August 13, 2014

Post-Grant for Practitioners

Challenging and Defending BioPharma Patents at the PTAB – What Practitioners Need to Know

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FISH & RICHARDSON

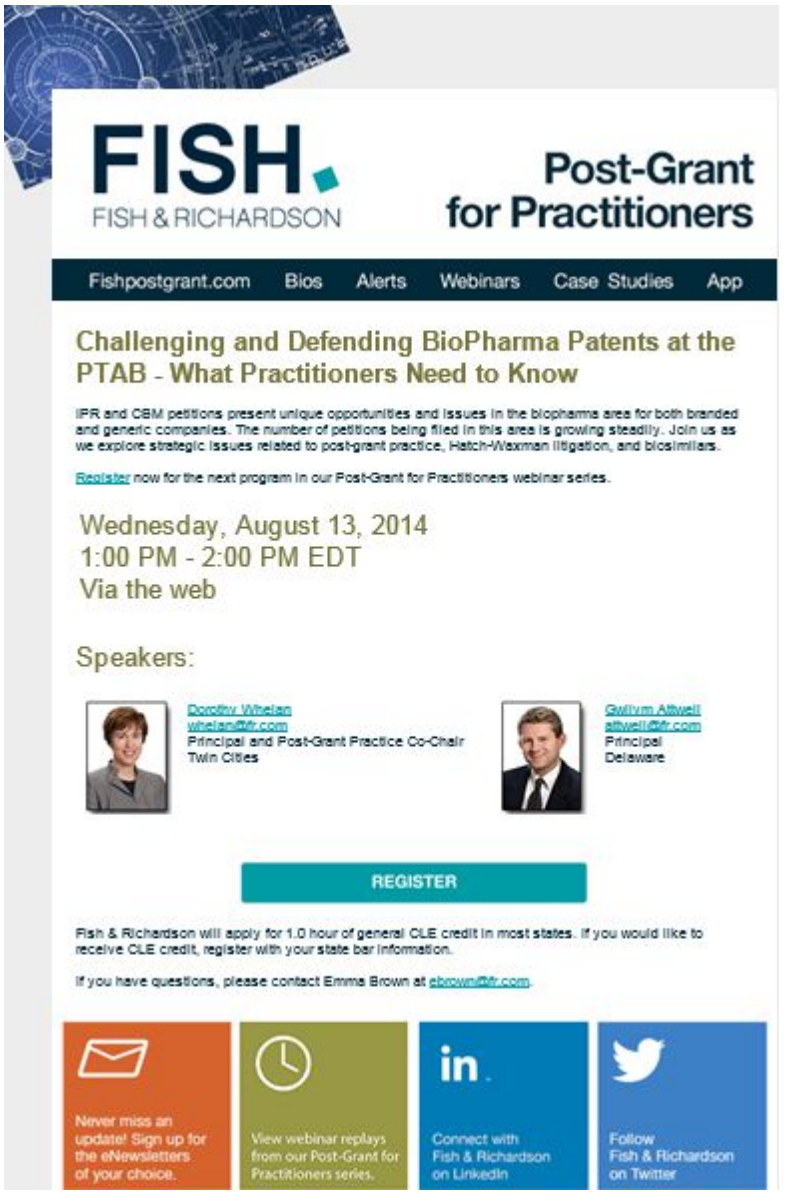
Webinar Series

Agenda

I. Overview of Webinar Series
II. Statistics
III. Bio-Pharma/Hatch-Waxman
IV. Biosimilars

Overview

- Where? … see invitation
- How often? … monthly
- When? … 2nd Wednesday
- Topics? …
  - Important decisions
  - Developments
  - Practice tips
- Housekeeping
  - CLE
  - Questions
  - Materials
    - http://fishpostgrant.com/webinars/



II. Statistics

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II. Statistics (IPR)

- IPR's Filed?
  - **1585** filed through August 7, 2014
  - **116** filed in July 2014
  - **93** bio-pharma petitions

- Application of Threshold: Reasonable Likelihood of Success
  - IPR continues to be instituted in most petitions evaluated (76% in 2014 v. 87% in 2013)
  - In many cases, however, IPR was ordered on only a subset of the grounds requested

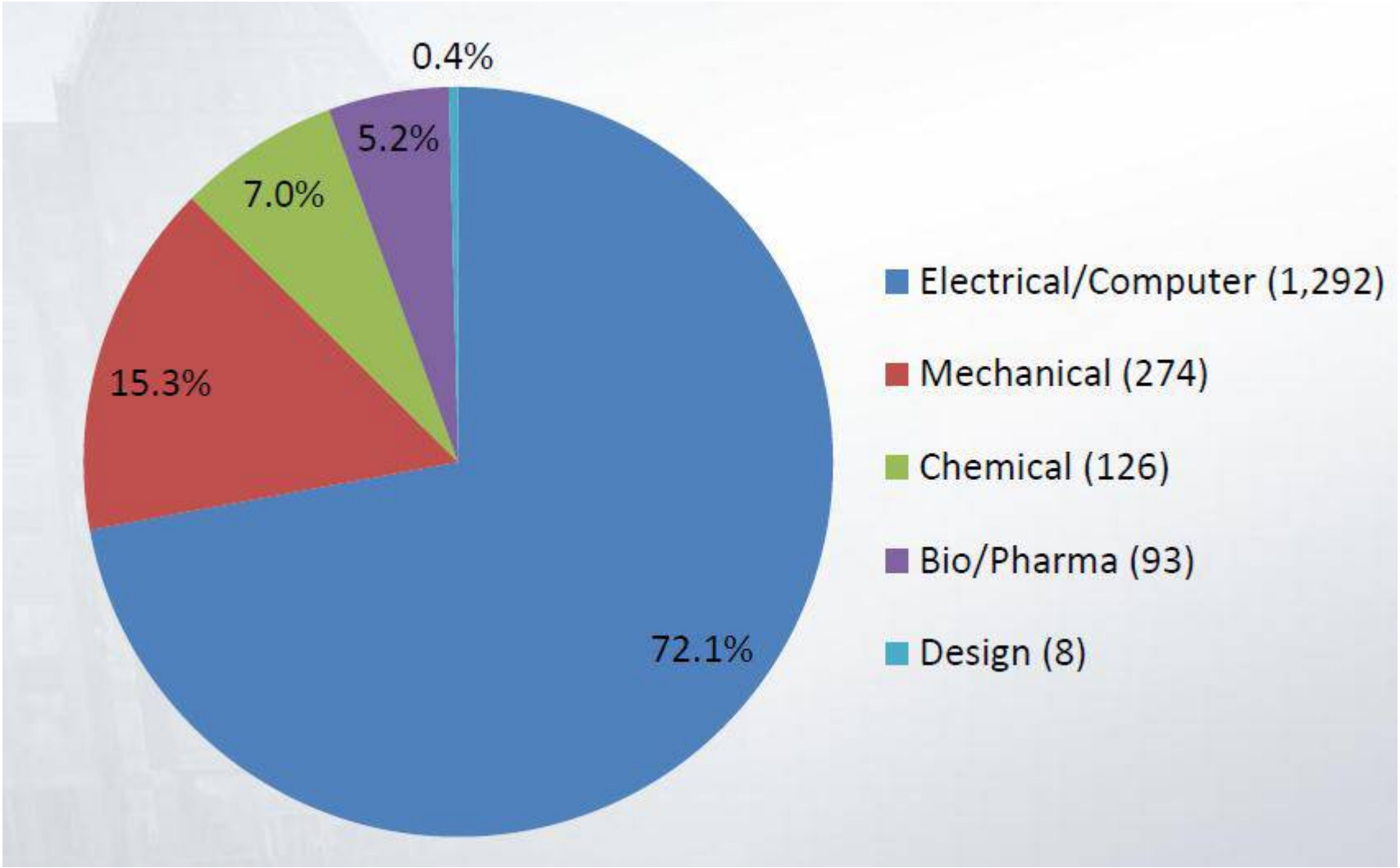
II. Statistics (CBM)

- CBM's Filed?
  - **201** filed through August 7, 2014
  - **10** filed in July 2014
  - **5** bio-pharma petitions
- Application of Threshold: More Likely Than Not
  - CBM also instituted in vast majority of Petitions evaluated (72% for 2014 v. 82% for 2013)
  - Here too, CBM is often ordered on only a subset of petitioned grounds and/or claims

II. Statistics (PGR)

- PGR2014-00008 filed August 5, 2014 by LaRose Industries
- First non-CBM post grant review petition filed
- Challenges raised under 102, 103, and 112
- PGR limited to “first to file” patents
- Must be filed within 9 months of patent issuance
- Implications for bio-pharma:
  - Can challenge patentability under 112 and 101 ***BUT*** estoppel is very broad

II. Statistics (technology breakdown)



US PTO, August 7, 2014

II. Statistics (Final Written Decisions)

- FWD's on the Merits Issued
  - IPR: **100** through July 31, 2014
  - CBM: **10** through July 31, 2014
- Most have found all challenged claims unpatentable
- One motion to amend claims granted to date

II. Stays (Statistics)

- Frequently updated listing of district court orders related to motions to stay is provided on our post-grant website, fishpostgrant.com/stays
- Webpage contains a tally of motions for stay granted and motions for stay denied, and provides the court orders
- Most motions for stay continue to be granted
- *Depomed Inc. v. Purdue Pharma L.P.*, C.A. 13-571 (JAP) (D.N.J.)
  - Non-HW bio-pharma case
  - Court granted stay

II. Stays (Statistics)

Unique Hatch-Waxman Issues

- Under 21 U.S.C. § 355(j), once a branded company sues a generic ANDA filer, the FDA will not grant the generic final approval for 30 months absent a court decision holding the patent not infringed, invalid, and/or not enforceable
- Purpose of stay is to give court time to resolve patent issues
- If generic files an IPR petition before or after being sued by branded company, and then moves to stay litigation, will this affect the 30 month stay?
- 21 U.S.C. § 355(j)(5)(B)(iii): FDA approval "shall be made effective upon expiration of the thirty month [stay] … or such shorter or longer period as the court may order because either party to the action failed to reasonably cooperate in expediting the action."

III. Bio-Pharma and Hatch-Waxman Issues

Benefits of PTAB for Generic Challengers?

- Lower burden of proof than district court (preponderance vs. clear and convincing);
- PTAB has been a hospitable forum for obviousness-based challenges (useful in challenging formulation claims)
- Limits ability of patent owner to tell an invention story (no live testimony)
- Broader claim construction standard than district court (BRI vs. plain meaning)
- Less expensive than district court
- PTAB has shown a willingness to consider prior art already of record and/or considered by Examiner during original prosecution

III. Bio-Pharma and Hatch-Waxman Issues

First ANDA filer vs. subsequent ANDA filers

- What effect will a successful IPR/CBM/PGR challenge have on the 180 day exclusivity to which first filer is entitled?

BACKGROUND – Hatch Waxman

- Manufacturer of generic version of branded drug files an Abbreviated New Drug Application ("ANDA") when it wishes to enter the market.
- ANDA includes a statement ("Paragraph IV certification", "P4") that patent(s) covering the drug and listed in the FDA's Orange Book are invalid, unenforceable, and/or not infringed.
- Exclusivity vests in the first ANDA filer regardless of whether an infringement suit is filed by the patent owner (*see* 21 USC §355(j)(5)(B)(iv)(II)(bb)).
- Subsequent generic filers are not eligible for the exclusivity period.

III. Bio-Pharma and Hatch-Waxman Issues

- Exclusivity rights may be forfeited based on the occurrence of one of six specified events, as set forth in 21 USC §355(j)(5)(D)(i).
- IPR could possibly factor into “failure to market” forfeiture event. BUT statute requires a “court” to enter a final decision from which no appeal can be taken.
- An IPR determination of invalidity, even if subsequently affirmed by the Federal Circuit, would not be sufficient, nor would it trigger a lifting of any 30 month stay.
- Consequences?

III. Bio-Pharma and Hatch-Waxman Issues

Representative cases - U.S. Patent 7,879,828

Apotex v. Wyeth LLC, IPR2014-00115 (November 1, 2013);

Initiative for Responsibility in Drug Pricing LLC v. Wyeth LLC, IPR2014-01259 (August 8, 2014*) ("IRDP")*

- Both petitions challenge claims 1-23 of U.S. Patent 7,879,828 entitled "TIGECYCLINE COMPOSITIONS AND METHODS OF PREPARATION"
- Patent is Orange Book listed; other listed patents expire April 9, 2016 (RE40183; claims to drug substance) and October 8, 2030 (US Patent 8,372,995; claims to particular crystalline forms of tigecyline)
- Patent is subject of a Hatch-Waxman suits by generic challengers other than Apotex (Wyeth Holdings Corp. et al. v. Sandoz, Inc., C.A. No. 09-955-LPS-CJB (D. Del.). ; Pfizer Inc. et al. v. Aurobindo Pharma Ltd. et al., C.A. No. 1:14-cv-00872-SLR (D. Del.); Pfizer Inc. et al. v. CFT Pharmaceuticals LLC, C.A. No. 2:14-cv-00714-LA (E.D. Wis.); Pfizer Inc. et al. v. CFT Pharmaceuticals LLC, C.A. No. 1:14-cv-00781-SLR (D. Del.); Pfizer Inc. v. Fresenius Kabi USA LLC, C.A. No. 1:13-cv-01893-SLR (D. Del.))
- IPR instituted for Apotex petition - oral hearing scheduled for January 23, 2015; no decision as of yet whether or not to institute IRDP proceeding

U.S. Patent 7,879,828

Representative claim language

1. A composition comprising tigecycline, lactose, and an acid selected from hydrochloric acid and gentisic acid, wherein the molar ratio of tigecycline to lactose is between about 1:0.2 and about 1:5 and the pH of the composition in a solution is between about 3.0 and about 7.0.

Reference[s]	Basis	Claims challenged
CN '550	§ 103(a)	1-23
CN '550, Pawelczyk, and Naggar	§ 103(a)	1-23
CN '550, Naggar, and Zhang	§ 103(a)	1-23
CN '550 and Trivedi	§ 103(a)	1-23
CN '550, Trivedi, Pawelczyk, and Naggar	§ 103(a)	1-23
CN '550, Kirsch, and Herman	§ 103(a)	1-23
Lawter, CN '550, and Trivedi	§ 103(a)	1-23

U.S. Patent 7,879,828

New type of player - *Initiative for Responsibility in Drug Pricing LLC*

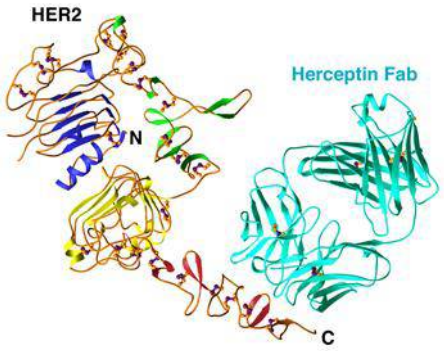
- IRDP = Albert J. Berger, Emeritus Professor of Physiology and Biophysics at the University of Washington School of Medicine
- “IRDP seeks to improve Americans’ access to low-cost generic pharmaceuticals by invalidating patents, such as the ’828 Patent, that are unjustifiably delaying generic competition.”
- “IRDP is not affiliated with any pharmaceutical company, and is therefore not susceptible to the considerations that often result in settlements between brand name and generic pharmaceutical companies that, in IRDP’s view, do not serve the public interest. IRDP agrees with Apotex that the claims of the ’828 Patent should be canceled and the instant petition therefore adopts the grounds of invalidity advanced by Apotex (repeating the language of Apotex’s petition when appropriate) on which the Board instituted review in IPR2014-00115.”

III. Bio-Pharma and Hatch-Waxman Issues

Phigenix, Inc

Phigenix, Inc. v. Genentech, Inc. and Immunogen, Inc., IPR2014-00842 (May 29, 2014)- U.S. Patent 7,575,748; and *Phigenix, Inc. v. Immunogen, Inc.*, IPR2014-00676 (April 22, 2014)- U.S. Patent 8,337,856

- U.S. Patent 7,575,748 – directed to "Methods of treatment using anti-ErbB antibody-maytansinoid conjugates"; U.S. Patent 8,337,856 – directed to "Cancer Treatment"
- Phigenix planning to "leverage licensed patented technology to establish a strong first-mover advantage in Personalized Medicine and forge a lasting leadership position in the rapidly evolving cancer diagnostic and therapeutics industry."
- Presently asserting US Patent 8,080,534 against Genentech over Genentech's anti-cancer drug Kadcyla, a HER2-targeted treatment for metastatic breast cancer.
- No decision on institution as yet in either petition



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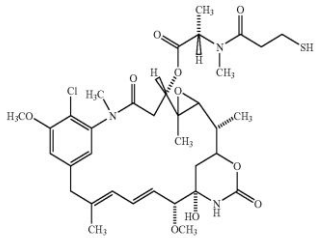
III. Bio-Pharma and Hatch-Waxman Issues

U.S. Patent 7,575,748

1. A method for the treatment of a tumor in a mammal, comprising the steps of (i) identifying said tumor as being characterized by overexpression of an ErbB2 receptor and as being a tumor that does not respond, or responds poorly, to treatment with an anti-ErbB antibody, and (ii) intravenously administering to the mammal a therapeutically effective amount of a conjugate of a humanized antibody huMab 4D5-8 covalently linked via a thioether linking group with a maytansinoid DMI having the structure



at a dose of between about 0.2 mg/kg and about 10 mg/kg (antibody-maytansinoid conjugate weight/body weight) and at a frequency of dosing selected from the group of dosing frequencies consisting of bolus, less than about 1 time per week, one time per week, two times per week, more than two times per week, and continuous infusion, whereby said tumor characterized by overexpression of an ErbB2 receptor and that does not respond, or responds poorly, to treatment with an anti-erbB antibody, is treated.

III. Bio-Pharma and Hatch-Waxman Issues

U.S. Patent 7,575,748 – asserted grounds

Ground	Claim(s)	Basis for Unpatentability
1	1-20 and 25-27	Obvious (§103) over Chari 1992 and HERCEPTIN® Label 1998
2	1-20 and 25-27	Obvious (§103) over Chari 1992, HERCEPTIN® Label 1998 and Baselga 1999
3	1-20 and 25-27	Obvious (§103) over Chari 1992 and HERCEPTIN® Label 1998 in view of Morgan 1990
4	1-20 and 25-27	Obvious (§103) over Chari 1992 and HERCEPTIN® Label 1998, and further in view of Morgan 1990, Hudziak 1998 and/or Rosenblum 1999
5	1-20 and 25-27	Obvious (§103) over Chari 1992 and HERCEPTIN® Label 1998, further in view of Morgan 1990, Hudziak 1998 and/or Rosenblum 1999, and further in view of Baselga 1998 and/or Pegram 1999
6	1-20 and 25-27	Obvious (§103) over Cohen 1999 in view of HERCEPTIN® Label 1998 and Morgan 1990

III. Bio-Pharma and Hatch-Waxman Issues

U.S. Patent 8,337,856

1. An immunoconjugate comprising an anti-ErbB2 antibody conjugated to a maytansinoid, wherein the antibody is huMAb4D5-8.

Ground	Claim(s)	Basis for Unpatentability
1	1-8	Obvious (§103) over Chari 1992 in view of HERCEPTIN® Label
2	1-8	Obvious (§103) over Chari 1992 and HERCEPTIN® Label, further in view of Hudziak 1998 and/or Rosenblum 1999
3	1-8	Obvious (§103) over Chari 1992 and HERCEPTIN® Label, further in view of Hudziak 1998 and/or Rosenblum 1999, and further in view of Baselga 1998 and/or Pegram 1999
4	6, 8	Obvious (§103) over Chari 1992 and HERCEPTIN® Label and further in view of Morgan 1990
5	1-8	Obvious (§103) over Chari 1992 and Carter 1992 and common knowledge in the art
6	1-5, 7	Obvious (§103) over Liu 1996 in view of HERCEPTIN® Label
7	6, 8	Obvious (§103) over Liu 1996 in view of HERCEPTIN® Label and further in view of Morgan 1990
8	1-8	Obvious (§103) over Cohen 1999 in view of Chari 1992

III. Bio-Pharma and Hatch-Waxman Issues

Stem cells

BioGatekeeper, Inc. v. Kyoto University., IPR2014-01286 (August 12, 2014) - U.S. Patent 8,058,065

- U.S. Patent 8,058,065 – directed to "Oct3/4, Klf4, c-Myc and Sox2 produce induced pluripotent stem cells"
- Single claim challenged and on only one ground
- Who is BioGatekeeper, Inc.?

III. Bio-Pharma and Hatch-Waxman Issues

U.S. Patent 8,337,856

- 1. A method for preparing an induced pluripotent stem cell by nuclear reprogramming of a somatic cell from a mammalian species, comprising:

a) introducing into the somatic cell one or more retroviral vectors comprising a gene encoding Oct3/4, a gene encoding Klf4, a gene encoding c-Myc and a gene encoding Sox2 operably linked to a promoter; and

b) culturing the transduced somatic cell on a fibroblast feeder layer or extracellular matrix in a cell media that supports growth of ES cells of the mammalian species, wherein one or more pluripotent cells are obtained.

III. Bio-Pharma and Hatch-Waxman Issues

CBM Developments

Amneal Pharmaceuticals et al. v. Jazz Pharmaceuticals, CBM2014-00149 (June 24, 2014)

- A covered business method patent is a "patent that claims a method or corresponding apparatus for performing data processing or other operations used in the practice, administration, or management of a financial product or service, except that the term does not include patents for technological inventions." AIA § 18(d)(1).
- Patent at issue entitled "Sensitive Drug Distribution System and Method"
- Listed in Orange Book as a patent covering Risk Evaluation and Mitigation Strategies
- Patent was subject of a Hatch-Waxman suit by generic challenger

III. Bio-Pharma and Hatch-Waxman Issues

CBM Developments

- Claim 1 reads as follows (emphasis added):

1. **A computerized method of distributing a prescription drug** under exclusive control of an exclusive central pharmacy, the method comprising:

receiving in a computer processor all prescription requests, for any and all patients being prescribed the prescription drug, only at the exclusive central pharmacy from any and all medical doctors allowed to prescribe the prescription drug, the prescription requests containing information identifying patients, the prescription drug, and various credentials of the any and all medical doctors;

III. Bio-Pharma and Hatch-Waxman Issues

CBM Developments

Claim 1 (cont'd)

requiring entering of the information into an exclusive computer database associated with the exclusive central pharmacy for analysis of potential abuse situations, such that all prescriptions for the prescription drug are processed only by the exclusive central pharmacy using only the exclusive computer database;

checking with the computer processor the credentials of the any and all doctors to determine the eligibility of the doctors to prescribe the prescription drug;

confirming with a patient that educational material has been received and/or read prior to shipping the prescription drug;

checking the exclusive computer database for potential abuse of the prescription drug;

III. Bio-Pharma and Hatch-Waxman Issues

CBM Developments

- Petitioner argued that the patent qualified for CBM:

"The challenged claims simply recite methods for centralized distribution of retail goods, specifically drugs, through a central pharmacy that encompasses steps such as interfacing with financial businesses, such as insurance companies, in order to secure payment for the prescription, rendering them incidental to a financial product or service. And these claims are directed towards methods and not any technological invention. The claims' recitation of a generic computer processor does not change this conclusion. Moreover, the claimed distribution methods are not novel or nonobvious and do not solve a technological problem with any technological solution. CBM review is, therefore, appropriate."

III. Bio-Pharma and Hatch-Waxman Issues

CBM Developments

- "Financial product or service" has been interpreted broadly—but will the PTAB interpret it so broadly as to include this patent?

- Implications for Hatch-Waxman litigation/generic challengers?
- There are 4 additional CBM petitions that have been filed against Jazz Pharmaceuticals, each of which relates to a patent for a drug distribution system and method:

  CBM2014-00150

  CBM2014-00151

  CBM2014-00153

  CBM2014-00161

Decisions on petitions expected in December, 2014

IV. Biosimilars

- Not governed by Hatch-Waxman regulatory scheme
- Attractive option for FTO purposes because faster than district court litigation
- IPR is particularly advantageous if 112/101 defenses also exist
- PGR less applicable to biosimilars because limited to “first to file” patents and must be filed within 9 months of grant

Post-Grant for Practitioners

- In Fish & Richardson's initial 7-part webinar series titled "Challenging Patent Validity in the USPTO," we explored details regarding several of the post grant tools, with 3 sessions dedicated to Inter Partes Review (IPR), and a final session walking through several hypotheticals, to help listeners understand how these apply to common situations.

- Audio and slides for these webinars are posted online at:

  http://fishpostgrant.com/webinars/

- If you listen to these webinars, you will be well positioned to engage in a conversation over whether and when to use those tools and how to defend against them.

Resources

- F&R web sites:
  - Post-Grant for Practitioners: http://fishpostgrant.com/webinars/
  - General: http://fishpostgrant.com/
  - IPR: http://fishpostgrant.com/inter-partes-review/
  - PGR: http://fishpostgrant.com/post-grant-review/
  - Rules governing post-grant: http://fishpostgrant.com/
  - Post-Grant App: http://fishpostgrant.com/app/ New!
- USPTO sites:
  - AIA Main: http://www.uspto.gov/aia_implementation/index.jsp
  - Inter Partes: http://www.uspto.gov/aia_implementation/bpai.jsp

Thank You!

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