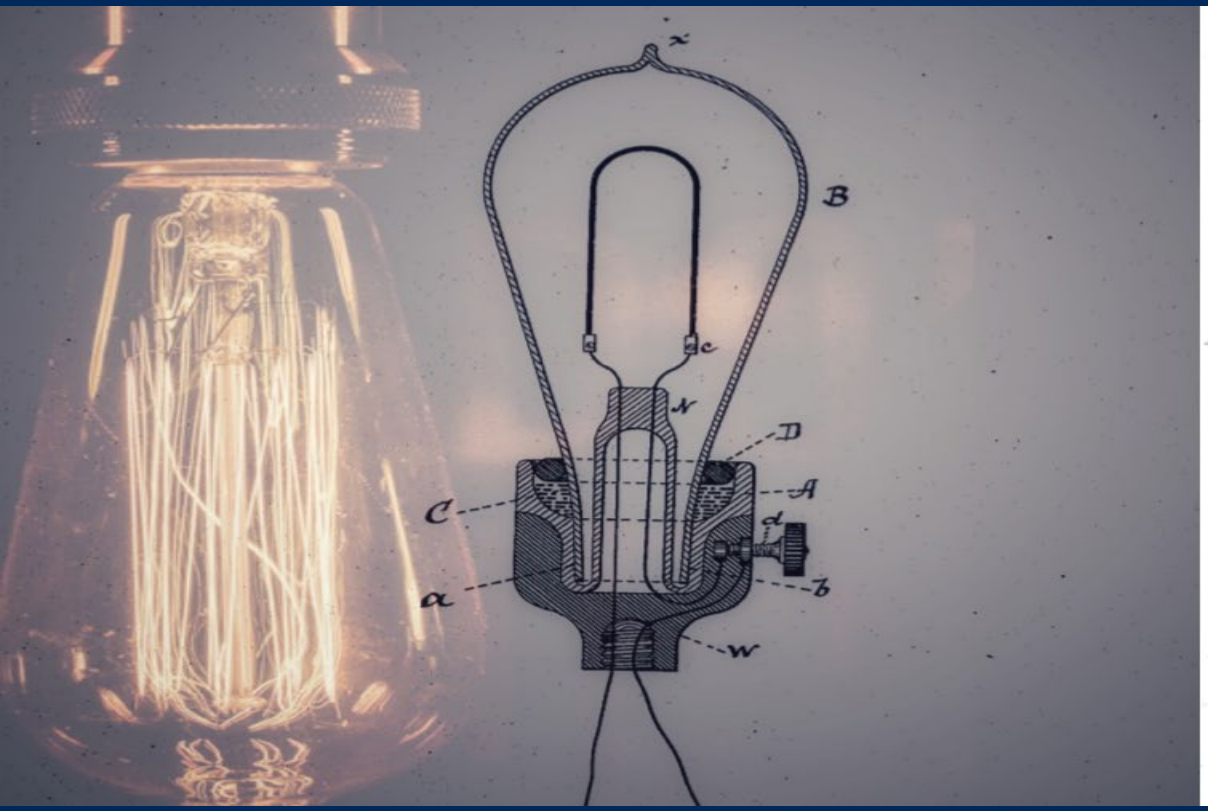
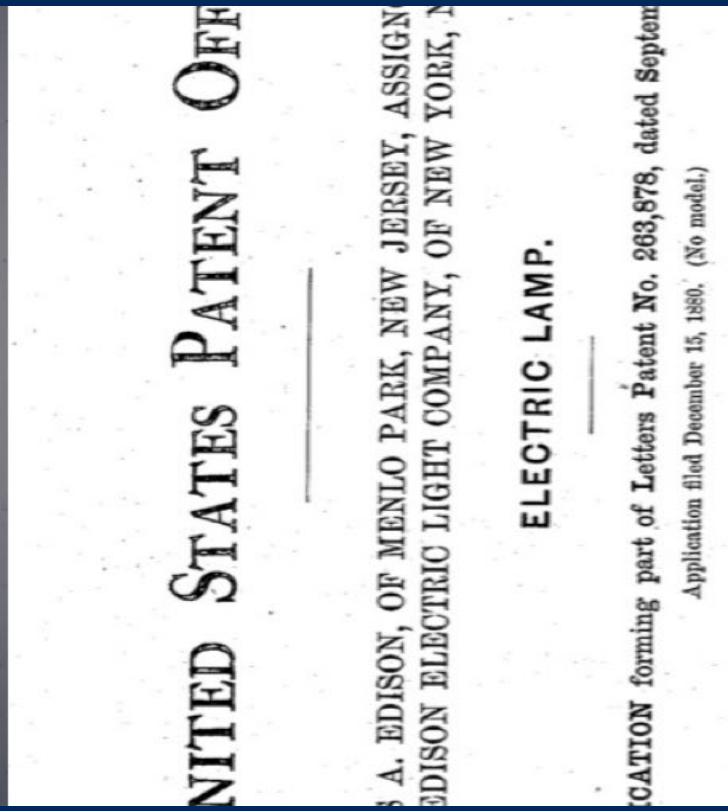
Case Studies in Chemical Patenting

CHEM 6961 / 4961 01 Aspects and Tools of Chemical Practice

Rensselaer Polytechnic Institute





NITED STATES PATENT OFF

S A. EDISON, OF MENLO PARK, NEW JERSEY, ASSIGN
EDISON ELECTRIC LIGHT COMPANY, OF NEW YORK, N

ELECTRIC LAMP.

CATION forming part of Letters Patent No. 263,878, dated Septem

Application filed December 15, 1880. (No model.)

CULHANE MEADOWS PLLC

Big Law for the New Economy®

April 18, 2022
Jeff B. Vockrodt
jvockrodt@cm.law

www.inventiveadventures.com

United States Utility Patent

"Everything that can be invented has been invented."

– Charles Holland Duell,
Commissioner of the
US Patent Office 1889

CULHANE MEADOWS PLLC
Big Law for the New Economy

Case Studies in Chemical Patenting

- **Basics of U.S. Utility Patent**
- Statutory Criteria for Patenting
    - Statutory Subject Matter / Eligibility
    - Enabling Disclosure / Written Description of the Invention
    - Novelty / Anticipation
    - Non-Obviousness
- Categories of Chemical Patent Claims
    - Process Patents
        - Methods of Manufacturing (The Kroll Process)
        - Methods of Therapeutic Use (Rogaine®)
        - Other Processes of Use (Activated Sludge)
    - Composition of Matter Patents
        - Novel Chemical Compositions (Diamond Match)
        - Species Selection Patents (Zyprexa®)
        - Enantiomer Patents (Plavix®)
        - Polymorph Patents (Nucynta ER®)

What is a U.S. Patent?

An agreement between U.S. Government and Inventor

- Inventor is given property rights in invention for twenty (20) years (from filing)
- Government (and the public) is given information on how to make and use the invention
- Patents are obtained at the U.S. Patent & Trademark Office after examination (called “patent prosecution”)

Three types of Patents

Utility patents

- covers all types of inventions (e.g., mechanical, chemical, biotech, business methods)

- Provisional provides a relaxed format and filing date effective to remove prior art, yet not count against the patent's term.

Design patents

- covers the ornamental aspects of a structure or apparatus (i.e., the "look" of an object, not function).

Plant patents

- covers asexually reproduced plants found in cultivated areas

Anatomy of a Patent

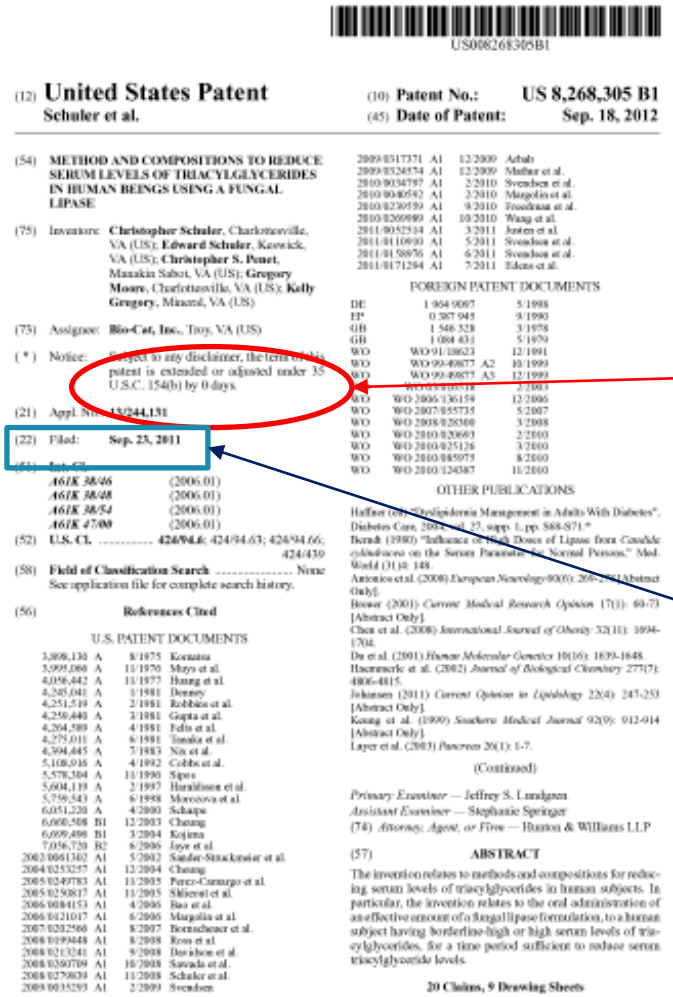
Title

Inventors

Patent Owner (Assignee)

U.S. Application No. and Filing Date

References reviewed by Patent Examiner



US008268305B1

(12) **United States Patent**
Schuler et al.

(10) **Patent No.: US 8,268,305 B1**
(45) **Date of Patent: Sep. 18, 2012**

(54) **METHOD AND COMPOSITIONS TO REDUCE SERUM LEVELS OF TRIACYLGLYCERIDES IN HUMAN BEINGS USING A FUNGAL LIPASE**

(75) Inventors: **Christopher Schuler**, Charlottesville, VA (US); **Edward Schuler**, Keswick, VA (US); **Christopher S. Penet**, Manakin Sabot, VA (US); **Gregory Moore**, Charlottesville, VA (US); **Kelly Gregory**, Mineral, VA (US)

(73) Assignee: **Bio-Cat, Inc.**, Troy, VA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **13/244,131**

(22) Filed: **Sep. 23, 2011**

(51) Int. Cl.
A61K 38/46 (2006.01)
A61K 38/48 (2006.01)
A61K 38/54 (2006.01)
A61K 47/00 (2006.01)

(52) **U.S. Cl.** **424/94.6**; 424/94.63; 424/94.66; 424/439

(58) **Field of Classification Search** ..... None
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

3,808,130	A	8/1975	Komatsu
3,995,060	A	11/1976	Mayo et al.
4,058,442	A	11/1977	Huang et al.
4,245,041	A	1/1981	Denney
4,251,510	A	2/1981	Robbins et al.
4,259,440	A	3/1981	Gupta et al.
4,264,580	A	4/1981	Felix et al.
4,275,011	A	6/1981	Tanaka et al.
4,364,445	A	7/1983	Nix et al.
5,108,916	A	4/1992	Cobbs et al.
5,578,304	A	11/1996	Sipos
5,604,119	A	2/1997	Hunkeler et al.
5,756,543	A	6/1998	Morozova et al.
6,051,220	A	4/2000	Schaupe
6,068,508	B1	12/2003	Chuang
6,699,498	B1	3/2004	Kojima
7,056,720	B2	6/2006	Joye et al.
2002/0061362	A1	5/2002	Sandor-Stuckinsior et al.
2004/0253257	A1	12/2004	Chuang
2005/0249783	A1	11/2005	Perez-Camargo et al.
2005/0250817	A1	11/2005	Shkvorel et al.
2006/0084153	A1	4/2006	Bao et al.
2006/0121017	A1	6/2006	Margolin et al.
2007/0202560	A1	8/2007	Bornscheuer et al.
2008/0199448	A1	8/2008	Ross et al.
2008/0213241	A1	9/2008	Davidson et al.
2008/0260708	A1	10/2008	Sawada et al.
2008/0279839	A1	11/2008	Schuler et al.
2009/0035293	A1	2/2009	Svendsen
2009/0317371	A1	12/2009	Arbab
2009/0324574	A1	12/2009	Muthur et al.
2010/0034797	A1	2/2010	Svendsen et al.
2010/0040582	A1	2/2010	Margolin et al.
2010/0260759	A1	9/2010	Freudman et al.
2010/0269989	A1	10/2010	Wang et al.
2011/0052534	A1	3/2011	Jorsen et al.
2011/0110930	A1	5/2011	Svendsen et al.
2011/0158976	A1	6/2011	Svendsen et al.
2011/0171294	A1	7/2011	Edens et al.

FOREIGN PATENT DOCUMENTS

DE	1 964 9097	5/1998
EP	0 387 945	9/1990
GB	1 546 328	3/1978
GB	1 084 431	5/1979
WO	WO 91/18623	12/1991
WO	WO 99/40877 A2	10/1999
WO	WO 99/40877 A3	12/1999
WO	WO 03/000818	2/2003
WO	WO 2006/136159	12/2006
WO	WO 2007/055735	5/2007
WO	WO 2008/028300	3/2008
WO	WO 2010/020693	2/2010
WO	WO 2010/025126	3/2010
WO	WO 2010/085075	8/2010
WO	WO 2010/124387	11/2010

OTHER PUBLICATIONS

Hoffman (ed.) "Dyslipidemia Management in Adults With Diabetes", Diabetes Care, 2004, vol. 27, supp. 1, pp. S88-S71.*
Berndt (1980) "Influence of 10-40 Doses of Lipase from *Candida cylindracea* on the Serum Parameters for Normal Persons." Med. World (31):6: 148.
Antonio et al. (2008) *European Neurology* 60(6): 269-271 [Abstract Only].
Bonne (2001) *Current Medical Research Opinion* 17(1): 60-73 [Abstract Only].
Chen et al. (2008) *International Journal of Obesity* 32(11): 1696-1704.
Du et al. (2001) *Human Molecular Genetics* 10(16): 1639-1648.
Hasenkamp et al. (2002) *Journal of Biological Chemistry* 277(7): 4806-4815.
Johansen (2011) *Current Opinion in Lipidology* 22(4): 247-253 [Abstract Only].
Kuang et al. (1999) *Southern Medical Journal* 92(9): 912-914 [Abstract Only].
Layer et al. (2003) *Pancreas* 26(1): 1-7.

(Continued)

Primary Examiner — Jeffrey S. Lundgren
Assistant Examiner — Stephanie Springer
(74) *Attorney, Agent, or Firm* — Hunton & Williams LLP

(57) **ABSTRACT**

The invention relates to methods and compositions for reducing serum levels of triacylglycerides in human subjects. In particular, the invention relates to the oral administration of an effective amount of a fungal lipase formulation, to a human subject having borderline-high or high serum levels of triacylglycerides, for a time period sufficient to reduce serum triacylglyceride levels.

20 Claims, 9 Drawing Sheets

Patent Number and Issue Date

Patent term adjustment

Filing date used to calculate term, if there are no US non-provisional priority applications.

Abstract

patents.google.com
patft.uspto.gov

CULHANE MEADOWS PLLC
Big Law for the New Economy

Anatomy of a Patent

Drawings

- Line figures, tables, graphs, photos with elements numbered and referred to in the specification.

Specification

- Includes background, summary of invention, description of figures, and detailed description of invention.

Claims

- Sentence-like constructs at the end of the patent that define the scope of protection for the invention (e.g., product, method of making and using product).

Case Studies in Chemical Patenting

- Basics of U.S. Utility Patent
- **Statutory Criteria for Patenting**
    - Statutory Subject Matter / Eligibility
    - Enabling Disclosure / Written Description of the Invention
    - Novelty / Anticipation
    - Non-Obviousness
- Categories of Chemical Patent Claims
    - Process Patents
        - Methods of Manufacturing (The Kroll Process)
        - Methods of Therapeutic Use (Rogaine®)
        - Other Processes of Use (Activated Sludge)
    - Composition of Matter Patents
        - Novel Chemical Compositions (Diamond Match)
        - Species Selection Patents (Zyprexa®)
        - Enantiomer Patents (Plavix®)
        - Polymorph Patents (Nucynta ER®)

Statutory Subject Matter / Eligibility

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

35 U.S.C. § 101

Patent *ineligible* subject matter:

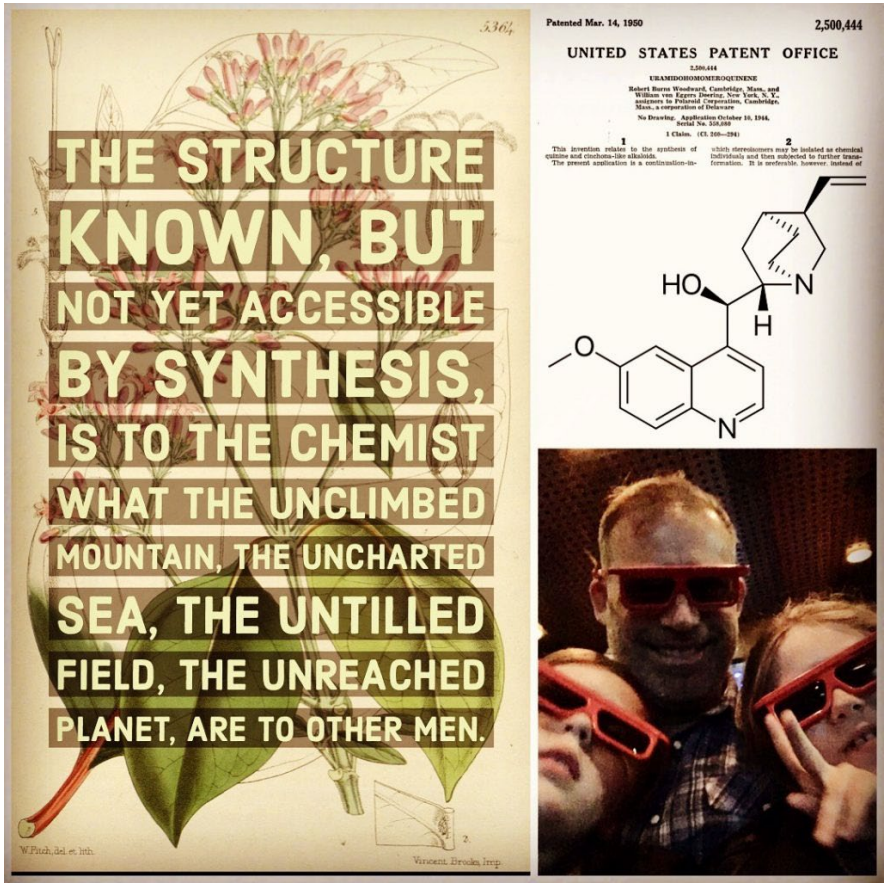
- **Natural products or phenomena**
- **Abstract ideas such as mathematical concepts**

Eligibility – Natural Products

Robert Burns Woodward invented the first ever process for synthesis of quinine, used to manufacture polarizing filters and for treating malaria.

He obtained several patents to ***methods of making*** and ***intermediate compounds*** used in the synthesis, including U.S. Pats. ***2, 395, 526***; ***2,500,444***; and ***2,475,932***.

He could not obtain patents to the natural products he synthesized because such subject matter is ineligible for patenting as a natural product.



www.inventiveadventures.com

CULHANE MEADOWS PLLC
Big Law for the New Economy

Eligibility – Abstract Ideas

***Diamond v. Diehr*, 450 U.S. 175 (1981).**

Supreme court reversed USPTO rejection for ineligible subject matter.

United States Patent [19]

Diehr, II et al.

[11] **4,344,142**

[45] **Aug. 10, 1982**

[54] **DIRECT DIGITAL CONTROL OF RUBBER MOLDING PRESSES**

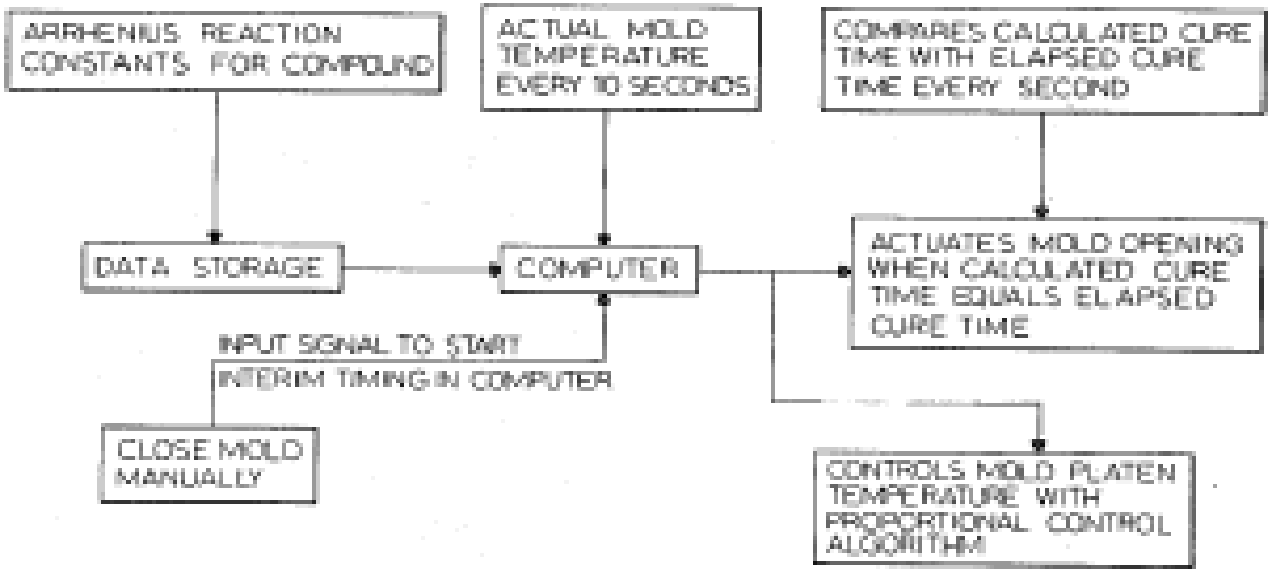
[75] Inventors: **James R. Diehr, II**, Troy; **Theodore A. Lutton**, Birmingham, both of Mich.

[73] Assignee: **Federal-Mogul Corporation**, Southfield, Mich.

3,718,721 2/1973 Gould et al. 264/40
3,819,915 6/1974 Smith ..... 235/151 X
3,980,743 9/1976 Smith 264/40.2

Primary Examiner—Joseph F. Ruggiero
Attorney, Agent, or Firm—Owen, Wickersham & Erickson

[57] **ABSTRACT**



Eligibility – Abstract Ideas

A method of operating a rubber-molding press for precision molded compounds with the aid of a digital computer, comprising:

. . .

repetitively performing in the computer, at frequent intervals during each cure, integrations to calculate from the series of temperature determinations the ***Arrhenius equation*** for reaction time during the cure, which is

$$\ln v = CZ + x$$

where v is the total required cure time, repetitively comparing in the computer at frequent intervals during the cure each said calculation of the total required cure time calculated with the Arrhenius equation and said elapsed time, and ***opening the press automatically*** when a said comparison indicates completion of curing.

The Supreme Court in 2012 noted that the *Diehr* case:

- "found the overall process patent eligible because of the way the additional steps of the process [besides the equation] integrated the equation into the process as a whole.“ *Mayo v. Prometheus*, 566 U.S. 66 (2012).

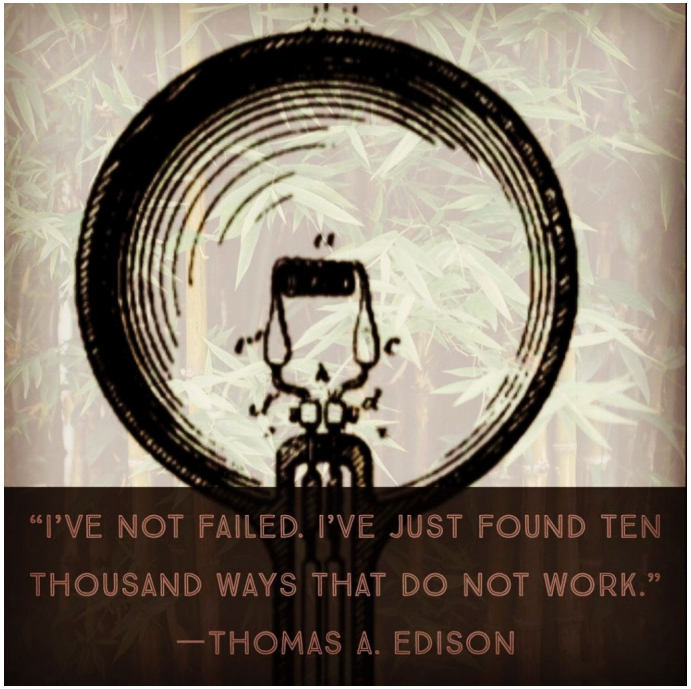
Enabling Disclosure / Written Description

The specification shall contain a ***written description*** of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as ***to enable*** any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor or joint inventor of carrying out the invention.

35 U.S.C. § 112

- **Written description requirement focuses on possession of the invention**
- **Enablement requirement focuses on whether practicing invention requires undue experimentation**

Enabling Disclosure / Written Description



www.inventiveadventures.com

Thomas Edison developed an improved lightbulb after painstaking development that studied fibrous materials all over the world to make carbonized filaments.

After ruling out several materials, Edison settled upon a particular bamboo from Japan. Microscopic inquiry revealed "that the fibres run more nearly parallel than in other species of wood."

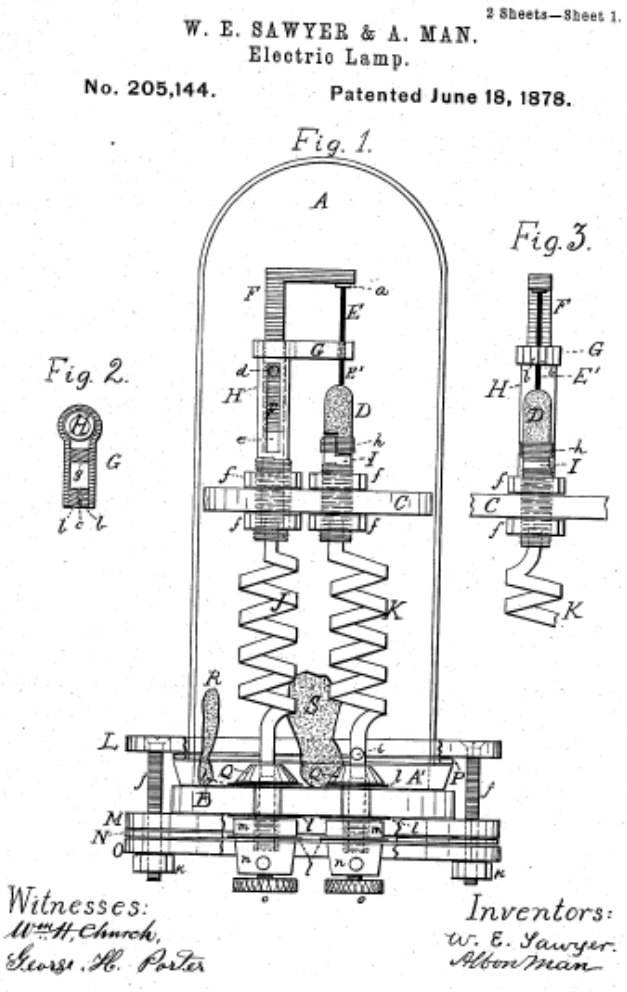
Westinghouse acquired the Sawyer patent and sued GE in case that went to the Supreme Court. *The Incandescent Lamp Patent*, 159 U.S. 465 (1895).

T. A. EDISON.
Electric-Lamp.

No. 223,898. Patented Jan. 27, 1880.

CULHANE MEADOWS PLLC
Big Law for the New Economy

Enabling Disclosure / Written Description


2 Sheets—Sheet 1.

W. E. SAWYER & A. MAN.
Electric Lamp.

No. 205,144. Patented June 18, 1878.

Fig. 1.

Fig. 2.

Fig. 3.

Witnesses:
Wm. H. Church,
Geo. H. Porter

Inventors:
W. E. Sawyer.
Alban Man

"If Sawyer and Man had discovered that a certain carbonized paper would answer the purpose, their claim to all carbonized paper would, perhaps, not be extravagant; but the fact that paper happens to belong to the fibrous kingdom did not invest them with sovereignty over this entire kingdom, and thereby practically limit other experimenters to the domain of minerals."

1. An electric lamp in which the globe and stopper, both of glass or other vitreous substance, are ground together and held together by a clamping device.

CULHANE MEADOWS PLLC
Big Law for the New Economy

Novelty / Anticipation

(a) Novelty; Prior Art.—A person shall be entitled to a patent unless—
(1)the claimed invention was patented, described in a printed publication, or in public use, on sale, or otherwise available to the public before the effective filing date of the claimed invention; or
(2)the claimed invention was described in a patent issued under section 151, or in an application for patent published or deemed published under section 122(b), in which the patent or application, as the case may be, names another inventor and was effectively filed before the effective filing date of the claimed invention.

35 U.S.C. § 102(a)

- **Novelty focuses on whether the claimed invention compared to the prior art is new.**

- **Inherent anticipation considers the natural and inevitable result of what is described in the prior art reference**

Novelty / Anticipation

Glenn T. Seaborg discovered plutonium in 1940, ushering in the atomic age. He went on to win the Nobel prize, isolating several trans uranium elements, two of which he patented.

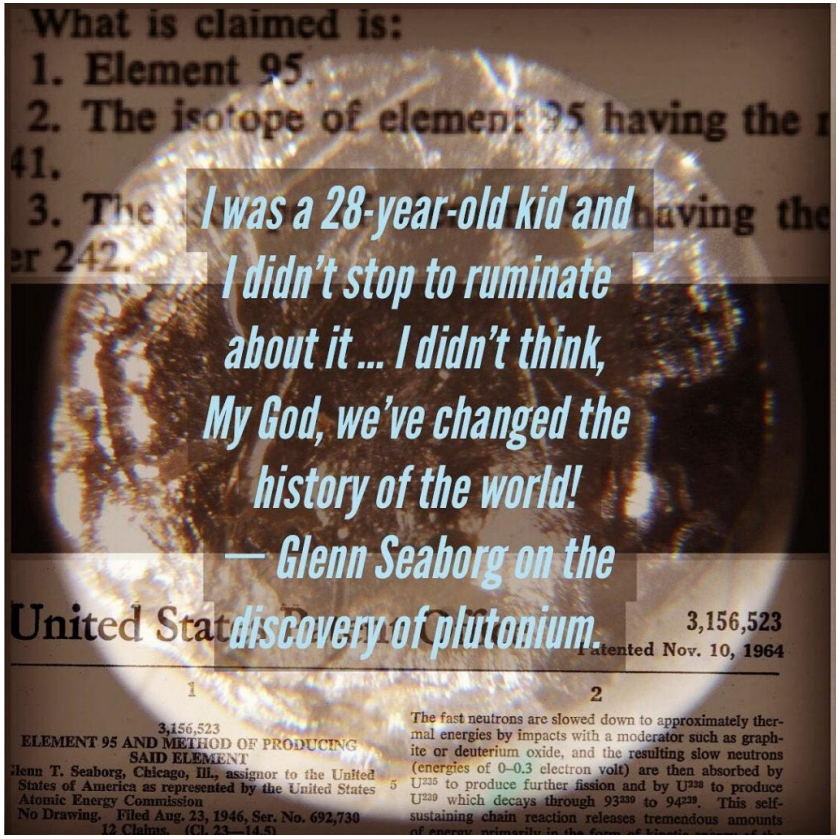
His patent application claiming Americium (Element 95) leading to U.S. Pat. 3,156,523 was rejected by the US Patent Office on the grounds that the element was likely an inherent product produced during nuclear fission reactions described in an earlier patent to Fermi et al.

What is claimed is:

1. Element 95.

2. The isotope of element 95 having the mass number 241.

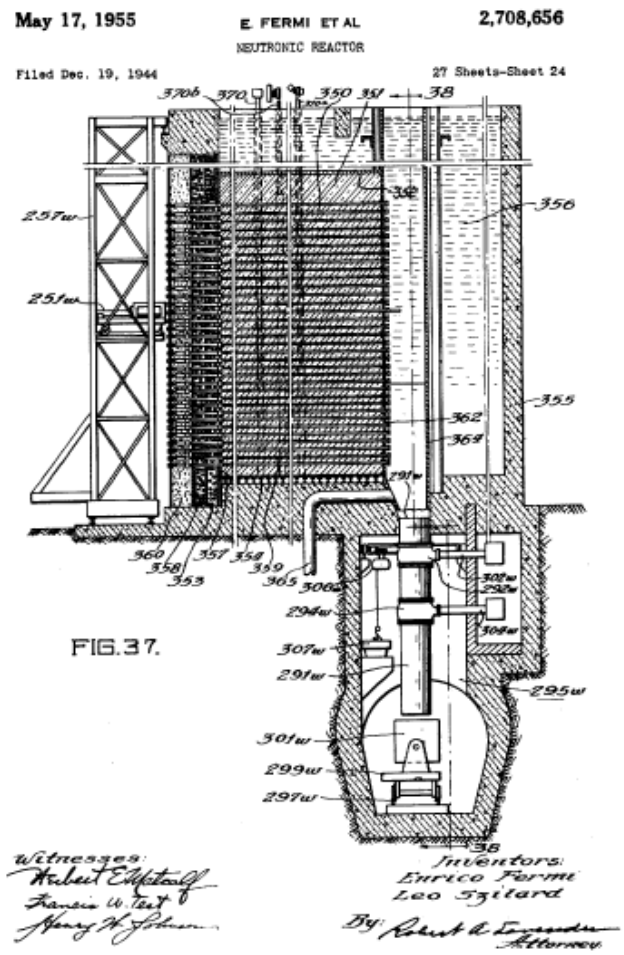
3. The isotope of element 95 having the mass number 242.



www.inventiveadventures.com

CULHANE MEADOWS PLLC
Big Law for the New Economy

Novelty / Anticipation



The Fermi et al. patent discloses several nuclear reactors. The patent does not mention elements 95 and 96.

The parties agreed “that the Fermi reactor in the exemplary operation relied on by the examiner "could have produced no more than one billionth of a gram of americium-241, and this one billionth of a gram would have been distributed throughout forty tons of intensely radioactive uranium reactor fuel."

The record before us . . . is replete with showings that the claimed product, if it was produced in the Fermi process, was produced in such minuscule amounts and under such conditions that its presence was undetectable.

The court reversed the Patent Office, allowing Seaborg’s application to become a patent.

CULHANE MEADOWS PLLC
Big Law for the New Economy

Non-Obviousness

A patent for a claimed invention may not be obtained, notwithstanding that the claimed invention is not identically disclosed as set forth in section 102, if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art to which the claimed invention pertains. Patentability shall not be negated by the manner in which the invention was made.

35 U.S.C. § 103

Obviousness is a question of law based on the following underlying factual inquiries:

- **Scope and content of the prior art**
- **Differences between the claimed invention and the prior art.**
- **Resolving the level of skill in the art**

Non-Obviousness - Exemplary rationales

Exemplary rationales that may support a conclusion of obviousness include:

A. Combining prior art elements according to known methods to yield predictable results;

B. Simple substitution of one known element for another to obtain predictable results;

C. Use of known technique to improve similar devices (methods, or products) in the same way;

D. Applying a known technique to a known device (method, or product) ready for improvement to yield predictable results;

Non-Obviousness - Exemplary rationales

E. "Obvious to try" – choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success;

F. Known work in one field of endeavor may prompt variations of it for use in either the same field or a different one based on design incentives or other market forces if the variations are predictable to one of ordinary skill in the art;

G. Some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention.

Obviousness - Requirements

To prove obviousness, the patent challenger (or examiner) must establish:

1. Some ***reason or motivation to modify*** a prior art reference to achieve the claimed invention.

2. An analysis addressing ***each of the claim limitations***.

3. That a person having ordinary skill in the art would have had a ***reasonable expectation of success***, although absolute predictability is not required.

Even then, secondary factors of non-obvious may include evidence of commercial success, long-felt but unsolved needs, failure of others, and unexpected results.

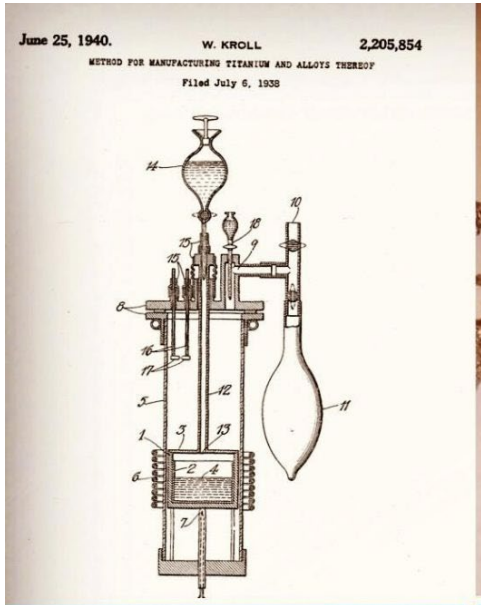
Case Studies in Chemical Patenting

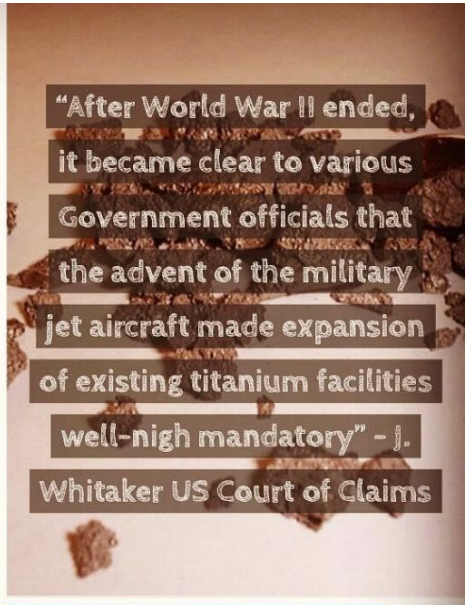
- Basics of U.S. Utility Patent
- Statutory Criteria for Patenting
    - Statutory Subject Matter / Eligibility
    - Enabling Disclosure / Written Description of the Invention
    - Novelty / Anticipation
    - Non-Obviousness
- **Categories of Chemical Patent Claims**
    - Process Patents
        - Methods of Manufacturing (The Kroll Process)
        - Methods of Therapeutic Use (Rogaine®)
        - Other Processes of Use (Activated Sludge)
    - Composition of Matter Patents
        - Novel Chemical Compositions (Diamond Match)
        - Species Selection Patents (Zyprexa®)
        - Enantiomer Patents (Plavix®)
        - Polymorph Patents (Nucynta ER®)

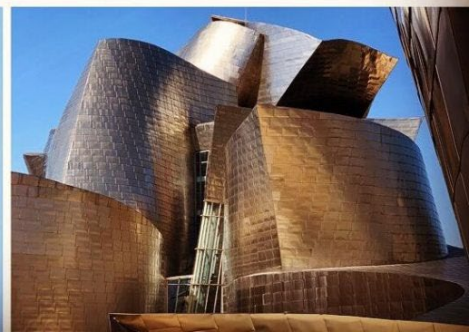
Methods of Manufacturing (The Kroll Process)

In 1937, William Kroll of Luxemburg invented the process we use to make titanium metal. His U.S. Pat. *2,205,854* claimed the "Kroll process"—reacting a titanium halide ($TiCl_4$) with an alkaline earth metal (Mg).

1. The method of producing cold malleable titanium consisting in causing a halide of titanium to chemically react with an alkaline earth metal at an elevated temperature below the boiling temperature of said metal and in the presence of a protective gas while maintaining normal pressure.


June 25, 1940. W. KROLL 2,205,854
METHOD FOR MANUFACTURING TITANIUM AND ALLOYS THEREOF
Filed July 6, 1938





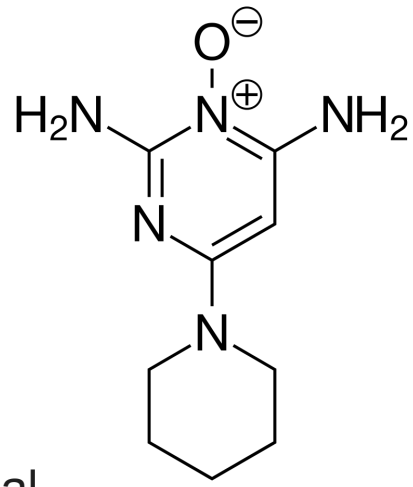
www.inventiveadventures.com

CULHANE MEADOWS PLLC
Big Law for the New Economy

Methods of Therapeutic Use (Rogaine®)

Upjohn Co. v. Medtron Laboratories, Inc., 751 F. Supp. 416 (S.D.N.Y 1990)

Rogaine (for men) (minoxidil), U.S. Pat. No. 4,596,812



1. A method of treating humans for alopecia which comprises topically applying to the human scalp an effective amount of a solution containing 6-amino-1,2-dihydro-1-hydroxy-2-imino-4-piperidinopyrimidine and a solvent.

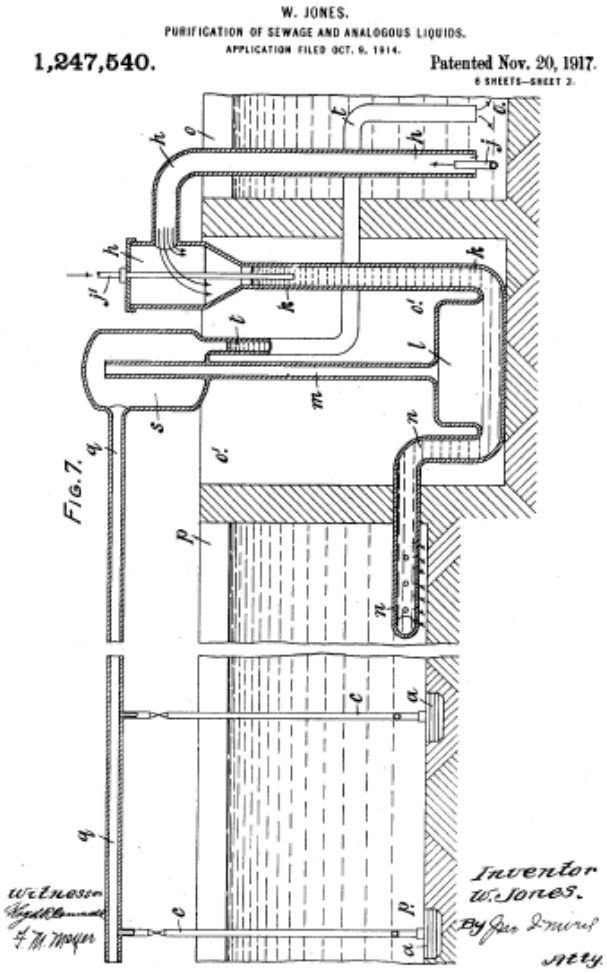
The only prior art cited as relevant by the PTO were the original patents on minoxidil as an anti-hypertensive agent (the "Anthony et al. patents"). These patents, also owned by Upjohn, did not disclose the topical hair growth compositions of the '619 and '812 patents.

Methods of Therapeutic Use (Rogaine)

While it was reported by Koblenzer that systemic, oral doses of diazoxide resulted in hair growth as a side effect, the only evidence of prior topical application of diazoxide was not published. Moreover, those results did not suggest either a safe or effective treatment. Even if Koblenzer's articles on oral administration were considered prior art, this prior art differs drastically from the '619 and '812 patents, which claim a safe and effective topical treatment for male pattern baldness.

Avoiding hindsight, this Court cannot consider as prior art Chidsey's discovery of minoxidil's hair growth properties when orally taken. One of ordinary skill therefore would not know that minoxidil, like diazoxide, caused hair growth when systemically given. It follows that one of ordinary skill in 1971 would not have had a reasonable expectation that topical minoxidil would be a safe and effective treatment for baldness.

Other Processes of Use (Activated Sludge)


W. JONES.
PURIFICATION OF SEWAGE AND ANALOGOUS LIQUIDS.
APPLICATION FILED OCT. 9, 1914.
1,247,540. Patented Nov. 20, 1917.
6 SHEETS—SHEET 3.
FIG. 7.
Witnesses
Inventor
W. Jones.
By

What is claimed is:—

1. The process of treating sewage and the like consisting in causing a local upflow in the liquid and supplying air locally into the liquid in its flow, and permitting the liquid to flow downward to another point.

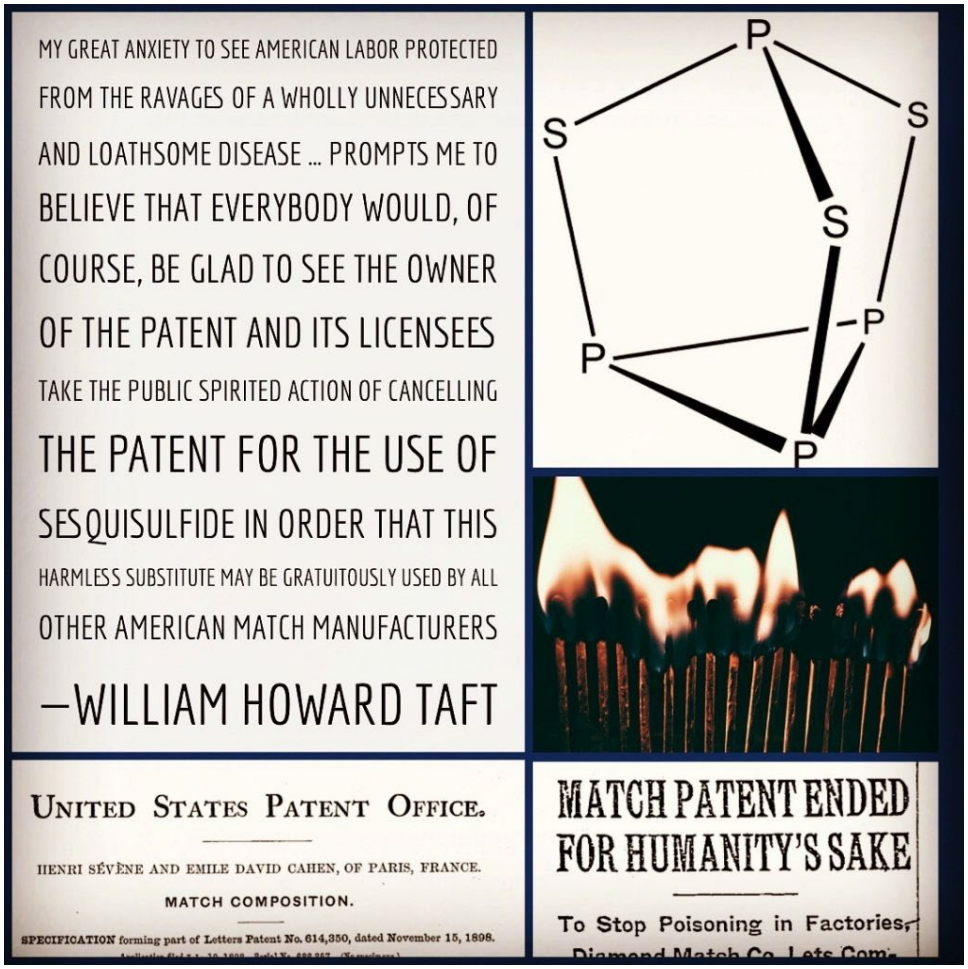
City of Milwaukee v. Activated Sludge, 69 F. 2d 577 (7th Cir. 1934)

The decree in this case enjoins appellant from operating its plant. . . . If, however, the injunction ordered by the trial court is made permanent in this case, it would close the sewage plant, leaving the entire community without any means for the disposal of raw sewage other than running it into Lake Michigan, thereby polluting its waters and endangering the health and lives of that and other adjoining communities. It is suggested that such harmful effect could be counteracted by chemical treatment of the sewage, but where, as here, the health and the lives of more than half a million people are involved, we think no risk should be taken, and we feel impelled to deny appellee's contention in this respect. . . . The decree is affirmed except as to the injunction, and as to it the decree is reversed.

Novel Chemical Compositions (Diamond Match)

French chemists Henri Sévène and Emile Cahen patented their non-toxic phosphorous sesquisulfide for matchmaking as U.S. Pat. ***614,350***, and sold it to the Diamond Match Co for $100,000 in 1900.

1. Inflammable material for matches having as an essential ingredient sesquisulfid of phosphorus, substantially as described.



www.inventiveadventures.com

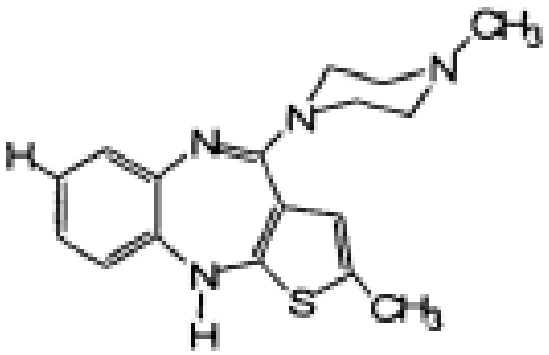
CULHANE MEADOWS PLLC
Big Law for the New Economy

Species Selection Patents (Zyprexa®)

Eli Lilly & Co. v. Zenith Goldline Pharms., 471 F.3d 1369 (Fed. Cir. 2006)

Zyprexa® (olanzapine), U.S. Pat. 5,229,382, which claimed

> 2-Methyl-10-(4-methyl -1-piperazinyl)-4H-thieno[2,3-b][1,5]benzodiazepine, or an acid addition salt thereof.

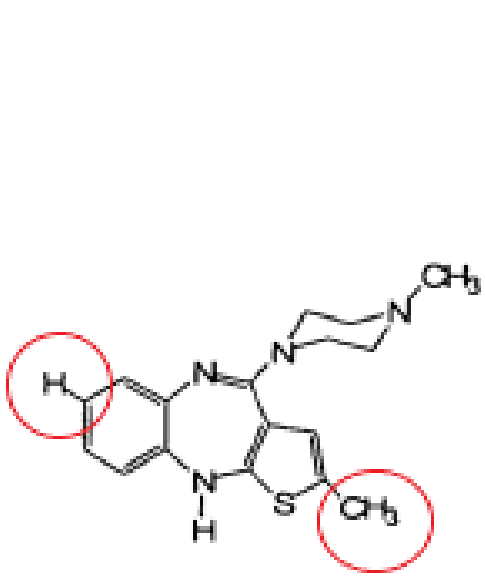


Olanzapine

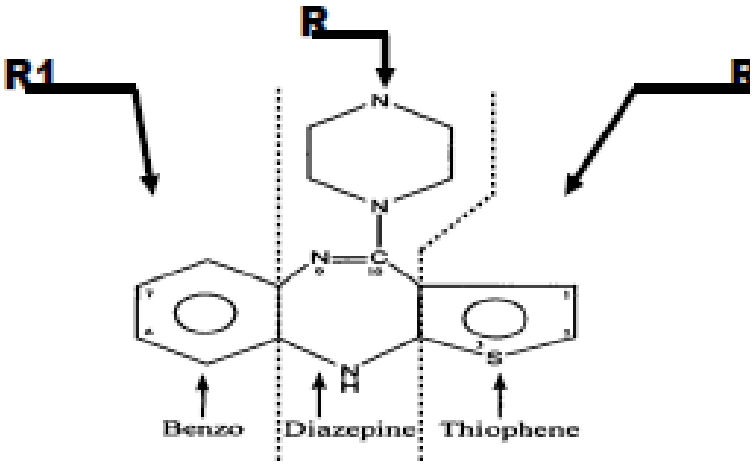
CULHANE MEADOWS PLLC
Big Law for the New Economy

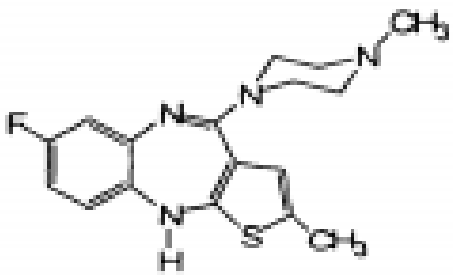
Species Selection Patents (Zyprexa®)

The **prior art** *included the thienobenzodiazepine genus as well as three known species Flumezapine, Ethyl Flumezapine, and Ethyl Olanzapine*

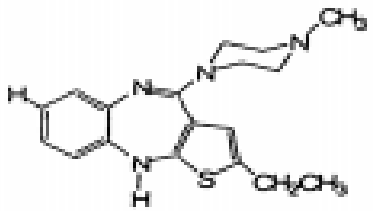


Olanzapine

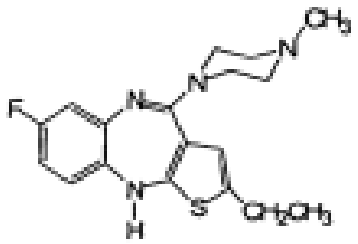




Flumezapine



Ethyl Olanzapine
(Compound '222)



Ethyl Flumezapine

CULHANE MEADOWS PLLC
Big Law for the New Economy

Species Selection Patents (Zyprexa®)

Anticipation – the defendants relied on an earlier cases *In re Petering* and *In re Schaumann* that found a species claim anticipated by a prior art genus.

The court distinguished those cases stating that "Petering and Schaumann expressly spelled out a definite and limited class of compounds that enabled a person of ordinary skill in the art to at once envisage each member of this limited class."

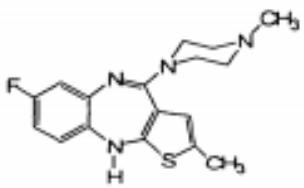
"By contrast, the number of compounds actually disclosed by Chakrabarti 1980a numbers in the millions (including all proposed alternative substituents)"

"Chakrabarti 1980a does provide a general structural formula with possible substituents of "R," "R1," and "R2," but it does not define them at all."

Species Selection Patents (Zyprexa®)

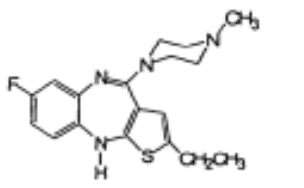
Obviousness – the court looked at whether it would have been obvious to make the slight changes in flumezapine, ethyl flumezapine, or ethyl olanzapine to arrive at the claimed invention:

Flumezapine caused extra-pyramidal symptoms (EPS) and an increase in liver enzymes and a muscle enzyme called creatine phosphokinase (CPK).



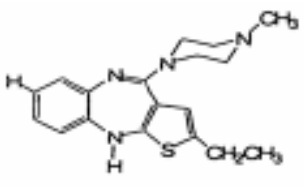
Flumezapine

Ethyl flumezapine caused widespread blood problems in dogs.



Ethyl Flumezapine

Ethyl olanzapine caused a significant increase in cholesterol in female beagle dogs.



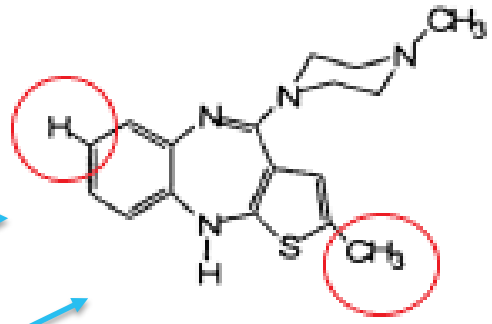
Ethyl Olanzapine
(Compound '222)

?

?

?

What is a ***lead compound*** for Obviousness?



Olanzapine

The homolog rule – adjacent homologs normally prima facie obvious

CULHANE MEADOWS PLLC
Big Law for the New Economy

Species Selection Patents (Zyprexa®)

Obviousness – the court focused on whether ethyl olanzapine would have been selected as a lead compound, because if that was the case then going from an ethyl group to methyl group would have been deemed obvious under the homolog rule.

"At the time of invention, the state of the art would have directed the person of ordinary skill in the art away from unfluorinated compounds like Compound '222" (ethyl olanzapine):

- Biological data was lacking for ethyl olanzapine
- Addition of halogen was thought important for anti-psychotic activity .
- Rejected arguments that some prior art suggested substituting fluorine with hydrogen would have avoided an undesirable metabolite

"Lilly established (1) a long-felt and unmet need; (2) failure of others; (3) industry acclaim; and (4) unexpected results. *Id.* The record shows a long-felt need for a safer, less toxic, and more effective clozapine-like drug; a decade (or more) of failure to find a replacement for clozapine; a reasonable amount of commercial success for olanzapine; and a number of awards for olanzapine as indicators of industry acclaim."

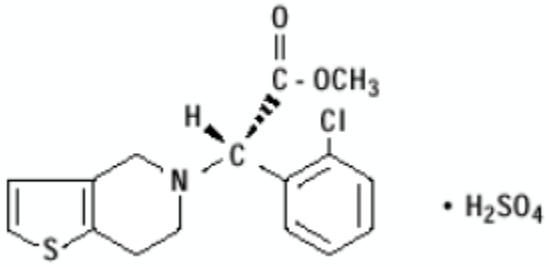
The court therefore upheld the validity of the Zyprexa patent.

Enantiomer Patents (Plavix®)

***Sanofi-Aventis v. Apotex Inc.*, 550 F.3d 1075 (Fed. Cir. 2008)**

Plavix (clopidogrel bisulfate) tablets, U.S. Pat. 4,847,265, claiming:

> 3. Hydrogen sulfate of the dextro-rotatory isomer of methyl alpha-5(4,5,6,7-tetrahydro(3,2-c)thienopyridyl)(2-chlorophenyl)-acetate substantially separated from the levo-rotatory isomer.



Prior art disclosed the compound as the racemate, and chemists would have recognized the compound would exist as a mixture of enantiomers.

Enantiomer Patents (Plavix®)

Novelty (Anticipation)

"The knowledge that enantiomers may be separated is not 'anticipation' of a specific enantiomer that has not been separated, identified, and characterized."

"[T]he reference patents would not have enabled a person of ordinary skill to obtain clopidogrel substantially separated from the levorotatory enantiomer."

Non-obviousness

"[O]n the state of the prior art, a person of ordinary skill would not have had the expectation that separating the enantiomers would be likely to produce an isomer having absolute stereoselectivity as to both the favorable antiplatelet activity and the unfavorable neurotoxicity"

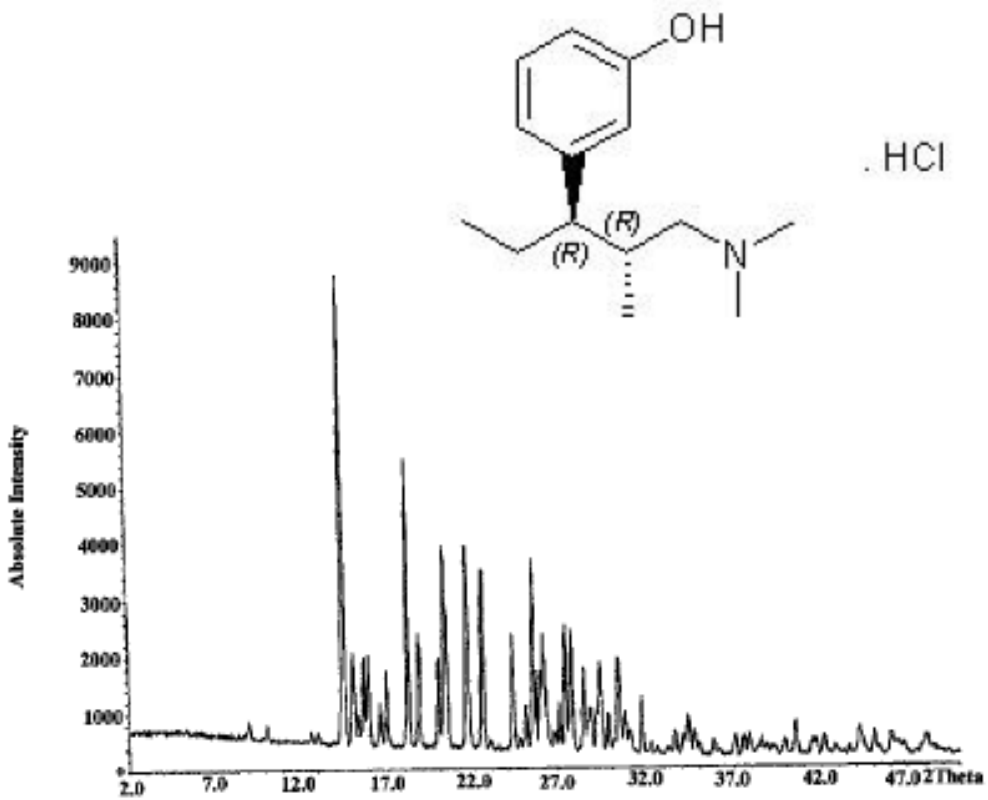
The court therefore upheld the validity of the patent to Plavix.

Polymorph Patents (NUCYNTA® ER)

***Grunenthal GmbH v. Alkem Labs. Ltd., 919 F. 3d 1333* (Fed. Cir. 2019)**

NUCYNTA® ER (extended release), a tapentadol hydrochloride tablet
U.S. Pat. 7,994,364 claiming:

1. A crystalline Form A of (-)-(1R,2R)-3-(3-dimethylamino-1-ethyl-2-methylpropyl)-phenol hydrochloride exhibiting at least X-ray lines (2-theta values) in a powder diffraction pattern when measured using Cu Kα radiation at 15.1±0.2, 16.0±0.2, 18.9±0.2, 20.4±0.2, 22.5±0.2, 27.3±0.2, 29.3±0.2 and 30.4±0.2.



CULHANE MEADOWS PLLC
Big Law for the New Economy

Polymorph Patents (NUCYNTA® ER)

***Grunenthal GmbH v. Alkem Labs. Ltd., 919 F. 3d 1333* (Fed. Cir. 2019)**

Form B of tapentadol hydrochloride was known in the art and previously disclosed in U.S. Patent No. 6,248,737 ("the '737 patent"), also assigned to Grünenthal. Form A was not known, and existence of polymorphs for this compound was not known.

Also known in the art at the time of filing was the concept of polymorph screening, which is the practice of characterizing all crystal forms of a chemical compound.

- "Byrn does not provide any guidance as to how the different solvents, varying temperatures, rates of agitation, or other variables used in polymorph screenings should be manipulated."

- "[T]here was little to no basis from which a POSA could expect a probability of success in producing Form A."

Conclusion

“Fifty years after we undertook to make the first synthetic polarizers we find them the essential layer in digital liquid-crystal. And thirty-four years after we undertook to make the first instant camera and film, our kind of photography has become ubiquitous.”

Edwin Land

Not only was [Edwin Land] one of the great inventors of our time but, more important, he saw the intersection of art and science and business and built an organization to reflect that.

Steve Jobs

Case Studies in Chemical Patenting

CHEM 6961 / 4961 01 Aspects and Tools of Chemical Practice

Rensselaer Polytechnic Institute

Thank You for your attention.

Please feel free to contact me if you have any questions!

CULHANE MEADOWS PLLC

Big Law for the New Economy®

April 18, 2022
Jeff B. Vockrodt
jvockrodt@cm.law

www.inventiveadventures.com