



Business Development Basics Course

Introduction To Intellectual Property

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Course Outline

- What is intellectual property?
- All about patents
 - Technical parts
 - Prosecution
 - Foreign patents
 - Costs



Course Outline Continued

- Why are patents important?
 - How claims influence the deal
 - How to read claims
 - Examples of deals
 - How third party issues effect value
- Exclusivity and Safe Harbor laws



Course Outline Continued

- How to work with an IP attorney
 - Freedom to operate issues
 - Opinion of counsel
 - Due diligence
 - Valuation of IP

- In the News – current topics



Intellectual Property

- Intellectual property is a **bundle** of **exclusive rights** over creations of the mind, both artistic and commercial.
- Two-thirds of the value of large businesses in the U.S. can be traced to intangible assets.
- Likewise, industries whose reliance on IP protections are estimated to produce 72 percent more value per added employee than non-IP industries



PRIMARY TYPES OF INTELLECTUAL PROPERTY

- **Copyright**
 - Property right in an original work of authorship that is fixed in a tangible form.
- **Trademark**
 - Distinctive sign that is used by a company to identify its products or services as its own.
- **Trade Secret**
 - Formula, practice, process, design instrument or information not generally known to the public that affords a commercial advantage over your competitors
- **Patent**



Patents

- A **patent** is a set of exclusive rights granted by a government to an inventor or assignee for a fixed period of time in exchange for disclosure of its secrecy
- A Constitutional Right
 - The Congress shall have power to promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries.
- Historically, patents date back to 1623 English Statute of Monopolies granted for **new** inventions.
- Jefferson was the father of our patent system and Congress enacted the first patent law in 1790.



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US005284654A

United States Patent [19]
Weber et al.

[11] **Patent Number:** **5,284,654**
[45] **Date of Patent:** **Feb. 8, 1994**

- [54] **METHOD FOR THE TREATMENT OF PARKINSON'S DISEASE**
- [75] **Inventors:** **Richard J. Weber**, Silver Spring; **Robert J. Plunkett**, Gaithersburg, both of Md.; **Scott E. Ewing**, Chicago, Ill.
- [73] **Assignee:** **The United States of America as represented by the Department of Health and Human Services**, Washington, D.C.
- [21] **Appl. No.:** **892,485**
- [22] **Filed:** **Jun. 3, 1992**

Related U.S. Application Data

- [63] Continuation of Ser. No. 401,141, Aug. 31, 1989, abandoned.
- [51] **Int. Cl.⁵** **A61K 35/14**
- [52] **U.S. Cl.** **424/93 V**
- [58] **Field of Search** **424/93 V; 435/2, 240.2**

- [56] **References Cited**
U.S. PATENT DOCUMENTS
4,902,288 2/1990 Ingram 424/534

OTHER PUBLICATIONS

- LeFur et al, Biol. Abstracts, vol. 73 (1981), 4433.
- Sladek et al, in Ann. N.Y. Acad. Sci., vol. 495 (1987) pp. 641-657.
- Backlund et al, in Ann. N.Y. Acad. Sci., vol. 495 (1987) pp. 658-669.
- Primary Examiner*—Jacqueline Stone
Attorney, Agent, or Firm—Office of Technology Transfer, National Institutes of Health

- [57] **ABSTRACT**
The present invention is directed to a method for the treatment of Parkinson's disease which affect the dopaminergic system by implanting into the brain of a host in need thereof an anti-neurodegenerative effective amount of activated leukocytes.

3 Claims, 1 Drawing Sheet



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METHOD FOR THE TREATMENT OF PARKINSON'S DISEASE

This application is a continuation of application Ser. No. 07/401,141 filed on Aug. 31, 1989, now abandoned, the entire contents of which are incorporated herein by reference.

BACKGROUND OF THE INVENTION

Parkinson's disease is a dopaminergic neurodegenerative disorder which afflicts an estimated 1% of the population over the age of fifty. The disease is primarily characterized by tremor, rigidity, impaired postural reflexes, and paucity of movement resulting from the loss of dopaminergic neurons in the substantia nigra which normally project to the corpus striatum. Because parkinsonian patients have a low concentration of dopamine in this region of the basal ganglia, current therapies have been directed at restoring normal levels of dopamine using the dopamine precursor L-dopa, with a peripheral decarboxylase inhibitor such as carbidopa. However, L-dopa's effectiveness diminishes with continued use and troublesome side effects often occur. Thus, alternative therapies are being sought. Strategies to promote functional recovery by implantation of fetal dopaminergic cells in specific dopamine-depleted areas of the brain are currently being evaluated in Parkinsonian animal models as well as in certain patients with Parkinson's disease. No doubt this investigational treatment will be confronted with some opposition on moral grounds.

The present invention has been accomplished with the above disadvantages in mind.

SUMMARY OF THE INVENTION

The present invention is directed to a method of treating neurodegenerative disorders which affect the dopaminergic system by implanting into the brain of a host in need thereof an anti-neurodegenerative effective amount of activated leukocytes.

BRIEF DESCRIPTION OF THE DRAWINGS

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(PHA), Sigma Chemicals Company, St. Louis, Mo.; lipopoly-saccharide (LPS), Difco Laboratories, Detroit, Mich.; and pokeweed mitogen (PWM). Examples of the lymphokines useful in activating the leukocytes to be utilized in the present invention are interleukin-2 (IL-2), Cetus Corporation, Calif.; and interleukin-3 (IL-3), Genzyme Corp., Boston, Mass. Examples of cytokines useful in activating the leukocytes utilized in the present invention are interleukin-1 (IL-1) and tumor necrosis factor (TNF), etc., both obtained from Collaborative Research, Lexington, Mass.

The activated leukocytes can be administered to the locus of the lesion by surgical implantation in a one time or a number of surgical implantations sufficient to elicit the desired response. The dosage amount to be implanted can be from about 1×10^5 to 1×10^7 cells. The cells can be administered in any known pharmaceutically conventional carrier such as normal saline. The dose, of course, will vary from patient to patient, depending on the severity of the lesions and/or the disease state and can readily be ascertainable by one skilled in the art.

The leukocytes can be activated either in vivo or in vitro. When activated in vitro, the thus produced activated leukocytes are surgically implanted to the lesioned area of the brain. When treating humans the leukocytes could be activated in vitro. In case of Parkinson's Disease the locus of the lesion is known to be in the striatum.

The present invention overcomes a number of disadvantages associated with the prior art therapies. For example, with respect to L-Dopa therapy, the present invention can reduce or totally eliminate L-Dopa therapy, thus decreasing or eliminating the untoward side effects associated therewith. The present therapy would also be an alternative to fetal implantation therapy, thus eliminating any moral issues raised by such a therapy.

Since in most instances it would be the patients' own auto-logous leukocytes which are activated, the cells to be utilized in the surgical procedure would be readily available and the chances of host rejection would be slim to none.



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ydopamine (6-OHDA), a catecholaminergic neurotoxin, was stereotactically injected into the pars compacta of the right substantia nigra following anesthesia with 350 mg/kg of chloral hydrate administered intraperitoneally. Ten days after lesioning, rats were tested for rotational behavior induced by D-amphetamine, a dopamine releasing agent. Rats in which the dopaminergic nigrostriatal pathway has been unilaterally destroyed rotate toward the side of the lesion when given amphetamine. The number of full body clockwise and counterclockwise turns of each rat was recorded in a rotameter as described by Ungerstedt, *Brain Res.* 24,485 (1970). Rats turning consistently at least 7 clockwise turns/min over a 90 minute period for 4 trials, which reflects a 98% or greater denervation of the striatum on the lesioned side were divided into three groups: unimplanted (n=10), sham-implanted (n=7), and implanted (n=13).

EXPERIMENT 2

Rats in the sham-implanted and implanted groups received 5 microliter stereotaxic injections of medium or a total of $3-7 \times 10^5$ activated leukocytes respectively, aimed at the following coordinates: A 0.20 mm, V 5.4 mm, L 2.2 mm (bevel rostral); A 0.20 mm, V 6.4 mm, L 3.2 mm (bevel rostral); A 1.60 mm, V 5.2 mm, L 2.0 mm (bevel rostral); A 1.60 mm, V 5.2 mm, L 2.8 mm (bevel caudal), using the technique described by Plunkett et al., *J. Neurosurg.* 69, 228 (1989). The needle was left in place for 2 min before being withdrawn at 1 mm/min. R. J. Plunkett, R. J. Weber, E. H. Oldfield, *J. Neurosurg.* 69, 228 (1989). The leukocytes were lavaged with 0.32M sucrose from the peritoneal cavity of normal Sprague-Dawley rats which had been injected intraperitoneally 48 hours earlier with 1 mg phytohemagglutinin (PHA). Analysis of the activated leukocytes by flow cytometry are described in Weber et al., *Cell Immunology*, 104, 400 (1978) revealed predominantly macrophages and T-lymphocytes. Monoclonal mouse IgG1 antibody to Thy 1.1, clone OX-7 culture supernatant and monoclonal mouse IgG2A antibody to rat macrophage antigen OX 41 ascites fluid were purchased from Pel-Freeze Biologicals (Rogers, AR); Fluorescein-labeled affinity-purified goat antibodies to mouse IgG(H+L) adsorbed with rat serum were purchased from KPL Laboratories, Inc. (Gaithersburg, Md.). Trypan blue exclusion immediately after harvesting and during the period of implantation confirmed cell viability (>95%).

FIG. 1 shows the results of all three groups which were tested weekly for amphetamine-induced rotation during the 13 weeks following implantation. Turning decreased an average of 47% at 8 weeks in the rats implanted with leukocytes ($p=0.006$; Wilcoxon signed rank). As can be seen by FIG. 1 neither the rats in the sham-implanted group nor those in the control group showed a significant decline in turning. Improvement was rapid in the implanted rats, with an average de-

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crease in amphetamine-induced rotation of 22% one week after implantation. In the two rats showing complete improvement, recovery was noted by the fourth and fifth week. Only two of the rats receiving leukocytes failed to show an increase in dopamine content or TH reactivity.

Punch biopsies were taken from the rostral striatum in 8 rats that failed to improve behaviorally (2 shams, 4 controls, and 2 unimproved implanted rats). Identical biopsies were taken in 7 of the leukocyte-implanted rats that improved. Dopamine content of the lesioned right striatum was determined by high performance liquid chromatography to be 0.1% of the intact left striatum in unimproved implanted rats. The results are reported in Table 1 below.

TABLE I

DOPAMINE LEVELS (pg/mcg protein)				
(mean \pm SEM)				
		Right caudate	Left Caudate	R/L
I.	Control (4)	3.0 \pm 1.8	103.3 \pm 20.4	2.9
II.	Sham (2)	1.5 \pm 0.6	91.4 \pm 33.8	1.6
IIIa.	Implant (7)	4.5 \pm 1.3	67.4 \pm 13.3	6.7
IIIb.	Improved Implant (2)	0.1 \pm 0.01	131.6 \pm 14.2	0.1
	Unimproved			

The dopamine content in the right striatum of rats implanted with leukocytes was restored to 6.7% of the left striatum.

Previous studies have shown that dopamine-rich grafts can provide complete compensation of amphetamine-induced turning in 6-OHDA lesioned rats and restore dopamine levels to 10-15% of normal. The results reported herein show here that stereotactically implanted leukocytes alone may be sufficient to bring about behavioral recovery.

All reference articles discussed, supra, are incorporated herein by reference.

While the invention has been described with regard to certain preferred embodiments, it is understood that various changes and modifications may be made without departing from the scope of the invention which is defined in the Claims.

We claim:

1. A method for treating the dopaminergic neurodegenerative disorder Parkinson's Disease by administering to a locus of a lesion of a patient suffering from said disorder an anti-neurodegenerative effective amount of in vitro activated leukocytes.

2. The method according to claim 1, wherein said anti-neurodegenerative effective amount is from about 1×10^5 to 1×10^7 cells.

3. The method according to claim 1, wherein said leukocytes are derived from said patient suffering from said dopaminergic neurodegenerative disorder.

* * * * *



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We claim:

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2. The method according to claim 1, wherein said anti-neurodegenerative effective amount is from about 1×10^5 to 1×10^7 cells.

3. The method according to claim 1, wherein said leukocytes are derived from said patient suffering from said dopaminergic neurodegenerative disorder.

* * * * *



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DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

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By dopaminergic neurodegenerative disorders is meant those disorders which affect the dopaminergic system, e.g., Parkinson's Disease and other such diseases which result in a loss of CNS regulated function.

Here we define terms

By host is meant any patient afflicted with such conditions, including humans, and is in need of said therapy. The leukocytes to be utilized from the present invention should be histo-compatible. Preferred leukocytes are autologous tissue.

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And we teach how to practice the invention

The leukocytes of the present invention are activated by conventional means known in the art where the known activators are brought into contact with the cells. Examples of known activators are plant mitogens, lymphokines and cytokines as are described in William E. Paul, *Fundamental Immunology*, Raven Press, New York, 1984, page 271-274 and page 299. Examples of

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groups.

The present invention has been accomplished with the above disadvantages in mind.

This is where we
sell the
invention to the
Examiner

Two red arrows originate from the text on the right. One arrow points to the first highlighted sentence, and the other points to the second highlighted sentence.



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United States Patent [19]
Weber et al.

US005284654A

[11] **Patent Number:** **5,284,654**
[45] **Date of Patent:** **Feb. 8, 1994**

[54] **METHOD FOR THE TREATMENT OF PARKINSON'S DISEASE**
[75] **Inventors:** **Richard J. Weber**, Silver Spring; **Robert J. Plunkett**, Gaithersburg, both of Md.; **Scott E. Ewing**, Chicago, Ill.
[73] **Assignee:** **The United States of America as represented by the Department of Health and Human Services**, Washington, D.C.
[21] **Appl. No.:** **892,485**
[22] **Filed:** **Jun. 3, 1992**

Here is what the Examiner found

Related U.S. Application Data
[63] Continuation of Ser. No. 401,141, Aug. 31, 1989, abandoned.
[51] **Int. Cl.⁵** **A61K 35/14**
[52] **U.S. Cl.** **424/93 V**
[58] **Field of Search** **424/93 V; 435/2, 240.2**

Here is where the examiner searched

[56] **References Cited**
U.S. PATENT DOCUMENTS
4,902,288 2/1990 Ingram 424/534
OTHER PUBLICATIONS
LeFur et al, Biol. Abstracts, vol. 73 (1981), 4433.
Sladek et al, in Ann. N.Y. Acad. Sci., vol. 495 (1987) pp. 641-657.
Backlund et al, in Ann. N.Y. Acad. Sci., vol. 495 (1987) pp. 658-669.
Primary Examiner—Jacqueline Stone
Attorney, Agent, or Firm—Office of Technology Transfer, National Institutes of Health

[57] **ABSTRACT**
The present invention is directed to a method for the treatment of Parkinson's disease which affect the dopaminergic system by implanting into the brain of a host in need thereof an anti-neurodegenerative effective amount of activated leukocytes.

3 Claims, 1 Drawing Sheet



- Invention Disclosure Form



Invention Disclosure Form - Confidential

1. TITLE OF INVENTION

The title should describe what the invention does, but not how it is made or how it works.

2. SEARCH TERMS (up to 10)

The OTM uses the Internet as a research tool when searching databases and markets. To make our searches efficient, please provide a short list of words, common industry phrases and/or categories.

3. BRIEF OVERVIEW OF THE INVENTION (3-4 paragraphs)

- Provide a short, general layperson's overview of the invention and how it works.
- What is the purpose of the invention? For example, "What problem does it solve?"
- Is it a new product, process, or composition of matter? Or is it a new use for or improvement to an existing product, process or composition of matter?
- What are the features and benefits of the invention?

4. TECHNICAL DESCRIPTION, DETAILS AND SUPPORTING DATA

Provide results, data or other evidence demonstrating how the invention works. Any papers or visual material that you may already have, published or unpublished, can be attached as answer to this question.

5. PRIOR METHODS, APPARATUS, DEVELOPMENTS AND PUBLICATIONS

- Provide a complete description of the closest known methods or apparatus in existence and the disadvantages or problems of each that are solved by the present invention.
- Cite any of your own publications and patents, and those of anyone else believed by you to disclose ideas most closely related to the invention.

Please attach all relevant publications, patents, advertisements, etc, if available.

6. STAGE OF DEVELOPMENT (2-3 paragraphs)

Describe the development status (concept only, laboratory tested, prototype, etc) and briefly indicate what further development may be necessary to commercialize it.

7. POTENTIAL LICENSEES

Identify companies that you think could benefit from the use of this technology.



Process steps for a patent

- Patent Assessment
- Provisional Application
- International Application -12 Months
- National Stage – 30 Months



Patent Assessment

- The process of determining if the preparation of a patent application is warranted
- Asking:
 - Is the invention **novel**?
 - Is the invention **inventive**?
 - Is the invention **commercially important**?



Provisional Applications

- Typically the first application filed
- They should be fully enabled
- Should not be a *cheap* application without claims
- Are never examined
- Die a natural death after 12 months



PCT Applications

- International application
- Filed by 12 month anniversary of provisional
- Begins 20 year period of patent life
- No substantive examination
- Circles globe for 18 months then lands



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National Stage

- Begins at 30 months
- This is where you LAND the PCT Plane
- \$\$\$ Pick your countries wisely \$\$\$



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(19) World Intellectual Property Organization
International Bureau



It's published!

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14 June 2001 (14.06.2001)

PCT

(10) International Publication Number
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(22) International Filing Date: 8 December 2000 (08.12.2000)

(25) Filing Language: English

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(30) Priority Data:
09/459,752 10 December 1999 (10.12.1999) US

(71) Applicant (for all designated States except US): COM-
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(72) Inventors: and

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02130 (US). SWINDLE, John [US/US]; 1908 31st Av-
enue West, Seattle, WA 98199 (US).

(74) Agents: WEBER, Kenneth, A. et al.; Townsend and
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Center, San Francisco, CA 94111-3834 (US).

(81) Designated States (national): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ,
DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,
NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM,
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian
patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European
patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE,
IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:
— Without international search report and to be republished
upon receipt of that report.

Where they want

to file

the priority dates

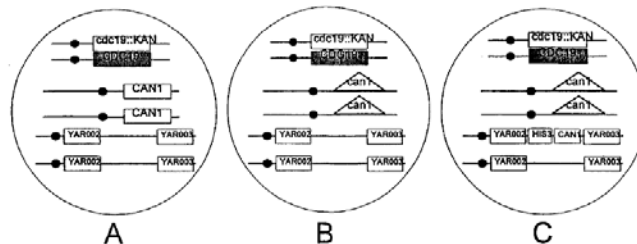
For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

Who owns it,
invented it, and
filed it.

(54) Title: A FUNCTIONAL GENE ARRAY IN YEAST

The invention

2446 A2





Jargon

- Patent Estate = Patent Portfolio
 - This is everything the company owns
- Patent Families
 - Each invention is a patent family comprising
 - U.S. and international applications and issued patents
- Members = Individual Patents or Applications



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PatBase - Microsoft Internet Explorer

Address: http://www.patbase.com/

Display results: (888888 888888)

Search 4: '(PWA(w00192446))' 1-1 of 1

Sorted by: Priority date desc Display format: Classic Print Save/export

1) Family numbers: 28311285 (US2802182709A)

Title: Functional gene array in yeast

Abstract: Source: US2002182709A This invention relates to functional gene arrays of yeast. Novel aspects include the individual yeast cells, methods for making the yeast and the arrays, the arrays and uses for the arrays. A diploid bearing special genetic properties has been constructed to facilitate cloning of heterologous genes capable of providing essential functions. A selection method, using this strain allows the identification haploid yeast strains dependent for life on heterologous essential genes. The arrays of these strains comprise a library of unique members where each member is dependent for survival on the function of a heterologous gene complementing a different essential host gene which has been inactivated by the insertion of a dominant selectable marker. These arrays provide screening platforms for agents that specifically target the activity of these heterologous genes.

International class (IPC 8): C12N1/18 C12N1/19 C12N15/00 C12N15/09 C12N15/81 C12Q1/02 C12Q1/68 (Advanced/Invention); C12Q1/68 (Advanced/Non-invention); C12N1/18 C12N1/19 C12N15/00 C12N15/09 C12N15/81 C12Q1/02 C12Q1/68 (Core/Invention); C12Q1/68 (Core/Non-invention)

International class (IPC 1-7): C12N1/18 C12N1/19 C12N15/00 C12N15/09 C12N15/10 C12N15/65 C12N15/74 C12N15/90 C12Q1/00 C12Q1/02 C12Q1/61 C12Q1/68

European class: C12N1/18 C12N15/81 C12Q1/68A8 C12Q1/68A8+565/201+565/101 M12Q1/68A8 M12Q1/68M10F

US class: 435/254.11 435/254.2 435/254.21 435/4 435/483 435/6

Figure 1

This tells us where the patent application was filed.

When was it published?

Family:	Publication number	Publication date	Application number	Application date	Links
Family: Australia	AU200120746 A5	20010618	AU20010020746D	2001208	
	AU784373 B2	20060323	AU20010020746	2001208	
	CA2294962 AA	20010614	CA20002294962	2001208	
	EP1242593 A2	20020925	EP20000994067	2001208	
	JP2003516149 T2	20030513	JP20010544322T	2001208	
	US2002182709 AA	20021205	US20020149562	20020609	
	US6232074 BA	20010515	US19990459752	19991210	
	US6998261 BB	20060214	US20020149562	20020609	
	WO0142446 A2	20010614	WO20000533329	20001208	
	WO0142446 A3	20011129	WO20000533329	20001208	

Priority: US19990459752 19991210 WO20000533329 20001208 US20020149562 20020609

command line: Search PatBase Group minesoft



Prosecution

- This is the process by which the applicant and the government determine if the invention merits a patent
- The patent office will search the invention for novelty and inventiveness
- The applicants will respond by argument or amending the claims
- From application to enforceable patent can take up to 5 years of your 20 year patent life



Estimated Costs in 2013 For Each Family in an Estate

- Patent assessments - \$4500
- Provisional applications - \$15000
- PCT applications - \$8000
- National stage - \$30k- \$60k
- Total for 1st 7 years - \$120k
- Lifetime of 20 years - \$220k



Business Development Basics Course

Examples of Deals Since July 2007

- 15 of top 20 deals since July 2007 were for Ph II or Ph III assets
- Phase III: GSK in-license of almorexant (insomnia) from Actelion
 - \$131M upfront in 2008 (Program abandoned in 2011)
- Ph III: Genzyme in-license of mipomersen (cholesterol) from Isis
 - \$175M upfront in 2008
- Ph II: Abbott in-license of bardoxolone (chronic kidney disease) from Reata
 - \$450M upfront in 2010
- Research Project: Roche RNAi collaboration with Alnylam
 - \$289M upfront in 2009



Considerations for IP License Deal

- Foremost considerations in an IP license deal:
 - Freedom-to-operate
 - Strength of patent being licensed
 - Effective patent term (term after product approval)
 - Period of regulatory exclusivity
- IP needs differ depending on the type of deal
 - Late stage product is not the same as research deal



IP Needs Differ Depending on Deal

- IP needs depend on technology and assets you seek
 - Late stage product not the same as research project
- What patent claims are needed?
- How strong are the patent claims?
- How long will patent protection last?
- How long will regulatory exclusivity last?
 - Regulatory submissions are valuable intellectual property
- What countries need patent protection?
- Is there freedom-to-operate (FTO)?



Patent Claims Needed Depend on Type of Deal

- For drug candidate, claim must describe commercial product
 - Does claim cover COM or use to be described in product label?
 - Does claim exclude generic competition?
- But for early research, claim may only need to inhibit others
 - Difficult to effectively exclude others from research activity, but seek competitive advantage in area of interest
- Types of claims
 - Composition of matter (COM)
 - Method of use
 - Process for making product
 - Others



Generally, Composition of Matter Claims are Most Ideal

- COM claims are directed to the drug or product itself
 - “A compound of formula A ...”
 - “A compound selected from the following ...”
 - “A pharmaceutical composition comprising [compound] and a pharmaceutical excipient.”
 - “A humanized antibody which binds the HER2 receptor ... [further description of Avastin]” Genentech US Patent 6,054,297
 - “An isolated DNA comprising an altered BRCA1 DNA having at least one of the alterations set forth in...” Myriad US Patent 5,693,473
- COM claims exclude *any* use of the composition of matter



Do Other Types of Claims in Later Patents Extend Exclusivity

- Claims to new salts or formulations of a compound
 - May be vulnerable to easy design-around by generic
 - These claims are more susceptible to patent challenge after the Supreme Court decision in KSR v Teleflex
- Claims to polymorphs and other solid forms
 - Polymorph is a particular crystalline form of a compound
 - Polymorphs can have different properties, e.g., solubility
 - Key question: can generic competitor access a different, but suitable polymorph?
 - No injunction if only a small amount of claimed polymorph is generic product (based on Supreme Ct. decision in eBay v MercExchange)
- Bottom line: Scrutinize these types of claims carefully



Claims Directed to Processes of Preparation

- Less valuable for small molecule drugs
 - Patents cover last step
 - Patent Covers key step with no easy design around
- More valuable for biologics, where FDA approval hinges on the process



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Two Types of Exclusivity: Patent and Regulatory

- Regulatory submissions are important intellectual property
- FDA provides data exclusivity after FDA approval
 - ANDA (Abbreviated New Drug Application) for a generic drug cannot get approved during FDA exclusivity period
 - 5 years for NCE (new chemical entity)
 - 7 years for Orphan Drug (disorder affects < 200,000 people in US)
 - 6 months more for pediatric exclusivity
 - 3 years for new use of an approved drug
- European Union provides 10 years of data exclusivity for NCE after market authorization (8+2+1 rule)
- In U.S., follow-on biologics (biosimilars) have 12 years of data exclusivity under the Biologics Price Competition and Innovation Act (March, 2010)



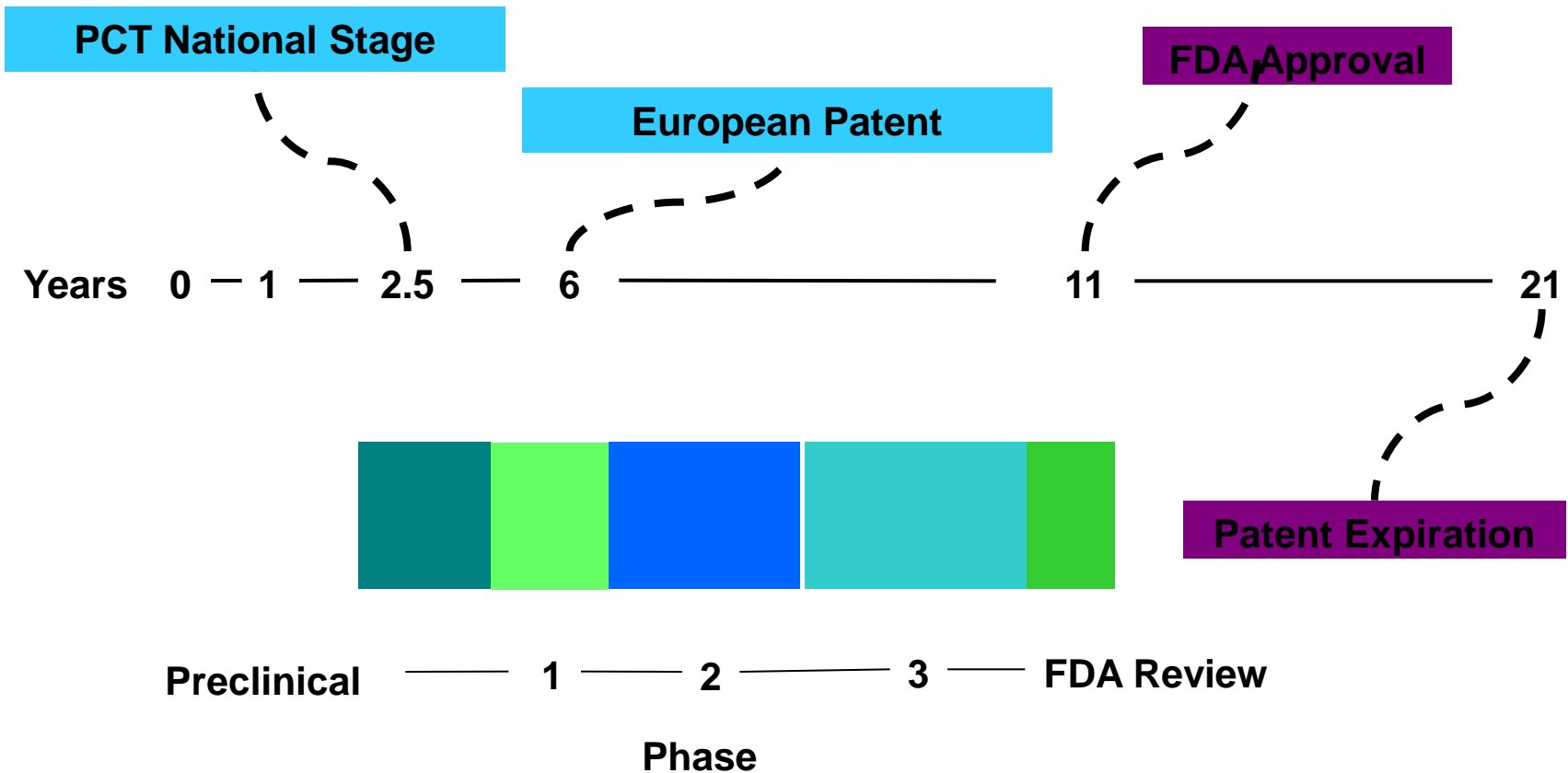
Regulatory vs Patent Exclusivity

- FDA exclusivity prohibits others from referencing clinical data for a period of time (e.g., 5 years for NCE)
- Patent prohibits others from making, using, selling or offering to sell the claimed invention
- FDA exclusivity may be as effective as patent exclusivity
 - Generic companies reference data, do not conduct full development
- Patent exclusivity usually longer (not always), but patents are susceptible to challenge
- Average “effective patent term” for pharma product =11.5 yrs



Business Development Basics Course

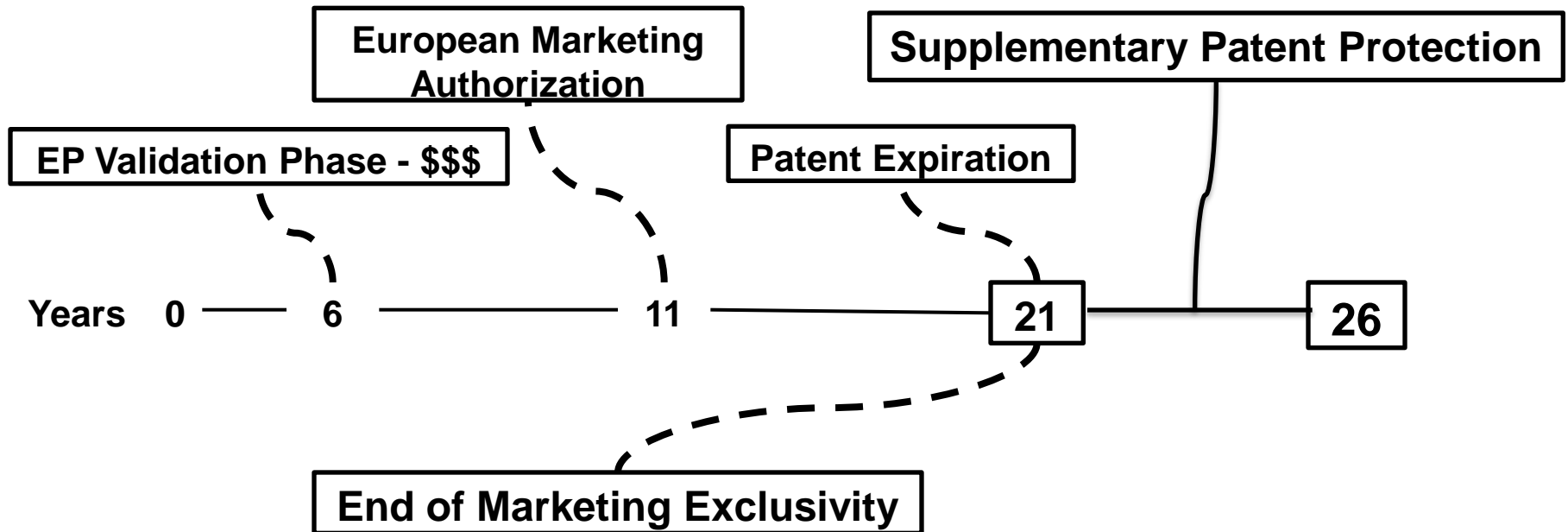
Example of How Important Timelines May Overlap





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Value of European Patent Comes Late Because of Long Marketing Exclusivity



Patent Expiration and End of Marketing Exclusivity are *independent* events, but roughly coincide



Hatch Waxman Act (1984)

- Enacted in 1984 to overcome Roche v. Bolar
- Bolar: patent infringement if generic company conducts clinical studies on a patented drug
- Bolar artificially extended patent term
- The Hatch-Waxman Act to promote generic competition was hotly negotiated and struck a careful balance between competing interests
- In 1984, generics accounted for about 17% of all prescriptions
- Today, generics account for about 69% of all prescriptions



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Hatch Waxman Act Balances Interests

- Benefits to Generics – the ANDA Process
 - Clinical studies before patent expires do not infringe patent
 - Can reference NDA data as part of the ANDA application
 - Can challenge the patent before coming to market with a Paragraph IV certification
 - Para IV certification keeps other generics out for 6 mos.
- Benefits to Pharma
 - Regulatory exclusivity (delays ANDA approval)
 - Patent term extension (PTE) for delays in regulatory approval (up to 5 years) based on a formula
 - After a Para IV certification pharma can bring a patent suit that triggers an automatic 30 month stay of FDA approval of the ANDA application



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Licensing Inventions from Federally Funded Research

- Bayh-Dole Act (1980): non-profits, including universities, and small businesses may retain title to “subject inventions” developed under federally-funded research
- Bayh-Dole has greatly spurred patenting of inventions made at universities; has enabled many start-ups and other commercial activity based on university research.

The catch:

- The government retains march-in rights with a non-exclusive license to practice the patent throughout the world (rarely happens)
- Requires manufacturing in the U.S. unless a waiver is obtained
- Disclosure requirement – must disclose subject inventions and patent applications to federal agency providing funding or could lose patent rights (Campbell Plastics case 2004)



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Patents Listed in FDA Orange Book

Revlimid® patents

Patent No	Patent Expiration	Drug Substance Claim	Drug Product Claim
5635517	Oct 4, 2019	Y	
6045501	Aug 28, 2018		
6555554	Jul 24, 2016		Y
6755784	Oct 23, 2020		
6908432	Aug 28, 2018		
7119106	Jul 24, 2016		Y
7189740	Apr 11, 2023		
7465800	Apr 22, 2026	Y	Y
7855217	Nov 24, 2024	Y	Y

← 2019

← 2026

Google FDA Orange Book.



Claims for Late Stage Product Deal

- Claims that covers the product can be narrow
 - Usually do not need to cover many other compounds
- Strong patent claim that can withstand generic challenge
- What if patent only claims method of use and not COM?
 - Not ideal, but:
 - OK if all indications on the product label are covered by the claims
 - Approval for new use of approved product gets 3 years FDA exclusivity
- Long effective patent term will enhance value of deal
- Usually want patent protection in broad geographic territory



Claims for Research Collaboration Deal

- IP desirable but less important than in a product deal
- Claims should cover basic technology
 - Product claims come in later patent applications as research bears fruit
- Claims tend to be broad in scope to establish dominant position in specialized area
 - Goal is to inhibit others; may be difficult to enforce
- Do not need broad geographic coverage
 - Can come later when protecting the future product
- Early COM claims should be broad enough to cover lead candidate and likely back-up compounds



Patent Must Cover the Label for Pharma Product

- After 5 years, FDA can approve a generic product within the label
- Product within the label but outside the claim is non-infringing
- Claim that reads “administering 5mg/day” is valuable if that is all the label allows!
- Combination therapy claims



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Top Ten Territories Account for over 93% of World

2007 Rank in Pharma Market Size (2002 Rank)	Pharma Market Country or Region	2007 Pharma Sales as % of Worldwide Market
1 (1)	USA	42.67%
2 (2)	EPO (38 countries)	30.84%
3 (3)	JAPAN	8.67%
4 (4)	CANADA	2.60%
5 (6)	CHINA	2.10%
6 (7)	BRAZIL	1.53%
7 (8)	SOUTH KOREA	1.49%
8 (5)	MEXICO	1.26%
9 (10)	AUSTRALIA	1.21%
10 (9)	INDIA	1.10%



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Countries Ranked 11-20 Account for Only About 4% of Worldwide Pharma Market

2007 Rank in Pharma Market Size (2002 Rank)	Country or Region	2007 Pharma Sales as % of Worldwide Market
11 (14)	RUSSIAN	0.81%
12 (13)	VENEZUELA	0.49%
13 (12)	TAIWAN	0.46%
14 (16)	ARGENTINA	0.40%
15 (15)	INDONESIA	0.35%
16 (23)	SOUTH AFRICA	0.35%
17 (21)	THAILAND	0.34%
18 (18)	PHILIPPINES	0.31%
19 (NA)	UKRAINE	0.26%
20 (12)	SAUDI ARABIA	0.21%



Working with Patent Counsel

- Freedom to operate analysis
- Opinion of counsel
- Due diligence



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Opinion of Counsel

*"I don't want a lawyer to tell me what I cannot do. I hire him to tell how
to do what I want to do."*
J.P. Morgan



A good lawyer should tell you what you cannot do, but also suggest ways to move forward. That requires that your lawyer know the deal background and your business goals.

*"A good lawyer knows the law. A great lawyer knows the judge."
- anonymous*



Good lawyers know the law. The best ones understand risk; they describe and weigh risk when advising a client in a negotiation.



Patentability versus FTO

- Patentability \neq Freedom-to-Operate
- A patent is the right to exclude others
- A patent does not grant the right to practice an invention
- Example:
 - Tom has a patent that claims the combination of A and B
 - Amy has a patent to “A”
 - Tom can exclude others from making, using, selling A + B
 - But Amy’s patent presents an FTO concern for Tom



Freedom to Operate

- How an attorney carries out a freedom to operate analysis
- Example
- Typical costs



General Steps For a Freedom to Operate Analysis

- Identify features of the product that might be subject to 3rd party patents
- Search features
- Create binders for each feature
- No validity issues addressed



PCR Diagnostic Kit

CinnaGen Inc.

Helicobacter pylori PCR detection Kit

Product	<i>Helicobacter pylori</i> PCR detection Kit
Description	A qualitative diagnostic kit for detection of <i>H. pylori</i> DNA in clinical samples like biopsy. Kit contains reagents for Polymerase Chain Reaction technique. Ready to use PCR mix, positive control and other qualified reagents along with an easy to follow protocol are included. Specific primers amplify conserved region in <i>H. pylori</i> genome. Using this kit, as low as 10 copies/ml of bacterial genome can be detected.
Storage	-20°C
	



- The PCR primers
- The bacteria
- The disease
- The polymerase
- The amplified target
- The label
- Special additives
- Hot start technology
- The box
- The caps on the tubes
- The blue plastic holder





Searching For Third Party Patents

- Each feature requires a search costing \$5-7K.
- Decide carefully how many features you will search
- Provide a binder for each feature searched
- There is no analysis beyond plain meaning of the claims.
- What do you do about air claims in applications?



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Dealing with an FTO Issue

Tom wants to market A + B and Amy has a patent to “A”

- Initial question – does Amy’s claim really cover A?
 - An infringement analysis determines whether A is within the scope of Amy’s claim
- Second question – is Amy’s claim valid?
- These may be difficult questions with no clear answer
 - > it often involves an assessment of risk
- Tom has choices:
 - Assume the risk / negotiate a license from Amy / challenge Amy’s patent (new opportunities to challenge with America Invents Act)



License Agreement Terms for FTO

Tom licenses A + B patent to Harry

- License agreement will have various terms regarding 3rd party patents that might interfere with commercialization of A + B
- Harry will want a representation of non-infringement:
 - “To the best of Tom’s knowledge, the commercialization of Licensed Product, as formulated and manufactured as of the Effective Date, does not and will not infringe the patent rights of any other Person”
- If a 3rd party license is needed, Harry wants to pay a lower royalty:
 - “Harry may deduct from the royalties otherwise due to Tom royalties payable for a Third Party License, provided that the deduction may not reduce Tom’s royalties by more than 50%.”



IP Due Diligence: When and How Much?

- Initial interest under CDA
 - Get copies of relevant patents / patent applications; summary of status
 - Determine exclusivity periods
 - Preliminary assessment of freedom-to-operate and patentability
- Greater diligence with Term Sheet goal
 - Conduct full freedom-to-operate analysis
 - Conduct full patentability analysis
 - Comprehensive interview of licensor attorney; ask for all useful information
- Especially for large deal, strive to complete diligence prior to execution of non-binding Term Sheet
- IP issues uncovered after finalized Term Sheet can be messy; may require additional reps and warranties in the agreement



The Due Diligence Checklist Covers Many Areas

- List of materials / information to obtain from target
- Ownership – requires a high degree of certainty
- Review of license agreements relating to target IP
- Patent validity
- Claim scope
- Patent terms and regulatory exclusivity
- Ex-U.S. filings
- Freedom-to-operate – sometimes most difficult
- Enforcement Issues



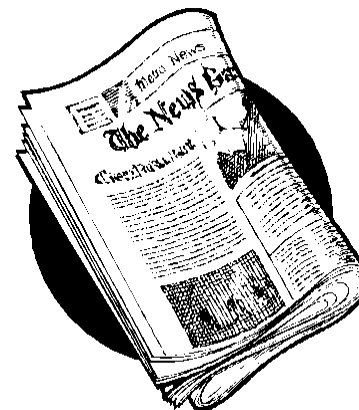
Opinions in Writing and FTO Analysis Performed by Other Side

- Should you get a legal opinion in writing?
 - Yes, for FTO issues that present a particularly important risk
 - Most other legal opinions should be communicated verbally
- Probe attorney for licensor regarding any FTO analysis they make have performed; ask if they have written opinions
- Ask to see the written opinion
 - Many attorneys will refuse request, but ...
 - Ask what triggered the opinion
 - Ask what references formed the basis of the opinion
- Few patent issues will be “black and white”
 - Attorneys tend to hedge when providing an opinion, but strive for an opinion that enables you to make a decision



Recent IP Developments

IN THE NEWS



REFORM OF INEQUITABLE CONDUCT
ELIGIBLE SUBJECT MATTER

- Mayo v. Prometheus (**diagnostic tests**)
- *Everyone (?)* v. Myriad Genetics (**genes**)



Reform of Inequitable Conduct

- Inequitable conduct impossible to “cleanse”
- Can infect all members of a patent family
- Prior standard was based on a sliding scale of materiality
 - Intent could be inferred from high materiality
 - Material if there is a substantial likelihood that a reasonable examiner consider it important
 - Negligence standard (should have known)
- Overruled by *Therasense v. Becton Dickinson*
 - Standard is no longer gross negligence or negligence (should have known)
 - Now must act with specific intent to deceive the PTO
 - Deliberate decision to withhold known material reference
 - “Material” means that the PTO would not have allowed the claim but for the omission



Supplemental Examination

- Cures inequitable conduct
- A Patent “shall not be held enforceable on the basis of conduct relating to information ... if the information was considered, reconsidered or corrected”
- Filing fee \$5,180; fee is \$16,120 if re-examination is ordered
- Material fraud is not removed
- Supplemental examination must be filed before inequitable conduct is raised in court



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SUPREME COURT OF THE UNITED STATES

Syllabus

MAYO COLLABORATIVE SERVICES, DBA MAYO
MEDICAL LABORATORIES, ET AL. *v.* PROMETHEUS
LABORATORIES, INC.

CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR
THE FEDERAL CIRCUIT

No. 10–1150. Argued December 7, 2011—Decided March 20, 2012

Although “laws of nature, natural phenomena, and abstract ideas” are not patentable subject matter under §101 of the Patent Act, *Diamond v. Diehr*, 450 U. S. 175, 185, “an *application* of a law of nature . . . to



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MAYO MEDICAL LABORATORIES, ET AL. v. PROMETHEUS LABORATORIES, INC.

A method of optimizing therapeutic efficacy for treatment of an immune-mediated gastrointestinal disorder, comprising:

(a) **administering** a drug providing 6-thioguanine to a subject having said immune-mediated gastrointestinal disorder; and

(b) **determining** the level of 6-thioguanine in said subject having said immune-mediated gastrointestinal disorder,

wherein the level of 6-thioguanine less than about 230 pmol per 8×10^8 red blood cells indicates a need to increase the amount of said drug subsequently administered to said subject and

wherein the level of 6-thioguanine greater than about 400 pmol per 8×10^8 red blood cells indicates a need to decrease the amount of said drug subsequently administered to said subject.



HELD NOT PATENTABLE:

A method of treating Crohn's disease comprising the steps of: **administering** drug X to a patient with Crohns and measuring the amount of drug X in the patient; and. **measuring** the amount of drug X in the patient where:

you give **more** drug x if the amount is *below* a given amount and **give less** drug X if *above* a given amount.



The Ruling in Mayo

- . . . the patents effectively claim natural laws or natural phenomena – namely the correlations between thiopurine levels and the toxicity and efficacy of thiopurine drug dosages ...
- . . .the claims inform a relevant audience about certain laws of nature; any additional steps consist of well understood, routine, conventional activity already engaged in by the scientific community.



The Solution in Mayo

- In Europe, not a problem with use claims?
- The solution is to take the “law of nature” and use it to recite an additional concrete “action” step
- Example: adjusting the dosing of the patient so that the thiopurine falls into the desired range
- What if the “administering” and “analyzing” steps are performed by different parties?
 - Under McKesson and Akamai, still infringement by inducement



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Everyone

v.

United States Court of Appeals for the Federal Circuit

THE ASSOCIATION FOR MOLECULAR
PATHOLOGY,
THE AMERICAN COLLEGE OF MEDICAL
GENETICS,
THE AMERICAN SOCIETY FOR CLINICAL
PATHOLOGY,
THE COLLEGE OF AMERICAN PATHOLOGISTS,
HAIG KAZAZIAN, MD,
ARUPA GANGULY, PHD, WENDY CHUNG, MD,
PHD, HARRY OSTRER, MD,
DAVID LEDBETTER, PHD, STEPHEN WARREN,
PHD, ELLEN MATLOFF, M.S.,
ELSA REICH, M.S., BREAST CANCER ACTION,
BOSTON WOMEN'S HEALTH BOOK COLLECTIVE,
LISBETH CERIANI, RUNI LIMARY,
GENAE GIRARD, PATRICE FORTUNE,
VICKY THOMASON, AND KATHLEEN RAKER,
Plaintiffs-Appellees,

v.

UNITED STATES PATENT AND TRADEMARK
OFFICE,
Defendant,

and

MYRIAD GENETICS, INC.,
Defendant-Appellant,

and



MYRIAD'S CLAIMS:

An isolated DNA coding for a BRCA1 polypeptide, said polypeptide having the amino acid sequence set forth in SEQ ID NO:2.



Current Topics in Intellectual Property

ARE GENES PATENTABLE?
A 3 YEAR ROLLER COASTER

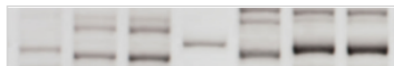
March 29, 2010 **2010 CLAIMS INVALID**
In ACLU Suit, Judge Rules Myriad's Genetic Patents Invalid

Last year, several doctors' groups, together with the ACLU and Public Patent Foundation, filed a lawsuit [seeking to invalidate patents on two genes](#) related to breast cancer and caused by Utah-based Myriad Genetics. The plaintiffs, who can be viewed as arguing

AUGUST 3, 2011 UNCATEGORIZED **2011 CLAIMS VALID**
Myriad Genetics Ruling That DNA Is Patent-Eligible

Like +1 0 Tweet 0 Share

We're seeing significant interest in the Myriad Genetics case. *Association for Molecular*



2012 MAYBE NOT VALID
SUPREME COURT VACATES FEDERAL CIRCUIT DECISION IN CASE CHALLENGING PATENTS ON BREAST CANCER GENES

by GenScott | April 11, 2012 | Announcements, Cases, Supreme Court | Comments Off



Myriad – Are Isolated Genes (or More Broadly Isolated Natural Products) Patentable?

- Highly political court case
- 2:1 decision that isolated genes are patentable
- One majority opinion focuses on the fact that isolated DNA requires cleaving DNA bonds or a different molecule for cDNA



Myriad – Are Isolated Genes (or More Broadly Isolated Natural Products) Patentable? (con't.)

- Second majority opinion focuses on
 - 1) Longstanding PTO practice
 - 2) Whether the claimed product has different properties than in the natural state
- Both majority opinions refer favorably to past court cases where isolated elements were found to be non-patentable
- Practice tips
 - Composition claims must recite “isolated”
 - Make certain pharmaceutical composition and treatment claims are well supported
 - Include data to support clinical indications



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Questions?

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Ken Weber
EMAIL: KWeber@Kilpatricktownsend.com