Hatch-Waxman 2023 Year in Review

Thursday, December 7

FISH.

Meet the Speakers

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Overview

Topics

- Important Decisions
- Developments
- Practice Tips

Housekeeping

- CLE
- Questions
- Materials
- http://www.fr.com/webinars

Agenda

- 2023 Trends for Hatch-Waxman Cases
- Patent Term Adjustment (PTA)/Patent Term Extension (PTE)
- Overlapping Ranges – Anticipation / Obviousness
- Update on the State of Section 112 (Enablement)
- U.S. Gov’t Agency Developments and their Impact on Hatch-Waxman Litigants
- Looking Forward to 2024

2023 Trends for Hatch-Waxman Cases

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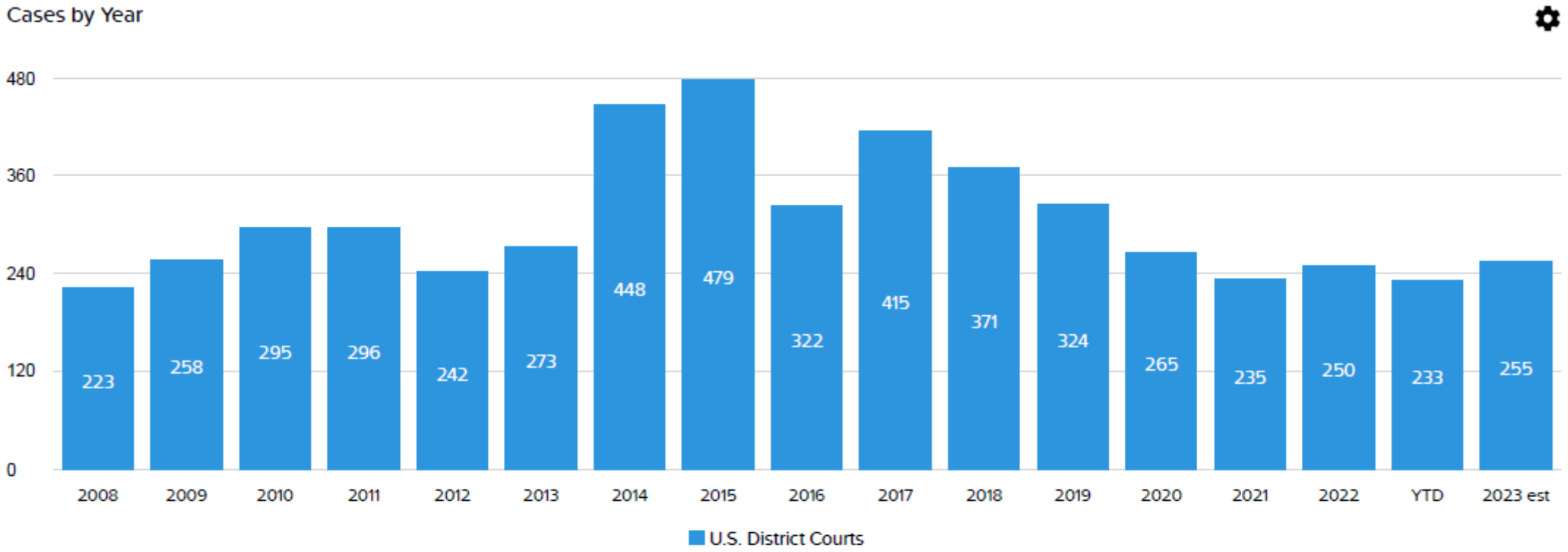
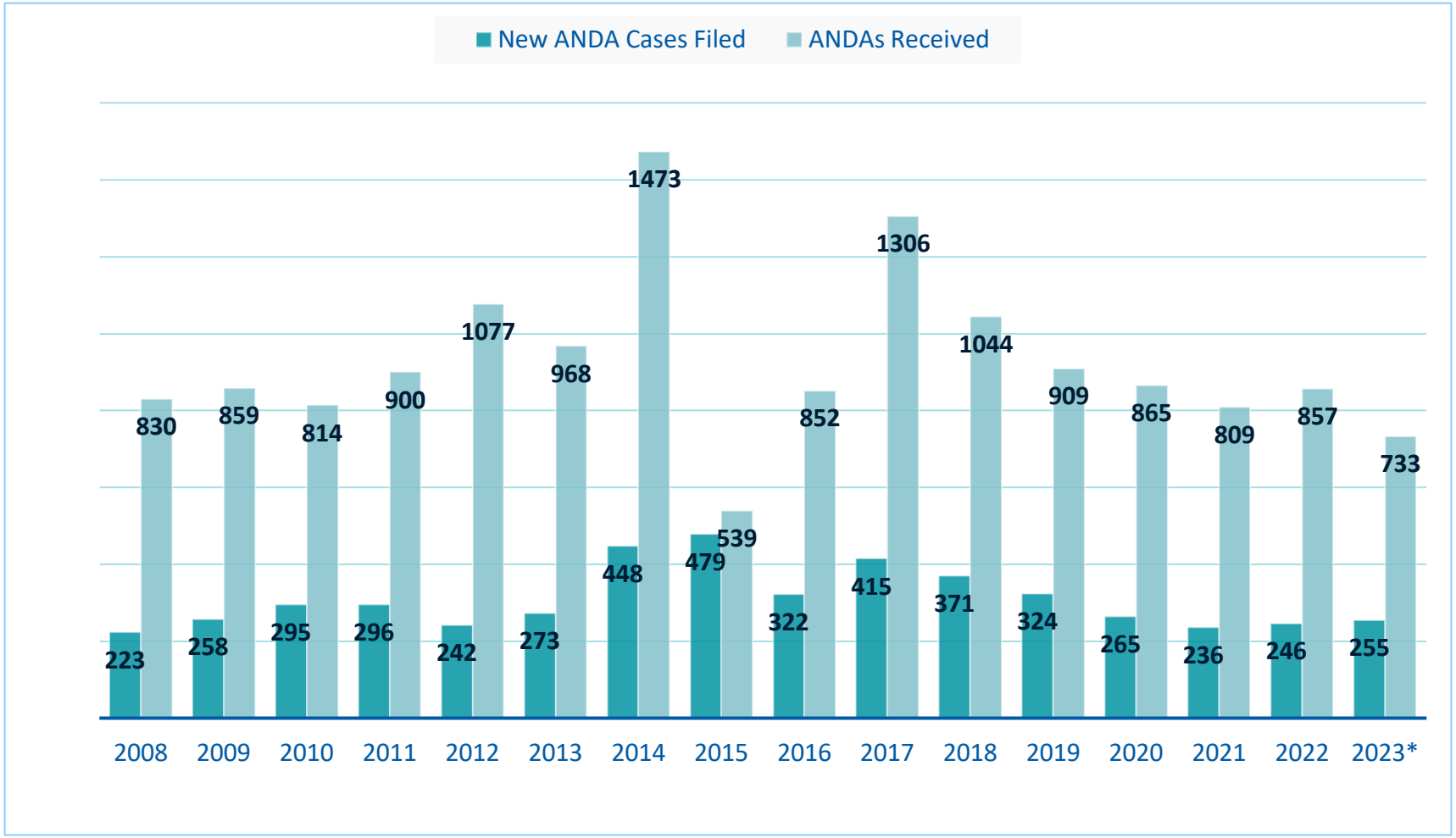
Number of ANDA Cases Filed



	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	YTD	2023 est
U.S. District Courts	223	258	295	296	242	273	448	479	322	415	371	324	265	235	250	233	255
Total	223	258	295	296	242	273	448	479	322	415	371	324	265	235	250	233	255

Source: docketnavigator.com (Case Type: Cases with ANDA Pleadings, through December 1, 2023)

ANDA Cases Filed v. ANDAs Submitted



**: estimated number of new cases filed for full year 2023*
Source: docketnavigator.com (Case Type: Cases with ANDA Pleadings); https://www.fda.gov/industry/generic-drug-user-fee-amendments/generic-drugs-program-monthly-and-quarterly-activities-report

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Busiest Venues for ANDA Cases in 2023

Courts		
D.Del.	257	65%
D.N.J.	90	23%
N.D.Cal.	16	4%
N.D.W.Va.	7	2%
E.D.Va.	5	1%
Other Courts	19	5%

Open ANDA Cases
(Between January 1 and December 1, 2023)

Courts		
D.Del.	142	57%
D.N.J.	87	35%
E.D.N.Y.	4	2%
N.D.W.Va.	3	1%
M.D.N.C.	2	1%
Other Courts	9	4%

New 2023 ANDA Cases
(through December 1, 2023)

Source: lexmachina.com (tag Patent: ANDA; data through December 1, 2023)

Busiest Judges for ANDA Cases

District Judges		
Colm Felix Connolly	79	20%
Richard Gibson Andrews	76	19%
Gregory Brian Williams	68	17%
Maryellen Noreika	41	10%
Leonard Philip Stark	28	7%
58 Other Judges		

Open ANDA Cases
(Between January 1 and December 1, 2023)

District Judges		
Richard Gibson Andrews	44	18%
Gregory Brian Williams	38	15%
Colm Felix Connolly	32	13%
Maryellen Noreika	20	8%
Karen McGlashan Williams	13	5%
34 Other Judges		

New 2023 ANDA Cases
(through December 1, 2023)

Source: lexmachina.com (tag Patent: ANDA; data through December 1, 2023)

Courts Requiring Case Narrowing Sooner

Revised April 26, 2022

IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF DELAWARE

PLAINTIFF,	:	
	:	
Plaintiff,	:	
	:	
v.	:	Civil Action No. [ ]
	:	**ANDA CASE**
DEFENDANT,	:	
	:	
Defendant.	:	

SCHEDULING ORDER FOR
HATCH-WAXMAN PATENT INFRINGEMENT CASES[1]

This __ day of _____, 20__, the Court having conducted an initial Rule 16(b) scheduling conference pursuant to Local Rule 16.1(b), and the parties having determined after discussion that the matter cannot be resolved at this juncture by settlement, voluntary mediation, or binding arbitration:

IT IS ORDERED that:

1. Caption Modification. The Caption shall be modified to include the words "ANDA CASE" immediately below the Civil Action Number.

[1] This form order is to be used in cases arising under 21 U.S.C. § 355 where all patents alleged to be infringed were the subject of a Paragraph IV certification of noninfringement and/or invalidity by Defendant(s).

5. Preliminary Disclosure of Asserted Claims. No later than seven days after the date of this Order, Plaintiff(s) shall serve Defendant(s) with a "Preliminary Disclosure of Asserted Claims" that lists each claim of each patent alleged to be infringed by Defendant(s), including for each claim the applicable statutory subsections of 35 U.S.C. § 271 asserted. Unless otherwise agreed to by the parties, Plaintiff(s) may assert no more than ten claims of any one patent and no more than 32 claims in total against any one Defendant. Plaintiff(s) shall produce with the Preliminary Disclosure of Asserted Claims a copy of the file

7. Invalidity Contentions and Preliminary Disclosure of Asserted Prior Art. Unless otherwise agreed to by the parties, no later than 30 days after service of the Preliminary Disclosure of Asserted Claims, Defendant(s) shall serve on Plaintiff(s) "Invalidity Contentions" that shall contain the following information:

(a) The identity of no more than 12 prior art references for any one patent and no more than 30 prior art references in total that Defendant(s) allege(s) anticipates each asserted claim or renders the claim obvious (the

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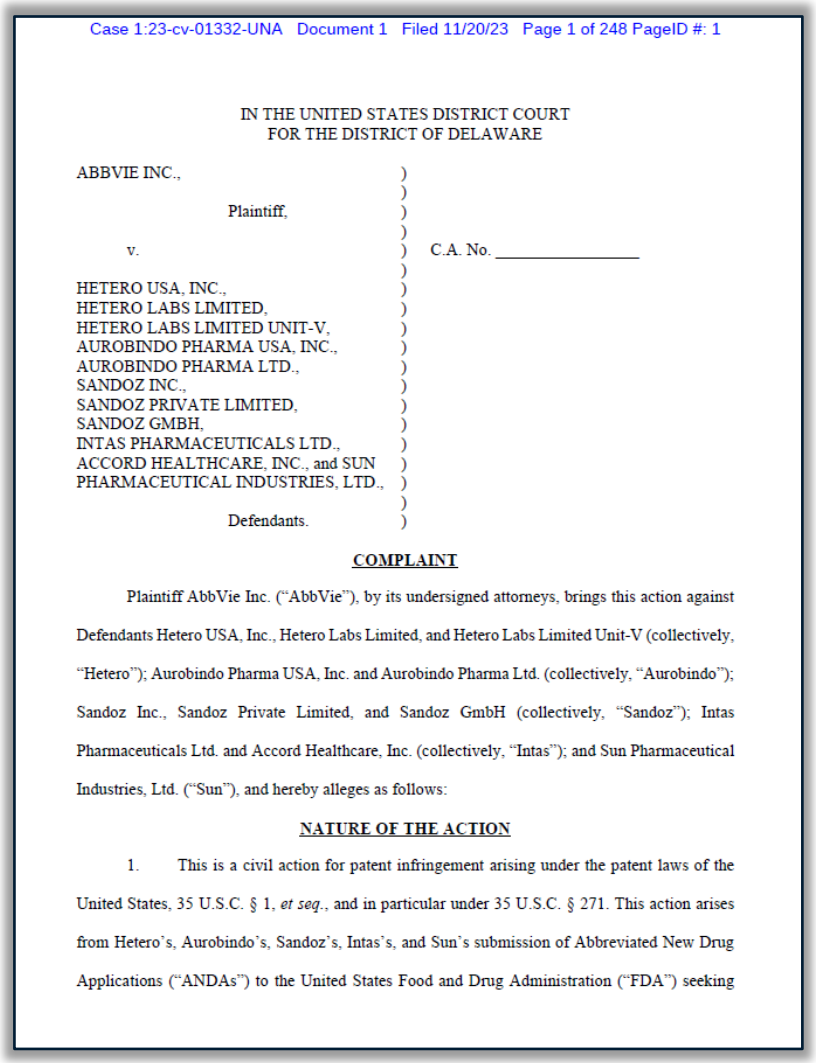
Early and Significant Case Narrowing Taking Hold

- ***Veloxis Pharmaceuticals, Inc. v. Accord Healthcare, Inc. et al.*, No. 22-00909-JDW, D.I. 40 (D. Del. Jan. 31, 2023) (Wolson, J. from E.D. Pa.)** (ordering early claim narrowing to 10 claims per patent and 50 total claims and invalidity contentions narrowed to 12 references or combinations per patent and 50 total references or combinations prior to *Markman* hearing; further ordering that 28 days after claim construction order, Plaintiff narrow to five claims per patent and 25 total claims and Defendant narrow to six references or combinations per patent and 25 total references or combinations)

- ***Hope Medical Enterprises, Inc. v. Accord Healthcare, Inc.*, No. 22-00978-RGA, D.I. 36 (D. Del. Mar. 31, 2023) (Andrews, J.)** (noting a narrowing to 32 total claims was "reasonable" and directing further reduction in advance of pretrial order)

- ***Exeltis USA, Inc. et al. v. Lupin Ltd. et al.*, No. 22-00434-RGA, D.I. 199 (D. Del. July 31, 2023) (Andrews, J.)** (after fact discovery closed, ordering narrowing to 40 claims and 7 invalidity arguments per claim before opening expert reports, and narrowing to 7 claims and 3 invalidity arguments per claim before pre-trial order)

RINVOQ® Hatch-Waxman Litigation



Case 1:23-cv-01332-UNA Document 1 Filed 11/20/23 Page 1 of 248 PageID #: 1

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ABBVIE INC.,

Plaintiff,

v. C.A. No. _____

HETERO USA, INC.,
HETERO LABS LIMITED,
HETERO LABS LIMITED UNIT-V,
AUROBINDO PHARMA USA, INC.,
AUROBINDO PHARMA LTD.,
SANDOZ INC.,
SANDOZ PRIVATE LIMITED,
SANDOZ GMBH,
INTAS PHARMACEUTICALS LTD.,
ACCORD HEALTHCARE, INC., and SUN PHARMACEUTICAL INDUSTRIES, LTD.,

Defendants.

COMPLAINT

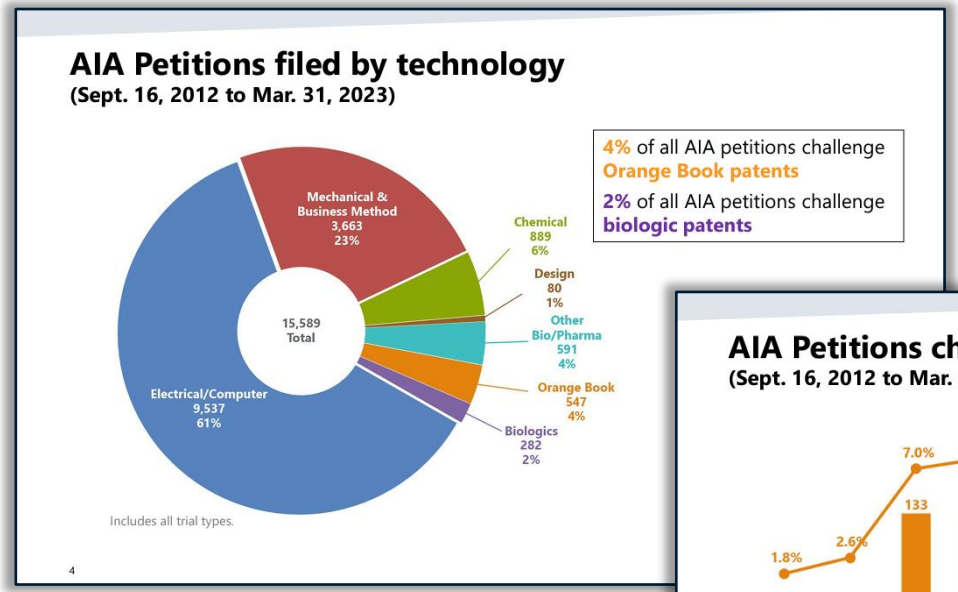
Plaintiff AbbVie Inc. ("AbbVie"), by its undersigned attorneys, brings this action against Defendants Hetero USA, Inc., Hetero Labs Limited, and Hetero Labs Limited Unit-V (collectively, "Hetero"); Aurobindo Pharma USA, Inc. and Aurobindo Pharma Ltd. (collectively, "Aurobindo"); Sandoz Inc., Sandoz Private Limited, and Sandoz GmbH (collectively, "Sandoz"); Intas Pharmaceuticals Ltd. and Accord Healthcare, Inc. (collectively, "Intas"); and Sun Pharmaceutical Industries, Ltd. ("Sun"), and hereby alleges as follows:

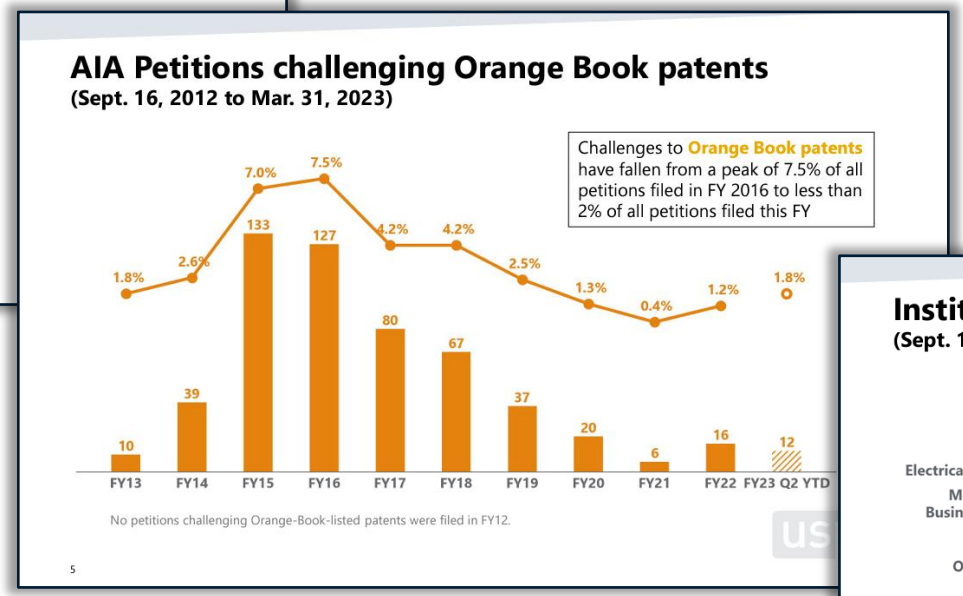
NATURE OF THE ACTION

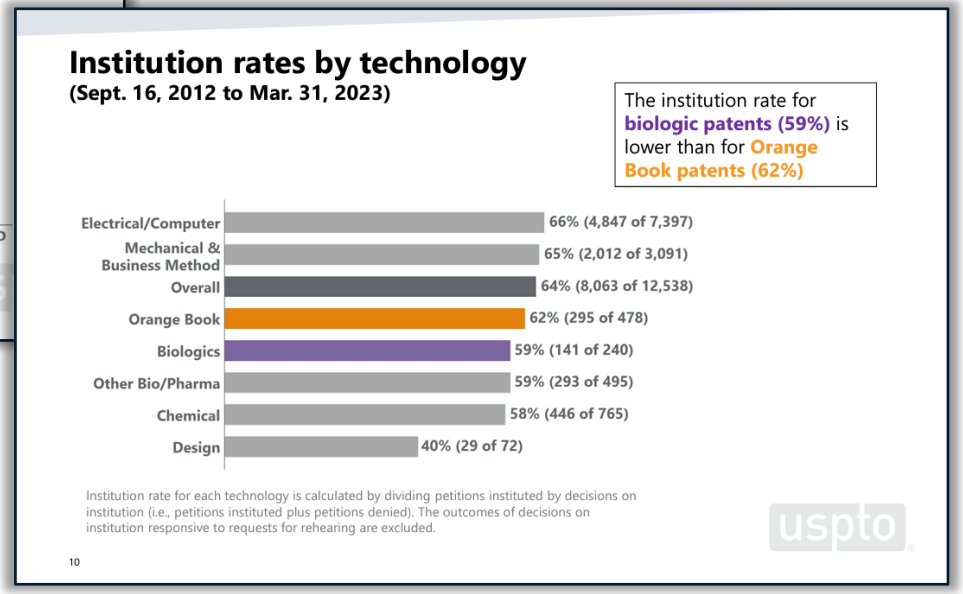
1. This is a civil action for patent infringement arising under the patent laws of the United States, 35 U.S.C. § 1, *et seq.*, and in particular under 35 U.S.C. § 271. This action arises from Hetero's, Aurobindo's, Sandoz's, Intas's, and Sun's submission of Abbreviated New Drug Applications ("ANDAs") to the United States Food and Drug Administration ("FDA") seeking

- 34 asserted patents
- 136 counts of infringement
- RINVOQ® has been approved to treat patients with seven different immune-mediated diseases

Orange Book Patents at the PTAB







Source: USPTO PTAB Orange Book patent/biologic patent study FY23 Q2 Update (through Mar. 31, 2023)

Patent Term Adjustment (PTA)/ Patent Term Extension (PTE)

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Statutory Additions to Patent Term

Patent Term Adjustment (PTA)

- Extension of patent term for delays at the PTO
- Based on delay in examination of the specific patent
- Governed by 35 U.S.C § 154

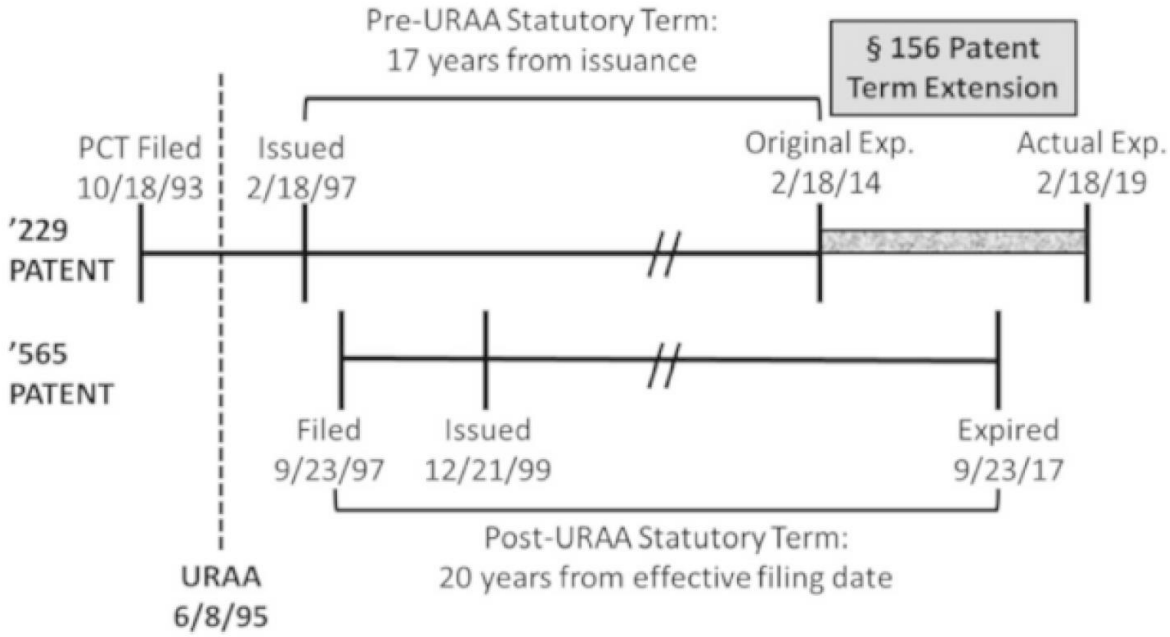
Patent Term Extension (PTE)

- Extension of patent term for delays in regulatory review by FDA or USDA
- Added to one patent of patentee's choice covering a specific product whose marketing approval was delay
- Governed by 35 U.S.C. § 156

Obviousness-type Double Patenting (ODP) v. PTE

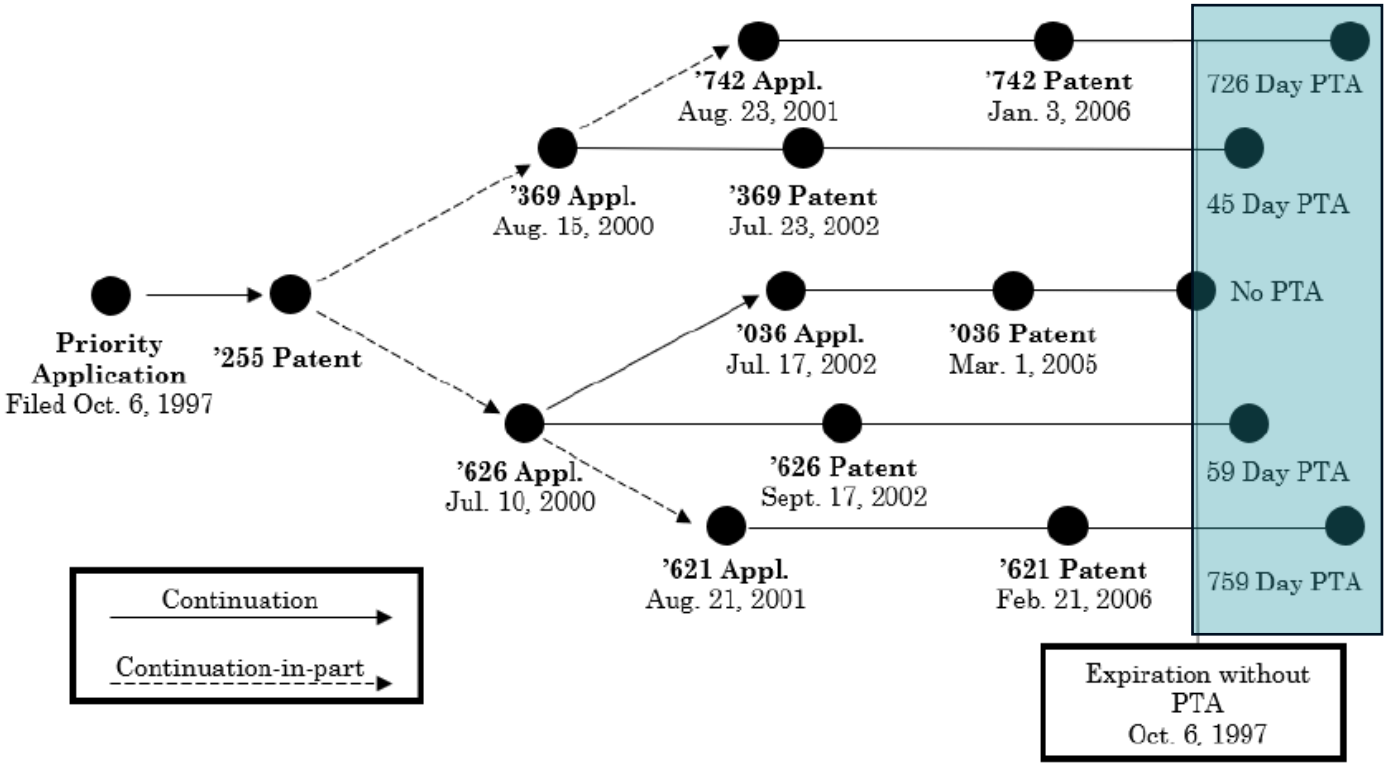
Novartis AG v. Ezra Ventures LLC, 909 F.3d 1367 (Fed. Cir. 2018)

- ODP does not invalidate a validly obtained PTE under § 156
- Fed Circuit declined to agree with arguments that would "mean that a judge-made doctrine would cut off a statutorily-authorized time extension." *Id.* at 1375 (internal citations omitted)



Obviousness-type Double Patenting (ODP) v. PTA

In re Cellect LLC, 81 F.4th 1216 (Fed. Cir. 2023)



Statutory Analysis of PTA v. PTE

PTA (§§ 154(b)(1)(B), 154(b)(2)(B))

(B) Guarantee of no more than 3-year application pendency.—Subject to the limitations under paragraph (2), if the issue of an original patent is delayed due to the failure of the United States Patent and Trademark Office to issue a patent within 3 years after the actual filing date of the application under section 111(a) in the United States or, in the case of an international application, the date of commencement of the national stage under section 371 in the international application, not including—

(i)–(iii) [providing for timing exceptions],

the term of the patent *shall* be extended 1 day for each day after the end of that 3-year period until the patent is i

(2) Limitations.—

***

(B) Disclaimed term.—

No patent the term of which has been disclaimed beyond a specified date may be adjusted under this section beyond the expiration date specified in the disclaimer.

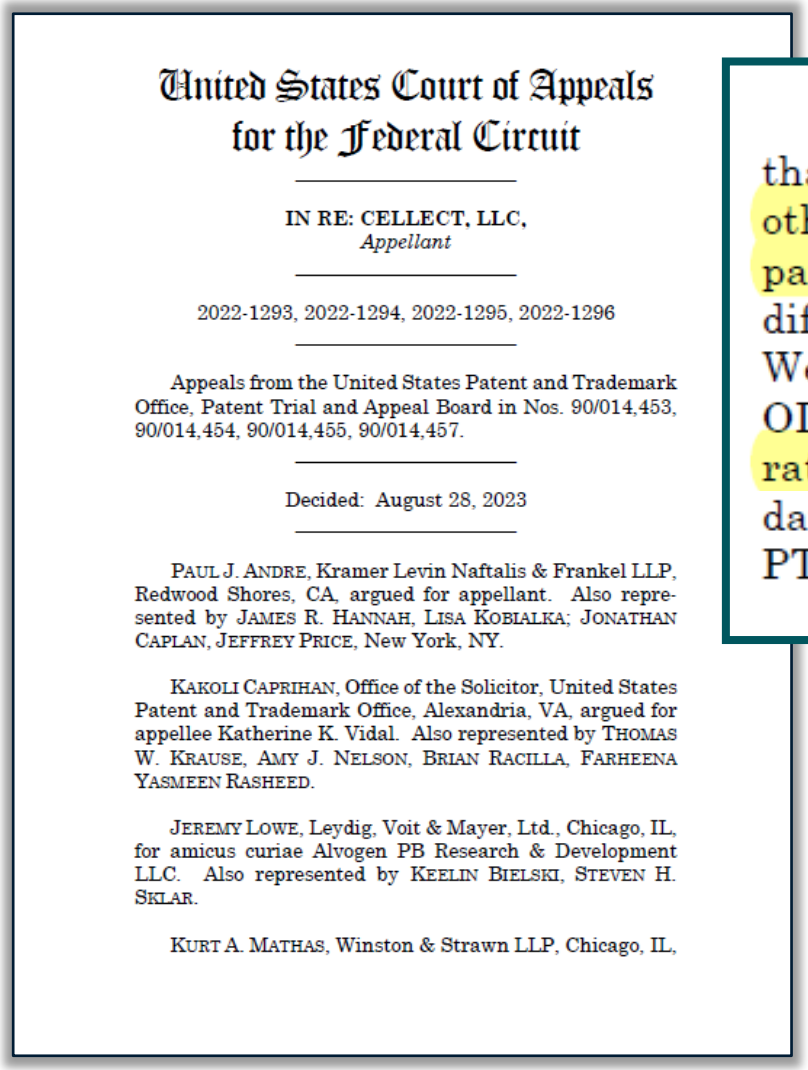
PTE (§ 156(a)(c)(3))

(c)(3) The term of a patent eligible for extension under subsection (a) *shall* be extended by the time equal to the regulatory review period for the approved product which period occurs after the date the patent is issued, except that . . . if the period remaining in the term of a patent after the date of the approval of the approved product under the provision of law under which such regulatory review occurred when added to the regulatory review period as revised under paragraphs (1) and (2) exceeds fourteen years, the period of extension shall be reduced so that the total of both such periods does not exceed fourteen years;

***

§ 156 does not include language expressly excluding patents in which a terminal disclaimer was filed from benefiting from a PTE.

Federal Circuit: PTA and PTE Treated Differently



United States Court of Appeals
for the Federal Circuit

IN RE: CELLECT, LLC,
Appellant

2022-1293, 2022-1294, 2022-1295, 2022-1296

Appeals from the United States Patent and Trademark Office, Patent Trial and Appeal Board in Nos. 90/014,453, 90/014,454, 90/014,455, 90/014,457.

Decided: August 28, 2023

PAUL J. ANDRE, Kramer Levin Naftalis & Frankel LLP, Redwood Shores, CA, argued for appellant. Also represented by JAMES R. HANNAH, LISA KOBIALKA; JONATHAN CAPLAN, JEFFREY PRICE, New York, NY.

KAKOLI CAPRIHAN, Office of the Solicitor, United States Patent and Trademark Office, Alexandria, VA, argued for appellee Katherine K. Vidal. Also represented by THOMAS W. KRAUSE, AMY J. NELSON, BRIAN RACILLA, FARHEENA YASMEEN RASHEED.

JEREMY LOWE, Leydig, Voit & Mayer, Ltd., Chicago, IL, for amicus curiae Alvogen PB Research & Development LLC. Also represented by KEELIN BIELSKI, STEVEN H. SKLAR.

KURT A. MATHAS, Winston & Strawn LLP, Chicago, IL,

Proceeding to the merits, we agree with the USPTO that PTA and PTE should be treated differently from each other when determining whether or not claims are unpatentable under ODP. PTA and PTE are dealt with in different statutes and deal with differing circumstances. We conclude that, while the expiration date used for an ODP analysis where a patent has received PTE is the expiration date before the PTE has been added, the expiration date used for an ODP analysis where a patent has received PTA is the expiration date after the PTA has been added.

We thus conclude that ODP for a patent that has received PTA, regardless whether or not a terminal disclaimer is required or has been filed, must be based on the expiration date of the patent after PTA has been added. We therefore further conclude that the Board did not err in finding the asserted claims unpatentable under ODP.

81 F.4th at 1226, 1229

Reaction to *In re Cellect*

Numerous pharma companies and organizations filed amicus briefs for rehearing petition

Post-In re Cellect Takeaways

- **Assume that courts will apply a bright line to the ODP analysis as it related to PTA and will not consider equitable concerns**
  - *Allergan v. MSN Labs*, 2023 WL 6295496 (D. Del. Sept. 27, 2023)
- **Monitor further developments**
  - USPTO's response to petition for rehearing due December 14

Overlapping Ranges – Anticipation / Obviousness

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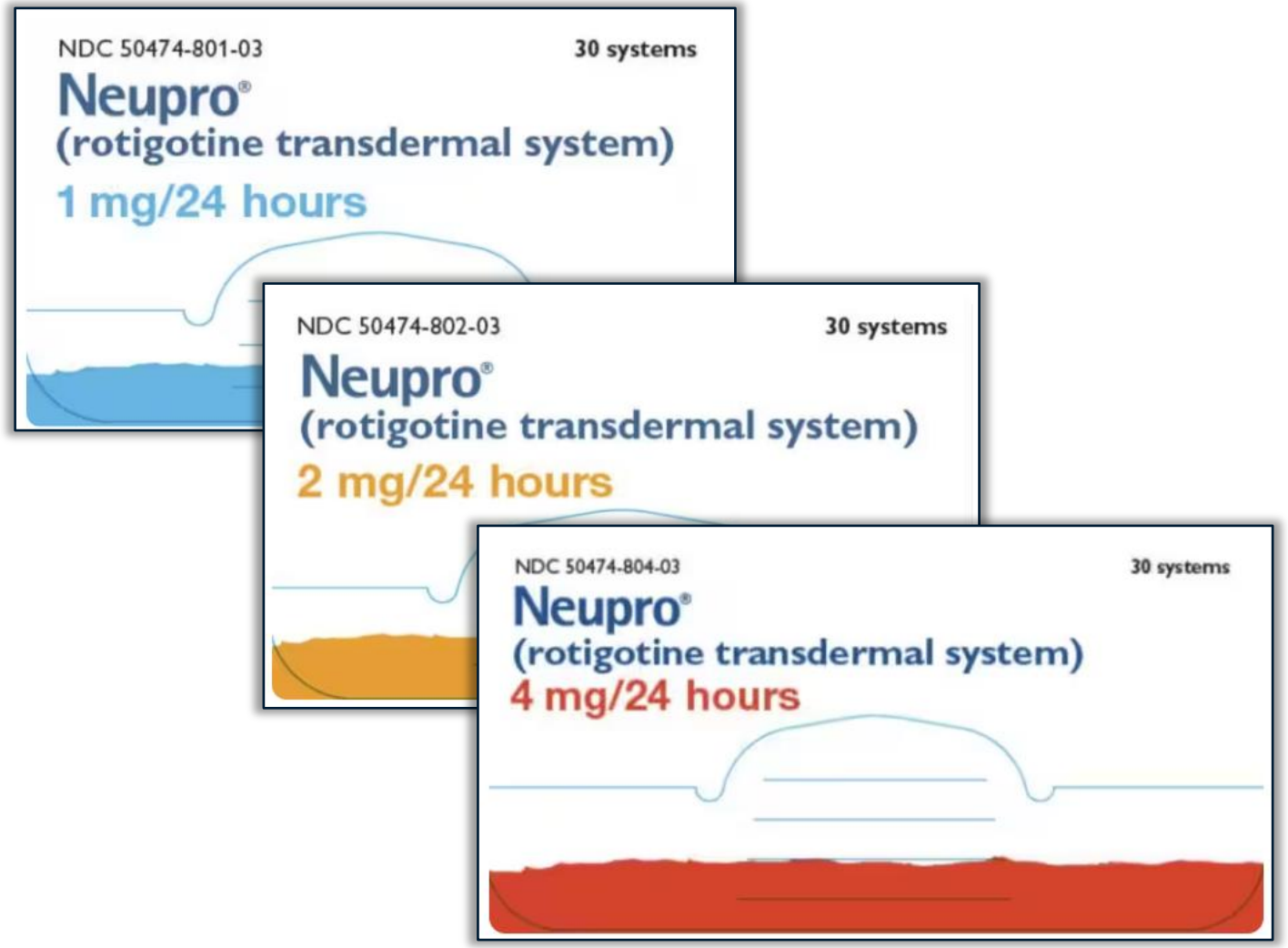
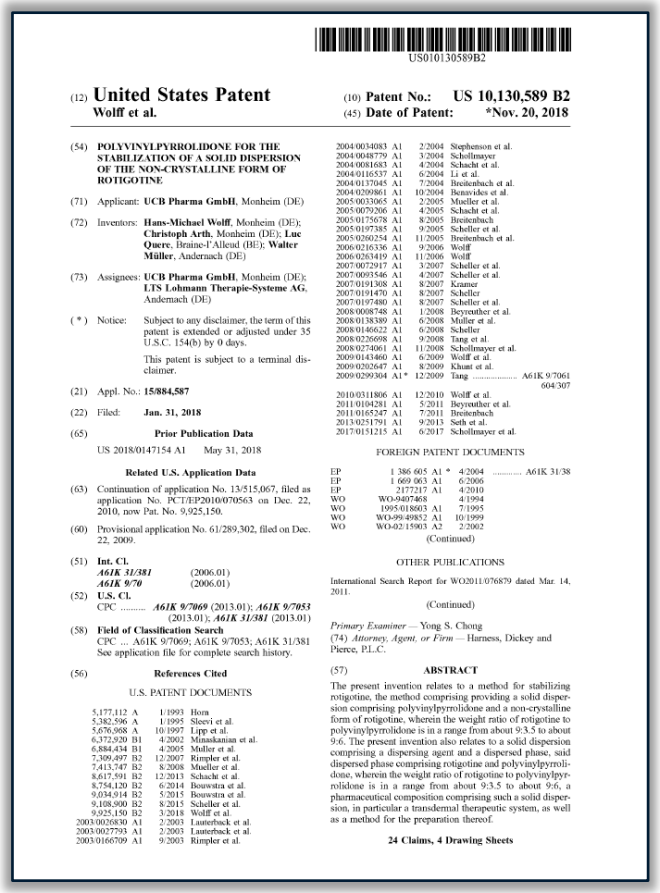
NEUPRO® Hatch-Waxman Litigation



D. Del. Takes a Look at Overlapping Ranges

UCB, Inc. v. Actavis Labs UT, Inc. (D. Del. 2021)



US010130589B2

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

(10) **Patent No.: US 10,130,589 B2**
(45) **Date of Patent: *Nov. 20, 2018**

(54) **POLYVINYLPYRROLIDONE FOR THE STABILIZATION OF A SOLID DISPERSION OF THE NON-CRYSTALLINE FORM OF ROTIGOTINE**

(71) Applicant: **UCB Pharma GmbH**, Monheim (DE)

(72) Inventors: **Hans-Michael Wolff**, Monheim (DE); **Christoph Arth**, Monheim (DE); **Luc Quere**, Braine-l'Alleud (BE); **Walter Müller**, Andernach (DE)

(73) Assignees: **UCB Pharma GmbH**, Monheim (DE); **LTS Lohmann Therapie-Systeme AG**, Andernach (DE)

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

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **15/884,587**

(22) Filed: **Jan. 31, 2018**

(65) **Prior Publication Data**

US 2018/0147154 A1 May 31, 2018

Related U.S. Application Data

(63) Continuation of application No. 13/515,067, filed as application No. PCT/EP2010/070563 on Dec. 22, 2010, now Pat. No. 9,925,150.

(60) Provisional application No. 61/289,302, filed on Dec. 22, 2009.

(51) **Int. Cl.**
A61K 31/381 (2006.01)
A61K 9/70 (2006.01)

(52) **U.S. Cl.**
CPC ***A61K 9/7069*** (2013.01); ***A61K 9/7053*** (2013.01); ***A61K 31/381*** (2013.01)

(58) **Field of Classification Search**
CPC ... A61K 9/7069; A61K 9/7053; A61K 31/381
See application file for complete search history.

(56) **References Cited**

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(Continued)

Primary Examiner — Yong S. Chong
(74) *Attorney, Agent, or Firm* — Harness, Dickey and Pierce, P.L.C.

(57) **ABSTRACT**

The present invention relates to a method for stabilizing rotigotine, the method comprising providing a solid dispersion comprising polyvinylpyrrolidone and a non-crystalline form of rotigotine, wherein the weight ratio of rotigotine to polyvinylpyrrolidone is in a range from about 9:3.5 to about 9:6. The present invention also relates to a solid dispersion comprising a dispersing agent and a dispersed phase, said dispersed phase comprising rotigotine and polyvinylpyrrolidone, wherein the weight ratio of rotigotine to polyvinylpyrrolidone is in a range from about 9:3.5 to about 9:6, a pharmaceutical composition comprising such a solid dispersion, in particular a transdermal therapeutic system, as well as a method for the preparation thereof.

24 Claims, 4 Drawing Sheets

U.S. Patent No. 10,130,589

> 1. A method for stabilizing rotigotine, the method comprising providing a solid dispersion comprising polyvinylpyrrolidone and a non-crystalline form of rotigotine free base, wherein the weight ratio of rotigotine free base to polyvinylpyrrolidone is in a range from about 9:4 to about 9:6.

- Claims 1, 2, 3, 7, 10, 11, and 12 of the '589 patent found invalid
  - **Anticipation**: Applying the "at once envisage" framework for anticipation articulated in ***Kennametal, Inc. v. Ingersoll Cutting Tool Co.***, 780 F.3d 1376, 1381 (Fed. Cir. 2015), the district court found that the Muller patents anticipate all asserted claims.
  - **Obviousness**: The asserted claims would have been obvious in view of multiple prior art references, including the Muller patents

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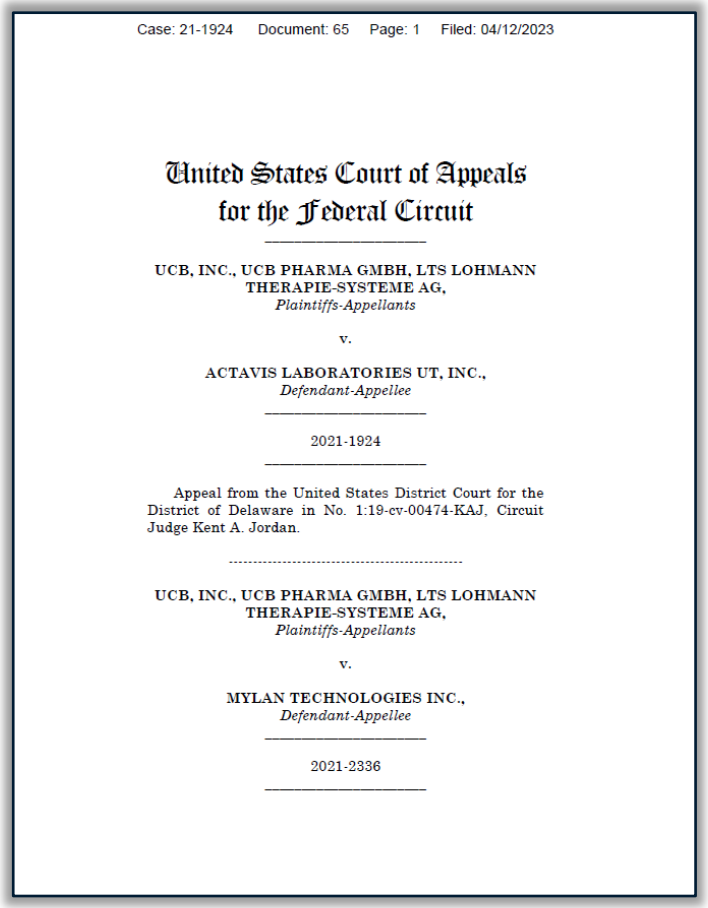
Fed. Cir. Splits with D. Del. on Overlapping Ranges

UCB, Inc. v. Actavis Labs UT, Inc., 2021-1924 (Fed. Cir. Apr. 12, 2023)



Case: 21-1924 Document: 65 Page: 1 Filed: 04/12/2023

United States Court of Appeals
for the Federal Circuit

UCB, INC., UCB PHARMA GMBH, LTS LOHMANN THERAPIE-SYSTEME AG,
Plaintiffs-Appellants

v.

ACTAVIS LABORATORIES UT, INC.,
Defendant-Appellee

2021-1924

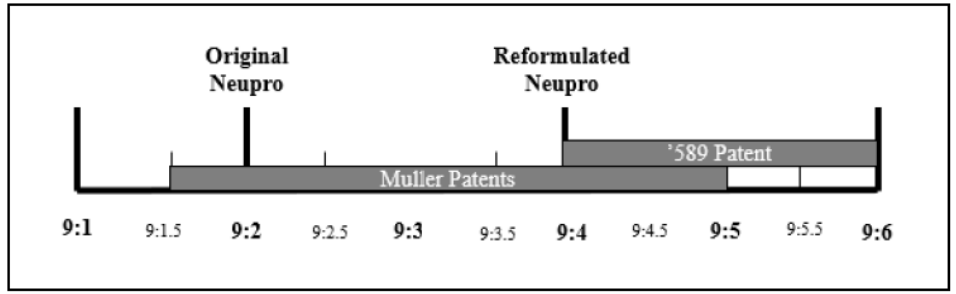
Appeal from the United States District Court for the District of Delaware in No. 1:19-cv-00474-KAJ, Circuit Judge Kent A. Jordan.

UCB, INC., UCB PHARMA GMBH, LTS LOHMANN THERAPIE-SYSTEME AG,
Plaintiffs-Appellants

v.

MYLAN TECHNOLOGIES INC.,
Defendant-Appellee

2021-2336

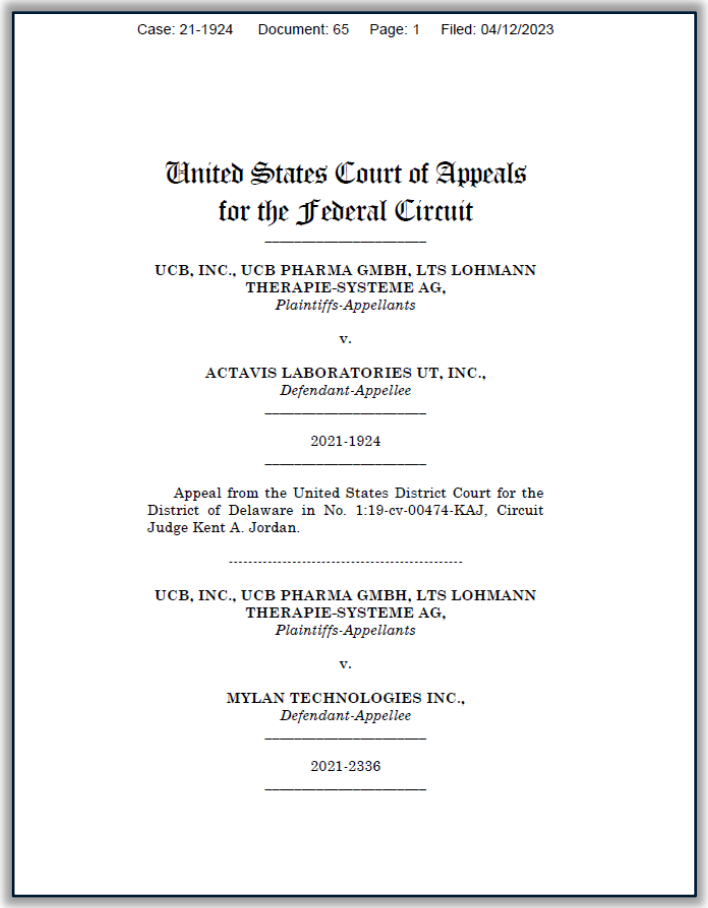


- District Court **erred** in applying *Kennametal* and the "immediately envisage" line of cases in its **anticipation** analysis
  - *Ineos* standard more appropriate for overlapping ranges: "[o]nce the patent challenger has established, through overlapping ranges, its prima facie case of anticipation, '**the court must evaluate whether the patentee has established that the claimed range is critical to the operability of the claimed invention**.'" *Genentech, Inc. v. Hospira, Inc.*, 946 F.3d 1333, 1338 (Fed. Cir. 2020) (quoting *Ineos*, 783 F.3d at 871) (emphasis added)

FISH.

Fed. Cir. Splits with D. Del. on Overlapping Ranges

UCB, Inc. v. Actavis Labs UT, Inc., 2021-1924 (Fed. Cir. Apr. 12, 2023)



Case: 21-1924 Document: 65 Page: 1 Filed: 04/12/2023

United States Court of Appeals
for the Federal Circuit

UCB, INC., UCB PHARMA GMBH, LTS LOHMANN THERAPIE-SYSTEME AG,
Plaintiffs-Appellants

v.

ACTAVIS LABORATORIES UT, INC.,
Defendant-Appellee

2021-1924

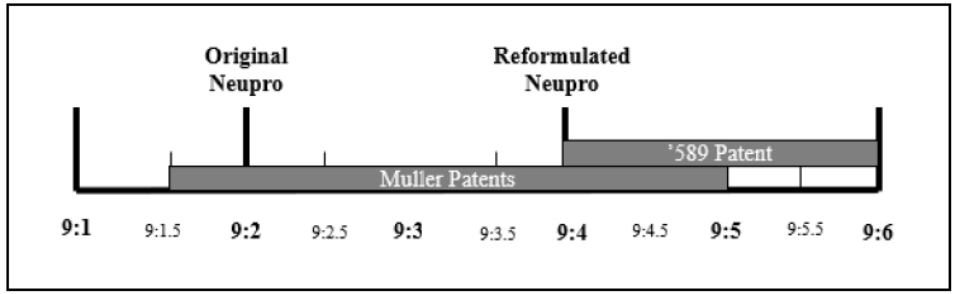
Appeal from the United States District Court for the District of Delaware in No. 1:19-cv-00474-KAJ, Circuit Judge Kent A. Jordan.

UCB, INC., UCB PHARMA GMBH, LTS LOHMANN THERAPIE-SYSTEME AG,
Plaintiffs-Appellants

v.

MYLAN TECHNOLOGIES INC.,
Defendant-Appellee

2021-2336



- Fed. Cir. **affirmed** District Court's finding that the claimed range of weight ratios of rotigotine to PVP overlap with that disclosed in the Muller patents and UCB failed to rebut this prima facie case of **Obviousness**
  - **Muller Prior Art Usable**: Due to the similarities in Form I and Form II, no "cataclysmic change" rendered pre-Form II prior art unusable
  - **No unexpected results**: The results obtained in the alleged invention and those in Muller patents, are "similar in kind . . . [and] with similar levels of stability (i.e., lack of crystallization)."
  - **No commercial success**: the Muller patents operated as blocking patents dissuading competitors from developing a rotigotine TTS

FISH.

Updates on the State of Section 112 (Enablement)

FISH.

35 U.S.C. § 112(a)

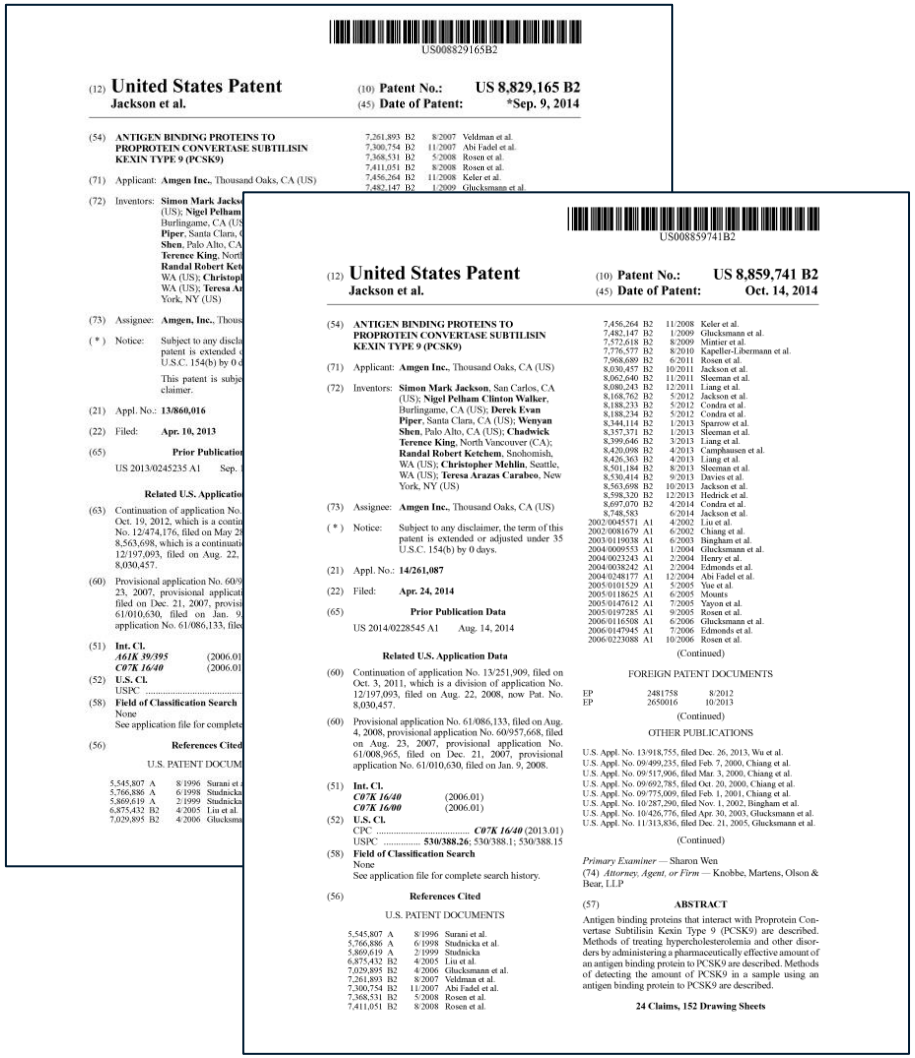
§ 112. Specification

(a) IN GENERAL.—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.

Enablement of Genus Claims (Amgen v. Sanofi)

- Amgen's patents describe antibodies that purportedly bind to the PCSK9 protein and lower LDL levels.
- Common patent specification disclosed amino acid sequences for twenty-six antibodies, and included three dimensional structures of two antibodies (including Amgen's Repatha).
- Sanofi contended that there are millions of antibody candidates within the scope of the claims, antibody generation is unpredictable, and practicing the full scope of the claims requires substantial trial and error.

Enablement of Genus Claims (Amgen v. Sanofi)



US008829165B2

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

(10) **Patent No.: US 8,829,165 B2**
(45) **Date of Patent: *Sep. 9, 2014**

(54) **ANTIGEN BINDING PROTEINS TO PROPROTEIN CONVERTASE SUBTILISIN KEXIN TYPE 9 (PCSK9)**

(71) Applicant: **Amgen Inc.**, Thousand Oaks, CA (US)

(72) Inventors: **Simon Mark Jacks** (US); **Nigel Pelham** Burlingame, CA (US **Piper**, Santa Clara, **Shen**, Palo Alto, CA **Terence King**, North **Randal Robert Ket** WA (US); **Christop** WA (US); **Teresa A** York, NY (US)

(73) Assignee: **Amgen, Inc.**, Thous

(*) Notice: Subject to any discla patent is extended U.S.C. 154(b) by 0 d This patent is subje claimer.

(21) Appl. No.: **13/860,016**

(22) Filed: **Apr. 10, 2013**

(65) **Prior Publicatio**
US 2013/0245235 A1 Sep.

Related U.S. Applicatio

(63) Continuation of application No. Oct. 19, 2012, which is a contin No. 12/474,176, filed on May 2 8,563,698, which is a continuati 12/197,093, filed on Aug. 22, 8,030,457.

(60) Provisional application No. 60/9 23, 2007, provisional applicat filed on Dec. 21, 2007, provisi 61/010,630, filed on Jan. 9, application No. 61/086,133, file

(51) **Int. Cl.**
A61K 39/395 (2006.01)
C07K 16/40 (2006.01)

(52) **U.S. Cl.**
USPC .....

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

(56) **References Cited**

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7,029,895	B2	4/2006	Glucksma

US008859741B2

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

(10) **Patent No.: US 8,859,741 B2**
(45) **Date of Patent: Oct. 14, 2014**

(54) **ANTIGEN BINDING PROTEINS TO PROPROTEIN CONVERTASE SUBTILISIN KEXIN TYPE 9 (PCSK9)**

(71) Applicant: **Amgen Inc.**, Thousand Oaks, CA (US)

(72) Inventors: **Simon Mark Jackson**, San Carlos, CA (US); **Nigel Pelham Clinton Walker**, Burlingame, CA (US); **Derek Evan Piper**, Santa Clara, CA (US); **Wenyan Shen**, Palo Alto, CA (US); **Chadwick Terence King**, North Vancouver (CA); **Randal Robert Ketchem**, Snohomish, WA (US); **Christopher Mehlin**, Seattle, WA (US); **Teresa Arazas Carabeo**, New York, NY (US)

(73) Assignee: **Amgen Inc.**, Thousand Oaks, CA (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.: **14/261,087**

(22) Filed: **Apr. 24, 2014**

(65) **Prior Publication Data**
US 2014/0228545 A1 Aug. 14, 2014

Related U.S. Application Data

(60) Continuation of application No. 13/251,909, filed on Oct. 3, 2011, which is a division of application No. 12/197,093, filed on Aug. 22, 2008, now Pat. No. 8,030,457.

(60) Provisional application No. 61/086,133, filed on Aug. 4, 2008, provisional application No. 60/957,668, filed on Aug. 23, 2007, provisional application No. 61/008,965, filed on Dec. 21, 2007, provisional application No. 61/010,630, filed on Jan. 9, 2008.

(51) **Int. Cl.**
C07K 16/40 (2006.01)
C07K 16/00 (2006.01)

(52) **U.S. Cl.**
CPC ***C07K 16/40*** (2013.01)
USPC **530/388.26**; 530/388.1; 530/388.15

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

(56) **References Cited**

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(Continued)

Primary Examiner — Sharon Wen
(74) *Attorney, Agent, or Firm* — Knobbe, Martens, Olson & Bear, LLP

(57) **ABSTRACT**

Antigen binding proteins that interact with Proprotein Convertase Subtilisin Kexin Type 9 (PCSK9) are described. Methods of treating hypercholesterolemia and other disorders by administering a pharmaceutically effective amount of an antigen binding protein to PCSK9 are described. Methods of detecting the amount of PCSK9 in a sample using an antigen binding protein to PCSK9 are described.

24 Claims, 152 Drawing Sheets

- 1. An isolated monoclonal antibody, wherein, when bound to PCSK9, the monoclonal antibody binds to at least one of the following residues: S153, I154, P155, R194, D238, A239, I369, S372, D374, C375, T377, C378, F379, V380, or S381 of SEQ ID NO:3, and wherein the monoclonal antibody blocks binding of PCSK9 to LDLR.

- 19. The isolated monoclonal antibody of claim 1 wherein the isolated monoclonal antibody binds to at least two of the following residues S153, I154, P155, R194, D238, A239, I369, S372, D374, C375, T377, C378, F379, V380, or S381 of PCSK9 listed in SEQ ID NO:3.

U.S. Patent No. 8,829,165

Amgen, Inc. v. Sanofi, 598 U.S. 594 (2023)

- "If a patent claims an entire class of processes, machines, manufactures, or compositions of matter, ***the patent's specification must enable a person skilled in the art to make and use the entire class***. In other words, ***the specification must enable the full scope of the invention as defined by its claims***. The more one claims, the more one must enable." *Id.* at 610.

Post-*Amgen v. Sanofi:* Antibody Claims

Bexalta Inc. v. Genentech, Inc., 81 F.4th 1362 (Fed. Cir. 2023)

- Genus claims to antibody or antibody fragments that "that binds Factor IX or Factor IXa and increases the procoagulant activity of Factor IXa" were invalid for lack of enablement. *Id.* at 1366.
- Facts of case were "materially indistinguishable from those in Amgen" where only eleven amino acid sequences were disclosed for "millions of potential candidate antibodies" with the claimed function. *Id.*
- Undisputed that "to practice the full scope of the claimed invention, skilled artisans must make candidate antibodies and screen them to determine which ones perform the claimed functions," which is "the definition of trial and error." *Id.*

Teva Pharmaceuticals International GmbH v. Eli Lilly Co., 2023 WL 6282898 (D. Mass. Sept. 26, 2023)

- Asserted Claims that "cover the entire functionally-defined genus of humanized anti-CGRP antagonistic antibodies" were invalid for lack of enablement where the specification disclosed only one covered antibody while the actual number of antibodies that could potentially antagonize CGRP is "mind-bogglingly large" and "not knowable." *Id.* at *22, 24.
- "[T]he claims did not identify any amino acid sequence or unique structure for a covered antibody; and a POSA could not predict whether an antibody would satisfy the claims based on its amino acid sequence or structure, and thus antibodies would have to be made and individually tested to determine whether they were viable candidates for antagonizing CGRP." *Id.* at *22.
- "[T]hese facts amount to nothing more than a 'roadmap' for a 'trial and error' process to identify and make antibodies within the scope of the Asserted Claims." *Id.*

Post-*Amgen v. Sanofi:* Method of Treatment Claims

Medytox, Inc. v. Galderma S.A., 71 F.4th 990 (Fed. Cir. 2023)

19. A method for treating glabellar lines in a patient in need thereof, comprising:

locally administering a first treatment of a botulinum toxin composition comprising a serotype A botulinum toxin in an amount present in about 20 units of MT10109L, a first stabilizer comprising a polysorbate, and at least one additional stabilizer, and that does not comprise an animal-derived product or recombinant human albumin;
…
wherein said greater length of effect is determined by physician's live assessment maximum frown and ***requires a responder rate at 16 weeks after the first treatment of 50% or greater***.

Substitute Claim to U.S. Patent No. 10,143,728

- Responder rate limit construed as range of 50-100%
- Specification contained "at most three examples of responder rates above 50% at 16 weeks: 52%, 61% and 62%." *Id.* at *10
- POSA "would not have been able to achieve responder rates higher than the limited examples provided in the specification." *Id.*

Post-*Amgen v. Sanofi:* Composition Claims

Orexo AB v. Sun Pharm. Industr. Ltd., 2023 WL 4492095 (D.N.J., August 11, 2023)

1. A pharmaceutical composition in the form of a tablet suitable for sublingual administration comprising:

buprenorphine, or a pharmaceutically acceptable salt thereof, provided in the form of microparticles,

a weak acid, provided in the form of particles, which particles are separate from the microparticles of buprenorphine, or a pharmaceutically acceptable salt thereof,

a disintegrant,

and naloxone or a pharmaceutically acceptable salt thereof…

U.S. Patent No. 9,439,900

- Specification disclosed dry mixing of buprenorphine and a weak acid
- Sun argued claims enabled because specification did not teach a POSA how to use its confidential process to make separate microparticles of buprenorphine and weak acid particles *Id.* at *23
- ***Amgen*** is inapposite because this case involved a single drug composition, not an entire genus

FISH.

Post-*Amgen v. Sanofi* Takeaways

- **Focus on scope of claims**
- **More predictability in underlying art = more likely experimentation will be "reasonable"**
- **Don't "monopolize" the genus**
- **Guidance can't amount to recipe for trial and error**
- **Challenges for antibody claims but need to consider implication for other types of claims**

U.S. Gov’t Agency Developments and their Impact on Hatch-Waxman Litigants

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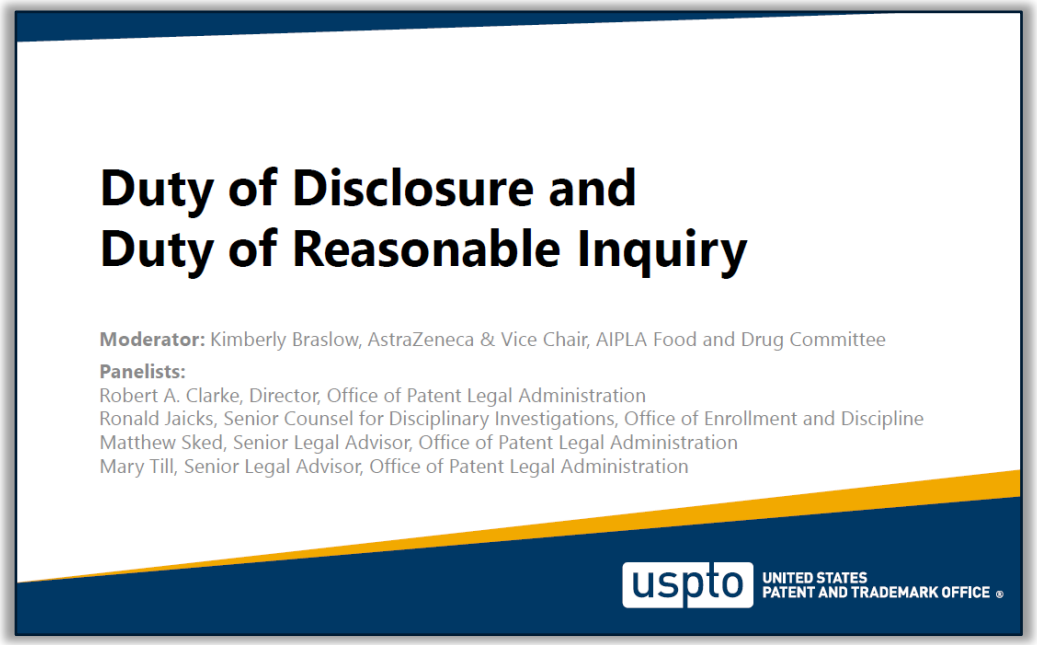
U.S. Gov’t Stakeholders for Orange Book Patents

FDA U.S. FOOD & DRUG ADMINISTRATION

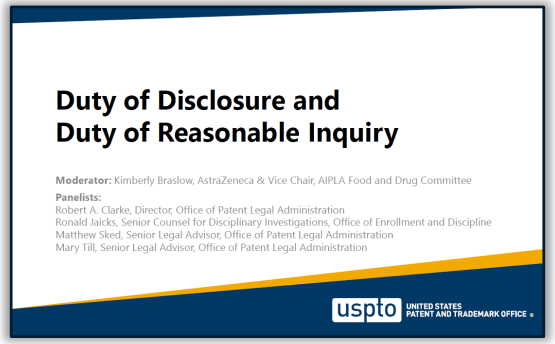
USPTO/FDA Collaboration Efforts - Update



February 23, 2023 USPTO Webinar

October 19, 2023 FDLI Webinar

2023 USPTO Webinar Takeaways



February 23, 2023 USPTO Webinar

- USPTO believes policy is useful regardless of whether *Belcher Pharmaceuticals LLC v. Hospira* (Fed. Cir. 2021) is a an outlier or not; **USPTO has not seen to date a deluge of cases like *Belcher***

- **The key factors to consider** in ensuring that consistent statements are made between the two agencies is
  - **the scope of the claimed invention** and
  - **the timing of the pending applications and submissions to the FDA**.

- Regulatory submissions involving **data from clinical trials conducted overseas** that are the basis for an approval **outside the US** would have to be provided to the USPTO if considered material information for a US pending application

- **Under what circumstances a paragraph IV certification served on a patent owner by an ANDA applicant would be material to the patent application?**
  - Is there a pending application that relates to the same active ingredient and claims of unpatentability in the Paragraph IV certification?
  - Does that basis for unpatentability relate to a presently claimed invention that is currently being prosecuted?
  - Does the information in that detailed statement trail to patentability of something that is currently pending at USPTO?

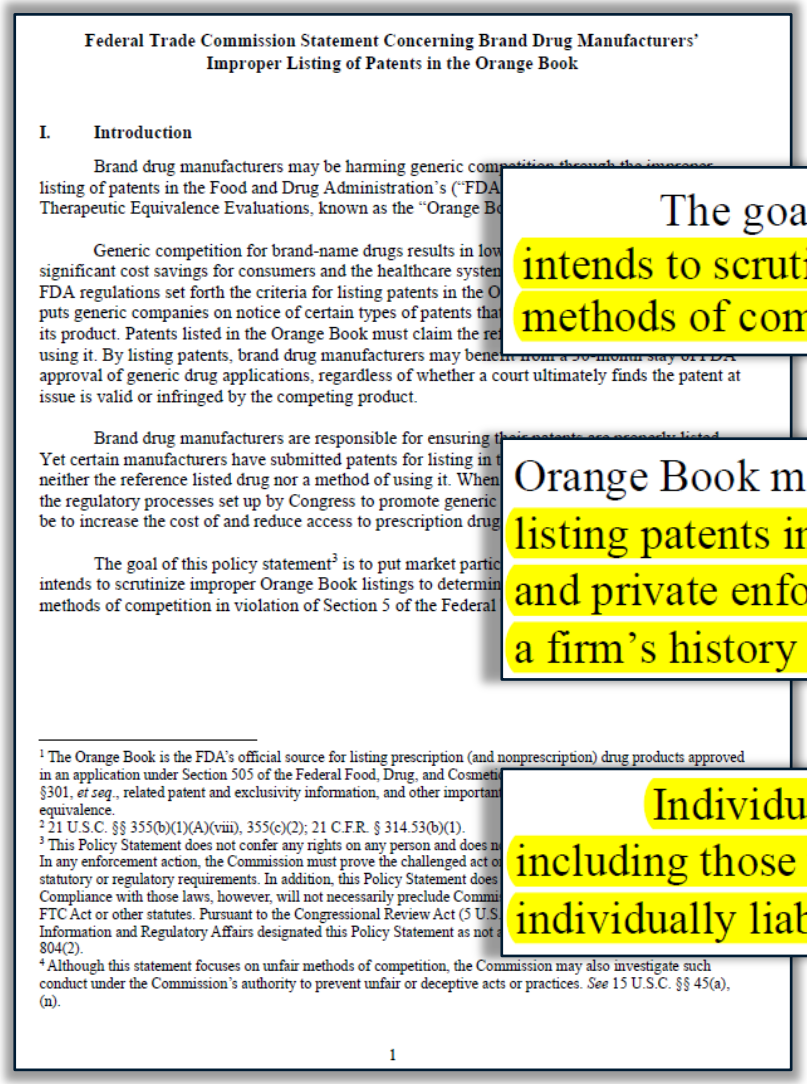
FDLI Webinar Takeaways

- **FDA Regulatory Counsel:**
  - "We have not, and we do not intend to be, involved in substantive patent dispute issues that would be consistent with our ministerial role."
  - The agency however is "**certainly exploring what we can do within the confines of the OBTA [Orange Book Transparency Act]** and our ongoing efforts over the years, and also requests that come into us over the years."
  - "Are there other areas of engagement that would be more beneficial in terms of getting to the prized goal of bringing down drug costs instead of perhaps looking at these sort of one-offs, like the provision of inconsistent statements? . . .**We don't have the raw data to see how pervasive this problem is**."

- **USPTO's Patent Trial and Appeal Board, Senior Lead Administrative Patent Judge:**
  - "When we really started thinking about that public proposal, all these questions came to mind because **there are regulatory and statutory interpretation issues that are really within the purview of the FDA**."
  - "And so, **there's a real mixed question there of a combination of FDA's position on what the statutory language means in combination with more of a patent law question about the scope of the claims**."
  - "We would take our lead from what the FDA is interested and willing to do on that. **And if they're not interested and don't see it within their current statutory authority to dive into those issues, then we'll help however we can**."

October 19, 2023 FDLI Webinar

FTC Has its Eye on Orange Book Patents



Federal Trade Commission Statement Concerning Brand Drug Manufacturers' Improper Listing of Patents in the Orange Book

I. Introduction

Brand drug manufacturers may be harming generic competition through the improper listing of patents in the Food and Drug Administration's ("FDA Therapeutic Equivalence Evaluations, known as the "Orange Bo

Generic competition for brand-name drugs results in low significant cost savings for consumers and the healthcare systen FDA regulations set forth the criteria for listing patents in the O puts generic companies on notice of certain types of patents tha its product. Patents listed in the Orange Book must claim the re using it. By listing patents, brand drug manufacturers may bene approval of generic drug applications, regardless of whether a court ultimately finds the patent at issue is valid or infringed by the competing product.

Brand drug manufacturers are responsible for ensuring Yet certain manufacturers have submitted patents for listing in neither the reference listed drug nor a method of using it. When the regulatory processes set up by Congress to promote generic be to increase the cost of and reduce access to prescription drug

The goal of this policy statement[3] is to put market partic intends to scrutinize improper Orange Book listings to determin methods of competition in violation of Section 5 of the Federal

[1] The Orange Book is the FDA's official source for listing prescription (and nonprescription) drug products approved in an application under Section 505 of the Federal Food, Drug, and Cosmeti §301, *et seq.*, related patent and exclusivity information, and other important equivalence.
[2] 21 U.S.C. §§ 355(b)(1)(A)(viii), 355(c)(2); 21 C.F.R. § 314.53(b)(1).
[3] This Policy Statement does not confer any rights on any person and does n In any enforcement action, the Commission must prove the challenged act o statutory or regulatory requirements. In addition, this Policy Statement does Compliance with those laws, however, will not necessarily preclude Commi FTC Act or other statutes. Pursuant to the Congressional Review Act (5 U.S. Information and Regulatory Affairs designated this Policy Statement as not 804(2).
[4] Although this statement focuses on unfair methods of competition, the Commission may also investigate such conduct under the Commission's authority to prevent unfair or deceptive acts or practices. *See* 15 U.S.C. §§ 45(a), (n).

1

The goal of this policy statement[3] is to put market participants on notice that the FTC intends to scrutinize improper Orange Book listings to determine whether these constitute unfair methods of competition in violation of Section 5 of the Federal Trade Commission Act.[4]

Orange Book may constitute an "improper means" of competition.[31] Accordingly, improperly listing patents in the Orange Book may also be worthy of enforcement scrutiny from government and private enforcers under a monopolization theory. Additionally, the FTC may also scrutinize a firm's history of improperly listing patents during merger review.[32]

Individuals who submit or cause the submission of improper Orange Book patent listings, including those who certify compliance under 21 C.F.R. § 314.53(c)(2)(ii)(R), may be held individually liable.[33] Further, if the FTC encounters false certifications filed under 21 C.F.R. §

FTC's September 14, 2023 Policy Statement

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FDA Supports FTC Attention on Orange Book Patents

FEDERAL TRADE COMMISSION
PROTECTING AMERICA'S CONSUMERS

For Release

FTC Issues Policy Statement on Brand Pharmaceutical Manufacturers' Improper Listing of Patents in the Food and Drug Administration's 'Orange Book'

FTC says improper listings could be investigated as potential violations of the FTC Act

September 14, 2023

Tags: Competition | Office of Policy Planning | Nonmerger | generic drugs | Health Care | Prescription Drugs

Give Feedback

The Federal Trade Commission today issued a policy statement, supported by the U.S. Food and Drug Administration (FDA), warning pharmaceutical companies that make and sell brand-name drugs that they could face legal action if they improperly list patents in the FDA's catalog of "Approved Drug Products with Therapeutic Equivalence Evaluations," commonly known as the "Orange Book."

Improperly listing patents in the Orange Book may harm competition from less expensive generic alternatives and keep prices artificially high, according to the policy statement. The FTC will scrutinize improper Orange Book patent listings as potential unfair methods of competition in violation of Section 5 of the FTC Act.

"Improper patent listings in the Orange Book illegitimately delay or lock out generic manufacturers from entering the market, depriving Americans of access to lower-cost medicines and drug products," said FTC Chair Lina M. Khan. "The FTC is making clear that improper Orange Book listings may be an unfair method of competition in violation of the FTC Act. We won't hesitate to use all our tools to combat illegal practices that are inflating the price of health care, including medicines."

*"**The FDA appreciates and supports the FTC's efforts to examine whether brand drug companies are impeding generic drug competition by improperly listing patents in the Orange Book**," said FDA Commissioner Robert M. Califf, M.D.*

*"The **FDA stands ready to assist the FTC** as part of our long history of collaboration to protect American consumers, including our continued engagement under the Executive Order on Competition in the American Economy to help identify and address efforts to block or delay generic drug and biosimilar competition."*

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FTC Takes Challenges 100+ Orange Book Patents

FEDERAL TRADE COMMISSION
PROTECTING AMERICA'S CONSUMERS

For Release

FTC Challenges More Than 100 Patents as Improperly Listed in the FDA's Orange Book

Improper listings may delay lower-cost generic drug competition, stall drug development, and stifle innovation

November 7, 2023 |

Tags: Competition | Office of Policy Planning | Bureau of Competition | Nonmerger | Health Ca
Prescription Drugs | Over-the-Counter Drugs and Devices

Today, the Federal Trade Commission (FTC) challenged more than 100 patents held by manufactu of brand-name asthma inhalers, epinephrine autoinjectors, and other drug products as improperly inaccurately listed in the Food and Drug Administration's (FDA) publication of "Approved Drug Products with Therapeutic Equivalence Evaluations," commonly known as the "Orange Book."

The Commission has also notified FDA that it disputes the accuracy or relevance of the listed information for these patents, which may require that the manufacturers remove the listing or certify under penalty of perjury that the listings comply with applicable statutory and regulatory requirements.

The FTC sent notice letters to 10 companies, which include: AbbVie, AstraZeneca, Boehringer Ingelheim Pharmaceuticals, Impax Laboratories, Kaleo, Mylan Specialty, and subsidiaries of Glaxo-Smith Kline and Teva. The notice letters and the patent listing dispute notifications provided to FDA identify specific patents that FTC contends are improperly listed for specific asthma and other inhaler devices, Restasis multidose bottles, and epinephrine autoinjectors, also commonly known as EpiPens.

Give Feedback

abbvie

AstraZeneca

Boehringer Ingelheim

Impax

kaléo®

Mylan

GSK

teva

Navigating New Gov’t Agency Developments

- Identify the FDA regulatory milestones and submissions for which an inquiry could be reasonable under the particular circumstances,
- Review PTO and FDA submissions for material inconsistencies,
- Draft procedures for coordinating patent prosecution and regulatory functions to help meet the PTO's clarified duties and potential FTC scrutiny,
- Conduct due diligence reviews related to the PTO duties for acquisitions or sales of life sciences entities and products, and
- Establish internal procedures to help minimize waiver of the privilege protecting attorney/client communications involving the foregoing

Looking Forward to 2024

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What to Watch for in 2024

- Stabilization of new ANDA cases filed and downward trend of new ANDAs submitted to FDA
- Impact of judicial changes in the District of Delaware
- Adoption of earlier and more significant claim narrowing by more judges and courts
- Push back against *In re Cellect*
- Increased §112 allegations by generic drug makers
- Government agency stakeholder impact on Hatch-Waxman litigants

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