the EPO gene[286].

The court analyzed that given the utter lack of experience in probing genomic libraries with fully degenerate probes and the crudeness of the techniques available in 1981; it would have been mere speculation or at most a probable deduction from facts then known by Dr. Fritsch that his generalized approach would result in cloning the EPO gene[287]. As expert testimony from both sides indicated, the court pointed out that success in cloning the EPO gene was not assured until the gene was in fact isolated and its sequence known. Based on the uncertainties of the method and lack of information concerning the amino acid sequence of the EPO protein, the court concluded that neither party had an adequate conception of the DNA sequence until reduction to practice had been achieved. As Lyn was first to achieve that goal, the court concluded that Amgen has priority over Chugai[288].

This case dealt with different issues relating to priority of inventorship in detail. It pointed out that in cases relating to gene sequences and related inventions, conception of an invention would not be considered to be complete until it is reduced to practice as the field is filled with uncertainty. As per the court conception of a method of sequencing the gene would not be enough to satisfy conception of the gene sequence. Conception is said to be complete only if the gene can be described by its physical properties or structure. In order to amount to conception, the idea should be workable by a person with ordinary skill in the art. The basic principles laid down in this case have

[285] Id. at 1207.
[286] Id.
[287] Id.
[288] Id.

changed the way in which courts look at priority of genes and related inventions.

Fiers v. Revel[289].

This interference among three foreign inventive entities relates to the DNA, which codes for human fibroblast beta-interferon, a protein that promotes viral resistance in human tissue[290]. Sugano's Japanese application disclosed the complete nucleotide sequence of a DNA coding for <<beta>>-IF and a method for isolating that DNA[291]. Revel's Israeli application disclosed a method for isolating a fragment of the DNA coding for <<beta>>-IF as well as a method for isolating messenger RNA (mRNA) coding for <<beta>>-IF, but did not disclose a complete DNA sequence coding for <<beta>>-IF[292]. Fiers, who was working abroad, based his case for priority on an alleged conception either in September 1979 or in January 1980, when his ideas were brought into the United States, coupled with diligence toward a constructive reduction to practice on April 3, 1980, when he filed a British application disclosing the complete nucleotide sequence of a DNA coding for <<beta>>-IF[293]. According to Fiers, his conception of the DNA occurred when two American scientists, Walter Gilbert and Phillip Sharp, to whom he revealed outside of the United States a proposed method for isolating DNA coding for <<beta>>-IF brought the protocol back to the United States[294]. On February 26, 1980, Fiers' patent attorney brought into the United States a draft patent application disclosing Fiers' method, but not the nucleotide sequence for the DNA[295].

[289] Fiers v. Revel, 984 F.2d 1164 (C.A.Fed.,1993).
[290] Id.
[291] Id. at 1166.
[292] Id. at 1167.
[293] Id.
[294] Id.
[295] Id.

In an interference decision, the Board held that Fiers failed to establish conception in the United States prior to his April 3, 1980 British filing date[296]. Specifically, the Board determined that Fiers' disclosure of a method for isolating the DNA along with expert testimony that his method would have enabled one of ordinary skill in the art to produce that DNA, did not establish conception, since "success was not assured or certain until the <<beta>>-IF gene was in fact isolated and its sequence known[297]." Accordingly, the Board held that Fiers was entitled only to the benefit of his April 3, 1980 British application date because only that application disclosed the complete nucleotide sequence of the DNA coding for <<beta>>-IF. That date was subsequent to Sugano's March 1980 Japanese priority date[298]. Fiers challenged the decision of the Board before the Appellate Court. The Court referred to Amgen and stated that conception does not occur unless one has a mental picture of the structure of the chemical, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it[299]. It further stated that it is not sufficient to define it solely by its principal biological property because an idea having no more specificity than its biological property would not be a conception[300]. The court further stated that when an inventor is unable to envision the detailed chemical structure of the gene so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, i.e., until after the gene has been isolated[301].

Based on the aforementioned analysis, the court determined that, irrespective of the complexity or simplicity of the method of isolation employed, conception of a DNA, like conception of any chemical substance, requires a

[296] Id. at 1168.
[297] Id.
[298] Id.
[299] Id. at 1168.
[300] Id. at 1369.
[301] Id.

definition of that substance other than by its functional utility. The court stated that the existence of a workable method for preparing a DNA establishes conception of that material[302]. Referring to its statement in Amgen that conception may occur, inter alia, when one is able to define a chemical by its method of preparation requires that the DNA be claimed by its method of preparation, the court recognized that, in addition to being claimable by structure or physical properties, a chemical material can be claimed by means of a process. Following that reasoning, the court stated that conception of a substance claimed per se without reference to a process requires conception of its structure, name, formula, or definitive chemical or physical properties[303].

The court reasoned that though the present invention has a particular biological activity or function, it has to be defined by something more than that in order to establish conception. It further stated that if inventors are allowed to get patents based on function or activity, inventors would file patent applications before they had made their inventions and before they could describe them, which is not consistent with the statute or the policy behind the statute, which is to promote disclosure of inventions, not of research plans[304]. The court went on to state that one does not need to have carried out one's invention before filing a patent application but one does need to be able to describe that invention with particularity.

Based on the aforementioned reasoning, the court finally concluded that the Board correctly decided that conception of the DNA did not occur upon conception of a method for obtaining it. And Fiers is entitled only to the benefit of his April 3, 1980 British filing date, since he did not conceive the DNA under section 102(g) prior to that date.

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[302] Id.
[303] Id. at 1170.
[304] Id.

The court in this case fortified the decision in Amgen and pointed out that conception of a method for isolating a DNA does not amount to conception of the sequence. As per the court, it is not enough if an invention is defined based on its function or activity; it has to be defined by its structure, name, formula, or definitive chemical or physical properties. Unlike in Amgen the court in this case said that conception can be proved even without carrying out the invention as long as the conception is clear enough to enable a person with ordinary skill to carry it out.

Kridl v. McCormick[305]

The invention in this case concerns the use of "antisense" recombinant DNA technology to make a virus-resistant plant or plant cell[306]. McCormick filed U.S. patent application 06/788,002 on October 16, 1985. The application was later assigned to Agracetus, Inc. and Kridl filed her U.S. patent application on March 28, 1986[307].That application was assigned to Calgene, Inc. Kridl raised an interference challenging prior conception of McCormick[308].

Based on pages from the laboratory notebook of Marcia Vincent dated January 18, 1984, describing an experiment in which a gene fragment was inserted into a cloning vector in both the sense and antisense orientations, one strand of which inserted gene fragment encoded a viral protein combined with Swain's testimony that he developed the strategy described in Vincent's notes in order to produce the antisense constructs of the invention and that he had communicated this strategy to Vincent, the Board of patent appeals concluded and the Federal Circuit agreed that McCormick had presented sufficient evidence to corroborate conception of the invention by at least January 18,

[305] Kridl v. McCormick, 05 F.3d 1446 (C.A.Fed.,1997).
[306] Id.
[307] Id. at 1448.
[308] Id.

1984 and that, as the first to conceive and the first to reduce to practice by filing a patent application[309].

The court started its analysis by stating that conception must include every feature or limitation of the claimed invention[310]. It further stated that conception must be proved by corroborating evidence which shows that the inventor disclosed to others his 'complete thought expressed in such clear terms as to enable those skilled in the art' to make the invention[311]. The court analyzed that one skilled in the art would have seen only one substantial use for the antisense constructs described in Vincent's notes, which is a means for imparting viral resistance to plants or plant cells because antisense constructs in plants were not known; only sense constructs were known at the time of conception, it would have been illogical to use novel constructs as experimental controls and it would also have been wasteful to attempt to generate sense constructs by a process that also generated antisense constructs because it was well-known how to make sense constructs alone[312].

Furthermore, the court stated that the antisense constructs do "speak for themselves" inasmuch as use to confer viral resistance was their only tenable utility and the conception of that utility was consistent with all of the other corroborated evidence[313]. Accordingly, the court concluded that McCormick's evidence was sufficient to prove conception of the invention, even though that evidence lacked explicit corroboration of the conception of antiviral utility[314]. The court finally stated that the evidence in no way contradicts Vincent's testimony that he conceived the utility of his invention when he conceived its

[309] Id. at 1449.
[310] Id. at 1449.
[311] Id. at 1450.
[312] Id.
[313] Id. at 1351.
[314] Id.

other features[315]. Therefore, the court concluded that McCormick conceived of the invention before Kridl.

The case elucidates the utility of laboratory notebooks for proving conception. As per this court, conception of an invention should be clear enough to enable a person with ordinary skill in the art to carry it out and conception of utility of the invention can be inferred from the state of the art.

Brown v. Barbacid[316] .

The case involves an interference between U.S. Patent No. 5,185,248 (the Barbacid patent) and U.S. patent application Serial No. 07/937,893 (the Brown application)[317]. The Barbacid patent and the Brown application both claim an assay for identifying new anti-cancer compounds that inhibit farnesyl transferase (FT), an enzyme involved in the control of cell growth[318]. The Barbacid patent application was filed on May 8, 1990, and issued on February 9, 1993. The Brown application was filed on December 22, 1992, but was accorded the benefit of an earlier related application filed on April 18, 1990[319]. Brown cited Notebook pages and autoradiographs from the inventor's (Dr. Reiss') experiments from August to October 1989, including experiments dated September 20 and September 25, 1989 to prove conception[320].

The court stated that Brown's physical evidence, such as Dr. Reiss' notebooks and auto radiographs, do not require corroboration to demonstrate the content of the physical evidence itself, namely that FT assay experiments took place on September 20 and 25, 1989[321]. However, the court reiterated that the gaps in facts stated in the notebooks relating to the limitations of the invention should

[315] Id.
[316] Brown v. Barbacid, 276 F.3d 1327 (C.A.Fed.,2002).
[317] Id. at 1331.
[318] Id. at 1331.
[319] Id. at 1332.
[320] Id. at 1334.
[321] Id. at 1337.

be corroborated by evidence[322]. Furthermore, the court pointed out that Inventor's testimony of conception and reduction to practice based on notebooks and experiments requires corroboration by independent evidence before it can be considered[323].

Moreover, the court went on to say that conception must encompass all limitations of the claimed invention and "is complete only when the idea is so clearly defined in the inventor's mind that only ordinary skill would be necessary to reduce the invention to practice, without extensive research or experimentation[324]. As per the court, Dr. Reis did not conceive every limitation of the invention when he conducted his FT assay experiment on September 20, 1989 because the laboratory notebook and autoradiograph themselves show that the September 20 experiment did not include the use of a test/candidate substrate (i.e., an inhibitor of FT), an element of the invention[325]. Likewise, in the only independent testimony corroborating Dr. Reiss' experiments, Dr. Casey did not suggest that the September 20 experiment included an FT inhibitor[326]. Thus, the court concluded that the physical and testimonial evidence regarding the September 20 experiments do not show conception or reduction to practice. Though the September 25 experiment contained all of the limitations of the invention, the court pointed out that Dr. Casey's testimony did not corroborate Dr. Reis testimony and does not prove conception on that date[327]. So, the court held that Brown failed to prove prior conception based on lab notebooks and experimental data due to lack of corroborative evidence.

This case illustrates the complications involved in maintaining lab notebooks. It states that lab notebooks have to be maintained in detail to be sufficient for poof of conception. If there are any gaps in the lab notebooks, they have to be

[322] Id.
[323] Id.
[324] Id. at 1336.
[325] Id.
[326] Id.
[327] Id.

corroborated by objective evidence. Expert testimony or attorney arguments themselves would not be sufficient to prove conception.

Singh v. Brake[328]

In a case involving an interference proceeding relating to invention of DNA construct, the Board of Patent Appeals and Interferences awarded priority of invention to patentee because applicant failed to establish that he had conceived of the plan to design DNA construct before patentee's priority date and because applicant failed to establish that he exercised reasonable diligence. The invention in this case relates to a patent application filed by Brake relating to a DNA construct including three basic components: (1) a segment, "L," which encodes an alpha-factor leader sequence; (2) a segment, "S," which includes a first codon, encoding either lysine or arginine, followed by a second codon, R2, encoding arginine; and (3) a gene, "Gene," which encodes a protein of interest, in particular, a polypeptide foreign to (i.e., not naturally produced by) Saccharomyces[329].

Singh raised an interference claiming that he conceived a plan to redesign the p60 DNA construct in order to obtain the desired gene product, without the additional amino acids, which followed the gene of interest in the yeast species, on October 1, 1982. Singh claimed that he realized the need to remove eight unwanted codons (twenty-four nucleotides) from the p60 DNA construct, and that he planned to accomplish this deletion by use of a technique known as "loop deletion mutagenesis[330]." On November 24, 1982, Singh wrote a laboratory notebook entry setting forth the undesired eight codons in the p60 DNA construct, as well as the twelve nucleotides on either side of that eight codon segment[331]. On that date, Singh also ordered a linear, 24-nucleotide

[328] Singh v. Brake, 48 Fed.Appx. 766 (C.A.Fed.,2002).
[329] Id. at 1364.
[330] Id. at 1367.
[331] Id. at 1366.

sequence that comprised the nucleotides of the flanking sequences[332]. This order was canceled on the same day, and a notation in Singh's laboratory notebook stated that Singh would perform the deletion experiment in a different way without changing codons[333]. Singh ordered another 24-mer for the deletion experiment. This 24-mer was precisely complementary to the flanking sequences set forth in the November 24 entry. DNA chemist Peter Ng testified that he synthesized the 24-mer for Singh on December 20, 1982. Singh affixed the order into his notebook on December 21, 1982, with a notation oligonucleotide for making in-frame deletion of alpha pro-IFN-D junction[334]. Singh claimed that these facts corroborate his testimony that he conceived the claimed DNA construct before January 12, 1983, which is the filing date of Brake, the patent applicant[335].

Despite the evidence, the court held that Singh failed to prove that he conceived the claimed construct prior to December 1, 1982[336]. Though Singh's notebook indicated the problem to be solved, namely, the need to eliminate the twenty-four nucleotides encoding the extraneous amino acids, the court held that the entry alone was insufficient to corroborate Singh's testimony[337]. The court stated that even if the entry expressed the problem, it did not provide the solution.

While it remains unclear exactly what Singh planned to do on November 24, 1982, his identification of preferred codons suggested to the court that his plans may not have included the use of loop deletion mutagenesis[338]. Nothing in Singh's notebook corroborated his testimony that the November 24, December 1, and December 21 entries were meant to be read together and therefore, the court stated that Singh did not have a definite and permanent idea of an

[332] Id.
[333] Id. at 1367.
[334] Id.
[335] Id. at 770.
[336] Id.
[337] Id.
[338] Id.

operative method of making the DNA construct prior to Brake 1's filing date[339]. According to the court, the notebook entries do not provide any protocol or outline of the loop deletion mutagenesis procedure.

Thus, after review of the record evidence in light of the proper legal standards, the court concluded that no evidence links the nucleotide Singh ordered on December 1, 1982, with a plan to design the claimed construct prior to January 12, 1983, which means that Singh had not conceived before Brake[340]. As Singh's laboratory notebook is unexplained as to content and relevance to the invention and uncorroborated the court held that he failed to prove reasonable diligence[341].

Like the earlier one, this case also points out the importance of maintaining detailed lab notebooks. It points out that lab note books have to be corroborated by evidence to prove date of conception.

Invitrogen Corp. v. Clontech[342].

The issue relating to conception arose in a patent infringement suit filed by Invitrogen against Clontech, in which Clontech responded by asserting non-infringement, invalidity, and unenforceability[343]. One of the grounds of invalidity was anticipation of the invention based on prior conception of the patented invention by Dr. Goff at Columbia University[344]. The patent in the case related to a mutant RT with DNA polymerase, but no RNase H, activity developed by Invitrogen. More particularly, Invitrogen altered a gene that originally encoded wild or natural RT, resulting in a mutant enzyme with the

[339] Id.
[340] Id.
[341] Id.
[342] Invitrogen Corp. v. Clontech Laboratories, Inc. 429 F.3d 1052 (C.A.Fed. (Md.),2005).
[343] Id.at 1060
[344] Id.

desired properties, which was reduced to practice on January 27, 1987[345]. Clontech claimed patent invalidity in the case by alleging anticipation by prior conception of the invention by Goff at University of Columbia[346].

The court started its analysis by stating that with unrecognized accidental duplication, the invention exists but remains unrecognized[347]. It further stated that the priority determination requires evidence that the inventor actually first made the invention, and that he understood his creation to have the features that, comprise the inventive subject matter[348]. In other words, the invention must be new and the inventor must be in a position to appreciate that a new invention has been made. The inventor must corroborate his belief or appreciation through objective evidence, which identify the novel features of an invention and which would be recognized by a person with ordinary skill[349].

Though Dr. Goff stated at the trial that he thought about the invention in question and suspected it because of failed experiments, the court pointed out that the notebook entries do not corroborate Goff's suspicion[350]. The court stated that neither the December 1984 entry, nor the May 1985 entry, indicated the alleged "focus" on H7 or H8.
The court rejected the 1984 entry as Goff stated at the deposition that the 1984 entry was not relevant to the H7 or H8 RT RNase H minus behavior[351].

Furthermore, the court stated that Clontech nowhere provides the court with expert testimony that properly explains the technical notebook entries advanced in support of its conception arguments[352]. As per the court, none of

[345] Id.
[346] Id.
[347] Id. at 1064.
[348] Id.
[349] Id.
[350] Id.
[351] Id. at 1068.
[352] Id.

the expert's testimony can be taken as conclusory as they are based on legal issues and extensive attorney arguments are not sufficient to substantiate the expert testimony[353]. So, as Clontech failed to prove prior conception through objective and corroborated evidence, the court held that the patent is not anticipated by prior conception.

This case brings out a new aspect for proving conception. It states that the inventor should appreciate the newness and completeness of his conception in order to be able to prove it. It further points out that conception has to be corroborated by objective evidence and that expert testimony and attorney arguments alone would not be sufficient.

The courts have interpreted rules for proof of prior conception differently when it comes to genes and related inventions. The principles laid down by the federal circuit can be summarized as follows:

a. In case of gene-based inventions conception of an invention will not be complete until the invention is reduced to practice. Conception of a method of isolating a gene would not be enough to prove conception of the gene sequence.
Completion of conception is tested from the point of view of a person with ordinary skill in the art. Conception is said to be complete only if is at a stage where it can be carried out by a person skilled in the art. Conception of utility can be presumed based on the state of the art.

b. To prove conception, the inventor must have realized the newness and completeness of his invention. Lab notebooks play a very important role in proving conception and diligence.

[353] id. at 1069.

c. To prove conception, Lab notebooks have to be corroborated by objective evidence. The requirement of corroborative evidence becomes more pertinent when there are gaps in lab notebooks.

d. Any prior art reference used to negate prior conception should have all elements and limitations of the invention.

e. Lab notebooks can be supplemented by expert testimony or attorney arguments and testimony or attorney arguments standing alone would not be enough to prove conception.

Section 102(a) and (b)

Section 102(a) provides that a patent will not be granted if the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent[354] and Section 102(b) provides that a patent will not be granted if the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application for patent in the United States[355]. As per the sections an invention will not be novel, if it is known or used in USA, patented or published anywhere in the world and on public use or sale anywhere. Novelty of gene related inventions has been challenged at the Federal Circuit based on prior patent or publication and public use or on sale.

Patent or Publication

An invention would not be patentable because of lack of novelty if it forms part of a granted patent or filed application before the priority date of the

[354] 35 USC Sec. 102.
[355] 35 USC Sec. 102.

invention. However, if the patent application is filed by the inventor in one country, he gets a grace period of twelve months for filing an application in another country, filing within which time would not negate novelty of his invention. Furthermore, an invention would also lack novelty if it forms part of a printed publication before the priority date. However, if the publication is by the inventor, the law grants a grace period of 12 months within which he can file for a patent without destroying the novelty of the invention. In order for a patent or publication to negate novelty of an invention, the patent or publication should contain all elements and limitations of the invention within a single reference.

In re Crish[356]

'In re Crish', the Court of Appeals for Federal Circuit held that claims for effective portions of gene's nucleotide sequence were anticipated by prior art, which identified gene-containing plasmid and effect in question[357]. The claimed invention in this case related to purified DNA molecules having promoter activity for the human involucrin gene (hINV)[358]. The application disclosed that the inventor had isolated and sequenced the promoter sequence of hINV from plasmid pSP64 <<lambda>> I-3 H6B using standard molecular biology techniques[359]. The inventor determined that the hINV promoter sequence was approximately 2.5 kb (kilobases) in size[360]. The application also identified and numbered each nucleotide in the hINV promoter sequence and designated it[361].

The federal circuit held that the invention is anticipated by existence of publications relating to the invention. The court started its analysis by reiterating the fact that novelty cannot be established by claiming properties

[356] In re Crish, 393 F.3d 1253 (C.A.Fed.,2004).
[357] In re Crish, 393 F.3d 1253 (C.A.Fed.,2004).
[358] Id. at 1254
[359] Id.
[360] Id.
[361] Id.

of a known material[362]. It stated that the promoter region of hINV was not new as hINV was known and used years before the date of invention[363]. Moreover, the court stated that promoter region of hINV was specifically identified by size and location in the Crish and Eckert publications[364].

As the discovery of properties of a known material does not make it novel, the court stated that identification and characterization of the nucleotide sequence of the promoter region of hINV, which is a part of the prior art does not make the claimed invention novel[365]. Furthermore, the court stated that the inventor's characterization that the pending claims cover a novel DNA sequence having promoter activity, while the references disclose only the starting material plasmid, is unsound because the claims encompassing the gene plus other nucleotides are anticipated by the starting material plasmid, which consists of the gene plus other nucleotides[366]. The court stated that the inventor cannot rely upon the inability of another worker to correctly sequence the promoter region of the hINV gene from plasmid afer he sequenced it accurately himself in order to prove novelty[367]. Finally, the court concluded that the invention is not novel because the plasmids used in the inventor's application and the inventor's prior publication were the same because both the application and the publication refer to the promoter region as approximately 2.5 kb in size and both the application and the publication refer to the same source for plasmid[368].

This case illustrates an aspect of publication, which is that existence of a larger sequence and a method of sequencing in a prior publication would anticipate a fragment or portion of the whole gene sequence.

[362] Id. at 1257
[363] Id.
[364] Id.
[365] Id.
[366] Id. at 1258
[367] Id. at 1259.
[368] Id.

Novo Nordisk Pharmaceuticals, Inc. v. Bio-Technology General Corp[369].

In a case relating to a process for producing "ripe" human growth hormone (hGH) protein in E.Coli bacteria through use of recombinant DNA techniques, the Court of Appeals, held that article previously published in non-patent printed periodical disclosed limitations in claim of patent negating the novelty of the patent.

Novo Nordisk Pharmaceuticals owns a patent disclosing a process whereby a proteolytic enzyme, preferably the enzyme dipeptidyl aminopeptidase I, cleaves a pre-hGH fusion protein in order to produce "ripe" hGH protein[370]. Bio-Technology General Corp. alleged invalidity of the patent by arguing that the Palvakis article published in 1981 anticipates the patent[371].

The court started its analysis by stating that anticipation based on a printed publication under section 102(a) requires the presence in the publication of each and every limitation of the claimed invention[372]. However, the court pointed out that a prior art reference may anticipate without disclosing a feature of the claimed invention if that missing feature is necessarily present, or inherent, in the single anticipating reference[373]. In order to anticipate, the court stated that a prior art disclosure must also be enabling, such that one of ordinary skill in the art could practice the invention without undue experimentation. The court held that Pavlakis article discloses the second and third limitations of the claim 1 in the patent[374]. These limitations require that the hGH protein be composed of a 191-amino acid sequence identical to that of

[369] Novo Nordisk Pharmaceuticals, Inc. v. Bio-Technology General Corp., 424 F.3d 1347 (C.A.Fed. (Del.),2005).
[370] Id. at 352.
[371] Id.
[372] Id. at 366.
[373] Id.
[374] Id. at 368.

pituitary-derived hGH and that the protein have the full biological activity of pituitary-derived hGH. In that regard, the court stated that the article states that the hGH1 protein, as predicted from the DNA sequence, appears identical in all respects to the major form of pituitary hGH[375]. Further, the court pointed out that the article discusses experimental tests used to characterize the hGH product, which were designed in order to determine whether the hGH1 protein had the same amino acid sequence and biological activity as pituitary-derived hGH. As per the court the article's discussion of the tests provides strong support for the conclusion that the Pavlakis article discloses the subject matter of claim 1 of the patent in question[376]. The court said that test results disclosed in the Pavlakis article indicated that the hGH1 protein had the same structure and chemical properties as pituitary-derived hGH. d hGH and accordingly, held that the article discloses a ripe hGH protein and therefore anticipates the patent[377].

Finally, the court stated that the 1981 Pavlakis article discloses the production of ripe hGH protein in an enabling manner because it discusses particular materials and a particular methodology to produce the hGH protein[378]. In other words, the court said that the article relies on standard recombinant DNA techniques that would have been understood by one of ordinary skill in the art at the time of its publication. Therefore, the court held that the Pavlakis article is sufficiently enabling for anticipating the patent in question[379].

The principle laid down in this case is that for an invention to be anticipated by prior art, the publication should anticipate all limitations in a single reference. Furthermore, the publication should have an enabling disclosure in order to anticipate the invention.

[375] Id.
[376] Id.at 1355
[377] Id.
[378] Id. at 1369.
[379] Id.

In re Ngai[380]

In 'In re Ngai' the Court of Appeals held that: inventor could not patent known kits for normalizing and amplifying RNA population by simply attaching new set of instructions[381]. Ngai argued in this case that the addition of new printed matter to a known product makes the product patentable. Rejecting his argument, the court pointed out, that the claimed invention is not patentable because the printed matter is not functionally related to the substrate and will not distinguish the invention from the prior art[382]. The court further stated that adopting Ngai's position would mean that anyone could continue patenting a product indefinitely provided that they add a new instruction sheet to the product[383]. Though Ngai is entitled to a patent on his invention of a new RNA extraction method, and the claims covering that invention were properly allowed, the court held that he is not entitled to patent a known product by simply attaching a set of instructions to that product.

This case points out that attaching instruction sheet to an invention would not be sufficient to satisfy the novelty requirement in order to make it eligible for a patent.

Scripps Clinic & Research Foundation v Genentech Inc[384].

In a case relating to a patent for ultra purification of blood-clotting factor using monoclonal antibodies, the court said that issue of invalidity of claims for anticipation by doctoral dissertation was not amenable to summary

[380] In re Ngai, 91 Fed.Appx. 153 (C.A.Fed.,2004).
[381] Id.
[382] Id. at 1338.
[383] Id.
[384] Scripps Clinic & Research Foundation v Genentech Inc., 927 F.2d 1565 (C.A.Fed. (Cal.),1991).

disposition[385]. This case concerns a patent relating to a substance called human Factor VIII: C, a complex protein that occurs naturally in normal blood and is essential to the clotting of blood[386]. One of the allegations of patent invalidity was based on anticipation by doctoral dissertation[387]. The court started its analysis by stating that Invalidity for anticipation requires that all of the elements and limitations of the claim are found within a single prior art reference[388]. The court went on to state that there must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention[389]. Though three successive declarations of Dr. Harris were filed by the parties, each explaining his dissertation, the court held that a decision on anticipation cannot be made in a summary judgment, as it requires ascertaining of facts.

The case lays down that the differences between the publication and the invention should be seen by a person with ordinary skill in the art.

To summarize, the cases lay down the following principles:

a. A publication must contain all elements and limitations of the invention in a single reference to negate its novelty.

b. The publication can be anticipatory only if it contains an enabling disclosure.

c. Anticipation by publication is seen from the point of view of a person skilled in the art.

d. Existence of a full sequence and a method of isolating the sequence in a publication would anticipate a fragment of the sequence.

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[385] Id.
[386] Id. at 1569.
[387] Id.
[388] Id.
[389] Id.

e. Addition of instructions would not attach novelty to an invention.

Public use and on sale

An invention will not be eligible for a patent if it forms part of public use within United States for more than one year before the date of application[390]. The public use must be in the natural and intended manner. The use need not be publicly accessible use and secret commercial use would be considered to be public use. Public use of an invention for purposes of testing or experiment would not be considered to be public use.

Another activity that would bar novelty of an invention is sale. An invention would not be novel if it is on sale in USA for more than a year before priority date of the invention[391]. The Supreme Court has set forth two conditions for an on-sale bar: (1) the invention must be the subject of a commercial offer for sale, and (2) the invention must be ready for patenting[392]. Secret commercial sale would give rise to an on sale bar.

Invitrogen Corp. v. Biocrest Mfg., L.P.[393]

The case relates to a patent invalidity claim relating to the introduction of recombinant DNA molecules into receptive E. coli cells to improve the cells' "competence," i.e., their ability to take up and establish exogenous DNA and replicate this DNA as they multiply[394]. Biocrest and other parties alleged that the patent owned by Invitrogen is invalid as it was part of public use[395]. Invitrogen used the claimed process before the critical date, in its own

[390] 35 USC Sec 102(b).
[391] 35 USC Sec. 102(b).
[392] Pfaff v. Wells Elecs., Inc., 525 U.S. 55, 67, 119 S.Ct. 304, 142 L.Ed.2d 261 (1998).
[393] Invitrogen Corp. v. Biocrest Mfg., L.P., 424 F.3d 1374 (C.A.Fed. (Tex.),2005).
[394] Id. at 1378.
[395] Id.

laboratories, to produce competent cells but it did not sell the claimed process or any products made with it. Invitrogen also kept its use of the claimed process confidential within the company[396]. Biocrest alleged that the Invitrogen's patent is invalid as the use of the invention within the company amounts to public use under Section 102(b) of the Patent Act[397].

The Court started its analysis by stating that analysis under Section 102(b) involves two separate inquiries, one evaluating whether "the invention" was complete and ready for patenting, and the other evaluating whether that invention was in public use[398]. One of the exceptions to public use bar is that the use is secret use. As there is no evidence that Invitrogen received compensation for internally, and secretly, exploiting its cells, the court stated that the use would not be public use under section 102[399]. It further stated that the fact that Invitrogen secretly used the cells internally to develop future products that were never sold is insufficient to create a public use bar to patentability[400].

Enzo Biochem, Inc. v. Gen-Probe, Inc[401].

Enzo is the assignee of the patent relating to nucleic acid probes that selectively hybridize with the bacteria that cause gonorrhea, namely, Neisseria gonorrhoeae, as well as methods for using those probes to detect the bacteria[402]. In June 1982, Enzo and Ortho Diagnostic Systems ("Ortho"), an affiliate of Cambridge Research Labs, entered into an agreement involving joint funding of research and development on "any human diagnostic product resulting from the program of research" "whether or not invented or developed

[396] Id.
[397] Id.
[398] Id. at 1380.
[399] Id.
[400] Id.
[401] Enzo Biochem, Inc. v. Gen-Probe, Inc., 424 F.3d 1276 (C.A.Fed.,2005).
[402] Id. at 1278.

by Enzo prior to the effective date of the agreement[403]." In August 1983, the parties executed an amendment that made it clear that a probe for gonorrhea was part of the agreement[404]. In an infringement suit filed by Enzo, Gen-Probe asserted patent validity stating that the contract between Enzo and Ortho amounts to an offer for sale under section 102(b) of the Patent Act[405].

The court started its analysis by stating the two-prong test put forward by the Supreme Court for the application of the on-sale bar, which is: First, the product must be the subject of a commercial offer for sale and Second, the invention must be ready for patenting[406]. The court stated that the Enzo-Ortho agreement created the necessary contractual obligations on the parties to constitute a commercial offer for sale[407]. Though the agreement states throughout its text that the parties are interested in cooperating in certain experimental work, that work is not preliminary production of the probe[408]. Instead, the court reasoned that provisions of the agreement relate specifically to supply of Ortho's worldwide requirements for what are clearly commercial purposes. The court stated that supply of worldwide requirements at reasonable times and prices surely means commercial supply, and the agreement constitutes an offer to sell under section 102[409].

The court evaluated Enzo's assertion of experimental use for negating On Sale bar and found that Enzo had asserted that the probe that it delivered to Ortho was its final product, which it deposited at the ATCC, and thus that it had reduced the invention to practice[410]. The court reasoned that the policy behind the rule that experimental use negates an on-sale bar is to give the inventor the opportunity to reduce an invention to practice, and thus that what occurs

[403] Id.
[404] Id. at 1280.
[405] Id.
[406] Pfaff v. Wells Elecs., Inc., 525 U.S. 55, 67, 119 S.Ct. 304, 142 L.Ed.2d 261 (1998).
[407] Id. at 1281.
[408] Id.
[409] Id.
[410] Id.

after a reduction to practice cannot be experimental use; consequently, it concluded that Enzo's use was not experimental[411].

The cases elucidate instances of public use and offer for sale.

To summarize, secret use for research purposes would not amount to public use and on sale bar arising out of a contract for unlimited supply cannot be negated by secret commercial use.

EUROPE

Article 54 of the European Patent Convention deals with novelty[412]. It provides that an invention will be considered to be new if it does not form part of the state of the art, which comprises everything made available to the public by means of a written or oral description, by use, or in any other way, before the date of filing of the European patent application[413]. The Article further provides that the content of European patent applications, whose filing dates are prior to the date referred to in paragraph 2 and which were published under Article 93 on or after that date, will be considered as comprised in the state of the art[414]. The Implementing regulations to EPC provide that biological material, which is isolated from its natural environment or produced by means of a technical process even if it previously occurred in nature, is patentable. They specifically provide that an element isolated from the human body or otherwise produced by means of a technical process, including the sequence or partial sequence of a gene, may constitute a patentable invention, even if the structure of that element is identical to that of a natural element. As per the regulations a gene sequence isolated from nature would be considered to be

[411] Id.
[412] Article 54, CONVENTION ON THE GRANT OF EUROPEAN PATENTS of 5 October 1973 text as amended by the act revising Article 63 EPC of 17 December 1991and by decisions of the Administrative Council of the European Patent Organisation of 21 December 1978, 13 December 1994, 20 October 1995, 5 December 1996 and 10 December 1998.
[413] See supra, Article 54(1) and (2).
[414] See Supra, Article 54(3).

novel in the light of what exists in nature even if its structure is same as the one existing in nature[415]. Novelty of genes and gene-based inventions has been the subject of uncertainty at the European Patent Office. Technical and Opposition Boards have been struggling to define appropriate tests for determining their novelty. A study of different decisions of the Boards elucidates the confusion and uncertainty surrounding the interpretation of novelty with regard to genes and gene based inventions.

Decisions of European Patent Office

Relaxin Decision.[416]

The opposition relates to a process for obtaining H2-relaxin, the DNA encoding it, their chemical structure and use of the protein[417]. The Board brushed aside the contention of the opponents that the subject-matter of the opposed patent lacks novelty since the patent owner isolated in a conventional way, the gene encoding relaxin, which was always present in the female human body by stating that the claimed DNA fragments encoding relaxin and its precursors (prepro- and pro-forms) are cDNAs, that is, DNA copies of human mRNA encoding relaxin, which do not occur in the human body[418].

The Board further stated that until a cDNA encoding human H2-relaxin and its precursors was isolated by the patent owner, the existence of this form of relaxin was unknown[419]. The Board went on to point out that it is established patent practice to recognize novelty for a natural substance which has been

[415] Rule 23c(a) and Rule 23e(2)- Patentable biotechnological inventions, PART II - IMPLEMENTING REGULATIONS TO PART II OF THE CONVENTION.
[416] Howard Florey/Relaxin(Oppositions by Fraktion der Grunen Im Europaischen Parlament; Lannoye), Opposition Division, 8 December 1994, (1995) E.P.O.R. 541.
[417] Id. at 542.
[418] Id. at 547.
[419] Id.

isolated for the first time and which had no previously recognised existence[420]. In view of the practice the Board held that the novelty of invention is assured.

The Board rejected the argument that the chemical structure of the DNA fragments in the claimed invention is completely undefined by stating that the DNA is defined in terms of the amino acid sequence it encodes, a generally acceptable terminology and one which is widely used and perfectly understandable to the skilled person[421]. Though a very large number of DNA sequences may fall under the scope of the claim, including sequences, which possibly occur in nature and differ from those exemplified in the patent, the Board stated that it has no bearing on the patentability of the claimed invention. In the light of the aforementioned reasoning, the Board held the invention to be novel[422].

The Relaxin case points out that cDNA sequence of a protein in human body is novel as it is different from what exists in the human body. As per the Board, isolation of a gene of a known protein for the first time through conventional methods would make the gene sequence novel. Furthermore, the case states that defining a DNA sequence in terms of the amino acid it encodes would be sufficient for patentability. This case cleared lot of doubts regarding novelty of genes by stating that natural existence of genes would not anticipate their isolation, as the isolated genes containing only the coding regions are different from their natural counterparts.

Amgen Decision[423]

The patent in the decision relates to the manufacture of the essential body

[420] Id.
[421] Id. at 548.
[422] Id.
[423] Kirin-Amgen/Erythropoietin v. (Oppositions by Genzyme; Elanex Pharmaceuticals; Merckle; Boehringer Mannheim; Behringwerke; AKZO Pharma, Technical Board of Appeal 3.3.4, 21 November 1994, (1995) E.P.O.R. 629.

protein erythropoietin (Epo) by recombinant DNA techniques, whose novelty was questioned on appeal to the Technical Board[424]. The Board started its reasoning by citing Decision T301/87, which held that the unknown presence of a particular nucleotide sequence in a Lawn gene bank could not be regarded as state of the art for the purpose of Article 54(1) EP in the absence of a known probe, or any other means, enabling the sequence to be identified[425]. Accordingly, in this case, as no probe was known for identifying the relevant gene, the Board found that the nucleotide sequence of the Epo gene was not part of the state of the art merely because the nucleotide sequence would have been present in the Lawn gene bank or possibly others and therefore not anticipated[426]. As to the Sugimoto disclosure, which is the only document said to anticipate the claims to transformed host cells and to the process, the Board agreed with the respondents that a cell fusion process, such as that disclosed in the reference, cannot be equated to the transfer of purified exogenous DNA, thus making the claim to DNAs, host cells in the present invention novel[427].

The Board further stated that r-Epo can be differentiated from u-Epo because it is reliably possible to check on a SDS-PAGE gel whether a given r-Epo exhibits a higher m.w. than a given u-Epo made available to the public, eliminating any doubts about confusion relating to novelty[428]. As no source of Epo other than u-Epo was available to the public in 1983, the Board concluded that the invention was not anticipated[429]. With regard to Epo secreted by fused cells and by the RCC-3-JCK tumour cells, the Board pointed out that the appellants have not been able to provide evidence about either the true nature of the product, or the enabling character of the teaching of the references[430]. Regardless of whether the cells are publicly available or not, the Board stated that it cannot take it as proved that these cells secrete an Epo supernatant comparable to

[424] Id.
[425] Id. at 665.
[426] Id.
[427] Id.
[428] Id.
[429] Id. at 666.
[430] Id.

that of the present invention. In view of the above reasoning, the Board concluded that the invention was novel[431].

Amgen decision lays down that a lawn gene bank will not anticipate a gene isolated from it in the absence of a known probe, or any other means, enabling the sequence to be identified. It further points out that availability of a protein to the public would not negate novelty of a more pure product of the same protein. It further reiterates that existence of general methods would not anticipate a specific process for isolating gene sequence of a particular protein. The case points out that existence of large sequences or gene banks, would not anticipate specific sequences.

Genentech I Decision (T158/91)[432].

The patent application was directed to a process for the synthesis of mature human growth hormone ("hGH") using a specific recombinant DNA process[433]. The Examining Division refused the application on the grounds of lack of novelty over a prior art reference that disclosed a recombinant DNA process of general applicability to the preparation of proteins in a mature form[434]. The prior art reference in particular disclosed those proteins where the corresponding DNA sequences were available at the time of its filing which included pre-hGH[435]. The patent applicant appealed and submitted further documents, which it claimed, showed that those skilled in the art had not and would not have relied on the teaching in the prior art reference as a reliable indication of how hGH could be prepared.

[431] Id.
[432] R. v. GENENTECH/Human growth hormone production, T158/91, Technical Board of Appeal 3.3.2 July 30, 1991, (2001) E.P.O.R. 60.
[433] Id.
[434] Id.
[435] Id.

The Board stated that the teaching in prior art reference was identical to the method of preparation described in the application[436]. However, the Board went on to say that in order to be novelty-destroying the teaching in prior art reference had to provide sufficient disclosure such that the invention could be put into practice with a reasonable expectation of success and without undue experimentation[437]. The Board pointed out that the sufficiency of a disclosure had to be examined in each case on its own merits, taking into account, for example, (a) the character of the technical field and the average amount of effort necessary to put into practice a certain written disclosure in that technical field; (b) the time when the disclosure was presented to the public and corresponding common general knowledge and (c) the amount of reliable technical details disclosed in a document[438].

The Board analyzed that in the present case, the DNA sequence for hGH was already known and therefore successful repetition of the disclosed teaching represented a reasonable expectation[439]. Moreover, the board said that documents filed during the examination procedure confirmed that, although the process disclosed was time-consuming and unpredictable, it had become routine for genetic engineering work[440]. As per the board the fact that the new documents filed by the applicant on appeal showed that the process did not always work in all cases did not mean that it did not work in a sufficiently reliable manner to be relied on[441].

Finally, the Board held that although the prior art reference did not provide the precise technical steps for the preparation of the gene coding for hGH, it would have enabled the skilled person equipped with the knowledge of the DNA

[436] Id. at 496.
[437] Id.
[438] Id. at 497.
[439] Id.
[440] Id.
[441] Id.

sequence for hGH and the common knowledge to carry out its preparation as claimed, thus making it not novel[442].

The Genentech decision lays down the following principles:

1. If the teaching in prior art reference provides sufficient disclosure such that the invention could be put into practice with a reasonable expectation of success and without undue experimentation, then it would be novelty destroying.
2. To make such a decision the Board would consider the following factors
(a) The character of the technical field and the average amount of effort necessary to put into practice a certain written disclosure in a technical field;
(b) The time when the disclosure was presented to the public and corresponding common general knowledge and
(c) The amount of reliable technical details disclosed in a document.
3. If steps in the prior art reference enable a skilled person equipped with the knowledge to carry out the invention, then the reference would be novelty negating.

Decision T223/92[443].

The patent in this case relates to Human immune interferon-gamma and DNA Sequence encoding for it[444]. The appellants cited a prior art reference describing an attempt to purify a protein whose existence and several of whose properties were known, in order to negate the novelty of the interferon-gamma per se, defined by the DNA-sequence coding for it and its amino-acid-sequence deduced from the DNA-sequence[445].

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[442] Id. at 493.
[443] R. v. GENENTECH/HIF-Gamma, T223/92, Technical Board of Appeal 3.3.2, July 20, 1993, (2003) E.P.O.R. 12.
[444] Id.
[445] Id. at 106.

The board stated that the invention in this case represents one of three groups of proteins, which were called interferons[446]. Though alpha and beta interferons have been purified to homogeneity and their amino acids had been determined first partially by direct amino acid sequence determination and later more completely by analysis of cloned cDNA sequences, much less information was available about the protein called interferon-gamma[447]. Though the prior art reference describes the attempt to produce, purify and characterise the gamma interferons, the Board stated that there remained obstacles as regards the identity and availability of the protein[448]. Because of the lack of a generally accepted standard for establishing the activity of the substance, the Board pointed out that no objective determination of an improved method for production was possible[449].

In contrast to the interferons referred in the reference, as the claimed invention relates to a protein called interferon-gamma defined by its amino acid sequence with the number of 146 amino acids from which the molecular weight of 17,400 can be calculated, the Board stated that the invention is different from what is stated in the prior art[450]. As a person with ordinary skill cannot realize the present invention from the reference, the Board concluded that the invention is novel[451].

The case points out that references citing general information without specific inputs relating to the invention based on which a person with ordinary skill cannot deduce the invention will not negate novelty of a claimed protein or DNA sequence.

[446] Id.
[447] Id.
[448] Id.
[449] Id.
[450] Id. at 107.
[451] Id.

Biogen I Decision[452].

The case relates to a European patent concerning DNA sequences, recombinant DNA molecules and processes for producing human fibroblast interferon" and claiming priority from two prior art references[453]. A Notice of Opposition was filed against the European patent and Revocation of the patent was requested on the grounds of Article 100 (a) EPC for lack of novelty and inventive step[454].

Citing the case law of the EPO (see T612/92 (FN4) of February 28, 1996), which states that the teachings of a document belonging to the prior art must be unambiguous before they can be taken into account for assessing novelty, the Board concluded that prior art references ('reference(s)') (1) and (2) are not novelty-destroying to the subject-matter of the first claim in the patent[455]. Both references (1) and (2) disclose a plasmid TpIF319-13 which carries the beta-IFN cDNA in the EcoRI site of pBR322 in such an orientation that it could theoretically be transcribed from the P4 promoter of pBR322 and"461 which, if so in practice, could be novelty-destroying for the subject-matter of Claim 1[456]. Though experiments were presented by the appellant to the effect that beta-IFN biological activity could be retrieved from host cells transformed with TpIF319-13, the Board found that these experiments did not conclusively show that the detected antiviral activity could be unambiguously attributed to beta-IFN[457]. The Board further stated that it is not convinced that the general teaching in references (1) or (2) constitutes unambiguous evidence for a recombinant plasmid expressing beta-IFN from the P1 promoter of pBR322[458]. Furthermore, the Board stated that though prior art reference (17) (as an expert opinion) disclosing that transcripts initiated at P4 are mostly 104 bp in

[452] BIOGEN/Human Beta-interferon(Opposition by Schering, Technical Board of Appeal 3.3.4, T207/94, (1999) E.P.O.R. 451.
[453] Id. at 453.
[454] Id.
[455] Id. at 461.
[456] Id.
[457] Id.
[458] Id.

length, as a few mRNA molecules are of greater length, but transcription stops into the bla gene before the EcoRI site, it does not seem possible that the beta-IFN cDNA would ever be transcribed from P4.

The Board further reasoned that the method according to a reference, which discloses a method for the isolation and screening of recombinant plasmids expressing beta-IFN cDNA or parts thereof, is not workable and that the document is not relevant to novelty because it does not provide any evidence that the method has been carried out[459] and because it discloses a generic method of cloning, which is not specific to the patent in question[460]. As none of the other references is concerned with making pharmaceutical preparations of beta-IFN and as they do not provide information on how to make sufficient amounts of the protein for such preparations, the Board concluded that all cited references do not destroy novelty[461].

The Biogen I decision elucidates that a prior art reference, which is ambiguous and which cites a general method of cloning a gene will not destroy the novelty of the gene sequence. In other words, a prior art reference has to be clear, certain and specific and should contain all elements in the subject matter of the claimed invention in order to negate novelty of a gene based invention.

Biogen II Decision[462]

The decision concerns a novelty issue among other issues relating to a method for the recombinant production of polypeptides displaying HBV antigenicity, and means therefore, including specific deposited recombinant DNA

[459] Id. at 461.
[460] Id. at 462.
[461] Id.
[462] BIOGEN/Hepatitis B Virus(Oppositions by Abbott; Takeda; Warcoin; Smith Kline Beecham; Institut Pasteur;Intervention by Medeva), Technical Board of Appeal 3.3.2, June 16, 1994, (1999) E.P.O.R. 361.

molecules[463]. Claims in question relate to specific DNA sequences, to fragments thereof and to DNA sequences which are degenerate as a result of the genetic code to any of the previous sequences, which encode a polypeptide with HBV antigenicity and a specific amino acid sequence or fragments thereof displaying antigenicity of HBsAg[464].

All prior art references relate to the cloning and structural analysis of HBV DNA of either adw or ady subtypes[465]. One reference reports the complete primary structure of the viral genome and identifies eight open reading frame regions, in particular the region, which contains the HBsAg gene, and other references disclose the location of the HBsAg gene in the genome, its nucleotide sequence and the deduced amino acid sequence of the encoded antigen[466]. The board stated that none of the references discloses sequences or fragments thereof identical with those recited in the claims at issue. The Board emphatically stated that small differences in a sequence like a difference in one amino acid would be sufficient for purposes of novelty[467]. It further stated that the sequences cited in the prior art references are not comparable to the invention in question[468].

Although the nucleotide sequences referred to in the invention are present in the references, the Board reasoned that they are not identified and characterised in their exact primary structure and thus they are not made available in the sense of Article 54 (2) EPC. In the light of aforementioned reasons, the Board held the claimed sequences to be novel[469].

The decision lays down a very important principle. It holds that even a very small difference such as a single amino acid, in the sequence of a gene or

[463] Id.
[464] Id. at 377.
[465] Id.
[466] Id.
[467] Id.
[468] Id.
[469] Id. at 378.

protein can make it novel and patentable. It further points out that existence of a fragment, as a part of a longer sequence does not anticipate the fragment.

R. v. RIJKSUNIVERSITEIT[470]

The patent in this case related broadly to a process for the incorporation of foreign DNA into the genome of monocotyledonous plants by incubating the protoplasts thereof with Agrobacterium or Rhizobium bacteria. Such technique was known for the genome of dicotyledonous plants, but was exemplified in the patent only in relation to the inoculation of Agrobacterium into two monocotyledonous species of the families Amaryllidaceae and Agaraceae (out of a total of 53 widely diversified such families)[471].

The closes prior art reference describes a study of the host range of Agrobacterium B6 performed by the authors on 48 species from 39 genera in 14 monocotyledonous families and also reviews all results made available on Agrobacterium tumorigenicity from 1911 onwards. Though the Board accepted that the strains cited in the reference[472], most probably contained the said plasmid, the existence of which in wild-type Agrobacterium was known since 1974, it stated that careful scrutiny of the reference revealed that none of the inoculations which were performed by the authors resulted in tumour formation, except that of Cordillyne stricta and that swelling occurred once, on one plant only and its nature remained to be established[473]. Furthermore, the Board stated that experiments specified in the reference had failed[474]. Accordingly, in view of the paucity of the positive results and the uncertainty attached to their significance, the Board concluded that the prior art reference does not teach the person skilled in the art that monocotyledonous plants can

[470] R. v. RIJKSUNIVERSITEIT, T612/92, Technical Board of Appeal 3.3.4, February 28, 1996, (2002) E.P.O.R. 9.
[471] Id.
[472] Id. at 84.
[473] Id.
[474] Id.

be infected with Agrobacterium, let alone that the T-DNA would be incorporated into the genome of the said plants[475]. Therefore, the Board held the invention to be novel in the light of the prior art.

The case elucidates that lack of specificity; successful experiments and certainty in a prior art reference would not anticipate a gene-based invention due to uncertainty in the field.

Unilever Decision (T386/94)[476]

The patent in this case relates to DNA molecules comprising the genes for preprochymosin and its maturation forms and microorganisms transformed thereby[477]. Two European patent applications claiming a priority right from June 17, 1981 and a priority right of January 16, 1981 were cited as anticipating the patent[478]. The Board did not deal with the first application as it was barred by res judicata[479]. With regard to the second patent application filed on January 16, 1981, disclosing the isolation of one recombinant clone containing a chymosin DNA sequence which was later on shown to be partially deleted, the Board stated that the disclosure of an incomplete clone cannot destroy the novelty of the subject-matter of the patent[480].

The Unilever decision lays down that a prior art reference discussing a partial sequence coding for a particular protein cannot negate the novelty of the complete sequence coding for the same protein.

[475] Id.
[476] Unilever/Chymosin(Oppositions by Celltech; Hansens Laboratorium), T386/94, Technical Board of Appeal 3.3.4, January 11, 1996, .(1997) E.P.O.R. 184.
[477] Id.
[478] Id. at 193.
[479] Id.
[480] Id. at 194.

Decision T109/91[481]

The patent in the case is directed to a composite plasmid comprising (A) a DNA replication region derived from a plasmid selected from a group of specified deposited plasmids and (B) a gene fragment derived from a plasmid capable of propagating in Escherichia coli and having at least a region expressing drug resistance[482]. The Opposition Division had rejected a novelty objection based upon EP-A-0 082 485 on the basis of lack of novelty[483].

The Board started its analysis by citing the closest prior art reference, which relates to novel vector plasmids and processes for producing the same by inserting DNA fragments containing a gene expressible in a microorganism belonging to the genus Corynebacterium or Brevibacterium into a plasmid derived from a microorganism belonging to the genus Corynebacterium or Brevibacterium[484]. The Board stated that a comparison of the features of the claimed invention and the plasmid in the prior art reference shows that both plasmids had been isolated from bacteria of the same species, namely Corynebacterium glutamicum and that both of them have the same BglII restriction site[485]. It went on to say that these common features provide a first indication that the claimed plasmid may well be the same as that described in the prior art reference[486]. Furthermore, the Board cited experiments, which showed that the restriction sites are the same for both plasmids[487].

In the Board's view slight differences in length are not decisive and cannot lead to the judgment that the plasmids must be considered as not being identical[488]. Rather, the Board considers the quality and quantity of the features, which

[481] Ajinomoto/Composite Plasmid(Opposition by Degussa), T109/91, Technical Board of Appeal 3.3.2, 13 January 1992, (1992) E.P.O.R. 163.
[482] Id.
[483] Id.
[484] Id. at 166.
[485] Id.
[486] Id.
[487] Id.
[488] Id. at 167.

correspond to each other in both plasmids as sufficient and convincing proof in view of which the mentioned tiny differences are negligible[489].

Based on the evidence, the Board concluded that the plasmid pCGl is the same as the claimed plasmid pHM 1519, making the claimed plasmid not novel in the light of the prior art.

The case elucidates that comparison of five percent of the DNA sequence might be sufficient to negate novelty of an invention.

Decision T301/87[490]

The patent in suit was broadly concerned with providing an improved route through recombinant DNA technology to certain types of interferons, and had been revoked by the Opposition Division on ground of lack of novelty among other grounds[491].

The Board stated that a gene sequence cannot be declared as not novel based upon hybrid phages contained in ' Lawn's gene bank', a public collection of some 240,000 fetal human chromosomes because the availability of the claimed fragment cannot be ascertained without undue burden[492]. The Board further stated that if an entity itself is disclosed in a priority document to the skilled person, it does not necessarily mean that a component part is also disclosed for purpose of priority if it cannot be envisaged directly and unambiguously as such, and requires considerable investigation to reveal its identity[493]. Accordingly, the Board stated that the contention that the reference to the 'II-206' sequence and corresponding deposition of a strain

[489] Id.
[490] Biogen/Recombinant Dna(Oppositions by Hoffmann la Roche; Upjohn; Boehringer Ingelheim Zentrale; Bender; Cetus; Hoechst; Boehringer Mannheim, T301/87, Technical Board of Appeal 3.3.2, 16 February 1989, (1990) E.P.O.R. 190.
[491] Id.
[492] Id.
[493] Id.

containing the total sequence in a recombinant form established by implication priority for a part of the sequence cannot be accepted for negating novelty. In the light of the reasoning, the court held the claimed sequence to be novel[494].

As per this case, existence of a gene library with thousands of sequences will not anticipate a gene fragment within it.

The Decisions of the EPO have attempted to define certain guidelines for genes and gene based inventions. The principles laid down by the cases can be summarized as follows:

a. cDNA sequence of a protein in human body is novel as it is different from what exists in the human body.
b. Isolation of a gene of a known protein for the first time through conventional methods would make the gene sequence novel.
c. A prior art reference has to be clear, certain and specific and should contain all elements in the subject matter of the claimed invention in order to negate novelty.
d. Lack of specificity, successful experiments and certainty in a prior art reference would not anticipate an invention.
e. A prior art reference disclosing a partial sequence coding for a particular protein cannot negate the novelty of the complete sequence coding for the same protein.
f. A lawn gene bank will not anticipate a gene isolated from it in the absence of a known probe, or any other means, enabling the sequence to be identified.
g. Existence of a gene library with thousands of sequences will not anticipate a gene fragment within it.
h. References citing general information without specific inputs relating to the invention based on which a person with ordinary skill cannot deduce the invention will not negate novelty of a claimed protein or DNA sequence.

[494] Id.

INDIA

In India, an invention is patentable only if it satisfies the requirement of newness specified under section 2(j), which defines a 'new invention' as any invention or technology which has not been anticipated by publication in any document or used in the country or elsewhere in the world before the date of filing of patent application[495]. Due to dearth of legislative history and judicial interpretation in India, the only source of explanation is the patent manual. The Manual provides that biological material such as recombinant DNA, Plasmids and processes of manufacturing thereof are patentable provided they are produced by substantive human intervention[496]. Based on the Manual's guideline, the patent office and courts might consider isolated gene sequences and related inventions to be patentable, as their isolation requires active human intervention.

Patent/Public Domain Analysis

Novelty filter determines the entry of inventions into the public domain based on the newness of the invention. An invention, which is new in the light of prior art, would be eligible for patent domain and an invention, which is not new, would enter into the public domain. The basic principles for determining novelty of a gene based invention are almost the same in all countries and therefore, there is not much variation in the size of patent or public domain based on differences in novelty criteria. Patent Laws of all countries consider isolated gene sequences to be patentable as they are different from their naturally existing counter parts. Existence of a partial sequence would not negate the novelty of the full sequence and existence of a full sequence in the prior art would not negate the novelty of a part of it. Furthermore, all three

[495] Section 2(l), Indian Patent Act, 1970 as amended in 2005.
[496] Annexure - I, Examination Guidelines for Patent Applications relating to Inventions in the field of Chemicals, Pharmaceuticals and Biotechnology, Manual of Patent Practice and Procedure, 2005.

countries require limitations in the prior art to be present in the invention in order to anticipate the invention. On a general basis, all three countries have uniform criteria for novelty.

The Comparative Study on Biotechnology Patent Practices done by USPTO, EPO and JPO, elucidates the uniformity in novelty related provisions. The study presents a case to explain the novelty requirement.
Case

The prior art (Y) is a structural gene encoding a functional polypeptide, the whole sequence of which is disclosed. The claimed invention (Y') is a partial DNA fragment of Y[497].

The three offices opined that inventions that relate to a partial sequence will fall within the scope of novelty when the invention has not been disclosed in concrete terms in publicly known literature. As the DNA fragment is an isolated compound that is different from the full-length gene compound, the patent offices stated that full-length gene sequence forming part of the state of the art is not novelty destroying to the DNA fragment[498]. The sequence would be novel in India also under the same logic.

Though the principles are overall uniform in all countries, USA by following the first to invent rule makes the novelty filter for genetic inventions a little tough to pass through when compared to India and Europe. Prior conception can destroy the novelty of an invention if it can be substantiated by proper evidence. So, lab notebooks of genetic inventions acquire more importance in USA then in other countries. So, it is very much possible to lose the novelty of an invention in USA if the inventor fails to maintain lab notebooks. Most novelty litigation in the US revolves around priority of conception. So, US

[497] Id.
[498] Id.

novelty is a little stringent, which means that there is a possibility of more genetic inventions getting into the public domain when compared to India and Europe. Furthermore, the US novelty criteria is also slightly more stringent than India and Europe because it requires reduction to practice to prove conception of gene related inventions. To conclude, the novelty requirement is overall uniform in all three countries with US criteria being a little more stringent than in other countries. On the whole, there is not much variation in the size of public or patent domain due to differences in novelty criteria.