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The face of the patent is not the "Whole Story": determining effective life of a pharmaceutical patent in the United States ☆

Anne Marie Clark *,[1], Heidi Berven [2]

Pfizer, 2800 Plymouth Road, Ann Arbor, MI 48105, USA

Abstract

This article provides an overview of the factors that may contribute to the effective term of protection for a pharmaceutical product in the USA—by patent and by FDA market exclusivities, identifies public and commercial sources for collecting relevant patent term and exclusivity data, and provides a strategy for ensuring that the effective term of protection has been calculated accurately.

Keywords: Patent term; Patent expiry; Pharmaceutical patents; Interference; Infringement; Terminal disclaimers; Maintenance fees; Correction certificates; FDA; Hatch–Waxman; Market exclusivity; NCE exclusivity; Orphan drug exclusivity; Pediatric exclusivity; OTC switches; ANDA exclusivity

1. Introduction

A number of legal and regulatory factors may influence the date on which a US patent covering a pharmaceutical product expires, as depicted in Fig. 1. Thus, US Patent Law, as enforced by the Patent and Trademark Office ("PTO"), effectively controls the term of such patents through various statutory provisions. For marketed pharmaceutical products, a body of regulations administered through the Food and Drug Administration ("FDA"), determines the period of market exclusivity that will be granted to a pharmaceutical product. At the interface of PTO and FDA governance is the action of the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the "Hatch–Waxman Act", after the senators that authored the legislation. The Hatch–Waxman Act compensates patent owners for delays in obtaining FDA approval for new pharmaceutical products, by rewarding them with patent term additions.

From the standpoint of competitive intelligence, it is frequently difficult to accurately determine the "patent life" of a competitor's patent. "Patent life" means the sum of the term of a patent that claims a pharmaceutical product, plus any market exclusivities granted to the pharmaceutical product. As a preliminary matter, such information can be critical in planning research directions and market entries. The information, however, is unavailable from a single public or commercial source. Moreover, errors can exist in databases regarding patent status, and changes frequently occur in relevant PTO and FDA law and regulations. As a result, the term of a patent cannot be determined algorithmically in some instances, but must be the result of a longitudinal, multi-source analysis. This article identifies public and commercial sources for collecting relevant term and exclusivity data, provides an overview of the factors that may contribute to effective patent term, and provides a strategy for ensuring that the term of a patent has been calculated accurately.

☆ This article is based in part on the authors' presentation given at the 226th American Chemical Society Meeting in New York City in September 2003.

* Corresponding author.

[1] Associate Director, Information Management, Pfizer Global Research and Development, Ann Arbor, MI. Ph.D. (Chemistry), The University of Louisville.

[2] Counsel, Pfizer, Inc., Ann Arbor, MI. Ph.D. (Chemistry), The Pennsylvania State University. J.D., The University of Iowa College of Law.

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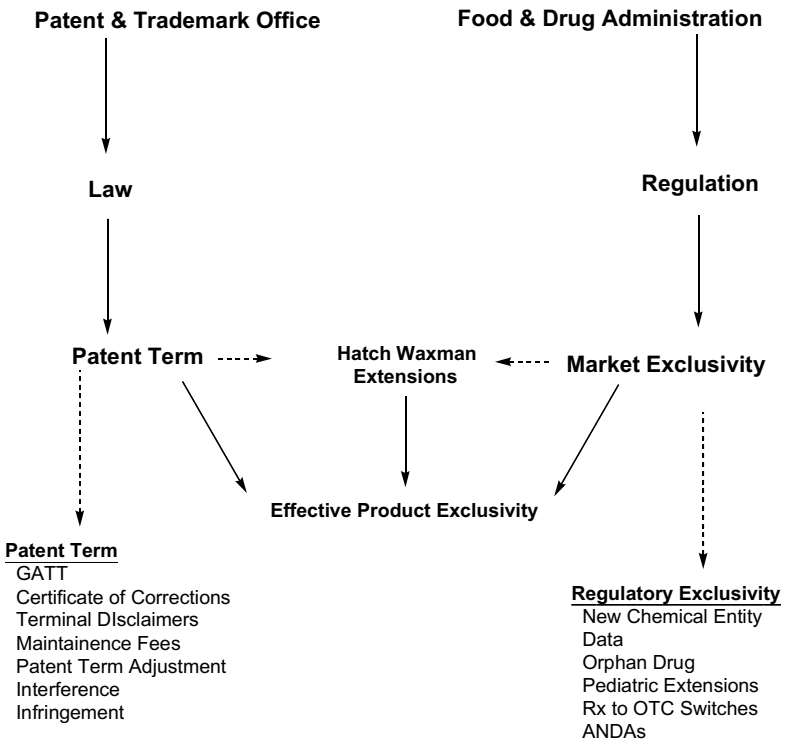


Fig. 1. Interface between patent term and regulatory exclusivity.

2. Public and commercial data sources [3]

2.1. Free services

2.1.1. Patent term data

Patent Application Information Retrieval (PAIR). PAIR is available from the PTO online at http://pair.uspto.gov/cgi-bin/final/home.pl. PAIR contains file history contents, and provides access to maintenance fee payment and patent term adjustment data on US patents and applications that have been published.

Official Patent Gazette (OG). The OG is available from the PTO online at http://www.uspto.gov/web/patents/patog/. The OG contains notices of expiration, reinstatement, certificates of correction, and other important information.

A list of *Patent Terms Extended Under 35 USC § 156* is available from the PTO online at http://www.uspto.gov/web/offices/pac/dapp/opla/term/156.html. The list contains expiry dates for drugs with Hatch–Waxman extensions and a link to a copy of the certificate of extension for most of them.

An OPS version of INPADOC, now available via Epidos, contains patent family and legal status information.

[3] This is an incomplete list. The comments reflect to the best of our abilities the supplier's representation of what is available and does not represent an endorsement by Pfizer.

2.1.2. Market exclusivity data

The *Approved Drug Products with Therapeutic Equivalence Evaluations (Orange Book)* is available from the FDA online at http://www.fda.gov/cder/ob/. The Orange Book contains drug patent expiry dates, Hatch–Waxman extensions and market exclusivity information such as new chemical entity (NCE), data or "other", and orphan drug exclusivity (ODE).

Orphan Drug Designations and Approvals are available from the FDA online at http://www.fda.gov/Orphan/designat/list.htm.

The list of *CDER New and Generic Drug Approvals* are available from the FDA online at http://www.fda.gov/cder/approval/index.htm. The list contains images of the New Drug Application (NDA).

2.2. Fee-based services

Inpadoc is produced by the European Patent Office, and is available through database vendors such as Dialog, Questel-Orbit, MicroPatent, Delphion and STN. Inpadoc contains patent family and legal status information.

IMS Patent Focus is produced by IMS Health, and is available through database vendors such as Dialog, Ovid, Questel-Orbit and STN. IMS Patent Focus contains evaluated patent position on pharmaceuticals.

IFI Claims (CLAIMS®) is produced by IFI Claims Patent Services, and is available through database

vendors such as Dialog, Questel-Orbit and STN. CLAIMS® Current Patent Legal Status Database references all actions noted in the *Official Gazette* that could affect the term of a patent, including: premature expirations, extensions, disclaimers and dedications.

LitAlert is produced by Thomson Derwent, and is available through Questel-Orbit and Dialog. LitAlert provides information relating to patents that have been the subject of infringement litigation.

Diogenes is produced by FOI Services, Inc., and is available through Dialog, and STN. Diogenes contains FDA information.

DOLPHIN is produced by Thomson Current Patents, and is available by subscription. Dolphin contains information on all aspects of pharmaceutical patents.

3. Factors affecting patent term

Referring again to Fig. 1, US Patent Law, as enforced by the Patent and Trademark Office, effectively controls the term of pharmaceutical patents through various statutory provisions. For example, the law guarantees a "base" patent term of either 17 years from the date of issue or 20 years from the date of filing, depending on whether the patent was filed before or after June 8, 1995. This "base" term is subject to further modification. For example, if required maintenance fees are not paid, a patent may go abandoned, thus truncating the patent term. Also, in some instances, a certificate of correction may issue, altering the patent priority date, and thus modifying the patent term. Further, the patent term may be terminally disclaimed to the effective life of a related patent. Additionally, the patent term adjustment provisions of the American Inventors Protection Act of 2000 allow for the extension of patent terms, as determined by the promptness and diligence of both applicants and examiners during the course of prosecution. Finally, a legal or administrative court can affect patent term, through the resolution of an infringement or interference action.

Patent term modifications due to these factors can occur at issuance or post-issuance, and a variety of patent information sources can be used to track term data. However, it is important to bear in mind that no single source reliably and accurately tracks all modifications.

3.1. Statutory patent term

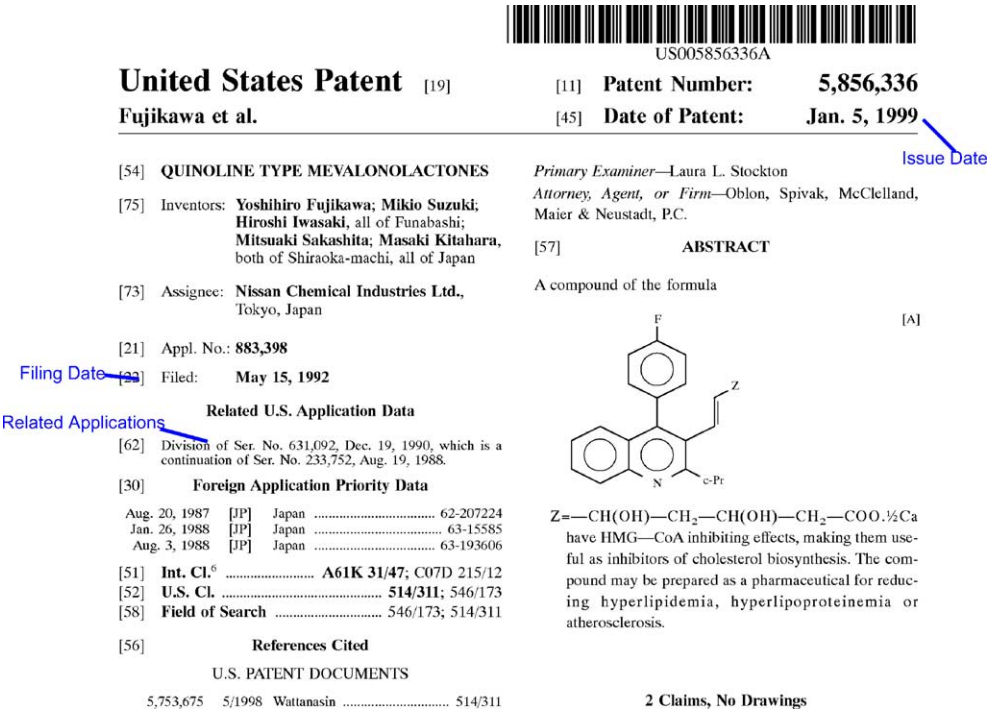
Prior to June 8, 1995, the statutory term of a US patent as provided by 35 U.S.C. § 154 was 17 years from the date of issue. After passage of the General Agreement on Tariffs and Trade (GATT), the statutory term as codified in 35 U.S.C. § 154 was changed to 20 years from the date of the first utility application filing for patent applications filed on or after June 8, 1995. For applications filed before June 8, 1995, the patent term is either 20 years from the date of filing or 17 years from the date of issue, whichever is longest.

When determining the patent term, the type of patent (which may be continuation, continuation-in-part or divisional application) should first be determined. A continuation patent is a second patent application for the same invention that is claimed in a prior, "parent" nonprovisional application that is filed before the first application becomes abandoned or patented. A continuation-in-part patent application is an application filed during the lifetime of an earlier, nonprovisional application that repeats some substantial portion or all of the earlier nonprovisional application, but that adds "new matter" not disclosed in the earlier nonprovisional application. A divisional patent application is a later application for an independent or distinct invention disclosing and claiming only a portion of the subject matter disclosed in the earlier or parent application. Related parent, continuation, continuation-in-part, and divisional applications that issue as patents may have the same or different expiration dates. It is important to determine the type of patent under review in order to ascertain whether a parent patent controls the expiration data of a continuation, continuation-in-part, or divisional patent. [4]

Much patent term data is available from public and fee-based services; however, errors in patent term data can exist, particularly for applications filed prior to the enactment of GATT. As a result, it is generally wise to check patent term data obtained by simple calculation using information provided on the front page, or "face" of a patent. Thus, in Fig. 2, depicting the face of US Patent No. 5,856,336, the filing date of the patent is provided in field 22, in the left column, or May 15, 1992. The issue date is provided in field 45, in the top right corner, or January 5, 1999. Related patents are listed in field 62, in the left column, indicating that the "parent" patent application to US Patent No. 5,856,336 was filed on August 19, 1988. Since US Patent No. 5,856,336 is not an originally filed utility application, but is a continuation application, the date used for the purposes of calculating the patent term would be August 19, 1988.

US Patent No. 5,856,336 was filed pre-GATT. Therefore, to determine the patent term, it is necessary to compare the patent terms as calculated from the first filing date, as opposed to the issue date. As indicated previously, prior to GATT, the term of a patent was 17 years from the issue date, or in the case of US Patent No. 5,856,336, January 5, 2016. Post-GATT, the patent

[4] Manual of Patent Examining Procedure (MPEP) §§ 201.06 (divisional applications), 201.07 (continuation applications), 201.08 (continuation-in-part applications).



US005856336A

United States Patent [19]

Fujikawa et al.

[11] **Patent Number: 5,856,336**

[45] **Date of Patent: Jan. 5, 1999**

Issue Date

[54] **QUINOLINE TYPE MEVALONOLACTONES**

[75] Inventors: **Yoshihiro Fujikawa; Mikio Suzuki; Hiroshi Iwasaki**, all of Funabashi; **Mitsuaki Sakashita; Masaki Kitahara**, both of Shiraoka-machi, all of Japan

[73] Assignee: **Nissan Chemical Industries Ltd.**, Tokyo, Japan

[21] Appl. No.: **883,398**

Filing Date [22] Filed: **May 15, 1992**

Related U.S. Application Data

Related Applications [62] Division of Ser. No. 631,092, Dec. 19, 1990, which is a continuation of Ser. No. 233,752, Aug. 19, 1988.

[30] **Foreign Application Priority Data**

Aug. 20, 1987 [JP] Japan 62-207224
Jan. 26, 1988 [JP] Japan 63-15585
Aug. 3, 1988 [JP] Japan 63-193606

[51] **Int. Cl.**[6] **A61K 31/47**; C07D 215/12
[52] **U.S. Cl.** **514/311**; 546/173
[58] **Field of Search** 546/173; 514/311

[56] **References Cited**

U.S. PATENT DOCUMENTS

5,753,675 5/1998 Wattanasin 514/311

Primary Examiner—Laura L. Stockton
Attorney, Agent, or Firm—Oblon, Spivak, McClelland, Maier & Neustadt, P.C.

[57] **ABSTRACT**

A compound of the formula

[A]

Z=—CH(OH)—CH_2—CH(OH)—CH_2—COO.½Ca have HMG—CoA inhibiting effects, making them useful as inhibitors of cholesterol biosynthesis. The compound may be prepared as a pharmaceutical for reducing hyperlipidemia, hyperlipoproteinemia or atherosclerosis.

2 Claims, No Drawings

Fig. 2. Calculating the term of patent filed pre-GATT (June 8, 1995): longer of 20 years from first filing or 17 years from issue.

term is 20 years from the date of first filing or in the case of US Patent No. 5,856,336, August 19, 2008. Therefore, the actual expiration date for US Patent No. 5,856,336 is January 5, 2016, *the longer of the two terms*.

3.2. Certificate of corrections

To perfect a claim for the benefit of foreign priority in a patented continuing application, a Certificate of Correction under 35 U.S.C. § 255 and 37 C.F.R. § 1.323 may be requested and issued after a patent is granted. A Certificate of Correction may be obtained, as long as the requirements of 35 U.S.C. § 119(a)–(d) or (f) have been satisfied in the parent application prior to issuance of the patent, and the requirements of 37 C.F.R. § 155(a) are met. A printed copy of the Certificate of Correction is attached to each printed copy of the patent, and is considered as part of the original patent.

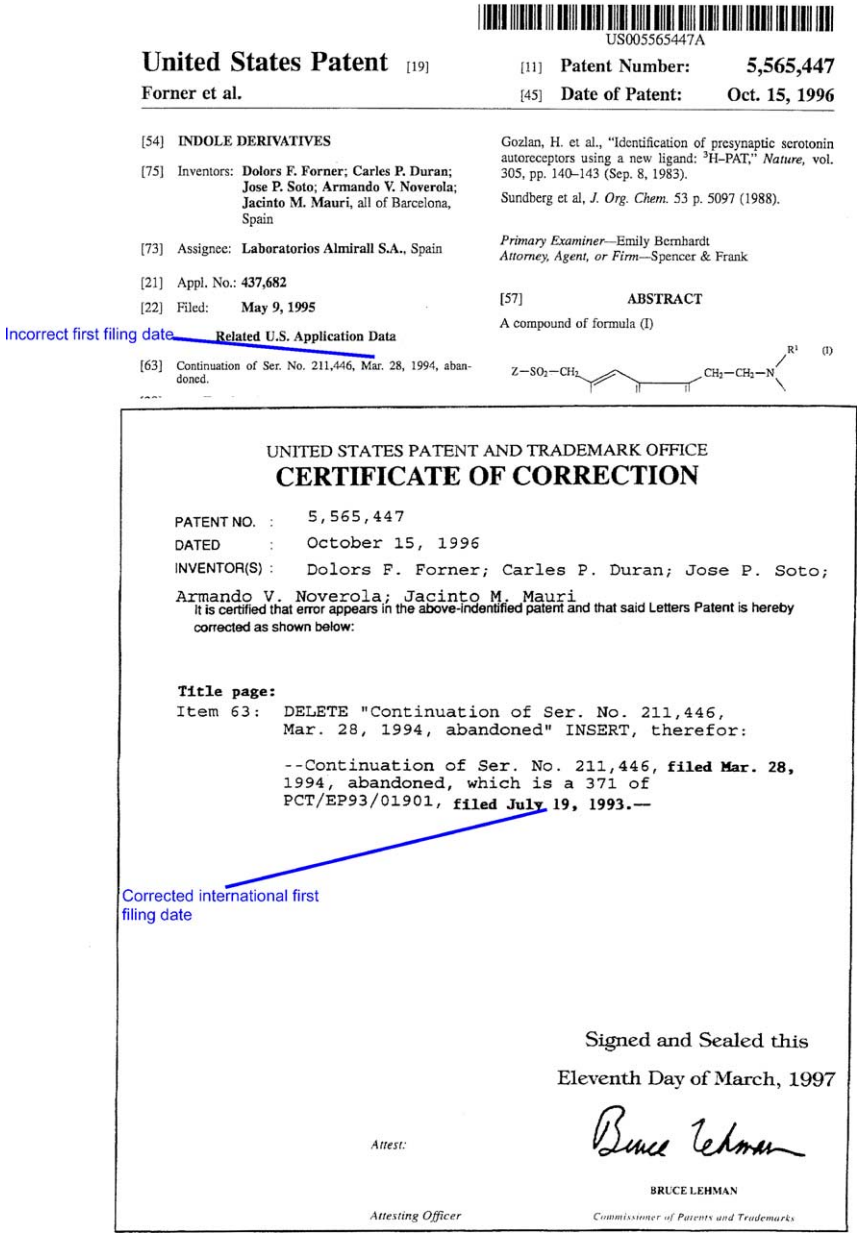
Certificate of Correction information is also available from the PTO. In addition, legal status databases will indicate that a Certificate of Correction exists for a particular patent, but will not provide additional, explanatory information. As a result, it is frequently necessary to examine the patent to determine whether there is a Certificate of Correction, and to examine the Certificate of Correction itself to determine the reason for the correction.

For example, a Certificate of Correction was issued for US Patent No. 5,565,447 to correct the priority claim. As indicated in Fig. 3, the face of US Patent No. 5,565,447 fails to indicate that the claim to priority reaches back to an earlier filed international application. As a result, the Certificate of Correction for US Patent No. 5,565,447, as reproduced in Fig. 3 provides the correct priority date for the patent of July 19, 1993, resulting in a corrected expiry date of October 15, 2013.

3.3. Terminal disclaimers

The patent statute prohibits a patent owner from obtaining patents on the same invention, or "double patenting". There are two types of double patenting. "Same invention" type double patenting is prohibited by 35 U.S.C. § 101, which provides that an inventor may obtain one patent, not a multiple of patents, for the same invention. The singular language of § 101 has been interpreted to provide an absolute bar to the issuance of a second patent for an identical invention. Thus, if a claim in the first patent is identical to a claim in the second, later issued patent, the second patent is deemed invalid on the basis of same invention double patenting.

"Nonstatutory" or "obviousness-type" double patenting is based on a judicially created doctrine grounded in public policy that is primarily intended to prevent prolongation of the patent term by prohibiting claims in a second patent that are not patentably distinct from claims in a first patent. It occurs when a claim of one patent is an obvious variation of a claim of another



US005565447A

United States Patent [19]
Forner et al.

[11] **Patent Number: 5,565,447**
[45] **Date of Patent: Oct. 15, 1996**

[54] **INDOLE DERIVATIVES**

[75] Inventors: **Dolors F. Forner; Carles P. Duran; Jose P. Soto; Armando V. Noverola; Jacinto M. Mauri**, all of Barcelona, Spain

[73] Assignee: **Laboratorios Almirall S.A.**, Spain

[21] Appl. No.: **437,682**

[22] Filed: **May 9, 1995**

Incorrect first filing date

Related U.S. Application Data

[63] Continuation of Ser. No. 211,446, Mar. 28, 1994, abandoned.

Gozlan, H. et al., "Identification of presynaptic serotonin autoreceptors using a new ligand: ^{3}H-PAT," *Nature*, vol. 305, pp. 140–143 (Sep. 8, 1983).

Sundberg et al, *J. Org. Chem.* 53 p. 5097 (1988).

Primary Examiner—Emily Bernhardt
Attorney, Agent, or Firm—Spencer & Frank

[57] **ABSTRACT**

A compound of formula (I)

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 5,565,447
DATED : October 15, 1996
INVENTOR(S) : Dolors F. Forner; Carles P. Duran; Jose P. Soto; Armando V. Noverola; Jacinto M. Mauri

It is certified that error appears in the above-indentified patent and that said Letters Patent is hereby corrected as shown below:

Title page:
Item 63: DELETE "Continuation of Ser. No. 211,446, Mar. 28, 1994, abandoned" INSERT, therefor:

--Continuation of Ser. No. 211,446, **filed Mar. 28,** 1994, abandoned, which is a 371 of PCT/EP93/01901, **filed July 19, 1993.**—

Corrected international first filing date

Signed and Sealed this
Eleventh Day of March, 1997

Attest:

BRUCE LEHMAN

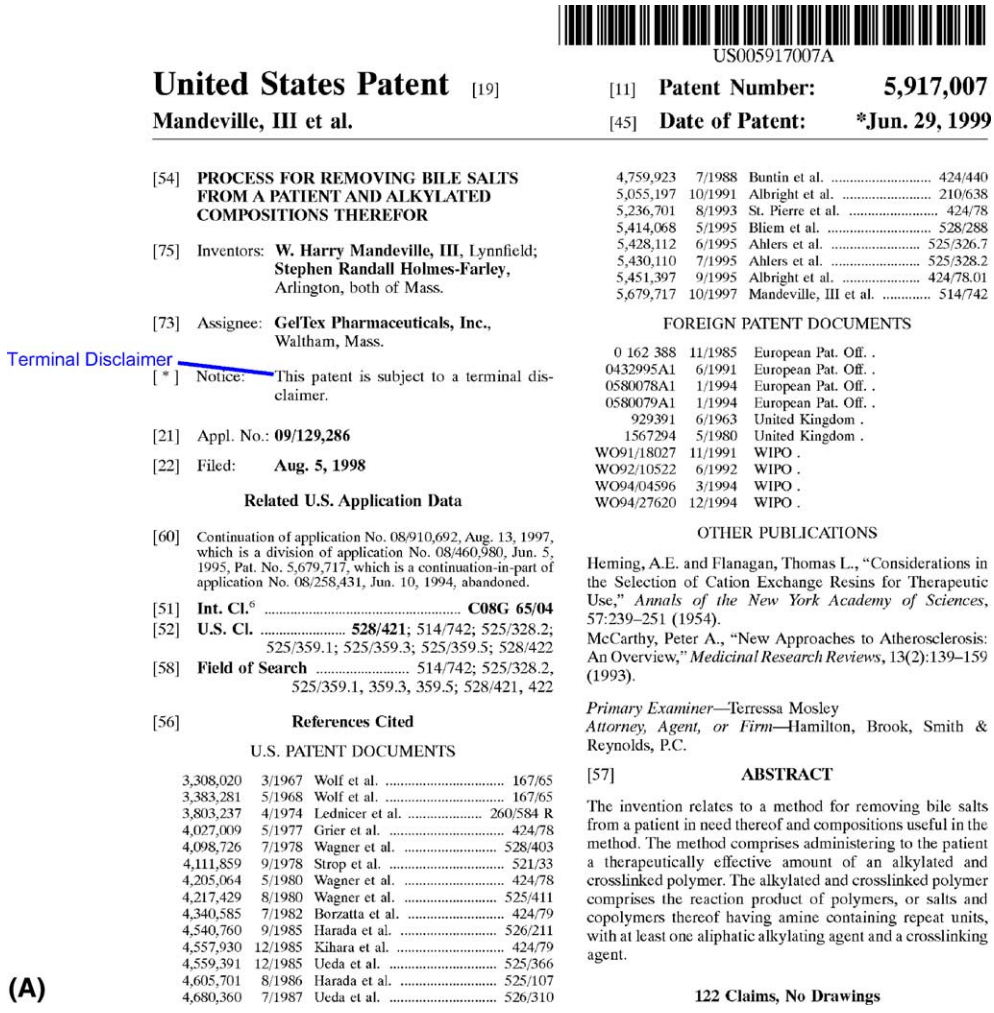
Attesting Officer *Commissioner of Patents and Trademarks*

Fig. 3. Certificate of Correction was issued for US Patent No. 5,565,447 to correct the priority claim. The face of US Patent No. 5,565,447 fails to indicate that the claim to priority reaches back to an earlier filed international application.

patent, and both patents are owned by the same person or company, or are subject to an obligation of assignment to the same person or company. The second patent is rendered invalid unless a "terminal disclaimer" is obtained according to 35 U.S.C. § 253. A terminal disclaimer is a written statement by the patent owner stating that the owner has disclaimed the period of the second issued patent that would extend beyond the expiration of a reference patent. The terminal disclaimer avoids the double patenting objection only so long as the patents are commonly owned.

The face of a patent will generally indicate whether a terminal disclaimer is operative, but generally will not provide additional information, such as the reference patent to which the terminal disclaimer has been made. For example, as depicted in Fig. 4A, US Patent 5,917,007 is subject to a terminal disclaimer, but the reference patent is not identified; as a result, the patent term for US Patent 5,917,007 is unclear.

In order to ascertain the correct patent term for US Patent 5,917,007, it is necessary to review the patent family of which US Patent 5,917,007 is a member. Patent family analysis reveals that US Patent 5,917,007 is a divisional patent of US Patent 5,679,717. Review of the face of US Patent 5,679,717 depicted in Fig. 4B indicates that it is also subject to a terminal disclaimer.



US005917007A

United States Patent [19]

Mandeville, III et al.

[11] **Patent Number: 5,917,007**

[45] **Date of Patent: *Jun. 29, 1999**

[54] **PROCESS FOR REMOVING BILE SALTS FROM A PATIENT AND ALKYLATED COMPOSITIONS THEREFOR**

[75] Inventors: **W. Harry Mandeville, III**, Lynnfield; **Stephen Randall Holmes-Farley**, Arlington, both of Mass.

[73] Assignee: **GelTex Pharmaceuticals, Inc.**, Waltham, Mass.

Terminal Disclaimer

[*] Notice: This patent is subject to a terminal disclaimer.

[21] Appl. No.: **09/129,286**

[22] Filed: **Aug. 5, 1998**

Related U.S. Application Data

[60] Continuation of application No. 08/910,692, Aug. 13, 1997, which is a division of application No. 08/460,980, Jun. 5, 1995, Pat. No. 5,679,717, which is a continuation-in-part of application No. 08/258,431, Jun. 10, 1994, abandoned.

[51] **Int. Cl.**[6] **C08G 65/04**

[52] **U.S. Cl.** **528/421**; 514/742; 525/328.2; 525/359.1; 525/359.3; 525/359.5; 528/422

[58] **Field of Search** 514/742; 525/328.2, 525/359.1, 359.3, 359.5; 528/421, 422

[56] **References Cited**

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3,383,281	5/1968	Wolf et al.	167/65
3,803,237	4/1974	Lednicer et al.	260/584 R
4,027,009	5/1977	Grier et al.	424/78
4,098,726	7/1978	Wagner et al.	528/403
4,111,859	9/1978	Strop et al.	521/33
4,205,064	5/1980	Wagner et al.	424/78
4,217,429	8/1980	Wagner et al.	525/411
4,340,585	7/1982	Borzatta et al.	424/79
4,540,760	9/1985	Harada et al.	526/211
4,557,930	12/1985	Kihara et al.	424/79
4,559,391	12/1985	Ueda et al.	525/366
4,605,701	8/1986	Harada et al.	525/107
4,680,360	7/1987	Ueda et al.	526/310
4,759,923	7/1988	Buntin et al.	424/440
5,055,197	10/1991	Albright et al.	210/638
5,236,701	8/1993	St. Pierre et al.	424/78
5,414,068	5/1995	Bliem et al.	528/288
5,428,112	6/1995	Ahlers et al.	525/326.7
5,430,110	7/1995	Ahlers et al.	525/328.2
5,451,397	9/1995	Albright et al.	424/78.01
5,679,717	10/1997	Mandeville, III et al.	514/742

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0432995A1	6/1991	European Pat. Off. .
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WO94/04596	3/1994	WIPO .
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McCarthy, Peter A., "New Approaches to Atherosclerosis: An Overview," *Medicinal Research Reviews*, 13(2):139–159 (1993).

Primary Examiner—Terressa Mosley

Attorney, Agent, or Firm—Hamilton, Brook, Smith & Reynolds, P.C.

[57] **ABSTRACT**

The invention relates to a method for removing bile salts from a patient in need thereof and compositions useful in the method. The method comprises administering to the patient a therapeutically effective amount of an alkylated and crosslinked polymer. The alkylated and crosslinked polymer comprises the reaction product of polymers, or salts and copolymers thereof having amine containing repeat units, with at least one aliphatic alkylating agent and a crosslinking agent.

122 Claims, No Drawings

(A)

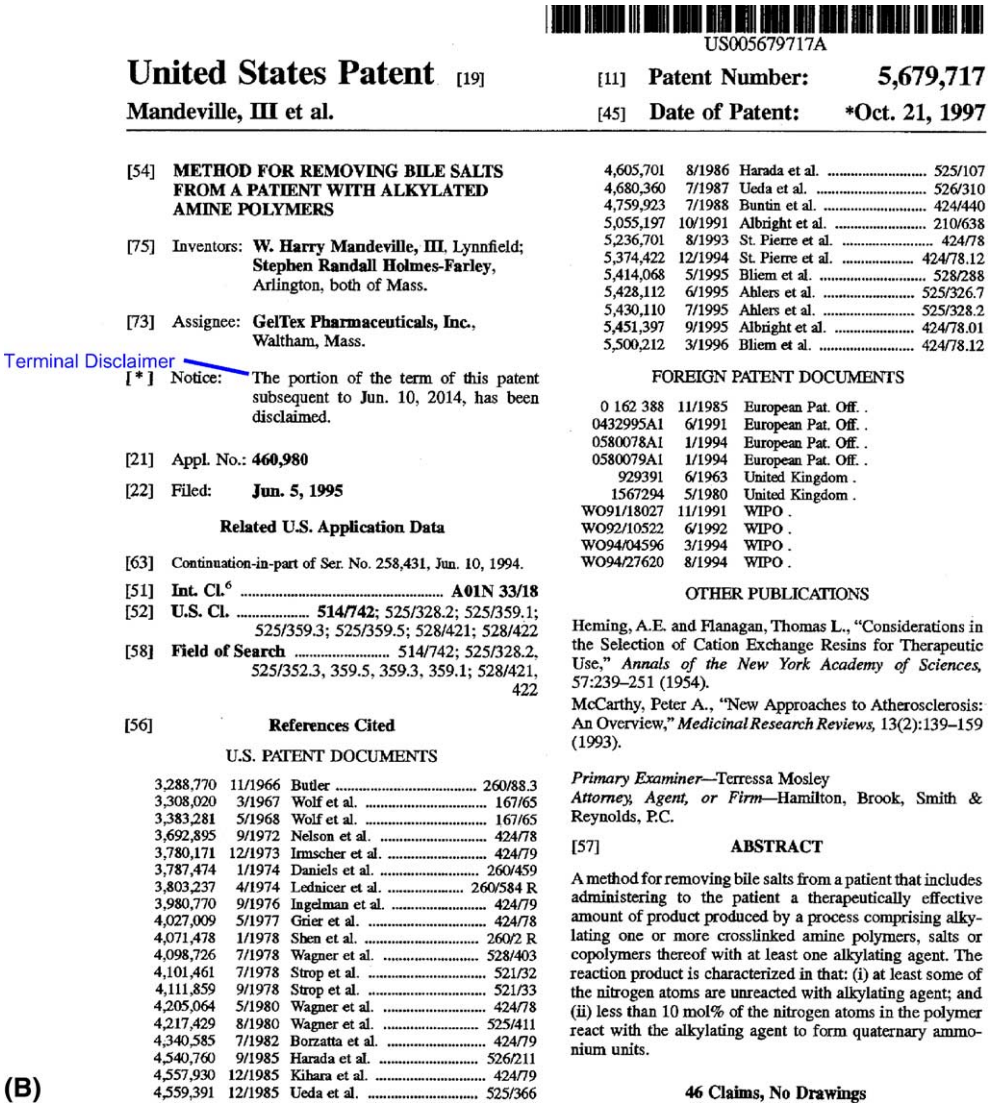
Fig. 4. (A) US Patent 5,917,007 is subject to a terminal disclaimer, but the reference patent is not identified. (B) Patent family analysis reveals that US Patent 5,917,007 is a divisional patent of US Patent 5,679,717. The face of US Patent 5,679,717 indicates that it is also subject to a terminal disclaimer. (C) A Certificate of Correction was filed to correct the date disclosed in the terminal disclaimer field on the face of US Patent 5,679,717.

Sometimes an expiration date is included in the terminal disclaimer statement. However, it is important to verify the date because it may be incorrect due to the patent term recalculation under GATT. Fig. 4C indicates that a Certificate of Correction was filed to correct the date disclosed in the terminal disclaimer field on the face of US Patent No. 5,679,717. So what is the term of US Patent 5,917,007? Ultimately, the file wrapper—the file the USPTO maintains for each patent application—is needed to calculate the term.

3.4. Maintenance fees

According to 35 U.S.C. § 41(b) and 37 C.F.R. § 1.362, all utility patents which issue from applications filed on or after December 12, 1980 are subject to the payment of maintenance fees. The maintenance fees are necessary to maintain the patent in force. As provided in Table 1, the fees are due at 3 1/2, 7 1/2, and 11 1/2 years from the date the patent is granted. The fees can be paid without a surcharge during the "window-period", which is the six-month period preceding each due date; e.g., three years to three years and six months, and so on, and with a surcharge from 3 1/2 to 4, 7 1/2 to 8, and 11 1/2 to 12 years. Maintenance fee information is available through the PTO PAIR system.

The Patent and Trademark Office does not mail notices to patent owners that maintenance fees are due. However, a reminder notice that maintenance fees may be due is included with correspondence from the PTO; for instance, the Notice of Allowance currently includes a reminder notice that maintenance fees may be due. In addition, a notice will appear in each issue of the PTO *Official Gazette* which will indicate which patents have been granted 3, 7, and 11 years earlier, that the window-period has opened, and that maintenance fee payments will now be accepted for those patents.



US005679717A

United States Patent [19]

Mandeville, III et al.

[11] **Patent Number: 5,679,717**

[45] **Date of Patent: *Oct. 21, 1997**

[54] **METHOD FOR REMOVING BILE SALTS FROM A PATIENT WITH ALKYLATED AMINE POLYMERS**

[75] Inventors: **W. Harry Mandeville, III**, Lynnfield; **Stephen Randall Holmes-Farley**, Arlington, both of Mass.

[73] Assignee: **GelTex Pharmaceuticals, Inc.**, Waltham, Mass.

Terminal Disclaimer

[*] Notice: The portion of the term of this patent subsequent to Jun. 10, 2014, has been disclaimed.

[21] Appl. No.: **460,980**

[22] Filed: **Jun. 5, 1995**

Related U.S. Application Data

[63] Continuation-in-part of Ser. No. 258,431, Jun. 10, 1994.

[51] **Int. Cl.**[6] **A01N 33/18**

[52] **U.S. Cl.** **514/742**; 525/328.2; 525/359.1; 525/359.3; 525/359.5; 528/421; 528/422

[58] **Field of Search** 514/742; 525/328.2, 525/352.3, 359.5, 359.3, 359.1; 528/421, 422

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3,980,770	9/1976	Ingelman et al.	424/79
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4,098,726	7/1978	Wagner et al.	528/403
4,101,461	7/1978	Strop et al.	521/32
4,111,859	9/1978	Strop et al.	521/33
4,205,064	5/1980	Wagner et al.	424/78
4,217,429	8/1980	Wagner et al.	525/411
4,340,585	7/1982	Borzatta et al.	424/79
4,540,760	9/1985	Harada et al.	526/211
4,557,930	12/1985	Kihara et al.	424/79
4,559,391	12/1985	Ueda et al.	525/366
4,605,701	8/1986	Harada et al.	525/107
4,680,360	7/1987	Ueda et al.	526/310
4,759,923	7/1988	Buntin et al.	424/440
5,055,197	10/1991	Albright et al.	210/638
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Primary Examiner—Terressa Mosley
Attorney, Agent, or Firm—Hamilton, Brook, Smith & Reynolds, P.C.

[57] **ABSTRACT**

A method for removing bile salts from a patient that includes administering to the patient a therapeutically effective amount of product produced by a process comprising alkylating one or more crosslinked amine polymers, salts or copolymers thereof with at least one alkylating agent. The reaction product is characterized in that: (i) at least some of the nitrogen atoms are unreacted with alkylating agent; and (ii) less than 10 mol% of the nitrogen atoms in the polymer react with the alkylating agent to form quaternary ammonium units.

46 Claims, No Drawings

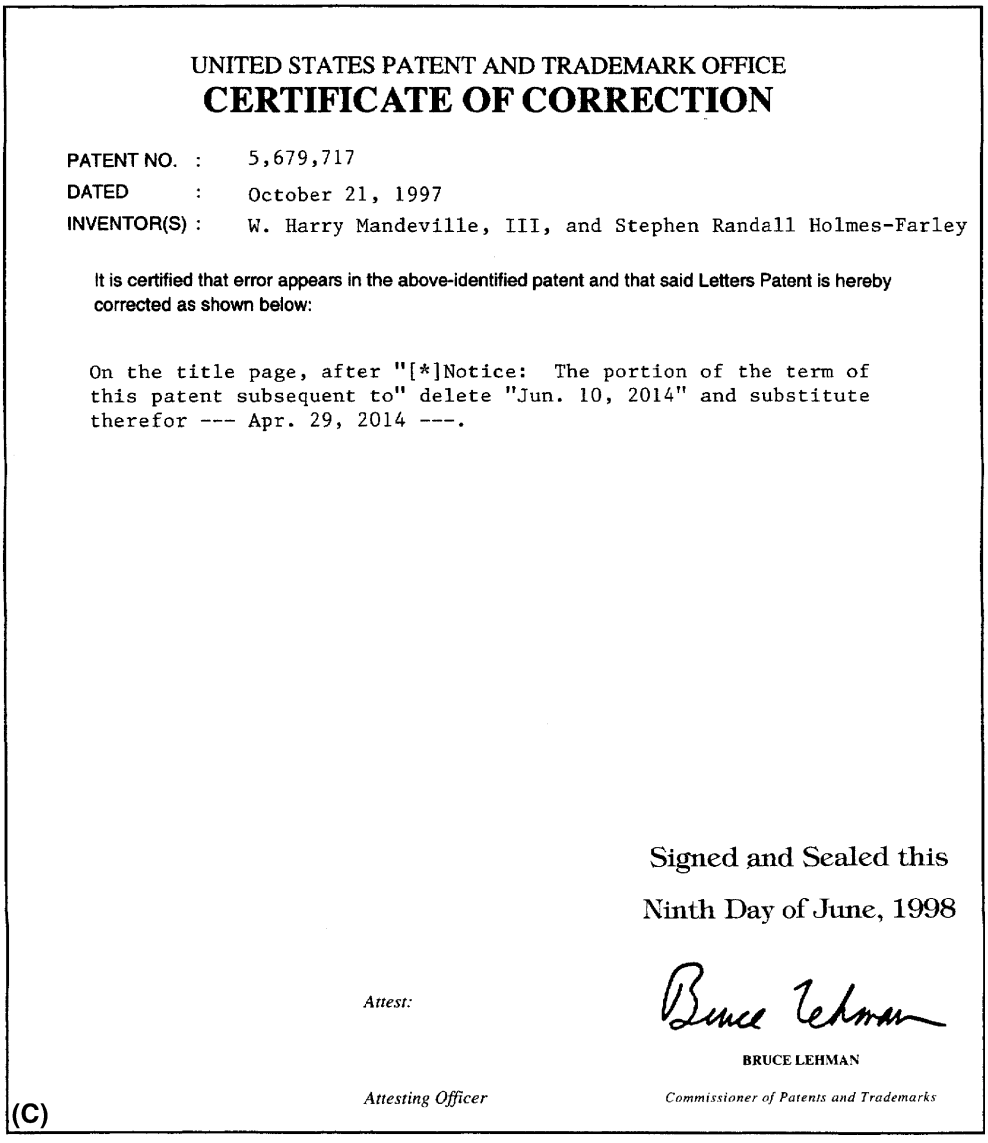
(B)

Fig. 4 (*continued*)

Failure to pay maintenance fees on time or during the six-month grace period may result in the expiration of the patent. The Office mails a Notice of Patent Expiration that records indicate that a patent has expired for failure to pay a required maintenance fee. An Official Gazette notice published after expiration of the grace period will indicate any patent that has expired due to nonpayment of maintenance fees.

However, according to 35 U.S.C. § 41(c)(1), the Director may accept the payment of any maintenance fee made within 24 months after the six-month grace period if the delay is shown to the satisfaction of the Director to have been unintentional, or at any time after the six-month grace period if the delay is shown to the satisfaction of the Director to have been unavoidable. A surcharge is typically required as a condition of accepting payment of any maintenance fee after the six-month grace period. If the Director accepts payment of a maintenance fee after the six-month grace period, the patent will be considered as not having expired at the end of the grace period, and a notice will appear in the Official Gazette indicating that the patent has been reinstated. An annual compilation of expirations and reinstatements is also published.

Caution must be exercised when stating that a patent has expired due to a failure to pay maintenance fees, because of the grace period, and the provision that the fee can be paid after the grace period if the delay was unintentional or unavoidable. For example, the maintenance fee for US Patent No. 5,104,361 was due on May 14, 2003, or 3 1/2 years from issue. The patent owner will have until November 14, 2003 to pay the maintenance fee, with a surcharge. After November 14, 2003 the patent will expire. However, it can be revived



UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 5,679,717

DATED : October 21, 1997

INVENTOR(S) : W. Harry Mandeville, III, and Stephen Randall Holmes-Farley

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

On the title page, after "[*]Notice: The portion of the term of this patent subsequent to" delete "Jun. 10, 2014" and substitute therefor --- Apr. 29, 2014 ---.

Signed and Sealed this

Ninth Day of June, 1998

Attest:

BRUCE LEHMAN

Attesting Officer

Commissioner of Patents and Trademarks

(C)

Fig. 4 (*continued*)

Table 1
Maintenance schedule for US patents

Fee due (no surcharge)	"Window" period (no surcharge)	Fee accepted with surcharge until	Patent expires	Revival possible
3 years	3 1/2 years	4 years	4 years + 1 day	Two years if payment delay unintentional; any time if delay unavoidable
7 years	7 1/2 years	8 years	8 years + 1 day	Same as above
11 years	11 1/2 years	12 years	12 years + 1 day	Same as above

with a fee either at any time if the delay in paying the fee was unavoidable, or before November 14, 2005 if the delay was unintentional.

3.5. Interference

Unlike other nations, the United States gives priority of invention to the person who is the *first to invent*, rather than the person who happens to be the *first to file*, a patent application. Frequently, competing patent applications are filed which claim the same invention. As provided by 35 U.S.C. § 135, a patent interference is a trial-like, administrative proceeding held within the Patent and Trademark Office, before the Board of Patent Appeals and Interferences (BPAI). The BPAI determines which of a number of competing applicants

was the first to invent and thus is entitled to receive a patent. Decisions of the BPAI can be subjected to review or appeal.

Patent interferences arise between pending patent applications, or between a pending application and an unexpired patent. Aspects of interference actions and their affect on legal status are also described in an article by Simmons and Spahl [1]. When an interference action occurs between pending patent applications, the winning party secures the invention embraced by the claims in controversy, and the losing party has to surrender those claims. Paper notice of the decision is added to the file wrappers of both the winning and losing applications. Assuming the winning application matures into a patent, the winning party to the interference will enjoy the right to exclude others from making, using, or selling the claimed invention as provided by the United States patent law.

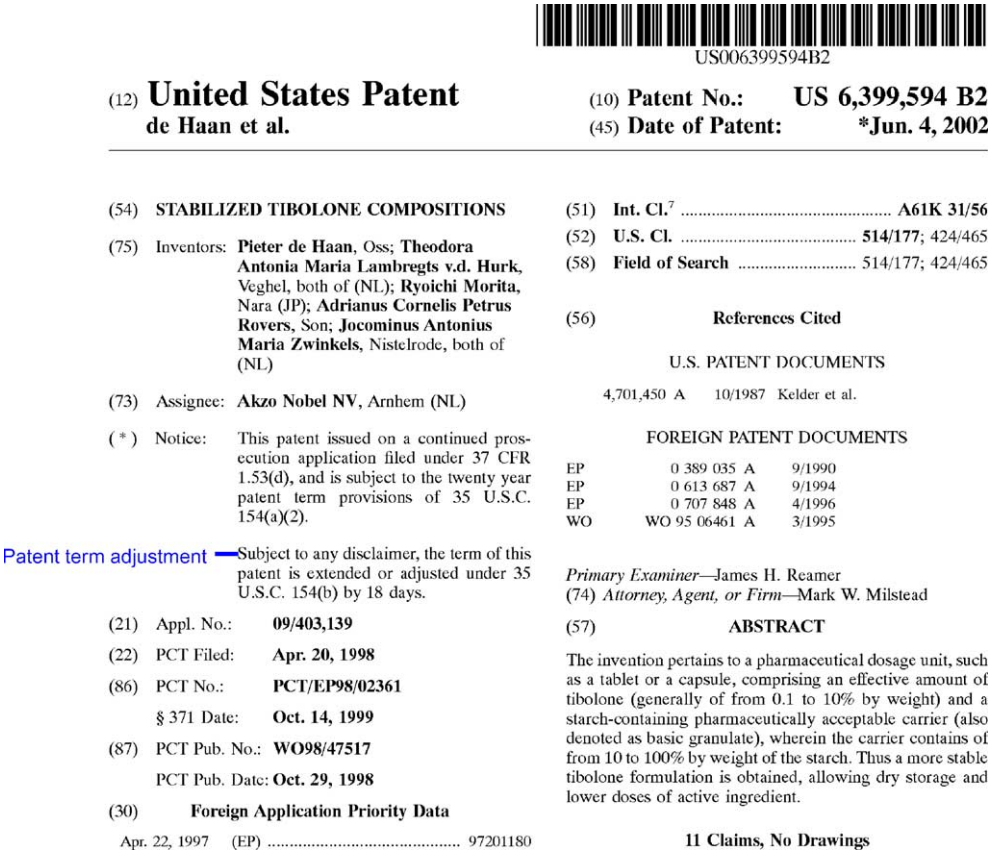
When an interference action occurs between a pending application and an unexpired patent and the patent loses, 35 U.S.C. § 135 provides that the subject claims are cancelled from the patent. The PTO is required to provide notice of the adverse decision, by indicating the result in the file wrappers of the winning application and losing patent.

The BPAI has its own web page [2]. The page provides links to BPAI Official Gazette Notices, as well as many of its recent interference trial opinions. Although the board itself can, and does, decide to publish certain of its opinions and orders, the provisions of 35 U.S.C. § 122 guaranteeing the confidential status of applications generally preclude, without prior permission of a patent applicant, publication of opinions and orders not otherwise available to the public. As a result, the BPAI web page is not a reliable source for information regarding interference opinions and orders.

Thus, in order to determine whether a patent was the subject of an adverse interference judgment, it is generally necessary to review the file wrapper. For example, US Patent No. 5,498,631 lost claims 1-12 due to an adverse interference judgment. This result was reflected in electronic copies of the patent available from the PTO website, and is noted in legal status databases. The electronic copies of patents do not always reflect an interference judgment.

3.6. Infringement

According to US Patent Law, a patent grants patent holders the right to exclude others from infringing—that is, making, using, or selling—the subject matter claimed by a patent. Patent owners have the right to bring civil suit against infringing parties, in order to enjoin their



US006399594B2

(12) **United States Patent**
de Haan et al.

(10) **Patent No.: US 6,399,594 B2**
(45) **Date of Patent: *Jun. 4, 2002**

(54) **STABILIZED TIBOLONE COMPOSITIONS**

(75) Inventors: **Pieter de Haan**, Oss; **Theodora Antonia Maria Lambregts v.d. Hurk**, Veghel, both of (NL); **Ryoichi Morita**, Nara (JP); **Adrianus Cornelis Petrus Rovers**, Son; **Jocominus Antonius Maria Zwinkels**, Nistelrode, both of (NL)

(73) Assignee: **Akzo Nobel NV**, Arnhem (NL)

(*) Notice: This patent issued on a continued prosecution application filed under 37 CFR 1.53(d), and is subject to the twenty year patent term provisions of 35 U.S.C. 154(a)(2).

Patent term adjustment — Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 18 days.

(21) Appl. No.: **09/403,139**
(22) PCT Filed: **Apr. 20, 1998**
(86) PCT No.: **PCT/EP98/02361**
§ 371 Date: **Oct. 14, 1999**
(87) PCT Pub. No.: **WO98/47517**
PCT Pub. Date: **Oct. 29, 1998**

(30) **Foreign Application Priority Data**

Apr. 22, 1997 (EP) 97201180

(51) **Int. Cl.**[7] **A61K 31/56**
(52) **U.S. Cl.** **514/177**; 424/465
(58) **Field of Search** 514/177; 424/465

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WO	WO 95 06461 A	3/1995

Primary Examiner—James H. Reamer
(74) *Attorney, Agent, or Firm*—Mark W. Milstead

(57) **ABSTRACT**

The invention pertains to a pharmaceutical dosage unit, such as a tablet or a capsule, comprising an effective amount of tibolone (generally of from 0.1 to 10% by weight) and a starch-containing pharmaceutically acceptable carrier (also denoted as basic granulate), wherein the carrier contains of from 10 to 100% by weight of the starch. Thus a more stable tibolone formulation is obtained, allowing dry storage and lower doses of active ingredient.

11 Claims, No Drawings

Fig. 5. US Patent No. 6,399,594 was subject to an adjustment of 18 days.

infringing behavior, and to be compensated for market damages associated with the infringement. A patent owner can initiate an infringement action against an allegedly infringing party who may or may not be a patent owner. [5] A patent owner's assertion of infringement is generally met with counter-assertions that there is no infringement, that the claims embracing the subject matter at issue in the infringement proceeding are invalid and thus unenforceable, or both.

Infringement actions are judicial proceedings within the purview of the federal courts. Decisions are available on the web pages of the federal courts, as well as from various commercial vendors such as Westlaw or Lexis, but not from the PTO. Other sources, such as LitAlert, provide patent litigation data that can be used to determine whether a particular patent was the subject of an infringement proceeding.

3.7. Patent term adjustments

Under 35 U.S.C. § 154(b)(1), patent terms may be adjusted when a variety of situations arise. For example, the PTO guarantees prompt response to applicants during prosecution, and if the pendancy of an application is greater than three years due to the failure of the PTO, the patentee may recover the time due to the delay as in increase in patent term. The formula employed to calculate the patent term adjustment due to PTO delay is complex, and takes a number of variables into account, including the promptness with which applicants have responded to PTO actions.

An adjustment is available in other instances as well. For example, if the issuance of an original patent is delayed due to interference proceedings under 35 U.S.C. § 135(a) or because the application is placed under a secrecy order under 35 U.S.C. § 181, the patent term can be extended for the period of delay. Furthermore, if the issuance of a patent is delayed due to appellate review by the Board of Patent Appeals and Interferences or by a Federal court and the patent is issued pursuant to a decision in the review reversing an adverse determination of patentability, the patent term can be extended for a period of time up to five years. However, a patent is not be eligible for extension under 35 U.S.C. § 154(b)(2) if the patent is also subject to a terminal disclaimer.

The total duration of all extensions of a patent under 35 U.S.C. § 154(b) cannot exceed five years. Adjustment information appears on the face of a patent. For example, US Patent No. 6,399,594 was subject to an adjustment of 18 days, as depicted in Fig. 5.

[5] Infringement actions may sometimes occur when the two parties in question each own patents that claim identical or equivalent inventions and they have not resolved the dispute through the interference process.

4. Factors affecting market exclusivity

The FDA grants exclusivity that also provides market protection. "Exclusivity" means exclusive marketing rights granted by the FDA upon approval of a drug. Patents and exclusivity work in a similar fashion but are distinctly different from one another. Patents are granted by the PTO anywhere along the development lifeline of a drug and can encompass a wide range of claims. Exclusivity was designed to promote a balance between new drug innovation and generic drug competition.

Exclusivity may run concurrently with patents and may be granted to an NDA applicant if the statutory requirements are met. See 21 C.F.R. § 314.108. More information on this and other aspects of the FDA's market exclusivity work are contained in an article by Holovac [3]. Information regarding whether a particular pharmaceutical product benefits from market exclusivity can be found in the FDA's Orange Book, referred to in Section 2, above. Market exclusivities are not generally covered by legal status databases such as INPADOC.

4.1. Hatch–Waxman extensions

Pharmaceutical products cannot be marketed without FDA approval. The Hatch–Waxman Act, as codified in 35 U.S.C. § 156, allows innovator pharmaceutical companies to regain part of a patent term that is lost due to the drug approval process. As a note, the provisions for patent term adjustment under 35 U.S.C. § 156 are separate *from* and in addition *to* the patent term extension provisions of 35 U.S.C. § 154(b), discussed above. The patent term extension provisions of 35 U.S.C. § 154(b) are designed to compensate the patent owner for delays in issuing a patent. In contrast, the patent term extension provisions of 35 U.S.C. § 156 are designed to restore term lost to pre-market regulatory review after the grant of a patent. In order to prevent a term extension under 35 U.S.C. 154(b) from precluding a term extension under 35 U.S.C. 156, 35 U.S.C. § 156(a)(2) specifies that the term has never been extended under 35 U.S.C. 156(e)(1).

35 U.S.C. § 156 allows patentees to extend one patent per product. The extension is granted by the PTO in collaboration with the FDA. As a preliminary matter, a patent holder/FDA applicant must demonstrate "due diligence" in dealings with the FDA in order to obtain the full measure of an extension. The amount of time is determined by adding half the time from Investigational New Drug (IND) to NDA to all of the time from NDA to approval. The maximum allowable extension is five years, but the statute provides that the sum of the extension and the remaining patent life cannot exceed 14 years from the date of approval. This provision does not shorten the usual patent term.

There were 587 pharmaceutical products with extensions as of March 3, 2003. Certificates of Extension copies can be obtained at the PTO website or as a Certificate of Correction. The extensions are added to the appropriate patent listed in the Orange Book. The extension will also be noted in legal status databases such as INPADOC and IFI as well as IMS.

Care should be taken in calculating the patent term if the term changed due to GATT. [6] The Hatch–Waxman extension will be added to the GATT-adjusted patent term subject to the 14-year cap. For example, because of the 14-year rule, maxaquin has an expiry date of February 21, 2006 (the approval date February 21, 1992 plus 14 years), not July 14, 2007 (September 17, 2004 patent expiry date plus the 1030 days Hatch–Waxman extension).

4.2. NCE exclusivity

The FDA grants five-year market exclusivity for New Chemical Entities (NCE) independent of patent status under 21 C.F.R. § 314.108. The NCE designation is granted to drugs that contain no active moieties that previously have been approved by the FDA under 21 C.F.R. § 314.108. NCE exclusivity begins at the time of New Drug Application (NDA) approval. It bars the FDA from accepting any Abbreviated New Drug Applications (ANDA) or 505(b)(2) applications for drugs containing the same active moieties for:

- five years if the ANDA or 505(b)(2) does not contain a paragraph IV certification to an Orange Book listed patent; or
- four years if the ANDA or 505(b)(2) contains a paragraph IV certification to an Orange Book listed patent.

NCE market exclusivity runs concurrently with the patent term if a patent is in force. For example, fondaparinux is a selective factor Xa inhibitor sold by Sanofi-Synthelabo. Fondaparinux is claimed in US Patent No. 4,818,816, which is listed in the Orange Book and expires on August 19, 2003. However, fondaparinux has NCE market exclusivity until December 7, 2006. This information is not available in patent legal status databases such as the PAIR system or INPADOC, but is available in the Orange Book and IMS Patent Focus.

4.3. Data or "other" exclusivity

According to 21 U.S.C. § 355(c)(3)(D)(iii) and 21 C.F.R. § 314.108(b)(4), the FDA also grants three-year data exclusivity for previously approved active ingredients, if the application contains reports of new clinical studies conducted or sponsored by the applicant that are essential for approval. Data exclusivity begins at the time of NDA or supplemental approval and bars the FDA from approving any ANDA or 21 U.S.C. § 505(b)(2) application that relies on information for which the exclusivity is granted. Data exclusivity can, but does not necessarily, prevent generic entry.

It is possible that data exclusivity will exist for certain indications for a drug but not for other indications. Thus a generic version of a drug could not be labeled for the listed indication but could be marketed for other indications. Alternatively, it is possible that data exclusivity will exist for certain formulations for a drug but not for other formulations.

For example, the anti-depressant drug, fluoxetine, has new dosage form exclusivity until February 24, 2006 for the weekly dosing formulation. However, generic versions of the drug with other formulations are commercially available. Fluoxetine does not have any patents currently listed in the Orange Book. [7] This information is not available in patent legal status databases such as the PAIR system or INPADOC, but is available in the Orange Book and IMS Patent Focus.

4.4. Orphan drug exclusivity

Under 21 C.F.R. § 316, orphan drug exclusivity (ODE) allows seven years of market exclusivity for pharmaceuticals that treat "rare" diseases, which are defined as diseases that effect less than 200,000 persons in the US. The ODE begins at the time of NDA approval and bars the FDA from approving any other ANDA, 505(b)(2) or NDA applications for the same drug for the same orphan disease for seven years. Whether or not a subsequent application is for the "same drug" depends on the chemical and clinical characteristics of the drug. [8] The FDA may also approve applications for the "same drug" for indications not protected by orphan exclusivity. For example, anagrelide, is an anti-coagulant sold by Roberts Pharmaceuticals. Anagrelide had no patents listed in the Orange Book when this paper was prepared. However, the anagrelide had orphan drug exclusivity that expired on March 12, 2004. This information is not available in patent legal status databases such as the PAIR system or INPADOC, but is available in the Orange Book and IMS Patent Focus.

4.5. Pediatric exclusivity

According to 21 U.S.C. § 505A, if the FDA requests that the applicant conduct clinical trials of a drug in

[6] Merck v. Kessler, 80 F.3d 1543 (Fed. Cir. 1996).

[7] After this paper was drafted, Lilly listed two additional patents in the Orange Book covering Fluoxetine. This demonstrates the need for continual monitoring of patent and exclusivity information.

[8] 21 C.F.R. § 316.

children, then an additional six-month exclusivity could be granted provided the sponsor has reasonably met the terms of the agency's written request. This pediatric exclusivity (PE) will be added to the term of each patent or other exclusivity listed in the Orange Book and will attach to any supplement subsequently approved in response to the terms of the written request if Waxman Hatch exclusivity is granted to that supplement. It should be noted that studies that are submitted and reviewed for pediatric exclusivity determination are reviewed for the pediatric exclusivity determination and may or may not result in a supplemental approval of an NDA.

For example, alendronate sodium has many patents listed in the Orange Book. Each patent has been extended by six months including US 4,621,077 that has a 1371 days Hatch–Waxman extension. The total extension for US 4,621,077 is 1371 days plus six months. The Hatch–Waxman extension will be noted in legal status databases such as INPADOC and IFI but not the pediatric exclusivity because it is not a patent term. The information is available in the Orange Book, Diogenes and IMS Patent Focus.

4.6. OTC switches

There are two market sectors for pharmaceuticals: the prescription (Rx) market and the over-the-counter (OTC) market. The exclusivities discussed previously are generally operative for Rx products; however they may apply to OTC products as well. Prescription drugs may be approved by the FDA for over-the-counter (OTC) sale. The drug may then be available, both as a prescription and an OTC product as long as some indications or dosages remain Rx. If no new clinical investigations are required for the OTC switch by the FDA, then no additional exclusivity will be granted. However, according to 21 U.S.C. § 355(c)(3)(D)(iv) and 21 C.F.R. § 314.08, if new clinical investigations are deemed essential to the approval of the OTC switch and are conducted or sponsored by the applicant, then the applicant will gain three years of market exclusivity. The OTC exclusivity only applies to the OTC market and does not impact the prescription market if Rx products remain.

For example, omeprazole (Prilosec), a heartburn treatment sold by Procter and Gamble, was granted OTC exclusivity because Procter and Gamble conducted additional safety studies [9] in support of the OTC switch. Prilosec OTC will have three years of market exclusivity preventing the launch of generic OTC versions. However, the OTC exclusivity has not prevented generic entry into the prescription market. This information is available in the Orange Book and from FDA press releases and pharmaceutical newsletters such as Scrip.

4.7. ANDA first filer exclusivity (180-days exclusivity)

According to 21 U.S.C. § 505(j)(4)(B)(iv), the first generic company to file a substantially complete ANDA with a paragraph IV certification asserting that the pioneer company's patent is invalid or not infringed may receive a 180-days period of exclusivity upon approval, during which no other generic versions of the drug can come to market. [10] The law has recently been changed, so that all "first applicants" are eligible for the 180-days period of exclusivity. First applicants are all applicants that file ANDAs with paragraph IV certifications on the same first day.

For example, the FDA approved Teva's ANDA for the ACE-inhibitor, moexipril, which is a generic version of Schwarz Pharma's Univasc. As a first filer, Teva became eligible for 180 days of marketing exclusivity. The information is available in the Orange Book and in Diogenes.

5. Conclusion

Ensuring that the life of a particular pharmaceutical patent has been calculated accurately requires careful consideration of data from a variety of public and commercial sources, covering both patent data and market exclusivity data. This article identified a range of complementary data sources that can aid in achieving this result, although in some instances, the only recourse is to order and analyze the file wrapper for a particular patent. As provided herein, a range of legal and regulatory factors may be at play in the patent life determination, and each of these factors should be examined, sometimes iteratively, before the correct answer can be obtained. In short, the strategy presented here is based on the premise that the data available on the face of a patent provides only part of the story as related to the patent life: the patent life calculation must be the result of a multi-source analysis.

Acknowledgements

The views expressed in this article do not constitute legal advice, and do not reflect an endorsement by Pfizer of any products or services described herein.

[9] In general a safety study can only be eligible for exclusivity purposes if the study broadens the original scope of the approval.

[10] This exclusivity is triggered not by the approval date of the generic application but rather by first commercial launch into the market place or a court decision.

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[2] See http://www.uspto.gov/web/offices/dcom/bpai/index.html, last visited September 17, 2003.

[3] Holovac MA. A balancing act in the United States drug industry: pioneer and generic drugs, the Orange Book, marketing protection and the US consumer. World Patent Inf 2004;26(2):123–9.