invention certain of our statements were not, from a scientific standpoint, precisely accurate."[66] As Judge Buffington indicated in his dissent, one cannot hold much respect for a decision that characterizes not just "ductile tungsten" as a "product of nature," but "a *wire* formed of ductile tungsten" as well.[67]

The other troublesome case is *Ex parte Frohardt.*[68] The rejected claim was directed to streptimidone, an antibiotic serendipitously produced in the fermentation broth obtained in the production of another antibiotic according to the teaching of a Belgian patent. The Belgian patent did *not* teach that streptimidone was present; it merely existed in the broth, unrecognized by any save Frohardt, Dion, and Ehrlich. The Board refused to equate "new" in 35 U.S.C. 101 with "previously unknown." It did not, however, go so far as to read 35 U.S.C. 101 as imposing an absolute novelty standard with regard to biological products. It distinguished *Ex parte Hillyer* [69] on the grounds that "(t)he claims in the present case are not limited to a pure compound or to the compound freed from the fermentation broth."

In *Ex parte Hillyer,* applicant had claimed as a composition of matter a particular chemical in a composition "substantially free from other compounds." It had previously existed as an unrecognized byproduct of prior art processes. The Board stated that the "claimed compounds existed only in undesirable polymeric byproducts of no recognized utility.[70] If the Board in *Frohardt* had equated the word "new" in 35 U.S.C. 101 with "previously unknown publicly in this country" (see 35 U.S.C. 102(a)), and tested the streptimidone claim under 35 U.S.C. 103, they would have confronted the fact that the prior art did *not* teach that streptimidone was present in the broth, hence, the art did not teach any advantage to isolating streptimidone in pure form.

Three recent cases appear to restore sanity. *In re Seaborg*[71]

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[66] Id., 650-651 (on petition for rehearing).
[67] Id., 648-650 (dissenting op.).
[68] 139 U.S.P.Q. 377 (POBA 1962).
[69] 102 U.S.P.Q. 126 (POBA 1953).
[70] Id., 128 (2-1 decision).

define the word "new" as used in §101 in any different manner.

. . .

Pure materials necessarily differ from less pure or impure materials and, if the latter are the only ones existing and available as a standard of reference, as seems to be the situation here, perforce the "pure" materials are "new" with respect to them.

. . .

Whether the claimed pure materials have the same usefulness or assortment of properties as the impure materials of the prior art, as the board here found, is a question having no bearing on the factual and legal matter whether pure materials are new vis-a-vis impure materials within the meaning of §101, although it is but one of the factors to be considered in determining their obviousness under 35 U.S.C. §103.[77]

As the CCPA pointed out, the novelty/nonobviousness distinction was also drawn in a racemic mixture case, *In re Williams:* "The existence of a compound as an ingredient of another substance does not negative novelty in a claim to the pure compound, although it may, of course, render the claim unpatentable for lack of invention.[78]

In *Bergy,* the applicant claimed

A biologically pure culture of the microorganism *Streptomyces Vellosus,* having the identifying characteristics of NRRL 8037, said culture being capable of producing the antibiotic lincomycin in a recoverable quantity upon fermentation in an aqueous nutrient medium containing assimilable sources of carbon, nitrogen and inorganic substances.[79]

The examiner rejected this claim as one directed to an unpatentable "product of nature," citing Manual of Patent Examining Procedure, Section 706.03(a): "a thing occurring in nature, which is substantially unaltered, is not a "manufacture.' "

What is the "thing occurring in nature"? Is it the organism,

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[77] Id., 1401-1402.

[78] In re Bergstrom, 427 F.2d at 1402, quoting from In re Williams, 171 F.2d 319 (1948).

[79] 596 F.2d 952, 967 (CCPA 1979).

only rarely hears patent cases; and because it is amply supported by precedent.

In *Scripps Clinic and Research Foundation v. Genentech, Inc.*, the district court commented: "There is no dispute over the patentability of a Factor VIII:C preparation. Although Factor VIII:C molecules occur in nature, a purified and concentrated preparation of Factor VIII:C as claimed in the patent constitutes a new form or combination not existing in nature, and hence is patentable under 35 U.S.C. 101.[82.1]

Chapter 4 will discuss the claim drafting problems created by the "product of nature" doctrine.

§ 3.05 "Altered" Products of Nature

Several cases have refused protection to plant and animal products from which the applicant merely excised the inedible or unusable portions. Thus, in *Ex parte Latimer,* the Commissioner of Patents stated that the fiber of the needle of the *Pinus australis* tree was an unpatentable product of nature.[83] A similar result was reached by the Patent Office Board of Appeals in *Ex parte Grayson* with regard to a claim to headless and deveined shrimp.[84] These decisions would themselves be more palatable if they were based on 35 U.S.C. 103, rather than on 35 U.S.C. 101. I do not know whether mermaids swim across the Mediterranean, but headless and deveined shrimp certainly do not. The proper objection to a claim to such shrimp was that it was obvious to anyone skilled in the culinary art that the shrimp would be more palatable if thus prepared, and that the method of so preparing them was in turn obvious.

One may envision circumstances which would justify a patent on a specifically prepared plant cutting or animal carcass. The first person to learn how to cook the deadly scorpionfish of the Orient so as to detoxify it, or the first person to excise the poisonous parts of the rhubarb plant, may well have made a patentable discovery thereby. Should they not be able to

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[82.1] 3 U.S.P.Q.2d 1481, 1487 n.6 (N.D. Cal. 1987).

[83] 1889 Comm'r Decis. 123, 127, reprinting 46 Off. Gaz. (Pat. Off.) 1638.

[84] 51 U.S.P.Q. 413, 414 (POBA 1941).

these customs cases, the Supreme Court followed the general legal principle that the customs law is construed, when ambiguous, in favor of the importer.[88] Third, it failed to provide any comprehensible standard for determining when a "product of nature" had been transformed into an "article of manufacture." This author suggests that the better approach was to consider the treated orange to be a "possible patentable

(*Text continued on page 3-25*)

[88] Id., 14.

manufacture" and then to invalidate the claim for what then would have been called "want of invention," and is now (35 U.S.C. 103) characterized as "obviousness." (Brogdex's claims to the *method* of treating fruit by washing them in boric acid solution and then coating them with gelatin were invalidated because the "substance" of his invention had been revealed twenty years before.)

The essential arbitrariness of the judicial treatment of "altered products of nature" is demonstrated by comparing the *American Fruit Growers* holding with the decision of the Second Circuit in *Steinfur Patents Corp. v. William Beyer, Inc.*[89] This case related to the fur industry. The process claims related to a method of "bleaching naturally dark-colored fur skins without impair[ing the qualities] of the leather or hair. The skins so bleached [could] then be dyed the same colors as formerly could be successfully applied only to white or naturally light-colored furs. This resulted in a commercial advantage, as the dark-colored skins were cheaper.[90] The product claims covered the products of various stages of the bleaching and dyeing process.

The court rejected the contention that the product claims to these bleached fur skins were invalid under the *American Fruit Growers* test:

> It can hardly be doubted that a naturally dark-colored skin which has been bleached and dyed a light color is an article of manufacture. Certainly it cannot be said of it, as of the orange, that there is no change in its "name, appearance or general character." In none of the three stages sought to be protected by the present patent were the dressed skins in their natural state. While it was true of the orange that impregnation of its rind with borax only protected the natural article against deterioration by mold and gave it no new beneficial uses, the same cannot be said of impregnation of the unbleached skin with ferrous sulphate. By such impregnation the skin attains a new quality which gives it a new beneficial use; it fits it to be used for bleaching by a method which could not without such impregnation be successfully employed. An orange has the

[89] 62 F.2d 238 (2d Cir. 1932).
[90] Id., 239.

by the Chinese [and Malay] gardeners . . . *as an insecticide.* . . ."[95]

Another commendable decision was *Binney & Smith Co. v. United Carbon Co.*, holding patentable two claims to a new form of carbon black utilizable as filler by the rubber industry.

> 1. Substantially pure carbon black in the form of commercially uniform, comparatively small rounded, smooth aggregates having a spongy porous interior.
>
> 2. As an article of manufacture, a pellet of approximately one-sixteenth of an inch in diameter and formed of a porous mass of substantially pure carbon black.[96]

Carbon black had previously been available only in the form of a finely divided powder, which could be inhaled by the workmen handling it. The patentees, by binding the powder into a less pernicious form, solved "a problem which had baffled other technological experts," and their claims were entitled to a "liberal construction."[97]

In *Funk*, the case involved a claim for certain mixed cultures of nitrogen-fixing bacteria. The Supreme Court noted, without citing *American Fruit Growers*, several of the considerations referred to in the latter decision:

> Each of the species of root-nodule bacteria contained in the package infects the same group of leguminous plants which it always infected. No species acquires a different use. The combination of species produces no new bacteria, no change in the six species of bacteria, and no enlargement of the range of their utility. Each species has the same effect it always had. The bacteria perform in their natural way. Their use in combination does not improve in any way their natural functioning. They serve the ends nature originally provided and act quite independently of any effort of the patentee.[98]

Previously, we pointed out the *Steinfur* distinction between

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[95] Id., 148-150.

[96] 125 F.2d 255, 257 (4th Cir. 1942); reversed on other grounds, 317 U.S. 228 (1942), on remand 64 U.S.P.Q. 366 (D. Md. 1945).

[97] Id., 259.

[98] 333 U.S. at 131.

rabarty microorganism "plainly qualifies as patentable subject matter":

> His claim is not to a hitherto unknown natural phenomenon, but to a nonnaturally occurring manufacture or composition of matter—a product of human ingenuity "having a distinctive name, character [and] use." Hartranft v. Wiegmann, 121 U.S. 609, 615, 7 S. Ct. 1240, 1243, 30 L. Ed. 1012 (1887). The point is underscored dramatically by comparison of the invention here with that in Funk. There, the patentee had discovered that there existed in nature certain species of root-nodule bacteria which did not exert a mutually inhibitive effect on each other. He used that discovery to produce a mixed culture capable of inoculating the seeds of leguminous plants. Concluding that the patentee had discovered "only some of the handiwork of nature," the Court ruled the product nonpatentable. . . .
>
> Here, by contrast, the patentee has produced a new bacterium with markedly different characteristics from any found in nature and one having the potential for significant utility. His discovery is not nature's handiwork, but his own; accordingly it is patentable subject matter under §101.[103]

It is unfortunate that the Supreme Court reiterated the *American Fruit Growers* test (which was based on *Hartranft*), instead of squarely separating the Section 101 issue of patentable subject matter from the Section 103 issue of obviousness. This final step was taken in *Diamond v. Diehr*. This case involved a claim to a computer-controlled process of curing rubber, rejected as a combination of nonstatutory calculation steps and conventional curing process steps. The Supreme Court agreed with the CCPA that the rejection should be reversed: "In this case, it may later be determined that the respondents' process is not deserving of patent protection because it fails to satisfy the statutory conditions of novelty under §102 or nonobviousness under §103. A rejection on either of these grounds does not affect the determination that respondents' claims recited subject matter which was eligible for patent

[103] Diamond v. Chakrabarty, 100 S. Ct. 2204, 2208 (1980).

CHAPTER 4

Claiming and Enforcing Utility Patents for Microbiological Inventions Under U.S. Law

§ 4.01 Conditions of Patentability

[1] Generally

It is not the purpose of this book to present a detailed exegesis of patent law principles. Rather, this treatise will focus on the application of those principles to "biological" invention. Recognizing, however, that some readers may come from a background in biotechnology, rather than in patent law, this author offers this brief overview of the conditions for patentability.

One of the key provisions of the Patent Act is Section 102, which sets forth seven conditions which negate patentability:

that an invention is not new."[1] As the CCPA stated in *Nickola v. Peterson*, "prior public knowledge or use in a foreign country would destroy novelty if the novelty requirement resided merely in the word 'new' in the absolute sense in which it appears in §101. . . ."[2]

The "date of the invention" referred to in paragraphs (a), (e), and (g) is itself given a specialized meaning by 35 U.S.C. §104, which bars, with minor exceptions, the establishment of the date of invention by reference to knowledge, use or activities in a foreign country, other than the filing of an application relied upon for "priority" purposes under 35 U.S.C. §§119, 365.

Paragraphs (b), (c), (d), and (g) penalize those who put off applying for a patent. A year's delay, after open and nonexperimental use, or after sales activity, vitiates patentability under paragraph (b). Secret use of an invention may be regarded as "abandonment" under paragraph (c), "suppression" under paragraph (g), or "public use" under paragraph (b). Application for patent abroad, but not in the U.S., is considered a dedication of the invention to the public here when the foreign patent issues, if the condition of paragraph (d) is met.

The "date of the application for patent" referred to in those paragraphs is given a specialized meaning by 35 U.S.C. §§ 119, 365, allowing a U.S. applicant, under stated circumstances, to enjoy the benefit of an earlier filing date on his application for a patent for the same invention in a foreign country (the so-called "convention priority" application), and 35 U.S.C. §120, giving him, under stated circumstances, the benefit of his filing dates on earlier related applications (so-called continuation, continuation-in-part, and divisional applications) in the United States.

Finally, paragraph (f) is a restatement of the "originality" requirement set forth in 35 U.S.C. §§101, 111.

35 U.S.C. §103 is the linchpin of the Patent Act. It represents Congress' attempt to codify the *Hotchkiss v. Greenwood* (1851) definition of "invention": a contribution to the useful art requiring greater "ingenuity or skill . . . than that of an ordinary

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[1] P. J. Federico, Commentary on the New Patent Act, 35 USCA at 1 (1954).
[2] 580 F.2d 898 (6th Cir. 1978).

when it satisfies the condition of 35 U.S.C. §102(b),[5] or when the inventive entity designated in the prior patent is different from that named in the later application.[6]

Not infrequently, several researchers will independently achieve the same discovery. In the field of mathematics, the classic example is the development of the calculus by Newton and Leibnitz. Since the patent system is intended to reward the "first inventor," a complex "interference procedure" has arisen for resolving doubts as to priority of invention as between applicants still before the Patent Office, or between an applicant and a patentee. Section 102(g) formally bars claims by later inventors.

Section 102(g) requires consideration of three concepts: conception; reduction to practice; and diligence. Conception is "the formation in the mind of the inventor of a definite and permanent idea of the complete and operative invention as it is thereafter to be applied in practice," and is effective when it is first manifested to others.[7] A "projected plan for research" may constitute a "conception."[8]

"Reduction to practice" comes in two flavors. The filing of a patent application complying with Section 112 is a "constructive" reduction to practice. Actual reduction to practice is a demonstration, satisfactory to those skilled in the art, of the capacity of the inventive idea to achieve its intended purpose. It frequently necessitates testing, to establish this capacity, and testing under actual working conditions may in some cases be required. It is not necessary that the invention be brought to the level of salability. The inventor need not personally reduce the invention to practice, as acts of others—employees, consultants, suppliers, customers—undertaken at his request will inure to his benefit.

Diligence is activity aimed at reduction to practice, or legally excusable inactivity.

There are two basic rules of priority of invention: (1) *A*, the first to reduce the invention to practice, is the inventor *unless*

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[5] In re Jaeger, 241 F.2d 723 (CCPA 1957).

[6] In re Bass, 474 F.2d 1276 (CCPA 1973).

[7] Mergenthaler v. Scudder, 11 App. D.C. 264, 1897 C.D. 724 (D.C. Cir. 1897).

[8] Lazo v. Tso, 480 F.2d 908 (CCPA 1973).

that there was no more concealment of the safes "than was inseparable from any legitimate use of them"; in *Manning v. Cape Ann Isinglass,* it referred to the use without "injunction of secrecy"; and in *Electric Storage Battery v. Shimadzu,* it noted the absence of effort to conceal the manufacturing methods "from anyone who had a legitimate interest in understanding them."[10] Despite these dicta, the courts have tended to regard secret use with the inventor's consent as a "public use" under 35 U.S.C. §102(b). Thus, Judge Learned Hand, in *Metallizing Engineering Company v. Kenyon Bearing and Auto Parts Company,* declared that the competitive use of an invention, in secret, beyond the "grace period" set forth in the statute, forfeits the right to apply for a patent. It was "the fiat of Congress that it is part of the consideration for a patent that the public shall as soon as possible begin to enjoy the disclosure." Eventually, as Judge Hand saw it, the inventor "must content himself with either secrecy, or legal monopoly."[11]

In the earlier case of *Macbeth-Evans Glass Co. v. General Electric Co.,* nine years of secret use for profit of a glassmaking method was held to have resulted in an abandonment or forfeiture.[12] Whether the defect is characterized as "public use" or "abandonment," it is clear that the courts will not permit an inventor "to hold back from the knowledge of the public the secrets of his invention," to retain the monopoly "for a long period of years" and "gather the whole profits of it," and then apply for patent only when forced to by the "danger of competition," lest they "give a premium to those who should be least prompt to communicate their discoveries."[13]

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[10] Worley v. Loker Tobacco, 104 U.S. 340 (1882); Hall v. MacNeale, 107 U.S. 90 (1883); Manning v. Cape Ann Isinglass, 108 U.S. 462 (1883); and Electric Storage Battery v. Shimadzu, 307 U.S. 5 (1939).

[11] 153 F.2d 516, 519-20.

[12] 246 F. 695 (6th Cir. 1917).

[13] Pennock v. Dialogue, 27 U.S. (2 Pet) 1 (1829).

tain predetermined desired properties."[15] Judge Smith also pointed out that "[s]hould a plant variety become extinct one cannot deliberately produce a duplicate even though its ancestry and the techniques of cross-pollination be known."[16] Thus, this prior publication did not meet the legal requirements for the bar stated in 35 U.S.C. §102(b) as it did not communicate where the necessary starting material could be obtained.

The *LeGrice* holding was not a "plant patent anomaly," it was the logical consequence of the application of the requirement that a publication be enabling in order to be anticipatory to unusual subject matter—a mutable, ephemeral, living invention. The *LeGrice* court made it clear it was applying traditional §102(b) standards.

The *LeGrice* holding was specifically applied to a utility patent application in *Ex parte Argoudelis* (1966). The examiner had cited a Japanese reference which disclosed that an antibiotic with properties identical to applicants' sparsogenin A had been obtained in Japan from the fermentation broth of a strain of actinomyces isolated from the soil of Chiba prefecture, Japan, and described the cultivation of this strain. Argoudelis relied on the *LeGrice* decision. The Board declared

> It cannot be denied that In re *LeGrice*, supra, applies to the publication cited in this application to the same extent that it applied to the publications cited in that case. Moreover, we have ourselves held that a written description of the character involved in a case such as the present one is not sufficient to enable a person skilled in the art to produce the invention.[17]

More recently, *In re Mancy* (1974) implied that a new organism could not be found obvious with respect to an organism reported in the literature unless the latter organism was available from a public depository: "Without *Streptomyces bifurcus*, strain DS 23, 219, . . . availability of which is supplied by appellant's deposit of the microorganism. . . , one skilled in the art would not find it obvious to produce daunorubicin by aero-

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[15] 133 U.S.P.Q. at 373.
[16] Id., 370.
[17] 157 U.S.P.Q. at 440.

able sources of carbon, nitrogen and inorganic substances, and separating daunorubicin formed during the culture.[19]

Prior art references disclosed that daunorubicin could be produced by aerobically cultivating *S. coeruleorubicus* 8899, *S. Coeruleorubicus* 31723, and certain cultures of *S. peucetius.*

The Board took the position that the "choice of a different strain of the same [species] is *prima facie* obvious," *i.e.* applicant was obligated to show an unexpected result from the use of the new strain.

The concept of *"prima facie* obviousness" is illustrated by the example of the homologous series in chemistry. All members of the alkane series possess similar chemical and physical properties, and the properties of the higher homologs could be predicted from the properties of the lower homologs. What makes chemistry interesting is the fact that such predictions are not always correct.

Thus, *In re Papesch* held that a triethyl-substituted heterocyclic compound was patentable over the homologous trimethyl-substituted compound when the prior art did not teach that the latter had the anti-inflammatory bioactivity of the

(*Text continued on page 4-13*)

[19] 182 U.S.P.Q. 303, 304 (CCPA 1974).

former.[20] Even more dramatic was *In re Lambooy,* which found that prior art riboflavin was a "metabolite" while the claimed "homolog" was an "antimetabolite."[21]

In *Mancy,* the Board relied on its prior decisions in *Ex parte Arzberger*[22] and *Ex parte Kropp.*[23]

In *Ex parte Arzberger,* without citation, the Board of Appeals affirmed the rejection of claims 1-4, based "on the general principle that the choice of a closely related microorganism or a different strain of the same microorganism is prima facie obvious." The applicant had discovered that a new strain of *Brevibacterium divaricatum,* specifically, NRRL B-2620, gave improved yields of L-glutamic acid as compared to prior art strains NRRL B-2311 and 2312. (Implicitly, the Board found that the yields were not improved to an unexpected degree, since it overturned the rejection of claims 5-10, reciting the presence of prior art growth promoters, since the "promoted" yields obtained were "unexpectedly increased.")

In *Kropp,* the applicant failed to show that the antibiotic produced by his *Streptomyces* strain was in any way noteworthy, and the Board seems to have held that the applicant had merely followed the teaching of the art that antibiotics may be obtained by culturing *Streptomyces* strains.

The CCPA reversed, relying on its *In re Kuehl* decision.

In *Kuehl,* applicant had used a *novel* aluminosilicate zeolite, ZK-22, as a catalyst in hydrocarbon cracking processes. The prior art showed the use of other zeolites as hydrocarbon cracking catalysts. The Patent Office felt that applicant, having discovered a new zeolite, had naturally tried it out as a catalyst, and that he had to show that it gave unexpected results. The CCPA disagreed, since "one having no knowledge of the [novel zeolite] would not find it obvious to crack hydrocarbons using it as a catalyst.[24]

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[20] 315 F.2d 381 (CCPA 1963).

[21] 300 F.3d 950 (CCPA 1962).

[22] 155 U.S.P.Q. 286 (POBA 1966).

[23] 143 U.S.P.Q. 148 (POBA 1959).

[24] 475 F.2d 658 (CCPA 1973). On the other hand, had Kuehl used 7K-22 in defiance of a prior generic claim in use of aluminosilicate zeolites as cracking catalysts, he would certainly have been deemed an infringer.

the organism, so it is not excluded as "prior art" on the basis of §112. It may be argued, however, that a culture deposit is not a "printed publication" within the intent of 35 U.S.C. §102(b). Does "printed" have its commonplace meaning, or did its meaning change as methods of information storage and retrieval changed?

Chisum's Law of Patents explains that "[i]n 1836, when provision for printed publications as a source of anticipation was first made, printing was the only means of making information widely available. . . . The trend of court decisions is toward a broad interpretation of printed that encompasses all material available to the public in a tangible form."[27]

No case has considered whether a culture deposit is *per se,* a printed publication. Several views of its status could be taken, based on analogy with the "thesis" and "microfilm" cases.

One possible view of the law is that any unrestricted deposit is "prior art." In *Hamilton Laboratories, Inc. v. Massengill* (1940), a "thesis" case, the Sixth Circuit suggested that "intent that the fruits of research be available to the public is determinative of publication."[28] A deposit of a culture, without restriction, is indicative of such an intent. This case did not suggest that indexing was necessary.

An NRRL (ARS) unrestricted deposit, since it becomes the property of the Department of Agriculture, is more likely to be considered indicative of an intent to disseminate the organism to the public than an ATCC deposit, since the depositor retains ownership of the latter.

The *Hamilton* test was severely criticized by the CCPA in *In re Bayer* [, 568 F.2d 1357, 1362 (CCPA 1978)], wherein it was called an "ill-conceived" expression of the applicable law. In *Bayer,* the applicant was also the author of the reference, and the fact that he filed a patent application "belie[d] any intent on appellant's part that the 'fruits of his research' were to be available to the public."

A second view was expressed by the CCPA in *In re Tenney* (1958). After World War II, the U.S. Government recorded all unpublished German patent applications on microfilm for

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[27] §3.04[3] at 3-22 (1981).

[28] Hamilton Labs., Inc. v. Massengill, 111 F.2d 584 (6th Cir. 1940).

DeGrunigen and *Gulliksen* decisions.[35] In *Bayer,* the examiner took the position that the thesis was available as a reference as of its date of receipt by the library. When received, these were accumulated in a library office accessible only to library employees. Eventually, the thesis were catalogued, bound, and finally shelved for use by the public. The Board affirmed, on a somewhat different ground. It felt that the thesis could not be available as a reference on the date of receipt, since it was not shelved. The Board held, however, that since applicant's thesis defense announced the availability of his thesis to his faculty committee, who then could obtain a copy thereof, or disclose the existence and location of the thesis to others, the thesis was "published" under 35 U.S.C. §102(b). Noting that the touchstone of 35 U.S.C. §102(b) is "public accessibility," the CCPA held that an "uncatalogued, unshelved thesis" was not, "by virtue of its accessibility to the graduate committee," a "publication." Since the CCPA opinion emphasized that the thesis was "unshelved," it cannot be said to have overruled the earlier Board decisions. The CCPA did, however, observe that "since appellant's thesis could have been located in the university library only by one having been informed of its existence by the faculty committee, and not by means of the customary research aids available in the library, the 'probability of public knowledge of the contents . . .' was virtually nil." [568 F.2d at 1361.]

Clearly, under these decisions, a deposit in the American Type Culture Collection would be effective as a reference at least from the date it was listed in the ATCC catalogue, or referenced in the literature. Before that time, the deposit would be analogous, one might argue, to the "uncatalogued, unshelved thesis" in *Bayer.* You cannot "browse" through a culture collection and discover a culture the way one can browse through library shelves of uncatalogued (or poorly catalogued) materials.

While an ARS deposit is necessarily available to USDA researchers, this does not necessarily render it prior art, in the absence of evidence that private individuals could obtain a

[35] 568 F.2d 1357 (CCPA 1978).

The National Institute of Mental Health has a complex system for reviewing grant proposals. The process begins with a grant application, which describes, inter alia, the "research protocol and design." A member of an initial review group (IRG), formed of eminent consultants, visits the applicant and prepares an "on site" visit report. After the IRG recommends approval or disapproval, an NIMM staff member summarizes their deliberations in the so-called "pink sheet," which, together with the application and any information added by the NIMM staff, is reveiwed by NAMMC, comprised of both public officials and outside experts. The D.C. Circuit, faced with an FOIA request for the applications, visit reports and "pink sheets" pertaining to eleven specified pharmaceutical research projects, held (1) a noncommercial scientist's research design is not literally a trade secret and therefore is not within the "trade secret" exemption (5 U.S.C. §552(b)(4); and (2) that the visit reports and "pink sheets" were exempt as "intra-agency memoranda" (5 U.S.C. §552(b)(5).[39]

In view of the reporting requirements for recombinant DNA research inventions, concern was expressed that such disclosures, if available under FOIA, might trigger 35 U.S.C. §102(b). This issue was debated by the interagency committee on Recombinant DNA Research[40] which, by a vote of 16-2, recommended:

> The legislation should provide that all records submitted to, or otherwise obtained by, the Secretary or his representatives under the legislation shall be available to the public upon request, except (a) information now exempt from disclosure under the Freedom of Information Act, and (b) other information the disclosure of which would cause the loss of proprietary rights.
>
> At the time of request, persons who have submitted records should be given an opportunity to identify those portions which they believe to be excepted from disclosure under the preced-

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for internal agency disclosure of trade secrets); Pennwalt Corp. v. Costle, — F. Supp. — (E.D. Pa. 1981), 530 PTCJ A-1 (1981) (enjoins EPA from disclosing trade secrets to the public); S. 1247 in 539 PTCJ A-5 (1981).

[39] Washington Research Projects Inc. v. DHEW, 504 F.2d 238, 244 (1974).

[40] Minutes of March 10, and 14, 1977.

filing. When theChrysler case was examined by an association of patent attorneys concerned with foreign patent effects of the FOIA, their legislative newletter concluded: "(W)hether or not the invention has been disclosed in fact to someone outside of the U.S. Government is of no relevance. The possibility of having access is sufficient for divulgation."

The patent group called for support of legislation pending in 1979 which would provide a "reasonable time" of secrecy for contractor inventions. Whether these bills will pass and whether they will provide relief remains to be seen. [O'Reilly, Federal Information Disclosure §10.13 (1980), citing EPC Art. 54(1); Nat'l Council of Patent Law Ass'ns "Legislative Letter No. 7" (June 1, 1979); S. 414 and S. 1215, 96th Cong., 1st Sess. (1979).]

[9] Sources of Information for Prior Art Searches

The most important sources of prior art in the field of biotechnology are conference abstracts and papers, technical articles, and books of the "annual review" variety. Material of a fairly clinical orientation may be searched on Index Medicus, or its on-line counterpart, MEDLINE. For material that emphasizes molecular biology, look in Chemical Abstracts or Biosis Previews. A number of specialized abstracting journals are helpful for monitoring current developments, *e.g.*, Derwent Biotechnology Abstracts, the Telegen Reporter, and the Royal Institute of Chemistry's Current Biotechnology Abstracts. The searcher should realize that these services cover journals more comprehensively than they do conference papers or books.

The second most important source of prior art would be published foreign patent applications. Ideally, these would be searched by a foreign patent attorney, knowledgeable in biotechnology, and having access to search facilities where these materials are grouped according to the International Patent Classification. American attorneys who rely on the examiners' collections of foreign art may be painfully surprised, since their collections are woefully incomplete, at least in biotechnology. It is better to use one of the on-line services, such as Derwent World Patent Index, or Pergamon Patsearch or

of a scientific paper might not be designated as one of the "joint inventors" of the invention described in that paper and claimed in a patent application filed shortly thereafter.

"Joint Inventorship" is recognized by 35 U.S.C. §116: "when an invention is made by two or more persons jointly, they shall apply for a patent jointly and each sign the application and the required oath. . . ." "Joint invention" itself has been defined by *Monsanto Co. v. Kamp*:[43]

> A joint invention is the product of collaboration of the inventive endeavors of two or more persons working toward the same end and producing an invention by their aggregate efforts. To constitute a joint invention, it is necessary that each of the inventors work on the same subject matter and make some contribution to the inventive thought and to the final result. Each needs to perform but a part of the task if an invention emerges from all of the steps taken together. It is not necessary that the entire inventive concept should occur to each of the joint inventors, or that the two should physically work on the project together. One may take a step at one time, the other an approach at different times. One may do more of the experimental work while the other makes suggestions from time to time. The fact that each of the inventors plays a different role and that the contribution of one may not be as great as that of another, does not detract from the fact that the invention is joint, if each makes some original contribution, though partial, to the final solution of the problem.

There are two types of contributions which a "co-author" may have made to a scientific study which would not be an "inventive contribution." First, the co-author may have diligently performed certain tedious or technically difficult tasks under the instructions of another.[44] Second, he may have been the administrative head of the laboratory, but not one provid-

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[43] 269 F. Supp. 818, 824 (D.D.C. 1967).

[44] Mineral Separation, Ltd. v. Hyde, 242 U.S. 261 (1916); Layne-New York Co. v. Allied Asphalt Co., 363 F. Supp. 299, 180 USPQ 81 (W.D. Pa. 1973); Mueller Brass Co. v. Reading Indus., Inc., 352 F. Supp. 1357, 1372 (E.D. Pa. 1972) aff'd 487 F.2d 1395 (3d Cir. 1973).

The "theory of the inventorship entity" states that when two individuals, *A* and *B*, have worked on a new development there are *three* possible inventorship entities: *A* alone, *B* alone, and *A* and *B* jointly. Consequently, the PTO has taken the position that a patent to *A* and *B* jointly may be prior art against an application filed later by *B*, unless *B* can show by affidavit that he developed the invention prior to the effective date of the patent as a reference.[49]

When the cited reference is a printed publication, and the applicant is one of the co-authors, the publication may be removed as a reference by obtaining a suitable affidavit from the other co-authors.

> We are of the opinion that the disclaiming affidavit of Senta Amon is effective in removing the Hirschler et al. article as a reference. The factual situation in the Harris case relied on by the examiner was quite different from that here present. In that case the reference sought to be overcome was a patent granted to joint inventors. The application for patent had been filed in the names of Harris and Epstein as joint applicants. Epstein had made the usual oath that he was the joint inventor with Harris of the invention described and claimed in the application, and on the basis of that sworn representation the patent was issued to Harris and Epstein as joint inventors. Epstein's later affidavit filed in the Harris application in the nature of a disclaimer of any common subject matter was inconsistent with his oath in the Harris and Epstein application. In the present situation the reference involved is not a patent containing a sworn statement as to inventorship, and we are of the view that an affidavit which points out that affiant took no part in writing the article and was not the inventor of the subject matter described in the article, but was merely listed as co-author of the article in order to receive credit for having collaborated on the research program under the directions of the present appellant, is properly acceptable and that the article may be considered the sole work of present appellant. Since the article is not a statutory bar, it is not effective as a reference. The rejection based on the Hirschler et al. article will, accordingly, not be sustained.[50]

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[49] MPEP §715.01(a).

[50] Ex parte Hirschler, 110 USPQ 384, 386 (POBA 1952).

a Rule 131 Affidavit. The Examiner apparently found this satisfactory.

The *Hirschler* rule has been drastically modified by *In re Katz* (1982). While *Hirschler*-style disclaimers may still be filed, they are not mandatory. In the *Katz* case, Dr. Katz, and two students working under his direction, were coauthors of a PNAS article. Eight months later, Dr. Katz filed an application as sole inventor of certain therapeutic immunosuppressive agents described in that article. While agreeing that the examiner could reasonably infer that the coauthors were also coinventors, the CCPA held that as soon as Dr. Katz came forward with an alternative explanation for the designation—that they were being rewarded for performing various assays under his supervision—the rejection should have been withdrawn. This procedure was successfully followed (after some travail) by Bertram Rowland during his prosecution of the Cohen and Boyer product application.

Patent applicants can minimize problems by preparing, before an application is filed, a written description of the contribution of each person who worked on the project and the basis for naming them (or not naming them) as inventors. If possible, this inquiry should be made before the article is published, and a review procedure should be provided whereby a putative coinventor may challenge the determination. Those who are not thought to be joint inventors may be asked to sign disclaimers.

When a patent is issued which fraudulently misstates the inventorship entity, the patent will be held invalid.[51] Normally, however, "misjoinder" and "nonjoinder" are disfavored defenses, and the patentee will be permitted to correct the statement of inventorship *via* a certificate of error under 35 U.S.C. §256.

(*Text continued on page 4-27*)

[51] Iron Ore Co. of Canada v. Dow Chemical Co., 177 USPQ 34 (D. Utah 1972), aff'd on other grounds 500 F.2d 189 (10th Cir. 1974)(intent to defraud University of Utah, employer of the actual sole inventor Cook).

[52] [Reserved.]

[11] It Is the Person Selecting Compounds or Organisms for Screening for a Particular Purpose, Not the Person Who Screens Them, and Finds One Satisfactory, Who Is the Inventor of that Satisfactory Compound or Organism

In *MacMillan v. Moffett* (1970),[53] Moffett, a recognized expert on anticholinergic compounds, selected sixty-nine such compounds as possible topical antiperspirants, from a field of over five-hundred possible or known anticholinergics, and sent samples to MacMillan, a topical antiperspirant expert, for testing. MacMillan found that U-5008 was "outstandingly effective" as a topical antiperspirant. The CCPA held that Moffett was the inventor since Moffett "thought specifically" about the tested compounds in connection with the discovered use. (The CCPA noted that the discovery of the special efficacy of U-5008 *might* be a separate, though subservient, patentable invention.)

[12] Appreciation that One Is Dealing With a Novel Substance or Organism May Be a Necessary Part of "Conception" and "Reduction to Practice"

It has been held that conception and reduction to practice of a novel substance is not established until the inventor appreciates that he is dealing with a new substance. The leading case is *Heard v. Burton* (1964).[54] For four years, Heard failed to appreciate that he was utilizing a novel form of alumina, rather than the gamma alumina known to the prior art. In *Silvestri v. Grant* (1974), the synthesis of ampicillin II was effective when researchers at Bristol Myers recognized that they were dealing with a new form of ampicillin, even though they had not yet appreciated all of its properties, or its structure.[55] The "appreciation" doctrine may be applicable, not

[53] 432 F.2d 1237, 1239 (CCPA 1970).
[54] 333 F.2d 239 (CCPA 1964).
[55] 496 F.2d 593 (CCPA 1974).

In *Alpert v. Slatin* (1962), this observation was elevated to the dignity of a rule of law: "In this type of research the inventor's mint cannot formulate a completed invention until he finally performs a successful experiment.[58] On the other hand, the "extensive testing on animals done at Merck" on nortryptyline, even after Engelhardt expressed his belief that it would act as an antidepressant, was held not to refute Engelhardt's contention that he had conceived of this use prior to the tests which confirmed it.[59]

[15] Conduct of Fermentation and RDNA Research Abroad May Result in Priority Problems

A significant amount of pharmaceutical research by U.S. companies is carried out in foreign facilities, often because the regulatory climate abroad is more temperate than in this country. During the furor over recombinant DNA research, several researchers sought refuge in other lands.

If research is conducted abroad, the researcher's patent rights are decidedly more vulnerable than if they were based on domestic research. 35 U.S.C. §104 provides:

> In proceedings in the Patent and Trademark Office and in the courts, an applicant for a patent, or a patentee, may not establish a date of invention by reference to knowledge or use thereof, or other activity with respect thereto, in a foreign country, except as provided in sections 119 and 365 of this title [35 U.S.C. §§119, 365]. Where an invention was made by a person, civil or military, while domiciled in the United States and serving in a foreign country in connection with operations by or on behalf of the United States, he shall be entitled to the same rights of priority with respect to such invention as if the same had been made in the United States.

What does this mean? It means that one who makes his invention in a foreign country cannot carry the date of his invention before the effective filing date of his U.S. application

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[58] 305 F.2d 891 (CCPA 1962).

[59] Rey-Bellet v. Engelhardt, 493 F.2d 1380 (CCPA 1974).

failing to subject the windshields "to conditions of vibration, temperature, pressure, moisture, and air flow, simulating those encountered in actual flight," for a reasonable time.[63]

The talisman is of course, the testing required by "persons qualified in the art.[64] In *Farrand Optical Co. v. United States* (1963), the inventor did not seek to "overcom[e] peculiar optical problems encountered in flight," and his window sill testing of his hemispheric view bombsight was deemed sufficient.[65] Similarly, in *Harrison v. Cadwell* (1930), the laboratory tests proved "conclusively the character of vulcanization obtained." The court warned of "very grave consequences for future inventions" if these tests were not regarded a reduction to practice.[66]

The environmental sciences are, however, a field in which it has proven difficult to predict the effects of man's activities.

Smith v. Bousquet (1940) held that field testing of a new pesticide was necessary to actually reduce it to practice. The Interference Examiner was of the opinion that Smith's laboratory tests sufficiently approximated natural conditions. The CCPA, however, noted that Mr. Vogel's report stated

> [I]t should be borne in mind that the results given . . . pertain to laboratory conditions. No data is at hand which throws any light on the possible performance of the chemicals used if applied under outdoor conditions where the influence of such factors as variable temperature, rain, sunlight, etc., would be felt. Neither is there any information relative to the possible effect on growing plants.[67]

"Biological controls" must contend not only with the physical factors enumerated in *Smith*, but also with complex ecological interrelationships. It is doubtful that the multitudinous factors involved can be satisfactorily simulated.

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[63] 253 F.2d 433, 436 (CCPA 1958).

[64] Sinko Tool & Mfg. Co. v. Automatic Devices Corp., 157 F.2d 974, 977 (2d Cir. 1946) (L. Hand).

[65] 325 F.2d 328, 333-34 (2d Cir. 1963).

[66] 39 F.2d 704 (CCPA 1930).

[67] 111 F.2d 157, 163 (CCPA 1940).

predictable that a tested invention would operate as alleged. . . ."[69]

[18] Reduction to Practice in Vaccine Cases

An early vaccine case, *Reichel v. Dorset* (1920), held that the potency of a hog chotera "antitoxin" had to be tested by immunizing a hog and exposing it to the disease, for a reduction to practice to occur. The claimed invention was characterized as "an important step in a difficult art."[70]

In *Dick v. Lederle Antitoxin Laboratories,* the Dicks asserted a variety of claims to scarlet fever toxin and antitoxin, and the methods of obtaining them. Judge Coffey, in attempting to determine the Dick's actual "date of invention," determined that the satisfaction of Koch's postulates would constitute a reduction to practice. Robert Koch (1843-1910) had devised a theoretical framework for ascertaining whether a particular organism is the cause of a particular disease:

> (1) The suspected organism must be found constantly in the proper tissues of an animal suffering from or which has died from the disease.
>
> (2) The organism must be cultivated artificially in a pure state.
>
> (3) The disease must be reproduced in a suitable animal by inoculation with the pure culture.
>
> (4) The organism must be cultivated again from the tissues of the experiment animal.[71]

Judge Coffey did not review the proof associated with the second, third, and fourth laws. With regard to the satisfaction of the first law, he stated:

> There are two significant articles by the Dicks in the American Medical Association Journal. In one, on October 6, 1923, Exhibit

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[69] 311 F.2d 249, 257 (CCPA 1962).
[70] 262 F. 652 (App. D.C. 1920).
[71] 43 F.2d 628, 632 (S.D.N.Y. 1930).

of derivatives which have been synthesized and tested. The question arises whether an inventor is "diligent" when he cre-

(*Text continued on page 4-35*)

ates additional exemplary species, instead of filing an application for patent upon his initial discovery. In *Engelhardt v. Judd* (1966), the CCPA stated:

> We recognize that an inventor of a new series of compounds should not be forced to file applications piecemeal on each new member as it is synthesized, identified, and tested for utility. A reasonable amount of time should be allowed for completion of the research project on the whole series of new compounds, and a further reasonable time period should then be allowed for drafting and filing the patent application(s) thereon, without subjecting the prior inventor or his assignee to the risk of forfeiture of valuable patent rights due to alleged concealment or suppression of the invention.[74]

The need for a reasonable limitation on the proliferation of examples is suggested, implicitly, by *In re Burndy* (1981): "Early filing of an application [for novel therapeutics] . . . is to be encouraged. Requiring specific testing of the thousands of prostaglandin analogs encompassed by the present claim . . . would delay disclosure. . . ."[75]

[20] Microbiology as an "Analogous Art"

In *Graham v. John Deere Co.* (1966),[76] the Supreme Court noted that those skilled in the technological arts had become more and more likely to turn to allied fields for solutions to their problems.

As additional uses are found for microorganisms, the question will arise whether microbiology is an art "analogous" to the new fields of application. By way of example, during the heyday of DDT, was a pesticide chemist expected to know that Bacillus popillae was an insect pathogen? Should a pollution control technologist have been charged with knowledge of the literature on energy-generating plasmids prior to Chakrabar-

[74] 369 F.2d 408, 412 (CCPA 1966).
[75] 642 F.2d 430, 434 (CCPA 1981).
[76] 383 U.S. 1, 19 (1966).

the mutant strain "prima facie obvious" [182 USPQ 303 (1974)]. Whether the mutant strain is, in fact, "obvious" over the parent strain may be determined by weighing the considerations set forth in §4.03 *infra.*

Second, it might be argued that 35 U.S.C. §102(g) is a source of prior art under 35 U.S.C. §103. This will be discussed in the next subsection.

[22] Prior Discovery of a Similar Strain by Another, Though Unpublished, May Be Prior Art if Not Abandoned, Suppressed or Concealed

In *Sutter Products Co. v. Pettibone Mulliken Corp.* (1970), the Seventh Circuit held that a prior inventor's machine, though not publicly known, was "prior art" under Section 103.[79]

35 U.S.C. §102(g) art has three important limitations: (1) it includes only inventions reduced to practice in this country; (2) it does not include inventions which have been "abandoned, suppressed or concealed" and (3) it does not include inventions which are commonly assigned. While §102(f) art is not so limited, §102(g) art, unlike §102(f) art, encompasses inventions of which the applicant had no knowledge at the time he made his invention.

A deposit in a foreign depository, at first glance, might seem incapable of operating as §102(g) art. This first impression is weakened, however, if this deposit is accessible to U.S. researchers, and U.S. researchers indeed are known to request subcultures from that depository. *A fortiori,* if the depository lists the deposit in a catalogue available in this country, it may operate as §102(g) art. (Though it may then be §102(a) or (b) art as well.)

A more interesting question is whether a *restricted* or *conditionally restricted* deposit is §102(g) art. A conditionally restricted deposit (*i.e.,* one which is to be released to the public when the patent issues), if timely made, probably would not be deemed "suppressed" or "concealed" by virtue of the re-

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[79] 428 F.2d 639 (7th Cir. 1970).

and operative invention and therefore was not even a "conception" for priority purposes. Even according it the status of a "reduction to practice," of course, the court's conclusions as to Hybritech's dates mandated its finding that the La Jolla work was not prior art.

As for the work of Oi and Herzenberg (Stanford), Judge Rich concluded that their work did not anticipate the invention because their work did *not* involve the detection or measurement of antigen. Moreover, their work did not address the importance of high-affinity monoclonal antibodies.

Hybritech might not have needed the assistance of Judge Rich had it more expeditiously had its notebooks witnessed by a non-inventor. Its May, August, and September, 1979, notebook entries were not witnessed until May, 1980. Judge Rich, on appeal, took the view 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."

[23] Effect of Patent Law Amendments Act of 1984

Until recently, one knotty problem for patent attorneys was the position taken by the PTO that the individuals named as joint inventors on an application must be joint inventors of the subject matter of all the claims in the application.[80.2] If, for example, one individual had constructed a new hybridoma and another had purified the secreted antibody, an examiner might reject a single application containing claims to both the hybridoma cell line and to the purified antibody even though these two claims certainly would not be considered to be directed to independent and distinct inventions. Section 104 of the Patent Law Amendments Act of 1984 amends 35 U.S.C. §116 to provide:

> When an invention is made by two or more persons jointly, they shall apply for patent jointly and each make the required oath.

[80.2] *See* Pearne, "Must Each Inventor Named in a Joint Patent Application Have Made an Inventive Contribution to Each of the Claims Thereof?," 58 JPOS 205 (1976).

quently in biotechnology patent litigation, as much scientific work is first divulged at conferences. In *Hybritech, Inc. v. Abbott Laboratories,*[80.4] in opposing Hybritech's motion for preliminary injunction, Abbott argued that five attendees at a conference received review copies of a manuscript prior to its delivery. The recipients were apparently all members of the Review Committee, and while it is not so stated in the opinion, there may have been an understanding that the manuscript was transmitted in confidence. The court found that the limited distribution "on this restricted basis" was not a "publication." The meeting itself was also prior to the "critical date" under Sec. 102(b). However, the court observed that there was an absence of "any evidence that the copies were distributed at the speech or made available on request after the speech."

In *Electro-Nucleonics Laboratories, Inc. v. Abbott Laboratories,*[80.5] the court stated that "the advance proof of a paper is printed publication pursuant to Section 102, when it has been printed and widely circulated among the participants in the symposium and any interested member of the public skilled in the art under consideration could have registered as a symposium participant and could have obtained a copy of the advance proof." However, it refused to accord "printed publication" status to a paper because it was presented in Europe at a workshop limited to Europeans, and because it was not possible "to accommodate all those who wished to attend." The court did not explain why it was relevant that the workshop was limited to Europeans, and it did not mention how many attendees there were. The court's analysis is therefore flawed.

§ 4.02 The Drafting of Claims

[1] The Legal Significance of the Claim

The basic requirement for claims is contained in 35 U.S.C. §112, paragraph 2:

[80.4] 4 U.S.P.Q.2d 1001 (C.D. Cal. 1987).

[80.5] 214 U.S.P.Q. 139, 146 (N.D. Ill. 1981).

to each of these points. A claim containing many limitations may avoid the prior art, but it may allow others to appropriate that which the inventor could rightfully regard as part of his discovery, yet failed to claim.[86] (If prolix, the claim might be invalid under 35 U.S.C. §112 by virtue of its incomprehensibility.[87])

A broad claim may catch infringers, but this is cold comfort if it allows them to bring in marginal prior art, or to charge the inventor with claiming organisms whose characteristics he has not freely disclosed to the public.

These considerations will be developed further in the remainder of this chapter.

In view of the fact that novel chemical compounds are among the fruits of biotechnology, and to serve as an analytical base for the drafting of claims to novel microorganisms and gene sequences, it is appropriate to review also some of the tenets of chemical patent practice.

The synthesis and characterization of a novel and nonobvious compound, coupled with the disclosure of at least one use for that compound, entitles its inventor to a patent covering that compound, *however* made or used.[88]

If a novel compound is not synthesized, but rather is found in nature, in an impure state, and its discoverer, upon purifying it, finds it to have properties nonobviously distinct from those of the natural mixture, he may advance a claim to the compound, provided it is limited so as not to cover the compound in its impure state.[89]

If a novel compound cannot be characterized, whether in the form of a precise chemical structure, or by enumerating all of its chemical or physical properties, protection may be obtained in the form of a "product-by-process" claim, but this

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[86] Keystone Bridge Co. v. Phoenix Iron Co., 95 U.S. 274 (1877).

[87] Victor Talking Machine Co. v. Thomas A. Edison, Inc., 229 F. 999 (2d Cir. 1916).

[88] Cf. Stow v. Chicago, 104 U.S. (14 Otto) 547 (1881); Potts v. Creager, 155 U.S. 597 (1895); Meta Frame Corp. v. Biozonic Corp., 352 F. Supp. 1006 (D. Mass. 1972).

[89] *See* §3.03, *supra.*

about 1.674 and 1.694, and exhibiting characteristic absorption bands in the infra red region of the spectrum when suspended in a hydrocarbon oil in solid form at the following frequencies expressed in reciprocal centimeters: 3420, 1643, 1609, 1580, 1523, 1302, 1231, 1209, 1121, 1080, 1050, 969, 943, 867, 844, 825, 805, 794, 788, 733, 713 and the acid salts of said substance.[92]

Perhaps the first such claim to be tested in the courts was that upheld in the Adrenaline case:

7. A substance possessing the herein-described properties of the suprarenal glands, having a whitish color, difficulty soluble in water at ordinary temperature, soluble in acids and forming salts therewith, soluble in alkalies, and melting at about 207° centigrade.[93]

In *Benger Labs. Ltd. v. R.K. Laros Co.* (1962),[94] Senior District Judge Kirkpatrick declared that "nothing in the law requires the courts to deny a patent to the inventor of a new and useful product merely because laboratory technique has not advanced to a point where the chemical structure can be recognized and described." The court held that a tripartite "fingerprint" of the composition satisfied §112.

The PTO formally recognized the propriety of these "fingerprint claims" in *Ex parte Brian* (1958), wherein appellants presented lengthy "fingerprint" claims to gibberellic acid. This is one of the few cases in which the PTO has given any precedential weight to the actions of examiners in other, but similar, cases.

Appellants have referred to numerous patents dealing with the subject matter involved in the present case, which have been allowed on the basis of claims identifying the products by their empirical formula and their physical and chemical characteristics coupled with their infra-red absorption spectra. Since the claims under consideration are similar to those in the patents, we do not feel disposed to reject them and thus upset such a

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[92] *See also* U.S. Pats. 2,982,689; 2,992,162; 3,015,607.

[93] Parke-Davis v. Mulford Co., 189 Fed. 95 (S.D.N.Y. 1911).

[94] 135 U.S.P.Q. 11, 14 (E.D. Pa. 1962).

The Manual of Patent Examining Procedure, §706.03(e) presently states

> An article may be claimed by a process of making it provided it is definite. . . .
>
> When the prior art discloses a product which reasonably appears to be either identical with or only slightly different than a product claimed in a product-by-process claim, a rejection based alternatively on either section 102 or 103 of the statute is appropriate. As a practical matter, the Patent and Trademark Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith. A lesser burden of proof is required to make out a case of prima facie obviousness for product-by-process claims because of their peculiar nature than when a product is claimed in the conventional fashion. . . .
>
> Where an applicant's product is incapable of description by product claims which are of different scope, he is entitled to product-by-process claims that recite his novel process of manufacture as a hedge against the possibility that his broader product claims may be invalidated. In re Hughes, 182 USPQ 106 (CCPA 1974).
>
> The fact that it is necessary for an applicant to describe his product in product-by-process terms does not prevent him from presenting claims of varying scope, Ex parte Pantzer and Feier, 176 USPQ 141 (Board of Appeals, 1972).

This rendered obsolete the rule in *Ex parte Brian* that "fingerprint" claims and "product-by-process" claims could not be directed to the same substance.[99]

Typically, microbiological applications present these claims in the form "The product of the process of claim *X*." In *Parke, Davis & Co. v. Amer. Cyanamid Co.*, a "fingerprint" claim contained a process limitation: "said acid being the acid derived from autolysis of mammalian liver tissue."[100]

A "product" claim in which the product is defined without any reference to the process of making it is infringed by any product "reading" upon the claim—even one made by a novel

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[99] 118 U.S.P.Q. 242.

[100] 207 F.2d 571, 572 (6th Cir. 1953).

ley's cytochalasin B did induce polyploidy in *C. gigas* as desired. This was considered to be the result of optimization within the ordinary skill in the art.

The pitfalls of using product-by-process claims to protect biotechnology inventions are further illuminated by *Scripps Clinic and Research Foundation v. Genentech, Inc.*[104.3] Scripps sought partial summary judgment on the issue of Genentech's infringement of certain claims of Scripps' reissue patent on Factor VIII:C. Claims 13, 14, 17, 18 and 34 were in product-by-process form, and related generally to immunopurification of Factor VIII:C by binding the Factor VIII:C/VIII:RP complex with monoclonal antibodies specific for Factor VIII:RP and subsequently eluting the VIII:C. The court followed established doctrine by holding that a product-by-process claim is infringed only by a product produced by following the same process described by the claim.

Scripp's product-by-process claims were strictly construed by the court. While it held that Factor VIII:C produced by Dr. Tuyddenham infringed claim 13, it held that it did not infringe claim 14 since Dr. Tuyddenham did not make use of a second adsorption by aminohexyl agarose as required by claim 14. Factor VII:C produced by immunopurification using monoclonal antibodies to Factor VIII:C rather than VII:RP was held to be outside the claims. Short shrift was given to the contention that Genentech's recombinant Factor VIII:C infringed the product-by-process claims.

Having held that the product-by-process claims were (with the aforestated exception) not literally infringed, the court held that such claims could not be extended by the "doctrine of equivalents":

> Scripps' contention that the accused Factor VIII:C infringed the product-by-process claims under the doctrine of equivalents, even though it was not produced according to every step in those claims, is merely an attempt to evade the limitation inherent in claiming the product of a process. Application of the doctrine of equivalents in this context would render meaningless the necessity of establishing infringement of a product-by-process claim by demonstrating that "the process of [the pa-

[104.3] 3 U.S.P.Q.2d 1481 (N.D. Cal. 1987).

Minor variations in wording, such as substitution of the terms "growing" or "culturing," for "cultivating," are not uncommon.

More important variations are attributable to the width of the brush used to depict the organisms, nutrient media, and operating conditions employed.

[b] Organisms Employed

The organism may be specified in claims of varying scope. Thus, in Kathrein, U.S. Patent No. 2,949,700 [1960], claims 6 through 13 descended the taxonomic ladder:

> 6. A process for the production of carotenoids which comprises cultivating under heterotrophic conditions an alga of the division Chlorophyta in an aqueous organic nutrient medium, at a temperature of from about 10° to about 40°C., said nutrient medium containing between about 0.5 and about 10 percent by weight of a carbohydrate, between about 0.1 and about 5 percent by weight of a proteinaceous material and between about 0.05 and about 4 percent by weight of urea.
>
> 7. The process of claim 6 wherein the alga is of the order Chlorococcales.
>
> 8. The process of claim 6 wherein the alga is of the family Oocystacea.
>
> 9. The process of claim 6 wherein the alga is of the genus Chlorococcum.
>
> 10. The process of claim 6 wherein the alga is of the genus Chlorella.
>
> 11. The process of claim 6 wherein the alga is of the genus Chlamydomonas.
>
> 12. The process of claim 6 wherein the alga is Chlorella vulgaris.
>
> 13. The process of claim 6 wherein the alga is Chlorella pyrenoidosa.

In order to forestall accusations of "overclaiming" (*see* §4.02 [12], claims reciting broad taxons often contain functional lim-

course, the invention lies in the "process engineering" of a crude fermentation method, the operating condition limitations will appear in the main claim.

[e] Supplementary Protection

It is not unusual for inventors to supplement the protection afforded by fermentation method claims by presenting

(a) Product-by-process claims;
(b) Claims to methods of producing the *organism;*
(c) Claims to the enzymatic synthesis method made possible by the enzymatic product of the fermentation;
(d) Claims to the preferred nutrient media (tailored to the needs of the subject organism); and
(e) Claims to methods of recovering the fermentation product.

[4] Claims to Other Microbiological Methods

[a] Isolation and Cultivation Methods

A number of patents have been issued for methods of isolating microorganisms (particularly mutants) from a culture medium. One example is Davis, U.S. Patent No. 2,571,115 [1949]:

> 1. The method of isolating nutritionally deficient bacterial mutants from a parent stock which comprises cultivating a mutant and nonmutant containing population in an enriched medium containing all of the nutritional substances necessary to support the mutant and nonmutant strains, eliminating from the medium the mutant strain growth supporting nutritional substance thereby preventing the growth of said mutant strains, sterilizing the growing nonmutant strain with penicillin which will sterlize growing bacteria but which will not sterilize the resting mutant strain, eliminating the penicillin, and cultivating the

1. A process for the manufacture of new strains of micro-organisms, which comprises the selection of two strains of a micro-organism whose genetical factors it is desired to combine, and having genetical markers which enable the strains to be easily distinguished and complementary nutritional requirements or complementary sensitivity to poisons; inoculating the strains in a medium deficient in the complementary poisons of the strains as the case may be; growing the heterokaryon so formed, or its conidia, in at least a similar medium, thereby favoring multiplication of heterozygous nuclei in which the factors of the marked strains are combined; recognizing the cells carrying these heterozygous nuclei by means of the markers and establishing a strain thereof; and selecting from the latter strain a stable recombinant strain which is produced from the heterozygous strain and which combines in a desired manner the different genetical factors of the originally selected strains.

[c] "Genetic Engineering" Methods

These claims cover methods of producing (a) cloning vectors, (b) recombinant plasmids, (c) transformed organisms, and (d) desired chemicals.

Probably the first U.S. patent in this field was Chakrabarty, U.S. Patent No. 3,923,603 *Discrete Plasmid Construction from Chromosomal Genes in Pseudomonas* [1975]. Claims 1 and 2 read:

1. A process for transferring chromosomal genes specifying a hydrocarbon degradative pathway for a given substrate from a first strain of Pseudomonas and imparting said chromosomal genes as part of a plasmid aggregate into a second strain of Pseudomonas which does not contain said chromosomal genes comprising the steps of:
a. introducing factor K, a transfer plasmid, into at least one organism of said first strain of Pseudomonas which mobilizes said chromosomal genes and forms a plasmid aggregate therewith,
b. admixing the resulting first strain of Pseudomonas with said second strain of Pseudomonas transferring said plasmid aggregate by conjugation,

first and second linear DNA segments has a gene for a phenotypical trait, under joining conditions where the termini of said first and second segments join to provide a functional DNA capable of replication and transcription in said unicellular organism;
growing said unicellular organisms under appropriate nutrient conditions; and isolating said transformants from parent unicellular organisms by means of said phenotypical trait imparted by said biologically functional DNA.

Other recent "genetic engineering" patents include Shine, U.S. Patent No. 4,264,731 [1981] and Debabov, U.S. Patent No. 4,278,765 [1981].

In this context, an interesting question has been asked: "To what extent will a patent granted on the basis of a demonstration in E. Coli preclude awarding a patent for doing something which is conceptually the same thing, but by perhaps quite a different route, in some other microorganism?[107] Similarly, it could be asked whether demonstrating a particular transformation in *E. Coli* is sufficient to support a claim covering similar manipulation of other organisms? In either case, expert testimony on the predictability of the results of the operation will control.

[5] Claims for Isolates: The Mystique of the "Biologically Pure" Culture

Harold Wegner suggested in 1974 that Mancy could have claimed his microorganism, which he had isolated from a soil sample, in the following manner:

1. A culture containing the microorganism, Streptomyces *bifurcus, strain* DS 23.219 (NRRL 3539), said culture being capable of producing the drug daunorubicin in a recoverable quantity upon fermentation in an aqueous nutrient medium containing assimilable sources of carbon, nitrogen and inorgan-

[107] Jackson, Patenting of Genes: Ground Rules, in ASM, Patenting of Microorganisms: Issues and Questions 23, 27 (1981).

ducing heteropolysaccharide.[110]

It is unfortunate that the "biologically pure culture" shibboleth has gone unchallenged. The claim containing such a limitation might be evaded by a putative infringer who deliberately allowed the culture to become contaminated with a slow growing, antibiotic prone, or otherwise noncompetitive or controllable second organism. The contaminated culture would not be "biologically pure." The patentee would be forced to rely on the uncertain support of the doctrine of equivalents. In *Ritter v. Rohm & Hass Co.*,[111] a district court held that a process employing a 95 percent acid solution did not infringe a claim reciting the use of "substantially anhydrous acid."

The term "pure culture" specifically may seem broader, but it is in fact narrower. The term "biologically pure" excludes non-living chemical impurities, the term "pure culture" does not.

"Biologically pure cultures" are biologically impossible. No culture can remain homogeneous. Bacteria exchange genetic information by conjugation, and mutate spontaneously. Gene sequences may be modified by mutagenic background radiation. Subculturing risks contamination from a variety of sources. The claim might well be attacked under Section 112.

There are a variety of ways by which the patent applicant may attempt to overcome these problems. The subtlest is for him to act as his own "lexicographer"[112] and define "purity" in a more palatable manner.

He may, for example, define a pure culture as a population of cells *derived* from a single cell by cell division (*i.e.*, a *clone*), or as a culture free of *deleterious* viable contaminating microorganisms. The Plant Variety Protection Act's definition of "uniformity" and "stability" may also furnish inspirational guidance.[113]

A court might not accept the definition if it regards it as

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[110] Cf. Goldberg, U.S. Patent No. 4,166,112 [1972] ["pure biological strain"].

[111] 154 U.S.P.Q. 518, 550 (S.D.N.Y. 1967).

[112] Feed Serv. Corp. v. Kent Feed, Inc., 528 F.2d 756, 188 U.S.P.Q. 616 (7th Cir. 1976).

[113] 7 U.S.C. §§1562, 1611, 2321 et seq.

rubbing of the fingers. I would not say that it is an adequate test to predicate rubber behavior on, but it is a rough and ready test; and if it responds to that test it is a pellet within the meaning of the claim. Finally, what on first impression appears to be reasonable certainty of dimension disappears when we learn that "approximately one-sixteenth of an inch in diameter" includes a variation from approximately 1/4th to 1/100th of an inch.[116]

In *United Carbon Co. v. Carbon Black Research Foundation,* the court sustained claims 1 and 2 of the reissue patent:

> Claims 1 and 2 of the Reissue Patent are as follows:
>
> 1. Substantially pure carbon black in the form of round smooth-surfaces aggregates less than one quarter of an inch in diameter, free from binders and porous throughout in such degree that approximately twice the number of pounds of aggregates of fairly uniform size can be placed in a container of a given size than is the case with the untreated black.
>
> 2. Substantially pure carbon black in the form of round smooth-surfaced aggregates less than one-quarter of an inch in diameter, free from binders and porous throughout in such degree that approximately twice the number of pounds of aggregates of fairly uniform size can be placed in a container of a given size than is the case with the untreated carbon black the aggregates being sufficiently hard and flowable to prevent the formation of dust, and yet sufficiently friable and dispensible for use as a component in the manufacture of rubber and other products.[117]

These claims clearly supplied objective standards for what the original claims had referred to facilely (and vaguely) as "substantially" pure.

There are many cases which interpret the term "substantially." Few have held the claims indefinite. Most interpret it as including variations which a person of ordinary skill in the art would know would not defeat the stated purpose of the inven-

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[116] 317 U.S. 228, 232-236 (1942).

[117] United Carbon Co. v. Carbon Black Research Foundation, 59 F. Supp. 384, 386 (D. Md. 1945) (United Carbon II).

Storch described three desirable bacterial strains, and two undesirable bacterial strains "which must be excluded from the pure flavor-producing cultures."

In *Bergstrom,* the applicant incorporated into his claim an *objective* standard of purity:

> 23. 7[3-hydroxy-2(3-hydroxy-1-octenyl)-5-oxocyclopentyl]-5-hepte in acid, *said acid being sufficiently pure to give a substantially ideal curve* on partition chromatography using an ethylene chloride: heptane: acetic acid: water (15:15:6:4) solvent system.[124]

Another term which might be used in a claim is "axenic culture" (from "a," not; "xeno," foreign). An axenic culture may include mutant progeny of a parent organism.

It may be argued that the term "culture" alone is sufficient. No reasonable microbiologist would interpret this term as encompassing the original soil or water sample. Support for this position may be gleaned from the legislative history of the plant patent act. The original proposal would have allowed protection of new varieties found in the wild. Commissioner Robertson warned that such protection might be unconstitutional. The bill was eventually amended to provide protection only for new varieties asexually reproduced in a *cultivated* state.[125] "(J)ust as the nurseryman goes beyond the plant hunter by trying to cultivate new varieties found by the latter, the microbiologist goes beyond the 'microbe hunter' when he cultures a newly discovered bacterium."[126] It is worth noting that fungi may be referred to either as "cultivars" or as "cultures."[127]

Even if there were merit to the assertion that a claim to a "culture" could reasonably be interpreted to cover the original chunk of soil, the limitation that it must be "capable of producing the antibiotic lincomycin in a recoverable quantity upon fermentation" should suffice to meet the objection.

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[124] In re Bergstrom, 477 F.2d 1394, 1395 (C.C.P.A. 1970).

[125] 35 U.S.C. §161.

[126] I.P. Cooper, *Arzberger Under the Microscope,* 78 Patent & Trademark Rev. 59 (Feb. 1980), and 7 Rutgers J. Computers, Tech. & L. 367 (1980).

[127] Cowan, *Dictionary of Bacterial Taxonomy.*

are the use of an organism to remove the toxic metabolic by-products of another organism to remove oxygen or depress oxidation-reduction potential for an anaerobic organism, or an organism to maintain a pH range critical for a second organism. In addition, one organism may produce a metabolic product, such as lactic acid, which both is beneficial to the growth of a second organism, such as a yeast, and at the same time helps to control contamination.[129]

The earliest "mixed" culture patent may have been Collett, U.S. Patent No. 952,418 (1910), teaching the use of a "mixture of lactic acid bacteria in the manufacture of cocoa." Another patent of interest is Gottas, U.S. Patent No. 2,867,945 *Process of Photosynthetic Conversion of Organic Waste by Algal-Bacterial Symbiosis* (1959).[130]

Patents have also been issued on cosynthetic methods for the production of complex organic compounds:

McCormick, U.S. Patent No. 2,998,352: Claim 1 reads as follows:

A process for the cosynthetic production of a tetracycline antibiotic selected from the group consisting of tetracycline, chlortetracycline, bromtetracycline, oxytetracycline, 6-demetocyltetracycline, and 7-chloro-6-demethyltetracycline which comprises cultivating at least two microorganisms of the genus *Streptomyces* one strain of which is of a species capable of producing a tetracycline antibiotic of the aforesaid group and the other strain of which is a strain selected from the group consisting of *S. aureofaciens, S. rimosus, S. hygroscopicus, S. plutonsis and S. albus* and is capable of acting cosynthetically therewith in an aqueous nutrient medium containing assimilable sources of carbohydrate, nitrogen and inorganic salts under submerged aerobic conditions until an enhanced quantity of said antibiotic is produced.

Sebek, U.S. Patent No. 2,887,161:

9. A process for the production of 1-dehydro-17-beta-hydroxy steroids which comprises: cultivating a species of the protozoan family Trichomonadidae selected from the genera Tri-

[129] Casida, *Industrial Microbiology,* 161 (1968).

[130] *See also* Matt, 1, 899, 217 (1933); Nouvel, 3, 3, 369, 969 (1968); Sakurai, 3, 932, 670 (1976).

> of a substantially neutralized mixtue of two types of bacteria, the first type being selected from the group consisting of *Streptococcus lactis, Streptococcus crenois, Lactobacillus bulgaricus* and *Streptococcus thermophilus,* and the second type being selected from the group consisting of *Streptococcus citrovorus* and *Streptococcus baracitrovorus,* said concentrate being stabilized by the admixture of a stabilizing agent and a nutrient medium so that the concentrate is stabilized against rapid loss of viability, said concentrate being frozen so that it can be stored for a long period of time without major loss in the viability of the bacteria.[131]

Ex parte Farr declared that Farr's invention was "not 'a discovery of nature' but rather the 'nonobvious manipulation, utilization or application of known things to produce a utilitarian tangible composition of matter.' "[132] *Farr* also interpreted the majority opinion in *Funk* as based on a finding of "aggregation," or "lack of invention" in the sense of being an obvious combination.

Proponents of "mixed culture" fermentations will certainly argue "nonobviousness" of the "mixed culture" over its component pure cultures. The McCormick patent refers to a "synergistic" increase in yield, and to the "surprising" fact that "both members of the cosynthesizing pair . . . need not be of the same species and indeed only one member of the pair need be derived from a normally-tetracycline-producing species of the genus Streptomyces.[133]

The difficulty inherent normally in producing a *compatible* mixed culture has been clearly explained by Casida:

> Simultaneous growth of two fermentation microorganisms in a single medium presents a problem in microbial ecology. Each organism must contend with the physiological, growth, and nutrient utilization activities of the other, and it is likely that their growth rates will differ so that one organism will outgrow the other. Thus, extensive studies of media and other fermenta-

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[131] File wrapper, U.S. Patent No. 3,420,742 (Paper No. 19). The patent was later the subject of two reissues, Re. 28,276 and Re. 28,488.

[132] Ex parte Farr, Appeal No. 822-58 on Ser. No. 404,526 [1964](Paper No. 19).

[133] U.S. Patent No. 2,498,352 col. 1.

claim drafters than a recognition of a real obstacle to patent protection. The claim might recite (1) the presence of the "main" organism in a certain range of frequency; (2) the absence of particular competing organisms; (3) the presence of desirable "background" organisms; and (4) an objective functional limitation on the claim (*e.g.*, a particularized leaching ability).

More detailed claims could be modeled after "alloy" claims, *i.e.*, a range of frequency for each organism of significance would be given.

The proliferation of "biologically pure culture" claims naturally leads one to wonder how these would be adapted to cover Professor Johnson's "mixed pure cultures." U.S. Patent No. 4,292,406 [1981] claims 1 and 2 read as follows:

> 1. The mixed culture system comprising a biologically pure strain of the microorganism Thermoanaerobacter ethanolicus, having the identifying characteristics of ATCC 31550 and a biologically pure strain of the microorganism Clostridium thermocellum, having the identifying characteristics of ATCC 31549, said culture system having the ability to produce ethanol in recoverable quantities upon fermentation in an aqueous nutrient culture containing cellulose material.
>
> 2. A mixed anaerobic, thermophilic culture system of the microorganisms Thermoanaerobacter ethanolicus and Clostridium thermocellum each of said microorganisms isolated in biologically pure culture, having the identifying characteristics of ATCC 31550 and 31549, respectively, and having the ability, when combined in a mixed culture system, to yield ethanol as a major product constituent upon fermentation in an aqueous nutrient medium containing cellulose material.

[7] "Organism-Plus-Carrier" Claims

Even before the epochal *Diamond v. Chakrabarty* decision, the Patent Office accepted the patentability of "compositions of matter" comprising a "living" organism together with a nonliving "carrier" or "nutrient medium."[137]

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[137] In re Bergy, 596 F.2d 952, 985-986 (CCPA 1979).

Still other compositions are used by the chemical industry:

Loughlin, U.S. 2,096,377 (1937): Claim 20:

20. An inoculum comprising essentially a bacterial culture of the species *Clostridium saccharobutyl-isopropyl-acetonicum* and a medium which contains fermentable sugary material, assimilable protein, and a small amount of water-soluble inorganic nitrogen-containing material and which has a pH value between 4.0 and 8.0.

Chibata, U.S. 3,953,291 (1976): Claim 11:

An *immobilized penicillin amidase-producing* microorganism comprising a penicillin amidase-producing microorganism tightly entrapped into the lattice of a semipermeable acrylotl polymer selected from the group consisting of homopolymer of N.N'-lower alkylene-bis-acryloylamide, bis (acrylogi-amidomethyl) ether or N,N'-acryloyl-ethylene-urea, copolymer of acryloylamide, and N,N'-lower alkylene-bis-acryloylamide copolymer of acryloylamide and bis-(acryloylamide and N,N'-acryloyl-ethyleneurea.

Frankenfeld, U.S. 3,347,668 (1967):

1. A proteinaceous adhesive composition comprising *Micrococcus cerificans* protein extract and water.

Perhaps the largest group of organism-plus-carrier claims pertains to therapeutic compositions, particularly, vaccines:

Smith, U.S. 3,364,117 (1968):

2. A vaccine composition comprising the attenuated strain of Salmonella choleraesius having the American Type Culture Collection reference number 15479 and a pharmaceutically acceptable diluent.

3. An injectable composition in unit dosage form comprising the attenuated strain of Salmonella choleraesuis having the American Type Culture Collection reference number 15479 and a pharmaceutically acceptable diluent, the number of viable bacteria in the unit being from 103 to 109.

The failure of the Supreme Court in *Chakrabarty* and *Diehr*

an organism in a "nutrient medium" necessarily encompass coactive ingredients.

If *Funk* is overruled, then claims to "organism-plus-carrier" compositions should certainly be submitted for "reissue" to eliminate the "carrier" limitation, if a "broadening" reissue is still permissible. A competitor might otherwise attempt to evade enforcement of the "organism-plus-carrier" claim by selling freeze dried cultures of the organism, allowing his customers to combine the organism with the carrier appropriate to the application desired.

Dependent claims may, of course, be phrased in "organism-plus-carrier" format to "supplement other patent protection."[142]

[8] Immunological Invention Claims

Antibodies, or, more accurately, immunoglobulins, are Y-shaped, multi-chain protein molecules, synthesized by cells of the immune system, which bind to and neutralize foreign objects called antigens. Each immunoglobulin molecule has antigen binding sites, formed by the genetically variable regions at the branched ends of the "Y." The portion of the antigen to which the antibody binds is called an epitope; a single antigen may bear several distinct epitopes. A vaccine is really a pacified antigen in a suitable carrier. It is a purified pathogen which has somehow been rendered less harmful, for example, an "attenuated" (less virulent) or "killed" pathogen, or an immunogenic but otherwise harmless fragment of a harmful antigen.

The body possesses both a humoral and a cellular immune system. The humoral immune system is maintained by a large number of differentiated small lymphocytes, each cell endowed with the capacity to produce a specific immunoglobulin. The antigen stimulates the proliferation and maturation of those lymphocytes whose immunoglobulins bind to that antigen. The small lymphocytes mature into plasma cells, which are prolific immunoglobulin factories. Typically, the antibody

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[142] Ex parte Ruschig, 147 U.S.P.Q. 46 (POBA 1965).

Heterospecific antibodies (those with dissimilar binding sites on the same molecule) have been constructed for special purposes.

Patents in the art have claimed (1) antigens; (2) carriers for haptens; (3) bridging agents; (4) immunization protocols; (5) antigen preparation techniques; (6) methods of purifying antigens or antibodies; (7) polyclonal antibodies; (8) label-antibody or label-antigen conjugates; (9) immunocyte and immortal cell lines used in constructing hybridomas; (10) fusion and selection protocols; (11) hybridoma cell lines; (12) monoclonal antibodies; (13) antibody-agent conjugates; (14) assay and purification methods employing antibodies; and (15) test kits.

Claims to antigens, and particularly to vaccines, have a long history in the Patent Office.

Early vaccine patent claims were directed to "a composition for injection purposes comprising viable *X* spore material in a medium containing *Y*."[143]

Later, we find claims reciting the vaccine claim in product-by-process form, perhaps with dependent claims to the stabilized or freeze-dried vaccines, or reciting the number of viable organisms per unit volume.[144]

One may also find composition claims to the strain in a pharmaceutically acceptable diluent, and to freeze-dried cultures of the strain.[145]

Ex parte Beard related to an equine encephalomyelitis ("blindstaggers") vaccine.[146] Prior to Beard's work, the only source of the vaccine was very limited—"bits of brain tissue of horses that had died of this disease." Attempts to prepare a suitable equine vaccine by growing the virus in guinea pigs and mice were fruitless; "it appeared that vaccination against equine encephalomyelitis required a homologous vaccine . . . one obtained by treating tissue from the same type of animal subjected to the virus. . . ."

Beard discovered that a suitable heterologous vaccine could be prepared from chick embryo tissue. It was "old to grow the

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[143] U.S. 1,989,014; U.S. 2,151,364.
[144] U.S. 3,184,384; U.S. 3,849,551.
[145] U.S. 3,364,117.
[146] 45 U.S.P.Q. 711 (POBA 1940).

X comprising cultivating a fused cell hybrid of an antibody *X*-producing cell and a myeloma cell and recovering antibody *X*."

One may also claim the method of producing the hybridoma cell line, though such claims are less useful.

Being chemicals, monoclonal antibodies are patentable as "compositions of matter." There is, unfortunately, a prevalent misconception that the patent protection available for monoclonal antibodies is necessarily narrow. In practice, monoclonal antibodies have been successfully claimed in terms of their immunological spectrum of reactivity.

Perhaps the first U.S. patent to issue which claimed a monoclonal antibody per se was Kung, U.S. Patent No. 4,361,549 (1982), which claimed:

> 4. A complement-fixing monoclonal antibody which reacts with essentially all normal human peripheral *T* cells, but not with normal human peripheral *B* cells, null cells, or macrophages.

Other claims of the Kung patent specified that the antibody was of murine origin (claim 5), that it was of class IgG (claim 4), the percentage of thymocytes, leukemic cells, etc., with which it reacted (claim 1), that it was of subclass IgG_2 (claim 2), or that it was produced by a hybridoma of particular origin (claim 3).

A somewhat more narrowly defined claim appears in Bieber, U.S. Patent No. 4,381,292 (1983). Here the claim, instead of being to a monoclonal antibody which reacts with a cellular antigen, is to one which reacts with a particular surface antigen, Leu 5.

Yet another example is Secher, U.S. Patent No. 4,423,147 (1983):

> 1. A monoclonal antibody produced by a murine derived hybrid cell line wherein the antibody is capable of specifically binding to an antigenic determinant of interferon-alpha.

Where necessary to distinguish over the prior art, a monoclonal antibody may be claimed in terms of its specific antigenic determinant (epitope), but this will not often be necessary.

In re Evanega[147.2] also examined the patentability of an immunoassay format. The claim was to a competitive immunoassay in which labeled antibody and sample antibody competed for the epitopes of particle-bound antigen. In Evanega's method, the mixture of bound and unbound species was centrifuged into "solid" (bound) and "liquid" (unbound) phases and the liquid phase enzyme activity was determined while there was still interphase, contact between the solid and liquid phases. The principal reference was Schuurs. After careful examination of the Schuurs reference, the Federal Circuit concluded that Schuur contemplated the physical isolation of the phases before the measurement of the enzyme activity. Two examples clearly spoke of removing the supernatant for assaying; the other examples said nothing about this issue. The court concluded that the "entirety" of the reference suggested the alleged distinction.

Claims to hybridoma cell lines can take several forms:

(1) specific claims to deposited lines;
(2) product-by-process claims, in which the hybridoma cell line is defined by the parental lines and the fusion protocol; and
(3) fingerprint claims, in which the hybridoma line is claimed in terms of the characteristics of the monoclonal antibody which it secretes.

In the next subsection, we look at claims to eukaryotic cell cultures. The comments made there are applicable also to hybridoma cell lines, and to hybridoma fusion partners as well.

[9] Claims to Inventions Relating to Eukaryotic Cell Cultures

In view of the paucity of decisions, even at the PTO Board of Appeals level, with regard to the patentability of these cytological inventions, it seems appropriate to review the patents already issued for whatever guidance they may offer. Present-

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[147.2] 4 U.S.P.Q.2d 1249 (Fed. Cir. 1987).

kidney fibroblast cell line designated BHK 21 in a nutrient medium therefor." Claim 2 is dependent on claim 1, and specifies a particular nutrient medium.

Sanders 3,418,210 [1968] Claim 3 reads "A standard bacteriological agar medium-containing hamster ascites tumor cell line having the reference BHK 21/C.13/T.6/Ascites, and mutants thereof, produced in accordance with the process of claim 1." Claim 6 is directed to a culture medium containing living organisms: "A substantially serum-free hamster ascites tumor cell medium comprising BHK 21/C.13/T.6 Ascites cell line of hamster ascites tumor cells produced in accordance with the process of claim 1, in agar, and Eagle/Hanks medium, which contains [additional substances]."

Kasza, 3,432,595 (1969) claim 1 covers: "The combination of viable canine melanoma 'cell line M' cells on a synthetic medium supporting the viability thereof, said medium comprising assimilable carbohydrate, assimilable protein or amino acids, nuclei acid, mineral, and vitamin components and, as a further element of the combination, a viable virus which is normally unindigenous to the canine melanoma 'cell line M' cells, but which may be indigenous to a canine or other test animal and to which the canine melanoma 'cell line M' cells are susceptible, growing in the culture of canine melanoma 'cell line M' cells as host."

Corlett, Jr., 3,683,550 [1972] Claim 17 reads: "A culture comprising granular pineapple bud clusters free-living apart from the donor pineapple plant, at least a portion of the bud clusters being in contact with aqueous nutrient, said bud clusters being characterized by the capacity to proliferate to form more granules without substantial differentiation into plantlets under first predetermined environmental conditions and the capacity to differentiate into a plurality of pineapple plantlets by modifying the environmental conditions." The dependent claims further specify the environmental conditions.

Smith, 3,709,782 [1973] Claim 3 is directed to "A continuous, established feline heteroploid cell line produced by the method of claim 1," while dependent claim 4 introduces the limitation, "in a culture medium therefor."

Apostolov, 3,935,066 [1966] claims the following.

C. Possessing a substantially constant degree of viral susceptibility;

D. Capable of maintaining substantial diploidy and not becoming senescent after at least thirty-six subculturings, while remaining free from morphological transformation and chromosomal anomalies; and

E. Retention of marker chromosomes; and a suitable culture medium therefor.

4. The diploid porcine embryonic cell strain of claim 3 which has been subcultured six times with eleven cell doublings and having American Type Culture Collection Accession No. CL 184 (ATCC No. CL 184).

5. A diploid porcine embryonic cell strain of claim 3 capable of being infected by and supportive of the growth of viruses selected from the group consisting of: transmissible gastroenteritis—(TGE) virus; porcine parvovirus—(PPV) virus; parainfluenza 3—(PI3) virus; rabies—(R) virus; enteric cytopathic porcine orphan—(ECPO) virus; bovine virus diarrhea—(BVD) virus; reovirus—(RV) virus; bovine enterovirus—(BEV) virus; bovine adenovirus—(BAV) virus; bovine parvovirus—(BPV) virus.

6. A diploid porcine embryonic cell strain of claim 4 capable of being infected by and supportive of the growth of a living, attenuated TGE virus.

[10] Claims to Inventions Relating to Tissue and Organ Cultures

No case law authority is available to guide patent draftsmen in the preparation of claims to tissue and organ cultures, or methods of using these cultures, so inspection of past patents is again called for.

Pincus, U.S. Patent 2,666,015 [1949] claimed

The method of hydroxylating 11-desoxycorticosterone in the 11-position which comprises perfucing an isolated functioning mammalian adrenal gland with blood plasma containing said

tissue completely enclosed in a container, at least a portion of the walls of said container being formed of a semipermeable membrane having pores extending therethrough with a maximum pore size of about 5 millimicrons.

Sanders, U.S. Patent 3,862,002 [1975] claimed a method of cultivating placental tissue to produce hormones such as estrogen, progesterone, ACTH, thyrotropin, gonadotropin, and samatotropin. He did not claim the preserved tissue culture, per se:

In a process for producing physiologically active substances, the steps comprising culturing viable placenta tissue in a culture medium at a temperature suitable to maintain viability and for a time period sufficient to provide an appreciable concentration of said substances in the culture medium, separating the culture medium containing said substances from said viable tissue, cooling the separated culture medium to about 5°C and acidifying the medium to a pH of about 3.5 to precipitate a glycoprotein fraction containing gonadotropin therefrom, separating the glycoprotein fraction containing the gonadotropin from the solution, contacting the residual culture medium with ether to extract fatty acids and steroid hormones therefrom, separating the ether phase from the culture medium phase, separating the fatty acids from said ether phase, and drying said ether phase to produce a residue including said steroid hormones.

As long as the claim is clearly limited to the tissue or organ maintained *in vitro* as a culture, there would appear to be no "product of nature" objection to patentability since the tissue or organ does not naturally function outside the body.

[11] Claims to Mutant Microorganisms

"Organism" claims will fall into two categories: (1) claims delimiting the scope of the claim by explicitly setting forth some morphological or biochemical trait of the organism, and (2) claims reciting that the organism has the "identifying characteristics" of a deposited "type specimen." Both forms of

able to the mutagenic effect of a deliberately introduced agent; rather than background radiation, that applicant had no (or very little control) over the genetic makeup of the progeny of the irradiated organisms, and that the real contribution of the applicant was the isolation of the mutant, for which the allowance of a *Bergy*-type claim would be a sufficient *quid pro quo*.

In response, applicant might contend that, according to 35 U.S.C. §103, "(P)atentability shall not be negatived by the manner in which the invention was made." He may have his patent even if he just "stumbled" upon the invention,[152] as Baruch discovered the superior "anti-knock" characteristics of tetramethyl lead when used in gasoline whose octane rating exceeded the critical value of 90,[153] or as a microbiologist may discover one or two methionine-auxotrophic mutants amid some 10,000 fungi surviving irradiation.[154]

Waddell Biggart recently indicated that some PTO examiners are routinely rejecting claims to newly developed "radiation mutants": "(1) under 35 U.S.C. §101, as a product of nature, since the mutant strain can occur as a result of natural mutational processes and may exist in nature; [and] (2) under 35 U.S.C. §102 or 35 U.S.C. §103 as being anticipated by or obvious over the parent strain used to engineer the mutant.[155]

With regard to the first rejection, in *Yoder Bros., Inc. v. California-Florida Plant Corp.*,[156] a plant patent case, the Fifth Circuit held that "recurring sports" were entitled to protection: "the purpose of the Plant Patent Act would be frustrated by a requirement that only those rare, never-before-seen, if not genetically impossible sports or mutations would be possible. The Fifth Circuit was interpreting 35 U.S.C. §103 as applied to plant patents, pursuant to 35 U.S.C. §161. Any qualms that this precedent is limited in value should be quieted by *In*

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[152] Gagnier Fibre Products Co. v. Fourslides, Inc., 112 F. Supp. 926, 48 U.S.P.Q. 9 (E.D. Mi. 1953); Schmidinger v. Welsh, 383 F.2d 455, 155 U.S.P.Q. 289 (3d Cir. 1967).

[153] California Research Corp. v. Ladd, 260 F. Supp. 752, 151 U.S.P.Q. 563 (D.C. D.C. 1966).

[154] Treichler, U.S. Patent No. 3,423,601 (1975) Col. 4.

[155] Biggart at 3-6.

[156] 537 F.2d 1347, 1382 (5th Cir. 1976).

Chakrabarty obtained a patent on a novel fused plasmid-transformed microorganism:

> 7. A bacterium from the genus *Pseudomonas* containing therein at least two stable energy-generating plasmids, each of said plasmids providing a separate hydrocarbon degradative pathway.[158]

There is a doctrine of "aggregation" which may pose patent difficulties for molecular geneticists. If plasmids can be arbitrarily selected and replicated in a host organism, a multiplasmid genetically engineered organism might be regarded as a mere, obvious aggregation for convenience of its genetic components. In the partially discredited yet still potent Supreme Court decision in *Lincoln Engineering Co. v. Stewart-Warner Corp.*, the Court declared:

> The mere aggregation of a number of old parts or elements which, in the aggregation, perform or produce no new or different function or operation than that theretofore performed or produced by them, is not patentable invention.[159]

It would be beyond the scope of this treatise to discuss the infirmities of the "aggregation" doctrine.[160] Instead, this treatise explores the manner in which the applicant may forestall an old combination rejection.

The applicant should point to any indications in the prior art that the plasmids employed were incompatible, as Chakrabarty did with regard to his genetically engineered *Pseudomonas*.[161] The applicant should point out how the *expression* of one plasmid (*e.g.*, in enzyme production), cooperates with the

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[158] In re Bergy and Chakrabarty, 596 F.2d 952, 970 (CCPA 1979) (consolidated cases).

[159] 303 U.S. 545, 549 (1938).

[160] For recent statements of the aggregation doctrine, *see* MPEP §706.03(i) and (j) and Anderson's Black Rock Inc. v. Pavement Salvage Co., 396 U.S. 57, 60-62 (1969).

[161] Tr. of Record, Pat. App. 77-535 at 9, 25-33.

Plasmids in recombinant bacteria are like carburetors in engines. Properly installed, they permit the bacteria engine to cough into useful life, producing the precious substances whose genetic information they encode, but plasmids are absolutely inanimate. Each building block of the plasmid (and plasmids can be built) is an absolutely dead bench chemical. All of the building blocks in the aggregate are little else. The chemical composition of the plasmid they form is absolutely definable. By every imaginable test, the new plasmids that confer near-miraculous properties on everyday organisms ought to be patentable, just like any other man-made chemical of value. And just as someone who makes, uses or sells an automobile containing a patented carburetor can be sued, so too one who makes, uses or sells a bacterium containing a patented plasmid should be subject to suit for infringement.

. . .

The plasmid question, we add, offers the Court an interesting opportunity to accomodate the interests of both parties in the present matter. Nothing in the legislative history of the Patent Act could be construed as proscribing patents on dead chemicals like plasmids. The grant of patents on plasmids could satisfy the needs of a burgeoning and bountiful industry, without

(Text continued on page 4-79)

Fig. 1 Vista general del área de estudio (A)

expression of other plasmid-mediated genes. The applicant should point out any difference in the transmissibility of the plasmid. In short, applicant must overcome the belief that each plasmid has the same effect it always has; as did, for example, the pencil point and the eraser in *Reckendorfer v. Faber.*[162]

The biologist's problem is similar to that of a metallurgist with a new alloy.[163]

Claims to transformed hosts are common in recent biotechnology patents. The narrowest of these claims are to the specific transformant deposited in a culture collection. However, broader claims are known. Some of the forms they take are indicated below.

1. Organism *O* which includes DNA coding for polypeptide *P.*
2. Organism *O* transformed by vector *V.*
3. Organism *O* adapted to exhibit activity *A* on condition *C.*
4. Organism *O* and any mutants thereof.
5. Organism *O* and any organism derived therefrom.

The Organism *O,* polypeptide *P,* vector *V,* etc., may be narrowly or broadly recited.

The "aggregation" problem is not limited to multiplasmid hosts of the *Chakrabarty* variety. It also applies to the chimeric plasmid type of transformant, in which Promoter *P* is placed in control of heterologous gene *G* on a vector *V* with various convenient restriction sites, bearing selection marker *M* and replicon *C,* and used to transform host *H.* If *P, G, V, M, C,* and *H* are all known in the art individually, an examiner might argue that it was obvious to combine them. The most effective counterargument is to point to the failures in the art.

The possibility of patenting plasmids per se was first suggested by Tom Kiley, Genentech's General Counsel:

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[162] 92 U.S. 347 (1876).

[163] *Compare* Ex parte Hehemann, 57 U.S.P.Q. 155 (POBA 1942); Becket v. Coe, 98 F.2d 332 (D.C. Cir. 1937); and Ex parte Brown, 71 U.S.P.Q. 112 (POBA 1946) *with* In re Cooper, 134 F.2d 630 (CCPA 1943).

re Seaborg, holding Element 95 (Americium) patentable even though undoubtedly produced previously through nuclear "recombinations" in prior art reactor operations.[157]

Turning to the second ground of rejection, this author suggests that the question was settled by *In re Mancy* (discussed in § 4.01[5].) While *In re Mancy* discussed fermentation processes, its reasoning is equally applicable to claims to the organisms themselves. Additionally, it should be observed that the characteristics and genetic makeup of the mutant strain obtained would not be predictable based on a study of the parent strain. If the mutant's phenotype and genotype are markedly different than those of the parent, then, unquestionably, it should be considered nonobvious. However, this author doubts that a showing of an "unexpected result" is, indeed, required, given the unpredictability of mutagenesis.

The reductio ad absurdum of the PTO argument is that all chemical compounds should be deemed unpatentable, since it is *conceivable* that they were created in millenia past. In particular, how could the PTO allow claims to fermentation products, such as tetracycline, when it is entirely possible that, in earlier times, a tetracycline-producing organism occurred in nature?

In MPEP 2100, the PTO noted "that the court did not limit its decision to genetically engineered living organisms." On July 29, 1980, Commissioner Diamond indicated that if the microorganisms claimed "were the result of human intervention and were not products of nature, such claims will not be rejected under 35 U.S.C. §101." Consequently, the PTO's present recalcitrance with regard to allowing claims to mutated organisms is misplaced, since the genotype of these organisms was changed as a result of human intervention (the application of mutagenic agents is merely a crude form of "genetic engineering").

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157 328 F.2d 996 (CCPA 1964).

claims have their place in patent practice. The second claim has less certain but potentially broader coverage than the first.

As W. Biggart has observed, the characteristics of the organism are inherently defined by the reference to the deposit.[148] He compares this practice to that of inserting a reference to a drawing into a claim, and particularly to the inclusion of a structural formula in a claim. *In re Papesch* (1963)[149] held that the properties of a compound claimed by formula are inherently incorporated into the claim. Thus, claims to compounds (and, by extension, organisms) may distinguish over the prior art by reference to distinctive properties that were not expressly recited in the claims.

Since each organism is uniquely determined by its genetic code, it is possible to claim organisms by claiming, broadly or narrowly, their nucleotide sequences. This prospect will be discussed further in § 4.03.

Wegner has suggested that had Mancy produced his new strain "by subjecting an old strain to radiation or chemical treatment to form a mutant," he would have been entitled to claim "The microorganism *Streptomyces bifurcus* strain DS 23, 219 (NRRL 34539).[150]

It is interesting to note that in 1975, Ciba-Geigy was issued a patent on the following:

> 1. A colony of a methionine-auxotropic mutant of a Cephalosporin C-producing strain of the genera Emericellopsis-Cephalosporium.[151]

Other patents making reference to the mutant character of the strain employed are available in the files.

It is possible that the Patent Office will take the position that random mutants cannot be claimed per se. The position, if taken, would be supported by the argument that applicant had no way of knowing whether a particular mutation was attribut-

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[148] Patent Resources Group, eds., Genetically Engineered Microorganisms and Cells, at 3-21 (1981).

[149] 137 U.S.P.Q. 43 (CCPA 1963).

[150] Wegner, Patent Protection for Novel Microorganisms Useful for the Preparation of Known Products, 5 IIC 285, 290 (1974).

[151] Treichler, U.S. Patent No. 3,923,601 [1975].

steroid, and subsequently isolating the 11-hydroxy steroids from the perfusion fluid.

He did not direct any claim to the excised gland, per se. Tucker, U.S. Patent 3,022,783, *Method of Preserving Tissue Such as Bones* [1960], however, also presented claims to "preserved tissue" and "preserved bone."

12. A preserved tissue for heterogeneous grafting universally compatible with human tissue comprising a healthy, viable dumb, animal body tissue combined with a normal saline bath including a soluble sodium sulfonamide compound, an antibiotic agent and blood components from the type of animal from which the tissue has been removed, said preserved tissue including muco-protein and muco-polysaccharides rendered extraordinarily permeable by said bath, said tissue being excessively antigen depleted and denatured by reaction producing sodium salt linked tissue protein which is amide ring bonded by double sulphur bonds, said tissue also including fibroblastic tissue converted from peripheral fibroblasts and also including growing tissue cells.

13. A preserved bone for heterogeneous grafting universally compatible with human bone comprising a healthy, viable dumb animal body bone combined with a normal saline bath including a sodium sulfonamide compound, an antibiotic agent and blood components from the type of animal from which the bone has been removed, said preserved bone including muco-protein and muco-polysaccharides rendered extraordinarily permeable by said bath, said bone being excessively antigen depleted and denatured by reaction producing sodium salt linked tissue protein which is amide ring bonded by double sulphur bonds, said bone also including osteoblastic bone tissue and growth produced periosteum converted in the bath from peripheral osteoblasts and also including growing bone tissue cells.

Jordan, U.S. Patent 3,093,831 [1963] presented several claims to a living, encapsulated gland, of which claim 1 is exemplary:

An implantable gland comprising living hormone-producing

1. A cell culture of a human epithelial heteroploid liver cell line, comprising a cell line in association with a nutrient culture medium, said cell line being a human epithelial heteroploid liver cell line, comprising cells characterized as follows: a. The cells form individually separated islands or discrete clumps when cultured in a growth medium; b. The cells have a morphology closely resembling that of hepatocytes of the human liver; c. The cells have a generation time not more than twenty-four hours; d. the cells manifest increased production of glycogen in the presence of 1 percent glucose in the said growth medium; and e. the cells are capable of supporting viruses.

2. A cell culture according to claim 1 wherein the islands or discrete clumps resemble liver lobules.

3. A cell culture according to claim 2, wherein the islands or discrete clumps have an average dimension of between 2 and about 3 mm.

4. A cell culture of a human epithelial heteroploid liver cell line, comprising a cell line in association with a nutrient culture medium, said cell line comprising a human epithelial heteroploid liver cell line, as deposited with the American Type Culture Collection under accession number CL 48.

Green, 4,003,789 [1977] Claim 1 reads "An isolated clonal cell line derived from a culture of mouse fibroblast 3T3 cell line, said clonal cell line having the characteristic of accumulating relatively large amounts of triglyceride fats while in a resting state and a suitable growth media therefrom" [sic]. Claim 3, on the other hand, covers "A cell culture comprising isolated 3T3-L1 cells in a suitable medium therefor."

Bordt, 4,070,453 [1978] Claims 3-6 and 11 are directed to cell strains:

3. A diploid porcine embryonic cell strain characterized by:

A. Freedom from i. specified viral contaminates as measured by cytopathology, hemadsorption, inclusion body staining, and fluorescent antibody techniques; ii. specified bacterial contaminants as measured by sterility testing; iii. mycoplasma contamination as measured by broth agar subculturing;

B. Nontumorigenicity in immunologically depressed hamsters;

ly, these patents may be found in Class 435, subclass 240, as well as in several other locations.

MacPherson 3,228,840 [1966] Claim 1 is directed to "a cell culture system comprising cells of the baby golden hamster

(*Text continued on page 4-69*)

On occasion, it may be difficult to identify the antigen. Under these circumstances, the physicochemical "fingerprint" of the antigen may be used to identify it. See Reinherz, U.S. Patent No. 4,443,427 (1984).

An example of an unusually broad monoclonal antibody claim may be found in Reading, U.S. Patent No. 4,474,893 (1984): "1. An antibody with binding affinity for two different desired antigens." (The Reading antibody was produced by a quadroma or trioma.)

The monoclonal antibody patents issued in the United States to date have claimed the antibody in qualitative terms, "directed against *X*," "specific for *Y*," or "reacting with *Z*." It is possible to follow the example of some European applicants by expressing the specificity of an antibody in quantitative terms, using rate or equilibrium constants.

With some knowledge of the amino acid sequence of your immunoglobulin, it is possible to claim it in structural rather than functional terms. A structural claim might be addressed to the "minimum binding site polypeptide" contained within the immunoglobulin unit.

It is also customary to present claims to immunoassay methods and test kits for use in such assays. The test kits include labeled or insolubilized antibodies or antigens which may also be claimed.

In *Electro-Nucleonics Laboratories v. Abbott Laboratories*,[147.1] a patent on a solid phase radioimmunoassay for a hepatitis associated antigen or its antibody was held invalid under 35 U.S.C. 102 and 103. The Coller patent, a 35 U.S.C. 102(E) reference, described a solid phase RIA for an antibody against hepatitis-associated antigen. It suggested that the antigen could be similarly detected if purified antibody were available. The court held that "the invention described in the '494 patent was an obvious response which was not possible until purified radioactively labeled antibody to the hepatitis B surface antigen was available." It therefore discounted evidence of commercial success and satisfaction of a longfelt need.

147.1 214 U.S.P.Q. 139, 144, 148 (N.D. Ill. 1981).

virus of the disease on chick embryo tissue" in a virulent form, but no reference had taught that a vaccine prepared from infected chick embryo tissue could be used to immunize horses. The Examiner pointed out, to no avail, that smallpox vaccine for humans had been made from chick embryo tissue. This antismallpox vaccine, applicant responded, used "live" virus, while Beard's vaccine was inactivated with formalin. In any event, the Board agreed with Beard that "the art point(ed) away" from his use of the vaccine in horses.

Other vaccine inventors have not fared as well.

Claims 1, and 9 of Bankowski's application for a patent relating to a Newcastle Disease virus vaccine were held invalid under 35 U.S.C. §103. Bankowski had used Sabin's rapid passage, rapid volume technique to attenuate the virus. The Sabin technique had previously been used in connection with poliomyelitis virus, and Bankowski applied it "without modification." The CCPA held that "in the absence of a showing of nonobviousness properties thus imparted to the attenuated vaccine . . . we think it would have been obvious . . . to utilize the Sabin rapid-passage technique. . . . (There are only a limited number of tissue-culturing techniques used in this art.)"[147]

The development of hybridomas and monoclonal antibodies has necessitated some experimentation in claim drafting.

Claims to methods of producing monoclonal antibodies are now common in the art. An early example is Koprowski, U.S. Patent No. 4,172,124 (1979):

> 1. A method of producing malignant tumor antibodies comprising immunizing an animal with tumor cells, forming fused cell hybrids between antibody producing cells from said animal and myeloma cells, cloning said hybrids and selecting clones which produce antibodies that demonstrate specificity for said tumor cells.

The wording of this claim is such that it would not cover antibody production where the fusion was performed prior to the issuance of the patent. It would be wise to supplement such a claim with one directed to "a method of producing antibody

[147] In re Bankowski, 138 U.S.P.Q. 75, 78 (CCPA 1963).

or humoral response to a particular antigen is the production of several different immunoglobulins, each produced by a specific lymphocyte clone. The heterogeneous antisera thus obtained is therefore said to be polyclonal in nature. Because the antisera thus obtained are heterogeneous, techniques have been developed for purifying a particular antibody.

A single immunoglobulin may react with several antigens, since each may bear the proper epitope. This phenomenon is known as cross-specificity or cross-reactivity.

Because of cross-specificity, use of purified antigen is desirable in antibody development.

Some foreign objects, such as low molecular weight molecules, are too small to elicit an immunogenic response. Such a response can be artifically obtained by coupling the small molecule, known as a hapten, to a carrier molecule large enough to capture the attention of the immune system.

For certain applications, the antibody may be further manipulated. For example, it may be conjugated with a label of some kind so that it can be assayed after being bound to its antigen. More recently, antibodies have been conjugated with therapeutic agents, the antibodies thus acting as carriers.

Monoclonal antibodies, that is, homogeneous antibodies produced by a single clone of cells, may be obtained from the blood of individuals afflicted with a form of cancer known as multiple myeloma. Here the antibody-producing cells multiply uncontrollably, so large quantities of antibody are produced. Each specific tumor (clone) in a patient suffering from multiple myeloma produces a single immunoglobulin.

The first hybridoma was created when Kohler and Milstein fused cultured mouse myeloma cells to normal spleen cells (the spleen is a lymphoid organ in which red blood cells and plasma cells are stored) from an immunized mouse. They showed that the resulting hybrid cells (hybridomas) produced homogeneous (monoclonal) antibodies against the immunogen used, and that these hybridoma cells grew continuously in culture. Hybridomas may also be obtained by fusing other antibody-producing cells with other "immortal" cells derived from any of several species. Hybridomas may be fused with each other to create quadromas.

The immunoglobulin molecule itself is no longer sacrosanct.

to expressly overrule the "two-part" patentability standard enunciated by Douglas in *Funk* leaves "organism-plus-carrier" claims open to assault. In its argument to the Supreme Court in *Chakrabarty,* the Government described a claim of this type as one in which "the invention apparently resides in nonliving material which is a part of the claim." The Government treated living material as analogous to the "secrets of nature" in *Funk* or the "algorithm" in *Flook,* and implied that patentability must be sought elsewhere.

In numerous cases, it has been held that a claim reciting a *well known* active ingredient in an *inert* carrier is unpatentable. Thus, in *Rosicky,* the CCPA stated "it would be obvious to one skilled in the art to utilize a carrier with the disclosed compounds of Cusic, et al."[138] In *Riden,*[139] the CCPA deemed the presence of a "relatively inert" surface-active agent equivalent to the use of the carrier in *Rosicky.* In *Ex parte Ligett,* the applicant failed to convince the Board of the existence of "coaction between the active ingredient and the fungicidal adjuvant.[140] (This argument was accepted, however, in *Rystan Co. v. Warren-teed Products Co., Inc.*[141])

If a court accepts the *Funk* reasoning that the nonobviousness of the bacterium cannot support the claim, certainly an inert "carrier," "diluent" or "adjuvant" cannot.

The word "inert" should be employed with great circumspection when drafting the patent specification. Any coaction between microorganism and the nonliving ingredients should be carefully explained. Thus, Mazocchi, U.S. Patent No. 1,989,-014 *Anthrax Vaccine* (1934) states that the ingredient saponin blocks the absorption of the anthrax organism into the host while promoting the growth of the bacilli. Smirnoff, U.S. Patent No. 3,911,110 *Insecticidal Compositions* (1975) explains that the enzyme chitinase is used to facilitate the penetration of the bacterium into the haemolymph of the insect. Claims to

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138 276 F.2d 656, 660 (CCPA 1960). *See also* In re Craige, 89 U.S.P.Q. 609 (CCPA 1951); Ex parte Miller, 81 U.S.P.Q. 261 (POBA 1947); Ex parte Billman, 71 U.S.P.Q. 253 (POBA 1946).

139 318 F.2d 761, 765-767 (CCPA 1963).

140 Ex parte Ligett, 121 U.S.P.Q. 324 (POBA 1958).

141 92 U.S.P.Q. 419 (N.D. Texas 1952).

Many of these organism-plus-carrier claims are directed to compositions useful as pesticides:

Edmond, U.S. 3,113,066 (1961):

1. A composition useful as a pesticide for lepidopterous insects comprising a major proportion of a *mineral oil* having a viscosity of about 40 to 120 SUS. at 100°F., an aromatic content below 25 wt. %, an olefinic content less than about 4 wt. %, and a total quantity of unsulphonatable residue of at least 50 wt. %, and dispersed within said oil about 20 to 120 x 75 x 109 *Bacillus thurinqieusis* spores per imperial gallon of said mineral oil.

Goldberg, U.S. 4,166,112 (1979): Claim 1:

A bacterial larvicide active against mosquito-like larvae comprising: (a) an effective larva killing concentration of spores of the pure biological strain of *Bacillus thuringiensis* var WHO/CCBC 1897 as an active ingredient; and (b) a carrier.

Other claims are directed to feed products:

Farr, U.S. 984,575 (1976):

1. A bacterial composition useful for changing the digestive system bacteria in animals when fed orally which comprises: live *Bactobacillus lactis* NRRL-B-5628 mixed with a growth medium and a freezing stabilizing agent and which mixture is cooled such that at least about 50 percent of the bacteria in the mixture are viable for about twenty-four hours.

Osasa, U.S. 4,147,773 (1979):

1. A powdery composition which contains 28-57 percent by weight of lacturose, less than 2.5 percent by weight of moisture and at least 8×10^{10} *of freeze dried viable cells of genus bifidobacterium* per gram of said composition.

Huber, U.S. 4,172,127 (1979):

9. A high-energy ration or feed suitable for use in a feedlot operation, for the fattening of a ruminant animal consisting essentially of a high-energy ration or feed for said ruminant animal and a minor amount of a culture of the microorganism *Peptococcus asaccharalyticus*.

tion conditions are required to balance the growth of the two or more organisms. This problem becomes either simplified or magnified if some form of symbiosis exists between the organisms, so that they are dependent on each other for growth.[134]

The *Funk* decision, though narrowly construed by *Farr* and *Bergy II* (in Judge Baldwin's concurring opinion), and clearly based on both factual and analytical errors, has not been overruled. It still casts a shadow over the future of "mixed culture" patents.

Professor Johnson draws an interesting distinction between "stable crude cultures" and "mixed pure cultures."

> A mixed pure culture is a mixture of pure cultures, propagated under conditions of strict asepis, the ratio of the numbers of each of the component cultures present being determined by the environmental conditions. A stable crude culture is a culture growing under non-aseptic conditions, the composition of which is entirely determined by the environmental conditions. It may be essentially a pure culture (as in vinegar manufacture) or have a large number of components (as in activated sludge). In actual practice, the situation is generally somewhere in the intermediate area bounded by a pure culture, a stable crude culture, an unstable crude culture, and a pure mixed culture.
>
> The stable crude culture was invented a long time ago. Wine, vinegar, beer, and the like have been made by it for a long time. More modern examples are production of yeast cells from sulfite waste liquor and other materials.[135]

According to Tuovinen and Nicholas, the use of microbes to leach out minerals from ores is, like sewage treatment, carried out on an industrial scale by "mixed populations" (Johnson's "stable crude cultures"). They declare that "it is difficult to establish patent rights over these varied bacterial populations.[136] This seems to this author to be more a challenge to

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[134] Casida, *supra* note 129 at 161-162.

[135] M. J. Johnson, Fermentation—Yesterday and Tomorrow, 1 Chem. Technol. 338, 341 (June 1971).

[136] Tuovinen and Nicholas, Patent Protection of Microorganisms with Special Reference to Ferrous Iron and Sulfur Oxidizing Bacteria, 17 Biotechnology and Bioengineering 1853, 1856 (1975).

chomonas, Tritrichomonas and Pentatrichomonas and Corynebacterium selected from the species *Corynebacterium simplex* and *Corynebacterium equi*, in a nutrient medium containing assimilable nonsteroidal carbon nitrogen sulfur and phosphorus, and 17-ketosteroid selected from the group of 17-ketostrane, 17-ketosomething and 17-ketostrane to effect simultaneous dehydrogenation on the 1,2-position and reduction of the 17-keto group to a 17 beta-hydroxy group, and isolating the thus-obtained corresponding 1-dehydro-17beta hydroxy steroid.

The earliest claim directed to the "mixed culture" per se appears to be Torok, U.S. Patent No. 1,894,135 (1935), teaching the use of a mixture of yeast and bacteria in particular proportions, for the making of dough. Nordsieck, U.S. Patent No. 2,121,442 (1937), directed to yogurt manufacture, claims:

7. A mixed culture of *bactobacillus acidophilus* and *Streptococcus thermophilus* habituated at 40°C. and in equilibrium, the culture having no unpleasant taste, odor or consistency and being adapted to coagulate sterile milk in seven hours at 40°C. with five percent inoculation.

A different approach to claiming a "mixed culture" appears in Das, U.S. Patent No. 4,138,498 (1979):

13. A composition for facilitating the adaptation of ruminants from roughage or normal pasture rations to a high energy starch ration, consisting essentially of a bacterial culture of Megasphaefa elsdenil and a propionic acid producing bacterial culture, said composition in unit dosage from containing 106 to 1012 microorganisms.

The reader is no doubt aware that a "mixed culture" claim was invalidated by the Supreme Court in *Funk* [Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127 (1948)]. However, the reader may not know that such a claim was held valid by the Board of Appeals in its unpublished *Ex parte Farr* opinion. The opinion quoted claim 5 (sic, 4) as illustrative:

A stabilized, mixed bacteria concentrate consisting essentially

The Patent Office has in fact granted at least one claim to a culture, per se:

> A freeze-dried culture of the attenuated strain of *Salmonella dublin* having the ATCC reference number 15480.[128]

[6] Mixed Cultures

"Mixed" cultures are cultures consisting of more than one strain of organism. Most "mixed" cultures are ineffectual because the strains mutually inhibit each other. Industrial microbiologists realized, however, that certain "mixed" cultures might prove advantageous:

> Dual or multiple fermentations are those fermentations in which more than one microorganism is employed. The organisms may be inoculated simultaneously into the growth medium, or one organism may be grown first in the medium, followed by the inoculation and growth of a second microorganism. Alternatively, after growth has occurred in the original media, two separate fermentations may be combined for further fermentation activity. The basic concept is that two or more microorganisms accomplish something that neither organism can be alone. Admittedly, in the state of present-day fermentation technology, this concept is more of a dream than a reality. The most obvious use of dual or multiple fermentations is to utilize one microorganism to produce a fermentation product that is then converted or changed by a second microorganism or further microorganisms into a different fermentation product possessing greater economic value. Thus, a yeast first produces ethyl alcohol, and then an Acetobacter species converts the alcohol to vinegar. Another approach is to use one microorganism to change or prepare the medium so that it becomes suitable for the growth of a second microorganism. For example, the first microorganism may provide amylase or protease activity for the second microorganism, which lacks these abilities. Further uses of dual or multiple fermentations

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[128] Smith, U.S. Patent No. 3,356,574 [1967]; cp. Smith U.S. Patent No. 3,364,117.

tion, and which was still within the inventive concept. The specification usually disclosed the same limitation on the variation permissible, though not with mathematical precision.

Use of the term "substantially" leads to uncertainty as to the scope of the claim. Thus *Ritter* says that "substantially anhydrous acid" is 96 to 100 percent acid;[118] *E. W. Bliss* says that a "substantial" amount cannot be less than 49 percent;[119] and *Lobdell* says it may denote "very much less than a majority."[120]

Most courts treat the term as no more than an explicit statement of the "doctrine of equivalents." In *J. R. Clark*, however, the Seventh Circuit declared that there is "more flexibility in substantially coincident than in coincident used alone."[121]

Another approach is to limit the claim by specifying the undesirable ingredients. Thus in *Ex parte Roundy*, applicant presented Claim 9 below:

> 9. In a process for preparing a cheese product in which proteolytic enzymes are utilized to develop cheese body characteristics, the step of admixing into the milk material a zymogen substance *which is free of steapsin and amylosin.*[122]

The exclusion of contaminants did not render the claim fatally indefinite. The same approach was taken by Pasteur when he claimed: "Yeast, free from organic germs of disease, as an article of manufacture."[123]

A combined approach was taken in Storch, U.S. Patent No. 561,291 *Ferment for Ripening Milk* (1896), claiming:

> A ferment for ripening milk or its derivatives, consisting of practically pure cultures of flavor-producing acid bacteria, substantially as set forth.

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[118] Ritter v. Rohm & Haas Co., 154 U.S.P.Q. 518, 550 (S.D.N.Y. 1967).

[119] E. W. Bliss & Co. v. Cold Metal Process Co., 122 U.S.P.Q. 238, 259 (N.D. Ohio 1959).

[120] In re Lobdell, 77 U.S.P.Q. 377 (C.C.P.A. 1948).

[121] J. R. Clark Co. v. Geuder, Paeschke & Frey Co., 119 U.S.P.Q. 161 (7th Cir. 1958).

[122] 79 U.S.P.Q. 96 (POBA 1948).

[123] Pasteur, U.S. Patent No. 141,072 [1873].

being unduly strained.[114]

Another approach is to state that the culture is "substantially pure." In *United Carbon Co. v. Binney & Smith Co.*, the Supreme Court held claims 1 and 2 of the original "carbon black" patent to be invalid for indefiniteness:

> 1. Substantial pure carbon black in the form of commercially uniform, comparatively small, rounded, smooth aggregates having a spongy or porous interior.
>
> 2. As an article of manufacture, a pellet of approximately one-sixteenth of an inch in diameter and formed of a porous mass of substantially pure carbon black.[115]

The Supreme Court relied heavily on the testimony of Mr. Wiegard:

> From it we learn that "substantially pure" refers, not to freedom from ash and other impurities, but rather to freedom from binders; "commercially uniform" means only the degree of uniformity demanded by buyers; "comparatively small" is not shown to add anything to the claims, for nowhere are we advised what standard is intended for comparisons; "spongy" and "porous" are synonymous; and relate to the density and gas content of aggregates of carbon black. Although sponginess or porosity is not a necessary attribute of a friable substance, it does contribute to the friability of aggregates of carbon black. It is of value only in that regard. A spongy or porous aggregate of carbon black may be so friable as to permit of the formation of dust; and, on the other hand, it is conceivable that it might not be sufficiently friable to mix satisfactorily with other substances such as those used in the manufacture of rubber products. The correct degree of friability can be ascertained only by testing the performance of the product in actual processes of manufacture of products of which carbon black is a component. A "pellet" of carbon black is "a spheroidal shaped aggregate that has substance and strength to it." For "strength" we have this rough and ready test: does it survive under gentle

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[114] Chicago Steel Foundry Co. v. Burnside Steel Foundry Co., 132 F.2d 812, 56 U.S.P.Q. 283 (7th Cir. 1943).

[115] United Carbon Co. v. Binney & Smith Co., 317 U.S. 228, 231-32 (1942) (United Carbon I).

ic substances.[108]

Upjohn was clearly following Wegner's lead when it proposed its claim 5 in *Bergy:*

> A biologically pure culture of the microorganism *Streptomyces vellosus* having the identifying characteristics of NRRL 8037, said culture being capable of producing the antibiotic lincomycin in a recoverable quantity upon fermentation in an aqueous nutrient medium containing assimilable sources of carbon, nitrogen and inorganic substances.[109]

While the CCPA holding (*Bergy I* and *II*) that "biologically pure cultures" of naturally occurring organisms are patentable was vacated, few would dispute that the CCPA is likely to adhere to this position. Judges Rich and Markey voted in favor of this decision originally. Judge Miller dissented, but on *unrelated* grounds. Judge Baldwin joined the majority in *Bergy II.* Judge Nies was not on the court during *Bergy I* or *II,* so she is the "unknown quantity." Nonetheless, this modest degree of uncertainty has not shaken confidence in *Bergy I*s significance, as is shown by the alacrity with which applicants have presented, and the PTO has accepted, "biologically pure culture" claims. This author warns, however, that this claim format is far from ideal.

Claim 5 was withdrawn by Upjohn in deference to General Electric, which was prosecuting the *Chakrabarty* case. Once this case was decided, Upjohn moved forward with other microbiological applications claiming microorganisms per se, and received a patent on: U.S. Patent No. 4,259,450, with a claim to "a biologically pure culture of the novel microorganism *Streptomyces espinosus* subsp. *acanthus.* . . ." Similar claims appear in other recently issued patents, such as U.S. Patent Nos. 4,263,404; 4,267,274. Steenbergen, in U.S. Patent No. 4,259,451, claims "a pure culture of a variant of *Agrobacterium radiobacter,* ATCC 31643, said culture being capable of pro-

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[108] H.C. Wegner, Patent Protection for Novel Microorganisms Useful for the Preparation of Known Products, 3 IIC 285, 290 (No. 3, 1974).

[109] In re Bergy, 596 F.2d 952, 967 (CCPA 1979) (Bergy II).

c. placing the mixture on minimal plates containing said given substrate as the sole source of carbon and
d. purifying the resulting conjugatants.

2. The process of claim 1 wherein the source of factor K is P. putida PRS1 K+.

A method claim is also presented in Chakrabarty, U.S. Patent No. 4,259,444 [1981], claim 11:

In the process in which a first energy-generating plasmid specifying a degradative pathway is transferred by conjugation from a donor Pseudomonas bacterium to a recipient Pseudomonas bacterium containing at least one energy-generating plasmid that is incompatible with said first plasmid, said transfer occurring in the quiescent state after the mixing of substantially equal volumes of cultures of said donor and said recipient, each culture presenting the respective organisms in a complex nutrient liquid medium at a population density of at least about 1,000,000 cells/ml, the improvement wherein after conjugation has occurred, the multi-plasmid conjugatant bacteria are subjected to DNA-cleaving radiation in a dosage sufficient to fuse the first plasmid and the plasmid incompatible therewith located in the same cell.

Cohen and Boyer, U.S. Patent No. 4,237,224 *Process for Producing Biologically Functional Molecular Chimera* [1980] claim 1 is for

A method for replicating a biologically functional DNA, which comprises: transforming under transforming conditions compatible unicellular organisms with biologically functional DNA to form transformants; said biologically functional DNA prepared in vitro by the method of:
(a) cleaving a viral or circular plasmid DNA compatible with said unicellular organism to provide a first linear segment having an intact replicon and termini of a predetermined character:
(b) combining said first linear segment with a second linear DNA segment, having at least one intact gene and foreign to said unicellular organism and having termini ligatable to said termini of said first linear segment, wherein at least one of said

thus treated population in an enriched medium capable of supporting the mutant strain.

Claims of the form "the method of producing the organism *X* wherein medium *A* is inoculated with organism *X* under condition *B*," and variants thereon, are also common. Cultivation method claims typically supplement either (1) claims to novel nutrient media or (2) claims to processes utilizing novel microorganisms.

[b] Mutation and Breeding Methods

A number of patents have been issued for general methods of mutating organisms with novel mutagenic agents. A recent claim of this type is Pacchetti, U.S. Patent No. 3,954,536 [1976]:

> 1. A process for mutant enriching cultures of edible yeasts comprising treating the cultures with 5-fluoro-uracil, said treatment with 5-fluoro-uracil being effected after a growth stage in rich media plus glucose and being followed by a growth stage in rich media plus glycerin.

Other method claims cover the production of a specific strain of microorganisms, and provide protection similar though inferior to claims to microorganisms per se. Thus, Murphy, U.S. Patent No. 4,264,737 [1981] claim 1 reads:

> The process of producing a hypotoxinogenic and genetically stable variant strain of Vibrio cholerae which comprises incubating a parent strain of V. Cholerae at a temperature of 40° to 42°C. and selecting therefrom a variant strain retaining the biotype and antigens of the parent strain and having a toxicity, as assayed in S49 mouse lymphosarcoma cells, reduced by a factor of at least 750.

An example of a claim to a "breeding" method is Pontecorvo, U.S. Patent No. 2,820,742 [1958]:

itations, *e.g.*, "a vitamin B-12 activity producing strain of fungi selected from the class consisting of Schizomycetes, Torula, and Eremothecium.[105]

In Armbruster, U.S. Reissue Patent No. 29,152 [1973], an objective test for qualifying strains was provided: that the strain, in the specified medium, "produces at least 50 percent more xylose isomerase activity than Streptomyces olivochromogenes ATCC No. 21,114 under identical conditions of cultivation."

Claims occasionally recite, with uncertain effect, that the strain in question is a "mutant," or that variant or mutant strains of the identical strains are covered.

"Markush group" claims to a group of select, deposited strains often appear in patents.[106]

[c] Nutrient Media

When the organism employed is "novel," the main method claim typically indicates only that the medium contains "assimilable" or "fermentable" carbon, nitrogen, phosphorus, etc., and its form, if pertinent (*e.g.*, aliphatic carbon of 6-12 atoms).

If the nutrient medium used as a substrate for the indicated organism is the "point of novelty," the fermentation method claim is likely to recite the components of the medium in some detail.

[d] Operating Conditions

Typically, the main claim will indicate whether the fermentatation is aerobic or anaerobic in nature, while dependent claims will recite temperature, pH, and pressure optima. If, of

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[105] Merck & Co., Inc. v. Chase Chemical Co., 155 U.S.P.Q. 139, 142 (D.N.J. 1967).

[106] Ex parte Markush, 1925 Comm. Dec. 126, 340 O.G. 839, sanctions claims of the form "An *X*, selected from the group consisting of *A*, *B* and *C*." For limitations on Markush practice, *see* MPEP §706.03(y).

tent] was followed to produce the defendants' article, or . . . that the article could not be produced by another process." *Cochrane,* 111 U.S. at 310. Scripps is therefore not entitled to application of the doctrine of equivalents in this context as a matter of law.

But process claims are entitled to a range of equivalents. The court's decision is anomalous in that it renders product-by-process claims narrower in scope than the corresponding process claims. It seems to this author that there could have been a genuine issue of material fact as to the equivalency of adsorption on anti-VIII:RP and adsorption on anti-VIII:C antibodies.

[3] Claims to Fermentation Methods

[a] Introduction

The classical format for a fermentation process claim is:

> A process for the production of *W* which comprising cultivating organism *X* in an aqueous nutrient medium, containing assimilable *Y*, under *Z* conditions, until a recoverable quantity of *W* is produced, and recovering said *W*.

(*Text continued on page 4-45*)

process not used by the patentee.[101] Product-by-process claims are usually deemed infringed only by a product made by the same process. Thus, in *Parke, Davis, supra, synthetic* folic acid did not infringe the "extract" claim.[102] When a product-by-process claim is presented because reference to the process is necessary to distinguish over the prior art, it is difficult to quarrel with this rule. When this claim format is forced on the applicant by his inability to determine the structure of the product, this rule appears harsh.

Product-by-process claims are often presented as a "fallback" should broad product claims be rejected or invalidated. They may also have value as protection against the import of products made abroad by a process patented in the U.S.[103]

Unsuccessful attempts have been made to broaden the scope of product-by-process claims to "substantially identical" products.[104]

Product-by-process claims cannot be obtained when the product is the same as or obvious from a product of the prior art, even if the latter is made by a markedly different process.[104.1] This principle is illustrated by *Ex parte Allen,*[104.2] which considered claims to polyploid oysters of the species *Crassostrea gigas* that had been made by applying hydrostatic pressure to oyster zygotes to induce polyploidy, and then cultivating the polyploid zygotes. The Examiner had found a reference which taught induction of polyploidy in oysters of the species *Crassostrea virginica* by chemical treatment. It was deemed *prima facie* obvious to apply the same method to other oyster species. Allen argued that there were phenotypic differences between the species, and that Stanley's chemical treatment was fatal to *C. gigas,* to no avail. The record also showed that when process parameters were modified, Stan-

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[101] 2 Chisum, Patents §8.05 (1981).

[102] *Supra,* note 100.

[103] Buono v. Yankee Maid Dress Corp., 77 F.2d 1345, 1348 (C.C.P.A. 1969). *See* Section 337 of the Tariff Act; In re Butter, 37 F.2d 623 (C.C.P.A. 1930); In re Brown, 29 F.2d 873 (D.C. Cir. 1928).

[104] Ex parte Lichty, 64 U.S.P.Q. 430 (POBA 1944). For further discussion of these claims, *see,* A.W. Deller, *Patent Claims* §§524, 531-547 (2d ed. 1971).

[104.1] In re Thorpe, 777 F.2d 695, 227 U.S.P.Q. 964 (Fed. Cir. 1985).

[104.2] 2 U.S.P.Q.2d 1425, 1427-28 (BPAI 1987).

long established practice in the particular art under consideration. Accordingly, we will not sustain the rejection of claims 10, 51, 58 and 59.[95]

A claim to an antibiotic was allowed in *Ex parte Sobin* (1963):

> 5. A substance effective in inhibiting the growth of fungi, selected from the group consisting of a white, acidic substance moderately soluble in water, very soluble in methanol, ethanol, acetone, butanol and carbon tetrachloride, insoluble in hexane, having the optical rotation A 25/D = -161° (C1% methanol) and capable of forming salts with organic bases; which contains the elements carbon, hydrogen and oxygen in substantially the following proportions by weight: Carbon—64.67; Hydrogen—6.29; Oxygen (by difference)—29.04—which displays in methanol a single peak at around 218.5 mu, E 1%/1cm = 358 in the ultraviolet region of the spectrum and when dissolved in carbon tetrachloride exhibits characteristic absorption in the infrared region at the following frequencies expressed in reciprocal centimeters: 2857, 1764, 1684, 1629, 1484, 1445, 1397, 1316, 1263, 1176, 1143, 1119, 1079, 1034, 952, 930, 921, 834, 737, 673; and the amine salts of said acidic substance.[96]

[b] "Product-by-Process" Claims

A "product-by-process" claim is one in which the product is in part defined by the process of making it. Originally, the PTO took the position that such claims could be presented only when there was no alternative, whereupon they would be considered, as the right to a patent is not to be determined by the limitations of the English language.[97] The "rule of necessity" was defended by the CCPA in *Hughes,* on public policy grounds, as it "may be more difficult [for a competitor] to determine from a product-by-process claim what product is covered thereby.[98]

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[95] 118 U.S.P.Q. 242, 245 (POBA 1958).

[96] 139 U.S.P.Q. 528 (POBA 1963). But cf. Ex parte Brockmann, 127 U.S.P.Q. 57 (POBA 1959).

[97] Ex parte Painter, 1891 CD 200, 57 OG 999 (Comm'r 1891).

[98] In re Hughes, 496 F.2d 1216, 1218 (C.C.P.A. 1974).

claim will not cover the same compound made by a different process.[90]

If no use, other than "in research," is known for a novel compound, then no patent protection can be obtained over the compound, per se.[91] The use disclosed, however, need not be one discovered by the discoverer of the compound. Nor is it required that the use be commercially feasible.

[2] Claims to Fermentation Products

This section focuses on those aspects of chemical product claiming which are most closely associated with biotechnology.

Frequently, the structurally complex products of biosynthesis are difficult to characterize, and therefore cannot be claimed by reference to their structural formulae. In such circumstances, applicants often present "fingerprint" or "product-by-process" claims to their products. These have been held sufficiently definite to satisfy the "distinct claiming" requirement of 35 U.S.C. §112. These two claiming expedients are discussed below.

[a] "Fingerprint" Claims

A "fingerprint" claim to a product is one which recites, in some detail, the physical and chemical properties of the product. An example may be found in Duggar, U.S. Patent No. 2,482,055:

> Substances effective in inhibiting the growth of Gram positive and Gram negative bacteria selected from the group consisting of a substance capable of forming salts with acids, containing the elements carbon, hydrogen, nitrogen, chlorine, and oxygen, being very soluble in pyridine, soluble in methanol and in acetone and being slightly soluble in ethanol and in water, its crystals having a refractive index parallel to elongation between

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[90] Cochrane v. Badische, 111 U.S. 293 (1884); Paeco, Inc. v. Applied Moldings, Inc., 194 U.S.P.Q. 353 (3d Cir. 1977).

[91] In re Kirk, 376 U.S. 936 (CCPA 1967); In re Joly, 376 U.S. 906 (CCPA 1967).

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

A patent is a deed to an invention, and one of the purposes of the claim is to set forth the metes and bounds of the invention, so that an innocent person may not unknowingly appropriate it.[81] In determining whether a culture or a microbiological process infringes a patent claim, the courts will look to the language of the claim in the first instance.[82] If a claim is so vague as to create a zone of uncertainty as to the rights of the public, it discourages invention by others, and the claim will be invalidated.[83]

Claims which recite quantitative limitations must be carefully supported. In *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*,[83.1] the court invalidated an assay claim reciting that the antibodies had an affinity exceeding 10^9 liters/mole. It criticized the claim because there was "no standard set of experimental conditions which are used to estimate affinities"; thus, it could not be determined with certainty whether a competitor infringed. However, the Federal Circuit reversed, finding that methods of calculating affinities were known in the art and that the methods were as precise as the subject matter permitted.

The claims cannot be so broad as to encompass the teachings of the prior art,[84] nor may they be so broad as to give the patentee a reward incommensurate with that he has disclosed to the public.[85]

A claim ought not be drafted without giving consideration

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[81] Armco Steel Corp. v. U.S. Steel Corp., 132 USPQ 542, 544 (W.D. Va. 1962); Continental Paper Bag Co. v. Eastern Paper Bag Co., 210 U.S. 405 (1908).

[82] Motion Picture Patents Co. v. Universal Film Co., 243 U.S. 502 (1916).

[83] Graver Tank & Mfg. Co. v. Linde Air Products Co., 339 U.S. 605, 607-609 (1950); United Carbon Co. v. Binney & Smith Co., 317 U.S. 228 (1942); Pope Mfg. Co. v. Gormully, 144 U.S. 224 (1892).

[83.1] 227 USPQ 215 (N.D. Cal. 1985), rev'd, 231 USPQ 81 (App. No. 86-531, decided Sept. 19, 1986).

[84] Graham v. John Deere & Co., 383 U.S. 1 (1966).

[85] O'Reilly v. Morse, 56 U.S. 112-114 (1854); 3M v. Carborundum, 155 F.2d 746 (3rd Cir. 1946).

> . . . Inventors may apply for a patent jointly even though (1) they did not physically work together or at the same time, (2) each did not make the same type or amount of contribution, or (3) each did not make a contribution to the subject matter of every claim of the patent.

The use of "suggestions" under 35 U.S.C. §102(f) or "prior work" under 35 U.S.C. §102(g) as 35 U.S.C. §103 prior art, whether standing alone or in combination with more conventional references, has been a source of some controversy in the patent profession. This has been particularly true when the suggestion emanated from or the prior work had been performed by another scientist in the same organization.

The Patent Law Amendments Act of 1984 alleviated this situation by amending 35 U.S.C. §103 to provide:

> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.[80.3]

Of course, the 1984 enactment also validates the treatment of suggestions and prior work by others as prior art under §103, save under the circumstances of the quoted proviso. Biotechnology companies entering into joint research arrangements with universities (or other companies) must study its language carefully. A mere license is insufficient to invoke the protection of the proviso; there must be an obligation to assign the invention to a common entity.

[24] What Is a "Printed Publication"?

Whether a disclosure constitutes a "printed publication" for purposes of 35 U.S.C. 102(b) is a question likely to arise fre-

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[80.3] Section 106(a) renders this provision retroactive in effect, except in the case of judicial and PTO decisions which have become final and unappealable or in the case of cases pending on the date of enactment.

striction. The contract of deposit, by its terms, impliedly rebuts any inference of intent to suppress. (If the pertinent application is abandoned, failure to lift the restriction may raise a presumption of abandonment, suppression or concealment.)

If the discoverer of the prior strain put off for too long a period the "publication" or claiming of the strain, suppression will be inferred, and the parent strain will not be §102(g) art.[80]

The importance of §102(g) art was keenly felt in *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*[80.1] Hybritech owned a patent claiming a sandwich assay using at least one high affinity monoclonal antibody. According to the court, Hybritech could not corroborate a date of conception earlier than May 6, 1980. The court also found that researchers at La Jolla (in November 1979) and Stanford (in July 1978) had actually reduced to practice the simultaneous sandwich assay using high affinity monoclonal antibodies. It accordingly held U.S. patent 4,376,110 invalid under 35 U.S.C. §102(g), without specifically addressing the dependent claims.

On appeal, the Federal Circuit reversed. In determining priority of invention as between Hybritech and La Jolla, the court found that Hybritech was first to conceive and show diligence during the critical period. The claim of conception, while "sparsely documented," was deemed adequate. The court referred to a January 1979 notebook describing a sandwich assay format, an April 1979 letter alluding to the possible uses of monoclonals in immunodiagnosis, and a failed attempt in May 1979 to use a monoclonal in a sandwich assay.

The Federal Circuit also declared that the district court's finding of a November, 1979, reduction to practice by the La Jolla group was in error because the key notebook page was not signed, witnessed or dated, because there was no intrinsic indication that it related to a sandwich assay; and because the affinity of the antibody used was unknown. (La Jolla, in fact, was involved unsuccessfully in an interference proceeding with Hybritech.) Judge Rich concluded that the notebook entry fell far short of showing the visualization of the complete

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[80] Engelhardt v. Judd, 369 F.2d 408 (CCPA 1966).

[80.1] 227 USPQ 215 (N.D. Cal. 1985), rev'd, 231 USPQ 81 (App. No. 86-531, decided Sept. 19, 1986).

ty's modification of a *P. aeruginosa* host for oil spill clean-up purposes?

It appears that the pertinent art includes not only "the art of the industry for which innovation is designed," but also arts dealing with "the kind of problem which the innovation is designed to solve." Initially, microbiology might not be considered to be a pertinent art, but once the trail is blazed, those skilled in the "product-function" art are expected to follow.[77]

[21] A Parent Strain, Undisclosed to the Art, May Be "Prior Art" Against a Mutant Strain Derived Therefrom

Consider the situation where *A* isolates a hitherto unknown strain, and sends a subculture to *B*. *B* then applies for a patent on a culture of that strain. Clearly the culture of the strain isolated by *A* is unpatentable to *B* by virtue of 35 U.S.C. § 102(f). (This is true regardless of whether *A* had publicly deposited, used or described the strain.)

Next, assume that *B* sought a patent on a *mutant* of the strain obtained from *A*. Under what theories might *A*'s strain be "prior art" under 35 U.S.C. § 103?

First, it might be argued that 35 U.S.C. § 102(f) is a source of prior art under 35 U.S.C. § 103. In *Dale Electronics, Inc. v. R.C.L. Electronics, Inc.* (1973), the First Circuit held that "the borrowing by the applicant of a sufficient body of lore to make the invention obvious bars entitlement under § 103.[78] The context showed that the court was relying on 35 U.S.C. §102(f). A National Beryllia salesman suggested BeO as a material having high thermal conductivity, and Dale then concluded that he could make a resistor core from BeO.

Of course, even if the strain discovered by *A* is considered §102(f) prior art, it does not, according to *In re Mancy*, render

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[77] *See* Chisum, *The Law of Patents* § 5.03[1] (1981).

[78] 488 F.2d 382, 386 (1st Cir. 1973). *See also* Ex parte Andresen, 212 USPQ 100 (POBA 1981). There is authority to the effect that this is not a proper use of 35 U.S.C. §102(f). In In re Bass, 474 F.2d 1276, 1286 (CCPA 1973), for example, Judge Rich attempted to limit the concept of prior art to the prior events enumerated in paragraphs (a), (b), (e), and (g).

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28, they reported that they had produced a case of experimental scarlet fever through employing a culture from a strain which fermented mannite. In the other, on January 26, 1924, Exhibit 29, they reported that they had produced experimental scarlet fever with a culture from a strain which did not ferment mannite. Thereupon they announced, in the article of January 26, 1914, that now, having used both types of the strain, that which fermented and that which did not ferment mannite, they had satisfied the first of Koch's laws; they had proved that this organism, which they had identified, was constantly present in cases of the disease; and they therefore announced the conclusion that the hemolytic streptococcus described caused the disease.[72]

This author believes that Dick correctly holds that the satisfaction of Koch's four postulates is *necessary* for a reduction to practice, but suggests that the claimed toxin, antitoxin or vaccine must also be obtained and tested for a reduction to practice to be achieved.

Thus, in *Ex parte Szabo,* a claim to an anti-cancer vaccine was rejected because the applicant failed to show its success in any test animal.[73]

[19] Deferring Filing While Developing a Series of Related Organisms or Compounds Before Filing for Patent, If Within the Bounds of Reason, Does Not Constitute Concealment or Suppression of the Invention

As will be discussed in § 4.02, a patent claim to a novel microorganism may in fact cover a large number of strains. Such a claim, or a claim to a fermentation method employing that organism, typically will be supported by several examples of strains falling within the claim and having similar utility. Similarly, fermentation products may be claimed generically, and these claims are normally supported by several examples

[72] Id., 633.

[73] 136 USPQ 305 (POBA 1961).

[17] A Therapeutic Agent Normally May Be Reduced to Practice by Demonstrating Its Safety and Efficacy in Appropriate Laboratory Animals

In MPEP 608.01(p), the PTO takes the position that

> proof of utility . . . may be established by clinical or *in vivo* or *in vitro* data, or combinations of these, which would be convincing to those skilled in the art. . . . More particularly, if the utility relied on is directed *solely* to the treatment of humans, evidence of utility, if required, must generally be clinical evidence, . . . although animal tests may be adequate where the art would accept these as appropriately correlated with human utility. . . . If there is no assertion of human utility, . . . or if there is an assertion of animal utility, . . . operativeness for use on standard test animals is adequate for patent purposes.

The PTO's qualification with regard to the treatment of humans should not be taken too seriously, for there are few human diseases for which acceptable animal models do not exist. *In re Krimmel* (1961) held that animal studies may show a reduction to practice of a drug which might be used in man:

> [W]e hold that when an applicant for a patent has alleged in his patent application that a new and unobvious chemical compound exhibits some useful pharmaceutical property and when this property has been established by statistically significant tests with "standard experimental animals," sufficient statutory utility for the compounds has been presented. By "standard experimental animals," we mean whatever animal is usually used by those skilled in the art to establish the particular pharmaceutical application in question. These may be mice in one case, rabbits in another, chickens in another, and monkeys in another.[68]

Shortly thereafter, *In re Hartop* (1962) declared that "running through *all* [the CCPA's reduction-to-practice] cases is the same . . . criterion, namely, . . . [would] one *skilled in the art* . . . accept a particular test . . . [as rendering it] reasonably

[68] 292 F.2d 948, 953 (CCPA 1961).

unless and until he communicates the invention to someone in the United States. It also means that a U.S. inventor having samples tested by a foreign laboratory does not thereby reduce his invention to practice until the results of the tests are conveyed to someone in this country.[60]

Evidence of acts abroad is admissible on the issue of the *origin* of the invention, however.[61]

[16] Field Testing of Microorganisms Intended for Pest or Pollution Control May Be Necessary to Achieve a "Reduction to Practice"

In *Larsen v. Marzall* (1952), the D.C. Court of Appeals indicated that laboratory tests could, under appropriate circumstances, constitute a reduction to practice:

> The governing considerations are two: First, do the tests employed—in actual use or in the laboratory—show that the product will serve the purpose for which it is designed . . .?
>
> Second, would the time, effort and expense of conducting actual field experiments be justified because of the small likelihood that they would yield substantially greater knowledge concerning the product's performance?[62]

Gaiser v. Linder (1958) is one of the classic "environmental testing" cases. It involved an airplane windshield equipped with "de-icing" means. The windshield was tested by forming a layer of frost to the coated glass, applying current to the coating, and observing whether the frost was uniformly dissipated. The CCPA was not convinced that "flight tests are not necessary," given the "definite possibility that some factor not present in the laboratory may cause failure in actual use," but assumed without deciding that the invention could be reduced to practice without flight tests. It faulted *Gaiser*, however, for

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[60] Dunlop Holdings, Ltd. v. Ram Golf Corp., 524 F.2d 33, 34 n.2, 188 USPQ 481 (7th Cir. 1975).

[61] Hedgewick v. Akers, 497 F.2d 405 (CCPA 1974).

[62] 195 F.2d 200, 202 (D.C. Cir. 1952).

only to fermentation products, but also to organisms themselves.

[13] Contemplation of a Use for a Product or Organism May Be a Part of Its "Conception"

The PTO has taken the position that a contemplated utility is a part of a complete conception.[56] In a microbiological context, this would mean that a novel organism would not be "conceived" until its discoverer suggested a use for it. In the case of a program of mutation and selection for an improved strain descended from a parent of known utility, conception would occur when the program was first suggested. If a novel strain were isolated, and identified as belonging to a family of strains having a known utility, the conception would occur when this identification was made. If the strain were a member of a hitherto unknown species, conception would not occur until its utility was delineated, unless the habitat of the strain had signalled its utility to its discoverer.

It should be noted that the CCPA has declared that the alleged need to recognize a utility for a substance in order to complete conception is "very much an open question."[57]

[14] In the Microbiological Arts, Conception and Reduction to Practice Will Often Be Simultaneous

Smith v. Bousquet [, 111 F.2d 157, 159 (1940)] involved the use of an old compound as an insecticide. Noting that "there is no known relation between chemical structure and insecticidal action" whereby the efficacy of a chemical as an insecticide may be predicted," the Interference Examiner declared:

> In the experimental sciences of chemistry and biology this element of unpredictability frequently prevents a conception separated from actual experiment and test.

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[56] D'Amico v. Brown, 155 U.S.P.Q. 534 (Pat. Off. Bd. Pat. Interf. 1967).
[57] Rey-Bellet v. Engelhardt, 493 F.2d 1380 (CCPA 1974).

This "inventorship entity" problem was raised during the examination of an early "recombinant DNA research" patent, Cohen and Boyer, U.S. Patent No. 4,237,224 [1980]. On July 18, 1979, several claims in application Serial No. 1,021 were rejected as unpatentable over three articles, the examiner noting "that the inventive entity of the instant application is different from the authors of the references."

On October 1, 1979, the applicants responded to this rejection:

> The rejection of Claims 1 to 11, 16 and 17, as unpatentable over publications, Cohen et al., Chang et al., and Morrow et al. are respectfully traversed. Indeed it is noticed that the inventive entity is different from the authors of the reference. However, it is well known, that senior authors normally publish contemporaneously with co-workers and graduate students. This is the situation here. The first two articles are by Cohen and Chang. Chang was a graduate student working under the direction of and in conjunction with Professor Cohen. In the absence of any basis for suggesting that Annie Chang, Professor Cohen's student, is in fact a co-inventor, rather than a co-author, it is believed to be inappropriate to reject the claims over the inventor's own publications.
>
> The Morrow article comes substantially after these references and also after an article, Cohen et al. Proc. Nat. Acad. Sci. USA 70, 3240 (1973) a copy of which accompanies this response. Professor Helling worked with Professor Boyer, while Ms. Chang, now Dr. Chang, worked with Professor Cohen. The mere fact that they are co-authors is an insubstantial basis for suggesting co-inventorship and it is submitted that there is no legal basis for rejecting the claims, where the inventors are co-authors of the references. So far as the Morrow article, it comes substantially after the other articles which establish applicants' reduction to practice of the subject invention. Therefore, this article is not appropriate as a reference.

On November 19, 1979, the Examiner reiterated the rejection, but referred the applicants to the *Hirschler* ruling [110 U.S.P.Q. 384 (1952)]. After blasting the line of decisions supporting the Examiner's position as "neither supported by logic nor reality," applicants' attorney overcame the references by

ing any substantive guidance as to the course of the study.[45]

Under the *Agawam* rule, in an employer-employee context, an employer may be deemed the sole inventor of discoveries made by his employee which were "ancillary" to the plan and preconceived design of the employer.[46] In *City of Milwaukee v. Activated Sludge,* involving a patented process of treating sewage with bacteria, the patentee (Jones) had employed Fowlers, Lockett, and Coombs, as chemists. Jones apparently was an engineer who solved the practical problems of exploiting the biochemical processes researched by Coombs and Fowler who joined Jones' employ after making the basic discovery of the aerobic activity of M-7 bacteria. The court held that the evidence did not displace Jones from his seat as "sole inventor," which he acquired in part because he perfected the devices for circulating the sludge in a finely divided form.[47]

Agawam was not controlling in a second microbiological case, *Larson v. Crowther.*[48] Larson was a professor of bacteriology and immunology at the University of Minnesota. Crowther was a skilled mechanic employed by the same institution. Crowther "had in mind that bacteria might be killed by subjecting them to the pressure of carbon dioxide gas and suddenly releasing it." Perfecting the necessary apparatus, he took credit for them in a report to Dr. Larson. Dr. Larson had been investigating the disruption of bacteria by the application of pressure, but the "crux" of the invention was "(t)he destruction of bacteria by the sudden release of pressure." Larson sought to rely on *Agawam* but the Eighth Circuit declared sharply that "(b)oth were employees of the University."

In the field of molecular genetics, we are likely to see various laboratories generating a series of articles and patent applications. This may create certain legal difficulties, as the authorship and inventorship entities will expand and contract as time goes on.

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[45] *See* 1 Rivise & Caesar, Interference Law and Practice §114 at 327 (1940).

[46] Agawam Co. v. Jordan, 74 U.S. (7 Wall.) 583 (1868); *See* Prager, Agawam v. Jordan, Annotated, 22 JPOS 737 (1940). *But see* Mayview Corp. v. Rodstein, 620 F.2d (9th Cir. 1980).

[47] 69 F.2d 577, 585-587 (7th Cir. 1934).

[48] 26 F.2d 780 (8th Cir. 1928) (vaccines).

Inpadoc, in order to search for pertinent foreign patents. Note, however, that on-line searching requires an ability to guess all the forms in which a concept might be expressed. A search on "promoters," for example, should cover "operon," "transcription control sequences," "5′ flanking sequences," and "regulons." One for "signal sequences" must cover "leader sequences." One for "liposomes" must cover "lipid vesicles" and "microcapsules." Moreover, bear in mind that only a small part of the foreign patent application (the title, and possibly the abstract) are searchable.

U.S. patents are the third most important source of prior art, because they represent work done at an earlier time than the work disclosed in a foreign application published on the same date. U.S. patents may be searched manually or by computer. The most pertinent classes are class 435 (former 195), "Molecular Biology and Microbiology," class 436, "Chemistry—Analytical and Immunological Testing," and new class 935, "Genetic Engineering." However, there are many other classes which occasionally are helpful.

It is now possible to search all the claims of a U.S. patent on-line, to obtain a statistical analysis of the classification of all U.S. patents containing a particular keyword, and to automatically find all later patents citing a pioneer patent. These resources may prove helpful. Often, it is desirable to do a quick manual search to help devise a comprehensive on-line search strategy, or a quick computer search to help select subclasses for manual search. In other words, manual and on-line searching are not mutually exclusive.

[10] A Co-Author of an Article Describing a Novel Strain Is Not Always a "Joint Inventor" of that Strain

While talking to attendees at the 1981 Battelle Memorial Institute Conference on Genetic Engineering, this author observed that few of the scientists appreciated why the coauthor

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[41] [Reserved.]

[42] [Reserved.]

ing paragraph. The Secretary should not release such portions unless (a) he has found the portions so identified not to be excepted and has given the submitter advance notice of this finding and an opportunity to rebut it, or (b) the public need to know so outweighs the interest of the submitter as to require release. Where the Secretary releases records or portions thereof because of the public need to know, he should notify the submitter, setting forth the urgent health or environmental needs which serve as the basis for his action.

In *Ex parte Suozzi* [, 125 USPQ 445 (POBA 1959)], a pre-FOIA case, an unclassified report distributed to government officials in their public capacity was held not to be a "publication" since their imparting, to the general public, of the information contained therein "would be merely permissive." Since FOIA disclosure of nonexempt government materials is mandatory, it might be argued that it represents "the other side of the coin." On the other hand, an analogy could be drawn with the *Bayer* case, comparing the government officials with the faculty committee, or to *Harris*, comparing the FOI process with declassification.

While the materials accessible under FOIA are not listed in a publicly available catalogue or index, it may be argued that this does not render them any less a "publication," since the agency's FOI Officer will locate documents responsive to a speculative subject matter request. The best that can be said at this time is that it is possible, though unlikely, that a report will be considered available as a reference when received by an agency. It ought not be considered a reference if it is marked "confidential business information" until the agency resolves its status. It certainly may be considered a reference once it is actually released to an FOIA requester.

FOIA may also have an impact on foreign patent protection. According to the leading treatise on FOIA disclosure law:

> A major concern of government contractors is the impact of the FOIA on patentability abroad. If trade secrets are shared with the government and face the possibility of disclosure, are the contractors in jeopardy of loss of patent rights? The European Patent Convention speaks in terms of "everything made available to the public" before the date of the European patent

copy.[36]

Note that since subcultures are sold by culture collections, a culture deposit might eventuate a §102(b) bar under the "on sale" clause, not merely the "printed publication" clause.

It could also be argued that an unrestricted deposit in the United States represents public knowledge or use by others in the United States under 35 U.S.C. §102(a). Again, it is uncertain whether the courts will emphasize its accessibility, or its actual dissemination, in reaching a conclusion. Note that a deposit outside the United States, while not in itself representative of "knowledge . . . in this country," may result in the evocation of §102(a) art when the depository distributes catalogues to persons in this country.

[7] Classified Publications Are Not Prior Art Until They Are Published

In *Ex parte Harris* [, 79 USPQ 439 (Comm'r 1948], the examiner relied on the declassification date of certain formerly classified reports on government-subsidized penicillin research. The Commissioner held that, absent any public announcement of the declassification, an overt act of publication, whereby these reports were communicated to the public, was necessary to render these publications "prior art."

[8] Effect of Disclosures to the Government

Under the Freedom of Information Act, much of the voluminous paperwork submitted to the government under penalty of law, or under contracts or grants, is available for public inspection.[37] While an exception is made for "trade secrets," it is the agency which decides whether the request covers a trade secret or not, often on an ex parte basis.[38]

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[36] Ex parte Deaton, 146 U.S.P.Q. 549, 551 (POBA 1965).

[37] 35 U.S.C. §552.

[38] *See generally:* Federal Information Disclosure, J. T. O'Reilly Ch. 10 (1980); Chevron Chemical Corp. v. Costle, 641 F.2d 104 (3d Cir. 1981)(allows

deposit in the Library of Congress. *In re Tenney* held that a microfilmed application, indexed under the wrong subject, was not to be considered a "printed" publication, in the absence of any showing that "the disclosure has achieved wide circulation." (The holding was based more on the fact that there was only one microfilm copy than on the fact that it was incorrectly indexed.)[29] Judge Worley, concurring, suggested the need to distinguish "dissemination . . . from technical accessibility."[30]

Under the *Tenney* view, a deposit could be considered "prior art" only if subcultures were in fact requested.

The third view was expressed in *Philips Elec. & Pharmaceutical Industries Corp. v. Thermal & Elec. Industries, Inc.* (1971). A microfilmed *and indexed* German application was held to be a reference. The index was available at the Library of Congress. *Tenney* was distinguished as a "misindexing" case. The Court held that the proponent of the reference must introduce either "proof of its dissemination" or proof "that a person interested in and ordinarily skilled in the art can locate it. . . ."[31] Similarly, in *Ex parte Garbo* (1962), the Government's disseminative intent, and the proper indexing of the microfilmed materials, was deemed controlling.[32]

In *Gulliksen v. Halberg* (1937),[33] the Patent Office Board of Appeals held that a thesis was available as a reference when received by a university library. On the renewed petition for rehearing, it held that the dates of binding and indexing were of no importance. Similarly, *Ex parte DeGrunigen* (1958) held that a thesis is available as a reference, at least once processed and shelved, whether or not it was catalogued.[34] *In re Bayer* (1978) suggests that the CCPA is less likely than the Board to regard a thesis as a reference, though it did not overrule the

[29] 254 F.2d 619, 626-27 (CCPA 1958).
[30] 254 F.2d at 628-29.
[31] 450 F.2d 1164, 1169-72 (3d Cir. 1971).
[32] 141 U.S.P.Q. 913 (POBA 1962).
[33] 75 U.S.P.Q. 252, petitions for rehearing denied, 75 USPQ 257 (POBPI 1937).
[34] 132 U.S.P.Q. 152 (POBA 1958).

The *Mancy* decision made it clear that the public received a *quid pro quo* for granting the claim allowed:

> While the patent will grant appellants a limited right to exclude others from producing daunorubicin by the use of *Streptomyces bifurcus*, the public receives not only the knowledge of appellants' discovery but also access to *Streptomyces bifurcus* through its deposit with the Department of Agriculture. See *In re Argoudelis, supra.*[25]

A new use of a *known* microorganism could, of course, be "*prima facie* obvious."

In re Kaufmann (1971), without indicating whether the Proteus OX-19 strain recited in claims 5 and 10 had been discovered by the applicant, held these claims obvious over the Huang patent, which disclosed that 6-aminopenicillanic acid could be produced by subjecting a penicillin to the action of a variety of penicillin ocylase-producing strains, including strains of species *Proteus rettgeri* and *Proteus sphingidus.*[26]

[6] Unrestricted Culture Deposits May Themselves Be "Prior Art"

A researcher seeking to improve a strain is likely to mutate and select strains repeatedly before filing an application. The "intermediate" strains created during this search are likely to be deposited with a culture collection well before any patent application is filed, and, indeed, even before any manuscript describing the strains is written, submitted, accepted, and published. If the culture deposit is itself "prior art," the effect on the patentability of similar strains is likely to be significant, since the effective filing date of the application may well be more than one year after the date of the deposit. (This problem, of course, arises only with regard to "unrestricted" deposits.)

The culture deposit of course enables the reproduction of

[25] 182 U.S.P.Q. at 306.

[26] 451 F.2d 1096, 1097-98 (CCPA 1971).

bically cultivating *Streptomyces bifurcus.*"[18] Finally, in *Ex parte Lundak* (1984), the Board of Appeals held that a written description of a novel cell line in a patent application, was, absent a deposit of the cell line, incapable of enabling the claims to the cell line. The Board cited *LeGrice* as authority supporting its position.

The issue of whether a reference was "enabling" was raised imperfectly in *Ex parte Goodall.*[18.1] The application claimed "a monoclonal antibody to hepatitis B surface antigen which is secreted by hybridoma cell line RF-HBs-1." The Examiner rejected the claim over Wands U.S. 4,271,145, which disclosed a hybridoma cell line, CRL-8017, which secreted an antibody deemed to be similar to that of Goodall. Appellants asserted that they had requested CRL-8071 from the culture collection, the ATCC, and that the ATCC had failed to provide it. Thus, they concluded, "the Wands disclosure is non-enabling and thus could not anticipate or render obvious their invention."

It appears that Goodall failed to put into the record any communications among ATCC, Wands and Goodall that might support the assertion of unavailability. Thus, while the Board thought that Goodall's argument "could give rise to very interesting issues," those issues were "not reached in this case" by reason of the inadequate documentation.

[5] The Use of a Novel Strain of Microorganism, Similar to a Strain Previously Known, and Used Similarly, Is Not "Prima Facie Obvious"

A liberal concept of nonobviousness was espoused by the CCPA in *In re Mancy.* The applicant had presented the following claim:

> 1. Process for the production of daunorubicin which comprises aerobically cultivating *Streptomyces bifurcus, strain* DS 23,219 (NRRL 3539), of [*sic,* or] a daunorubicin-producing mutant thereof, using an aqueous nutrient medium containing assimil-

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[18] In re Mancy, 182 U.S.P.Q. 303, 305 (1974).
[18.1] 231 U.S.P.Q. 831 (BPAI 1986).

[3] Mere Practice of Fermentation Process Abroad by Another Is Not Anticipatory "Knowledge" or "Use" Under 35 U.S.C. §102

The exclusion of foreign knowledge, use or invention, not embodied in a patent or printed publication, from the scope of 35 U.S.C. §102, is probably attributable to two considerations: (1) the difficulty of proving or disproving the foreign knowledge or activity; and (2) the notoriety of the foreign activity in the United States. While these considerations have questionable force in the modern world, the exclusion has been retained. Thus, the mere practice of a fermentation process abroad will not anticipate, under 35 U.S.C. §102(a) another's subsequent U.S. patent claim to that very process.

An early fermentation patent case, *City of Milwaukee v. Activated Sludge*[14] declared that even domestic knowledge of an invention reduced to practice abroad could not operate as an anticipation until the invention was patented or described in a printed publication. (Knowledge of the activated sludge process, reduced to practice in Manchester, England, had been communicated to various experts in the trade.) This author suggests that if the domestic knowledge of the foreign invention is sufficient to reduce the invention to practice, and is, though unpublished, characterizable as "public" knowledge, this knowledge, when proven, might constitute prior art.

[4] If an Organism Is Not Readily Available, Its Mere Description in a Printed Publication Is Not "Prior Art"

In re LeGrice, discussed in detail in Chapter 8, explained that a mere written description of a "rose floribunda plant" would not normally "enable" a person skilled in the art to reproduce the plant, since plant breeders "are not presently able to control the factors which govern the combination of genes and chromosomes required to produce a new plant having cer-

[14] 69 F.2d 577, 588-89 (7th Cir. 1934).

(2) *B* was the first to conceive the invention and was diligent from a time just prior to *A's* entry into the field. (The lack of diligence of *A* is irrelevant, unless it amounts to "abandonment, suppression, or concealment.") The various ingredients of priority, namely conception, reduction to practice, and diligence, are subject to "corroboration" requirements.

The remainder of this section will specifically apply these general principles to "biological" invention.

[2] Secret Practice of Fermentation Process May Vitiate Right to File for U.S. Patent Thereon

Like so many legal terms, the term "public use" in 35 U.S.C. §102 has taken on connotations distinct from those it bears in ordinary speech. The use of an improved corset spring in a pair of corsets used by one woman, "and in a position always withheld from public observation" was deemed by the Supreme Court to be a "public" use:

> [W]hether the use of an invention is public or private, does not necessarily depend upon the number of persons to whom it is known.
>
> [S]ome inventions are by their very character only capable of being used where they cannot be seen or observed by the public eye. An invention may consist of a lever or spring, hidden in the running gear of a watch. . . . Nevertheless, if its inventor sells a machine of which his invention forms a part, and allows it to be used without restriction of any kind, the use is a public view. . . . So, on the other hand, a use necessarily open to public view, if made in good faith solely to test the qualities of the invention, and for the purpose of experiment, is not a public use within the meaning of the patent law.[9]

In the corset case, the use was necessarily hidden. The Supreme Court has not squarely considered whether use under an "injunction of secrecy" would constitute "public use." However, in *Worley v. Loker Tobacco* it noted that "no one was excluded from the factory"; in *Hall v. MacNeale* it was observed

[9] Egbert v. Lippmann, 104 U.S. 333, 336 (1881).

mechanic acquainted with the business."[3] 35 U.S.C. §103 provides

> §103. Conditions for patentability; non-obvious subject matter
>
> A patent may not be obtained though the invention is not identically disclosed or described as set forth in § 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The Senate and House reports explain 35 U.S.C. §103 as a provision representing the view that "[a]n invention which has been made, and which is new in the sense that the same thing has not been made before, may still not be patentable if the difference between the new thing and that which was known before is not considered sufficiently great to warrant a patent." They define "prior art" as "what was known before as described in § 102."

In *Graham v. John Deere and Co.*, the Supreme Court held that in applying §103, the PTO and the courts should make "several basic factual inquiries:

> Under §103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background, the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented. As indicia of obviousness or nonobviousness, these inquiries may have relevancy.[4]

An inventor's own prior work may be treated as prior art

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[3] 52 U.S. (11 How.) 248, 252-53 (1851).

[4] Graham v. John Deere & Co., 383 U.S. 1, 17-18 (1966).

§102. Conditions for patentability; novelty and loss of right to patent

A person shall be entitled to a patent unless—

(a) 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, or

(b) The invention was patented or described in a printed publication in this or a foreign country or in a 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, or

(c) He has abandoned the invention, or

(d) The invention was first patented or caused to be patented, or was the subject of an inventor's certificate, by the applicant or his legal representatives or assigns in a foreign country prior to the date of the application for patent in this country on an application for patent or inventor's certificate filed more than twelve months before the filing of the application in the United States, or

(e) The invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or

(f) He did not himself invent the subject matter sought to be patented, or

(g) Before the applicant's invention thereof the invention was made in this country by another who had not abandoned, suppressed, or concealed it. In determining priority of 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 time prior to conception by the other.

As the subtitle of Section 102 indicates, it covers both "novelty and loss of right to patent." The "novelty" required by paragraphs (a), (e) and (g) "is not novelty in an absolute sense, as the statute defines what is to be looked to in order to show

protection under §101."[104]

Unfortunately, the term "product of nature," like Pavlov's bell, will probably summon the ghost of *American Fruit Growers* for many years to come.

§ 3.06 Patentability of the Obviously Desirable Product of a Nonobvious Process

Where it is evident that purification of a product would accentuate its desirable or reduce its undesirable characteristics, or where an altered form of a product is obviously desirable, patentability may be bottomed on the nonobviousness of all processes for successfully making the desired product.

In *Irani*,[105] involving a claim to crystalline anhydrous "ATMP," the examiner took the position that any one skilled in the art, knowing of Petrov's "glassy solid" (amorphous) form of ATMP, "would be motivated to attempt the preparation of crystalline anhydrous ATMP" by the knowledge that some compounds of its class existed in crystalline form and were useful as softeners, sequesterants, or chelating agents. The CCPA held that "even assuming that one skilled in the art could have predicted with reasonable certainty that crystalline anhydrous ATMP could be produced, we are not convinced by this record how this could be achieved. We note that neither the examiner nor the Board has contended that a suitable process would have been obvious.

In *Grose*, the CCPA was concerned with a synthetic crystalline zeolitic molecular sieve "fingerprinted" by its X-ray powder diffraction pattern. The CCPA declared that "[o]ne of the assumptions underlying a prima facie obviousness rejection based on a structural relationship between compounds, . . . that a method disclosed for producing one would provide those skilled with a method for producing the other," was inapplicable.[106] Following *Hoeksema*, the CCPA held that the product could not be obvious if there was no obvious process of preparing it.[107]

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[104] 209 U.S.P.Q. 1-10 (S. Ct. 1981).

[105] In re Irani, 427 F.2d 806, 807, 809 (CCPA 1970).

[106] In re Grose, 592 F.2d 1161, 1168 (CCPA 1979).

[107] Id., citing In re Hoeksema, 399 F.2d 269, 274 (CCPA 1968).

a visible and a latent alteration. In *Ex parte Mowry,* the Board drew a new distinction, validating a claim to an "erosion stable soil" (soil covered by a surface film of a water-scluable polymer) as the "soil has been chemically modified by having its electrolytic sites absorbed on the polymer molecules; [and as] this treatment has modified its physical properties and increased its utility by rendering it resistant to natural erosive forces."[99] One may wonder whether it is fair to limit *American Fruit Growers* to coated natural products in which the coating does not react chemically with the product. The *Mowry* holding was "followed" in *Ex parte Shepherd,* involving a claim to a "combination of soil and fumigant," even though there was no indication of any chemical reaction between the soil and the fumigant.[100]

In *Ex parte Chakrabarty,*[101] the Board apparently agreed that the claimed bacteria could not be considered "products of nature," as *"Pseudomonas* bacteria containing two or more different energy generating plasmids are not naturally occurring." Typical of the *Chakrabarty* claims was claim 7, to

> [a] bacteria from the genus *Pseudomonas* containing therein at least two stable energy generating plasmids, each of said plasmids providing a separate hydrocarbon degradative pathway.[102]

In 1971, Chakrabarty and Gunsalus had disclosed (1) that the genes governing the synthesis of the enzymes responsible for the degradation of (a) camphor and (b) octane constituted "plasmids" and (2) that the CAM and OCT plasmids were incompatible, *i.e.,* they would not both be replicated if placed in a single microorganism, presumably because the cellular maintenance site" for plasmids was already occupied. Chakrabarty overcame this problem of plasmid incompatibility by fusing the CAM and OCT plasmids with UV radiation.

The Supreme Court, without distinguishing the "law of nature" and "product of nature" doctrines, held that the Chak-

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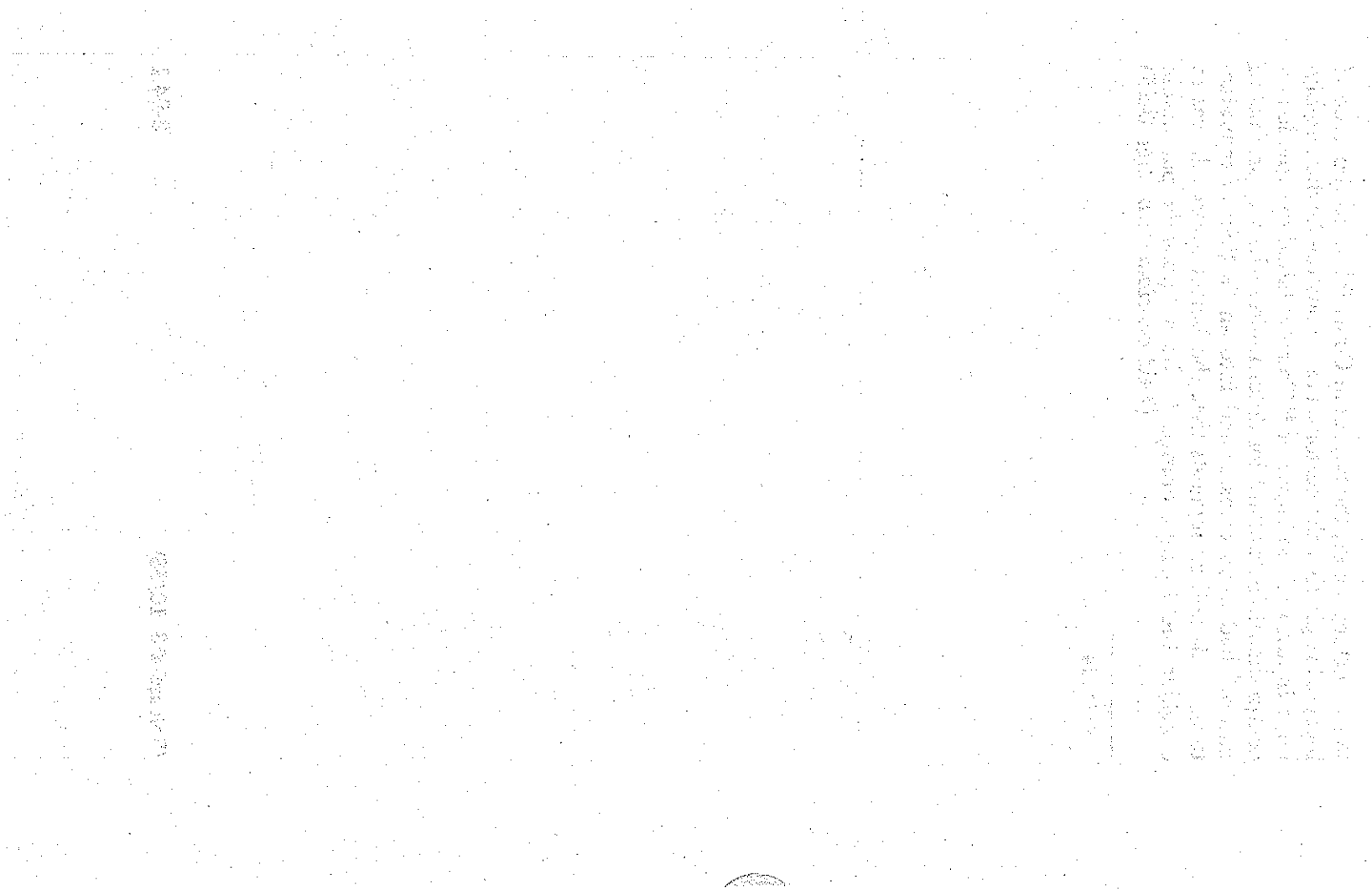
[99] 110 U.S.P.Q. 389 (POBA 1955).
[100] 185 U.S.P.Q. 480 (POBA 1974).
[101] In re Bergy, Pat. App. No. 77-535, Rec. 92-94.
[102] Id., 92.

same use whether or not impregnated with borax. A fur skin unimpregnated with ferrous sulphate cannot be used in the same way as one which has been so impregnated. The orange case does not, in our opinion, require a decision that the product patent in suit is invalid.[91]

It would be unfortunate if the result of these opinions was a rule that the patentability of an altered product of nature depended on whether the alteration was visible to the naked eye. This author believes that the increase in the utility of the dark-colored fur skins in *Steinfur* was not appreciably greater than the increase in the utility bruised mold-prone fruit in *American Fruit Growers.* More likely, the product claims to the bleached fur skins were held valid simply because the prior art did not teach a bleaching agent which acted quickly enough to bleach dark-colored fur before the immersion impaired the hair or the leather.[92] In *Brogdex,* the prior art taught the use of borax as a preservative for fruit, and Brogdex's product claims would have fallen for lack of novelty.

In *Dennis v. Pitner,*[93] the Seventh Circuit correctly distinguished between a "product of nature" rejection and an "obviousness" rejection in a factual context similar to that of the *Grayson* case. Claim 1 was directed to "(a)n insecticide and vermifuge comprising ground cube root with the fibrous element removed." Defendants contended that the patented article "is a product of nature, namely the powdered cube root, either as dust, extract, or concentrate—the latter being merely modified forms of the natural product." The court rejected the contention that "the cube roots utilized as an insecticide may not involve patentable invention under any circumstances."[94] It invalidated the claims, however, because it was "not persuaded that Dennis was the first to discover that the powder from the cube root could be used as an insecticide." Others had previously reported that the plant was "often cultivated for use as a fish poison" and that the extracts "has long been used

[91] Id., 240.
[92] Id., 241 ("carroting fur").
[93] 106 F.2d 142 (7th Cir. 1939).
[94] Id., 144-146.



claim the products, though natural in origin, which they have produced by nonobvious methods?

In 1931, the Supreme Court held in *American Fruit Growers, Inc. v. Brogdex Co.* that the following product claim was invalid:

> Fresh citrus fruit of which the rind or skin carries borax in amount that is very small but sufficient to render the fruit resistant to blue mold decay.[85]

The Third Circuit had held that the product claimed was a "combination of the natural fruit and a boric compound," and was patentable as "the complete article is found in nature and is thus an article of manufacture."[86]

Relying on the definition of "manufacture" given in the Century Dictionary, and on two custom cases interpreting this term, the Supreme Court declared

> Addition of borax to the rind of natural fruit does not produce from the raw material an article for use which possesses a new or distinctive form, quality, or property. The added substance only protects the natural article against deterioration by inhibiting development of extraneous spores upon the rind. There is no change in the name, appearance, or general character of the fruit. It remains a fresh orange, fit only for the same beneficial uses as theretofore.[87]

This *American Fruit Growers* case has some obvious faults. First, it may be argued that "resistance to blue mold decay" is a new and distinctive quality or property of the Brogdex orange, and that the borax treatment rendered bruised or scratched fruit, which normally would be attacked by the blue mold, secure, and therefore gave such fruit a marketing use it would not otherwise have. Second, it relied on custom cases, and under customs law, construing the goods to be "manufactured" would have led to the imposition of higher duties. In

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[85] American Fruit Growers, Inc. v. Brogdex Co., 283 U.S. 1, 6 (1931)(claim 26).

[86] Discussed at 283 U.S. at 11.

[87] Id., 11-12.

the *Streptomyces vellosus,* or is it the chunk of Arizona soil from which Bergy isolated it? The organism, per se, is not a "thing occurring in nature," since nowhere on the face of this earth, can one find *Streptomyces vellosus* existing apart from other organisms other than in a laboratory. (This is the fallacy of *General Electric.* The tungsten atom occurs in nature, but only bound to oxygen.)

Bergy's *Streptomyces vellosus,* under controlled fermentation conditions, could be used to produce the antibiotic lincomycin. The chunk of Arizona soil from which it was isolated could not be used in this manner. The *S. vellosus* was but a minor denizen of a "complex jungle of microorganism." Forced to battle for survival, it could hardly attain a significant population level without human assistance. Only a culture of *S. vellosus* free of competitive organisms would be an efficient producer of lincomycin.[80]

In the vitamin B-12 case,[81] the court declared

> The step from complete uselessness to great and perfected utility is a long one. That step is no mere advance in the degree of purity in a known product.

The CCPA decided, following the vitamin B-12 case, that Bergy's biologically pure culture was "a far cry" from "something preexisting, and merely plucked from the earth and claimed as such.[82] The lesson of *Bergy* is that a biologically pure culture is analogous to a chemically pure extract or distillate. Chemists isolate molecules; biologists isolate organisms. Both manipulate heterogeneous products of nature—the coal tars of the chemist, the topsoils of the biologist—in order to obtain something useful.

The *Bergy* decision, though vacated, remains significant because it reflects the views of four of the present judges of the CCPA; because the CCPA hears appeals from the decisions of the Patent and Trademark office; because the Supreme Court

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[80] *See* affidavits of Grady, Dietz, and Miller, referred to in 596 F.2d at 972.
[81] Merck & Co., Inc. v. Olin Mathieson Chem. Corp., 116 U.S.P.Q. at 490.
[82] 563 F.2d 1031, 1036 (CCPA 1974).

may be profitably compared with the ductile tungsten case. The CCPA upheld a claim to "Element 95, Americium" even though this element would have been produced in the course of prior art reactor operations, as the amount produced could not have exceeded one-billionth of a gram, distributed amidst forty tons of intensely radioactive uranium fuel.[72] (The court also upheld, in a companion case, a claim to Element 96, Curium.)

In re Bergstrom involved claims to compounds of the prostaglandin family, PGE2 and PGE3.[73] These were extracted from natural sources such as the human prostate gland. The examiner rejected the claims under Section 101 as directed to "naturally occurring substances," which were not "new." At first, the Board took the position that "a claim to a purified material cannot be allowed unless the purified material exhibits properties and utilities not possessed by the unpurified material."[74] Later, the Board referred to the *inherent* presence of PGE2 and PGE3 in the prior art reference.[75] While it was true that extracts from the human prostate glands were known to have hypotensive and smooth muscle-stimulating pharmacological activity, this activity and the presence and activity of PGE2 and PGE3 were not suspected *by* those skilled in the art.[76]

Rejecting both the examiner's and the Board's position, the CCPA said:

> The criteria for determining whether given subject matter is "new" within the meaning of §101 are no different than the criteria for determining whether that subject matter possesses the "novelty" expressed in the title of §102. The word "new" in §101 is defined and is to be construed in accordance with the provisions of §102. Thus, that which possesses statutory novelty under the provisions of §102 is also new within the intendment of §101. We have found no evidence of Congressional intent to

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[71] 328 F.2d 966 (CCPA 1964).
[72] Id., 997.
[73] 427 F.2d 1394 (CCPA 1970).
[74] Id., 1398.
[75] Id.
[76] Id.