Recent Developments: Biosimilar challengers in PTAB Proceedings

Moderator
Teresa Stanek Rea

Speakers
Hon. Michelle Ankenbrand
Julia Pike, Sandoz
Paul Golian, BMS
Melissa Brand, BIO

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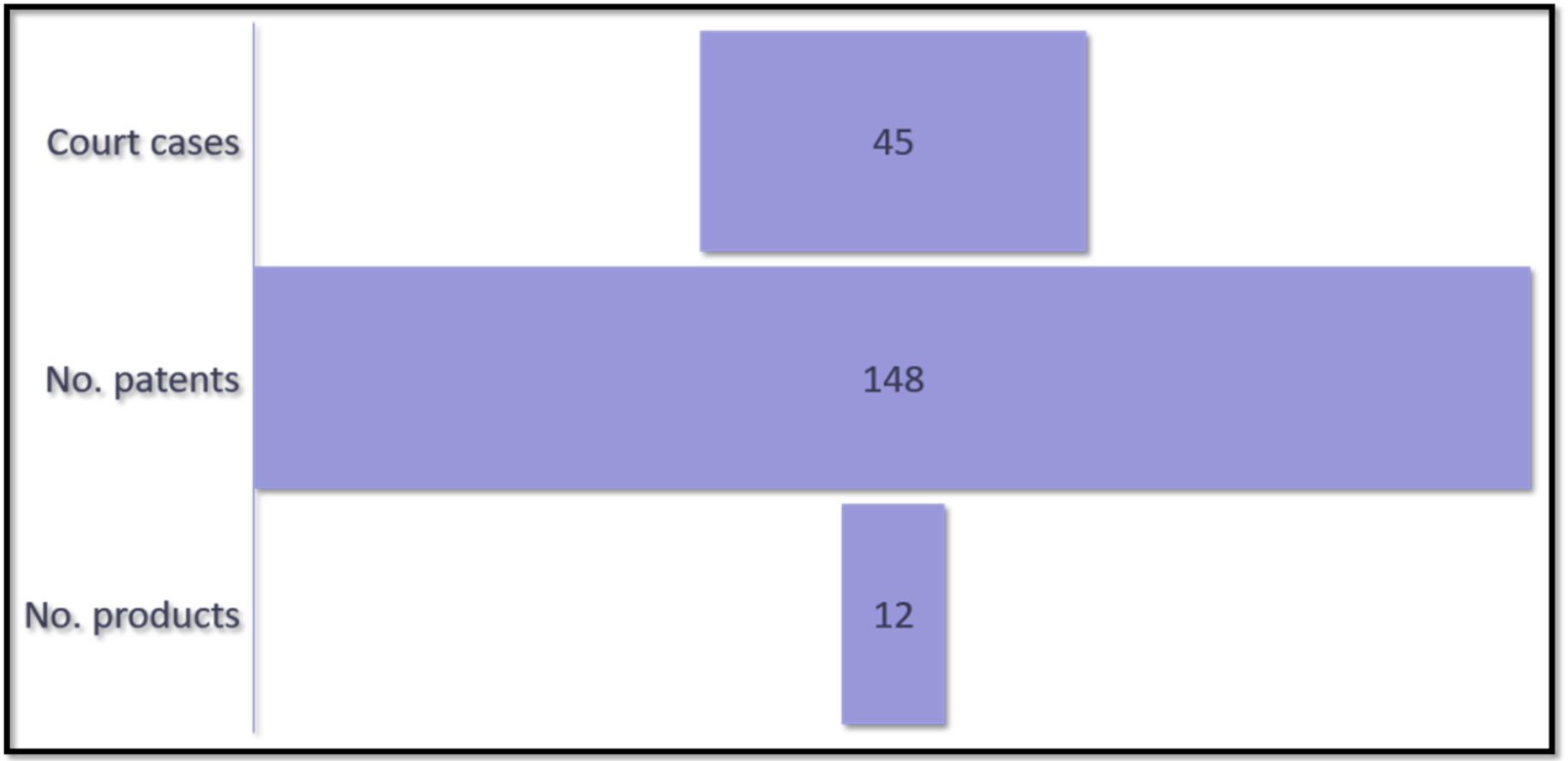
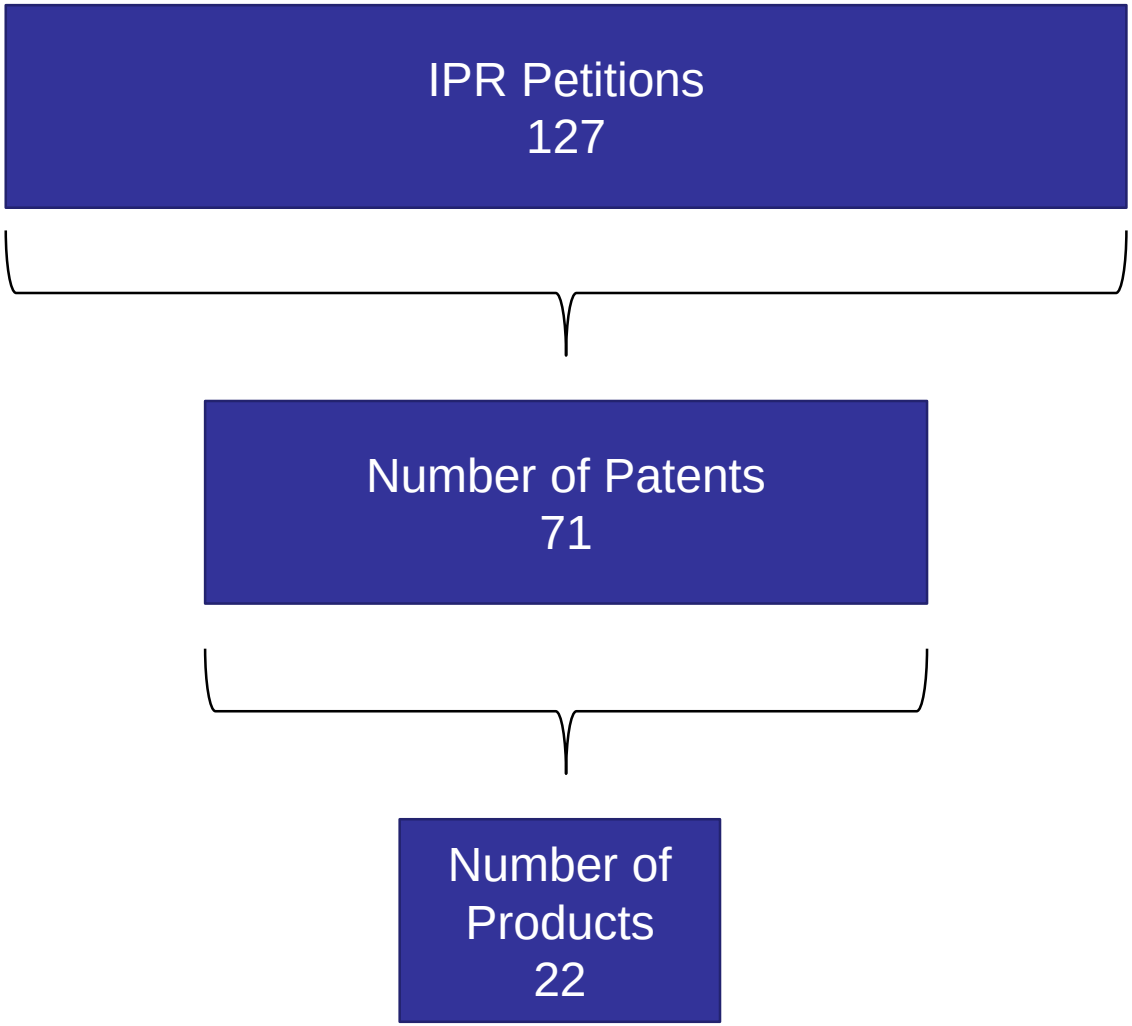
District court litigation involving biologics



IPR petitions involving biologics



IPR Challenges focus on a few drugs

Product	No. IPRs	Global sales, 2017*
Herceptin	32 IPRs	$7.44
Rituxan	27 IPRs	$9.24
Humira	20 IPRs	$18.43 billion
Lantus	13 IPRs	$5.73
Ajovy	8 IPRs	--
Emgality	8 IPRs	--

*From “The Top 15 Best-Selling Drugs of 2017” by Alex Phillippidis, Genetic Engineering & Biotechnology News, Mar. 12, 2018.

Biosimilars – Patent Dance

- **When you dance**
  - Patent lists are exchanged resulting in a first wave of litigations
  - IPRs may be filed on these patents, as well as on those left off the list
- **When you do not dance**
  - If the biosimilar applicant misses a dance step, the sponsor can immediately bring a DJ action for infringement.
    - As new information becomes available in the course of these litigations, raises the possibility of more IPRs over time
    - File IPR within 12 months but then an 18 month time course to reach final written decision

Timing of filing

- Most IPRs involve parallel district court proceedings. This is not the case with biosimilars
  - Typically IPRs are filed before any case or controversy in district court
  - Many biosimilar makers file petitions relatively early in the life cycle (clinical trials still pending) and well prior to seeking aBLA approval from FDA
  - Biosimilar makers can time their petitions to obtain a decision from the PTAB by the time they expect aBLA approval
  - Of approximately 98 biosimilar petitions, there was no parallel district court proceeding in approximately 81 of them

Frequent petitioners

- Mylan (86 petitions, incl. small molecules)
- Pfizer (26 petitions)
- Celltrion (18 petitions)
- Sandoz (15 petitions)
- Coherus (12 petitions)
- Hospira (8 petitions)
- Samsung Bioepis (6 petitions)
- Boehringer Ingelheim (4 petitions)

* PTAB statistics, as of February 15, 2019

Biosimilars Approved in the United States

aBLA / NDA No.	Biosimilar Brand Name	Biosimilar Scientific Name	aBLA / 505(b)(2) Holder	Date of Biosimilar License	Reference Product	Reference Product License Holder	U.S. Biosimilar Launch Date
aBLA 761024	Amjevita™	Adalimumab-atto	Amgen Inc.	Sep. 23, 2016	Humira®	AbbVie Inc.	
aBLA 761058	Cyltezo®	Adalimumab-abdm	Boehringer Ingelheim	Aug. 25, 2017	Humira®	AbbVie Inc.	
aBLA 761071	Hyrimoz™	Adalimumab-adaz	Sandoz Inc.	Oct. 30, 2018	Avastin®	Genentech	
aBLA 761028	Mvasi™	Bevacizumab-awwb	Amgen Inc.	Sep. 14, 2017	Avastin®	Genentech	
aBLA 125545	Retacrit®	Epoetin Alfa-epbx	Hospira / Pfizer	May 15, 2018	Epogen®	Amgen	Nov. 2018
aBLA 761042	Erelzi®	Etanercept-szzs	Sandoz Inc.	Aug. 30, 2016	Enbrel®	Immunex Corp. (Amgen Inc.)	
aBLA 125553	Zarxio®	Filgrastim-sndz	Sandoz Inc.	Mar. 6, 2015	Neupogen®	Amgen Inc.	Sept. 2015
aBLA 761080	Nivestym™	Filgrastim-aafi	Pfizer	Jul. 20, 2018	Neupogen®	Amgen Inc.	Oct. 2018
aBLA 125544	Inflectra®	Infliximab-dyyb	Celltrion Inc.	Apr. 5, 2016	Remicade®	Janssen Biotech	Nov. 2016
aBLA 761054	Renflexis®	Infliximab-abda	Samsung Bioepsis	Apr. 21, 2017	Remicade®	Janssen Biotech	Jul. 2017
aBLA 761072	Ixifi™	Infliximab-qbtx	Pfizer Inc.	Dec. 13, 2017	Remicade®	Janssen Biotech	
NDA 205692 [505(b)(2)]	Basaglar®	Insulin Glargine	Eli Lilly & Co.	Dec. 16, 2015	Lantus®	Sanofi Aventis US	Dec. 2016
aBLA 761075	Fulphila®	Pegfilgrastim-jmdb	Mylan / Biocon	Jun. 4, 2018	Neulasta®	Amgen	Jul. 2018
aBLA 761039	Udenyca™	Pegfilgrastim-cbqv	Coherus	Nov. 2, 2018	Neulasta®	Amgen	Jan. 2019
aBLA 761088	Truxima®	Rituximab-abbs	Celltrion / Teva	Nov. 28, 2018	Rituxan®	Genentech	
aBLA 761074	Ogivri™	Trastuzumab-dkst	Mylan GmbH / Biocon	Dec. 1, 2017	Herceptin®	Genentech	
aBLA 761091	Herzuma®	Trastuzumab-pkrb	Celltrion / Teva	Dec. 14, 2018	Herceptin®	Genentech	
aBLA 761100	Ontruzant®	Trastuzumab-dttb	Samsung Bioepis	Jan. 18, 2019	Herceptin®	Genentech	

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As of Jan. 31, 2019

From Venable/Fitzpatrick Biologics/HQ website https://biologicshq.com/statistics/

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Biosimilar Applications Pending in the United States

Biosimilar Name	Scientific Name	aBLA / 505(b)(2) Holder	Reference Product	Reference Product License Holder	FDA Status
SB5	Adalimumab	Samsung Bioepis	Humira®	AbbVie	Accepted Sep. 2018
Grastofil™	Filgrastim	Apotex	Neupogen®	Amgen	Accepted Feb. 2015
TPI G-CSF	Filgrastim	Adello Biologics	Neupogen®	Amgen	Accepted Sep. 2017
TX-01	Filgrastim	Tanvex BioPharma	Neupogen®	Amgen	BLA Submitted Oct. 2018
ABP 710	Infliximab	Amgen	Remicade®	Janssen	Submitted Dec. 2018
Lapelga™	Pegfilgrastim	Apotex	Neulasta®	Amgen	Accepted Dec. 2014
LA-EP2006	Pegfilgrastim	Sandoz	Neulasta®	Amgen	Accepted Nov. 2015; Rejected Q2 2016
Rixathon®	Rituximab	Sandoz	Rituxan®	Genentech	Accepted Sep. 2017; CRL May 2018
Kanjinti™ (ABP 980)	Trastuzumab	Amgen / Allergan	Herceptin®	Genentech	Submitted Jul. 2017; CRL Jun. 2018; Resubmitted Dec. 2018
PF-05280014	Trastuzumab	Pfizer	Herceptin®	Genentech	Accepted Aug. 2017; CRL Apr. 2018
Lusduna™ Nexvue™	Insulin Glargine	Merck	Lantus®	Sanofi Aventis US	Tentative Approval Jul. 2017
Unknown (Semglee in the E.U.)	Insulin Glargine	Mylan / Biocon	Lantus®	Sanofi Aventis US	CRL Jun. 2018

CRL = Complete Response Letter

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As of Jan. 31, 2019

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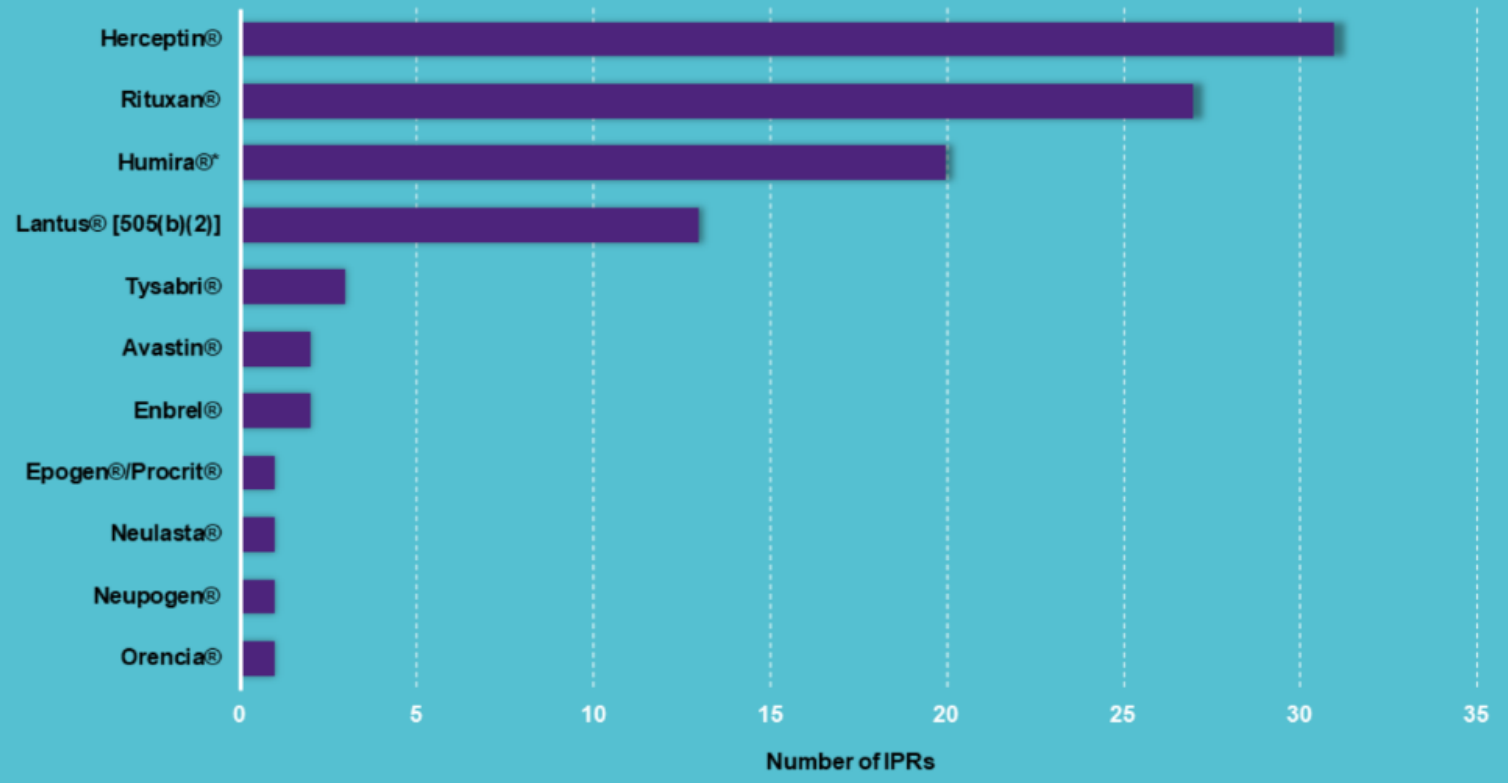
Biosimilar-Related IPRs by Reference Product



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*Considering IPR2017-00826 and IPR2017-01008 as one IPR, and IPR2017-00827 and IPR2017-01009 as one IPR.

As of Jan. 31, 2019

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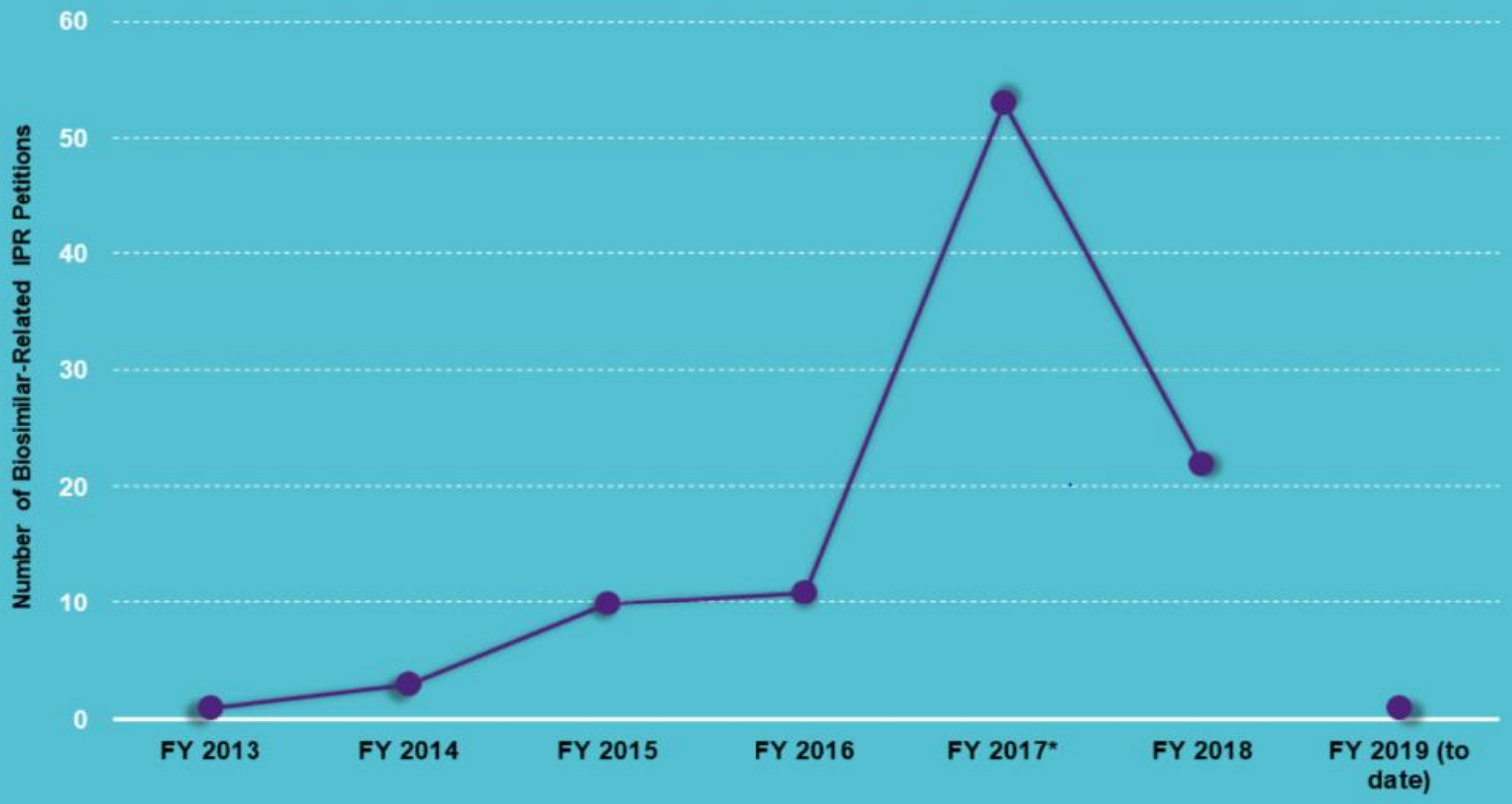
Biosimilar-Related IPR Petitions by Fiscal Year



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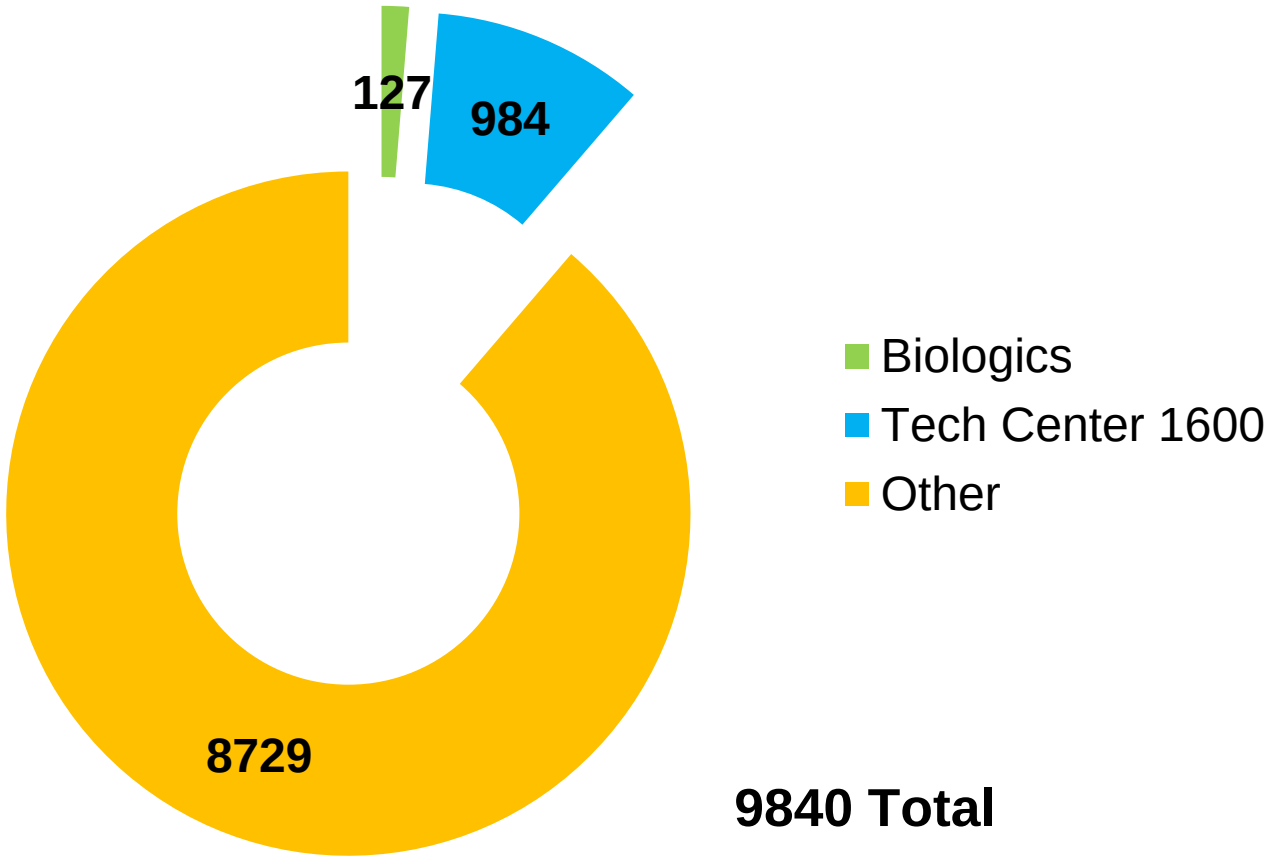
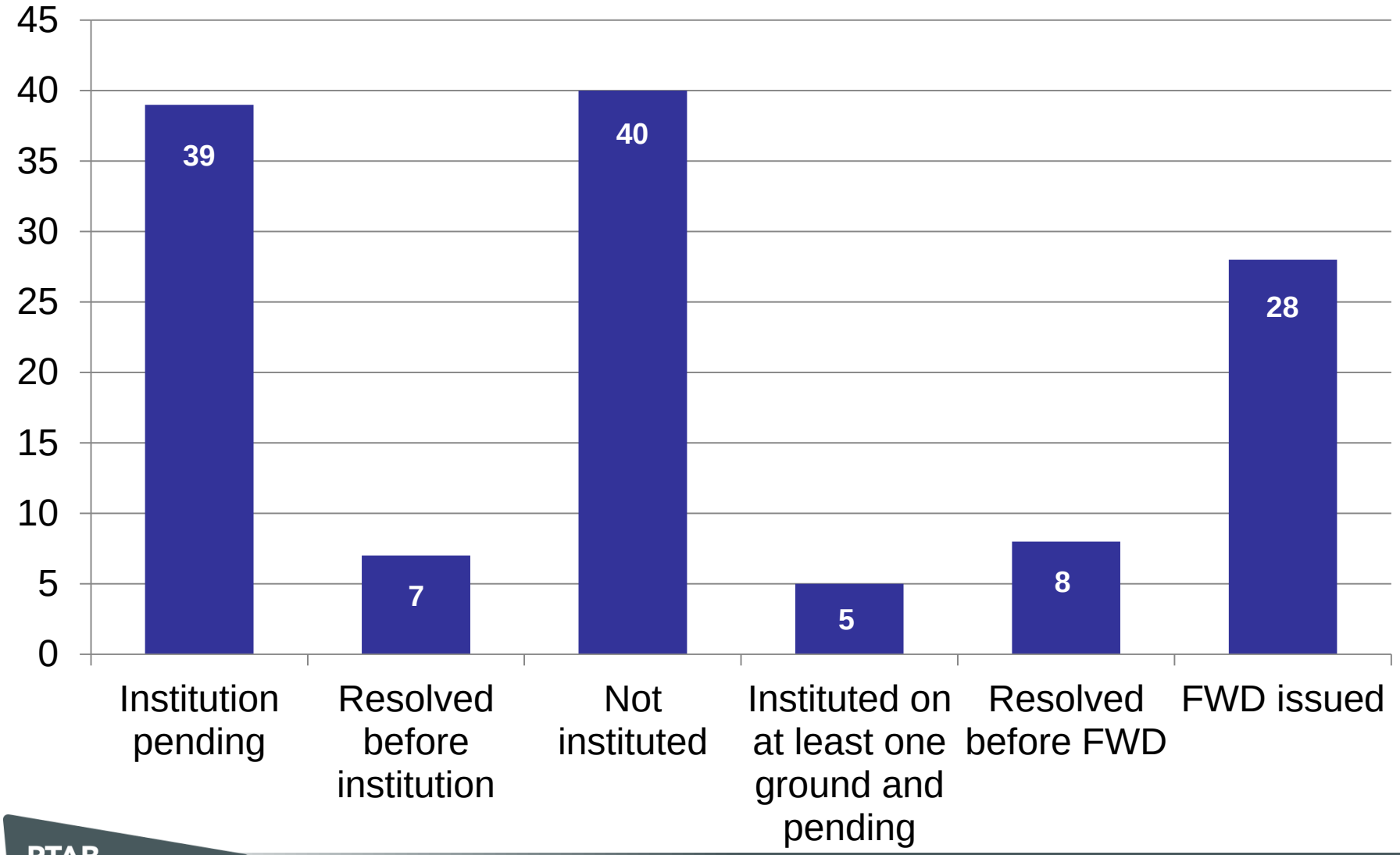
PTAB Fiscal Years run from October 1 – September 30.

As of Jan. 31, 2019

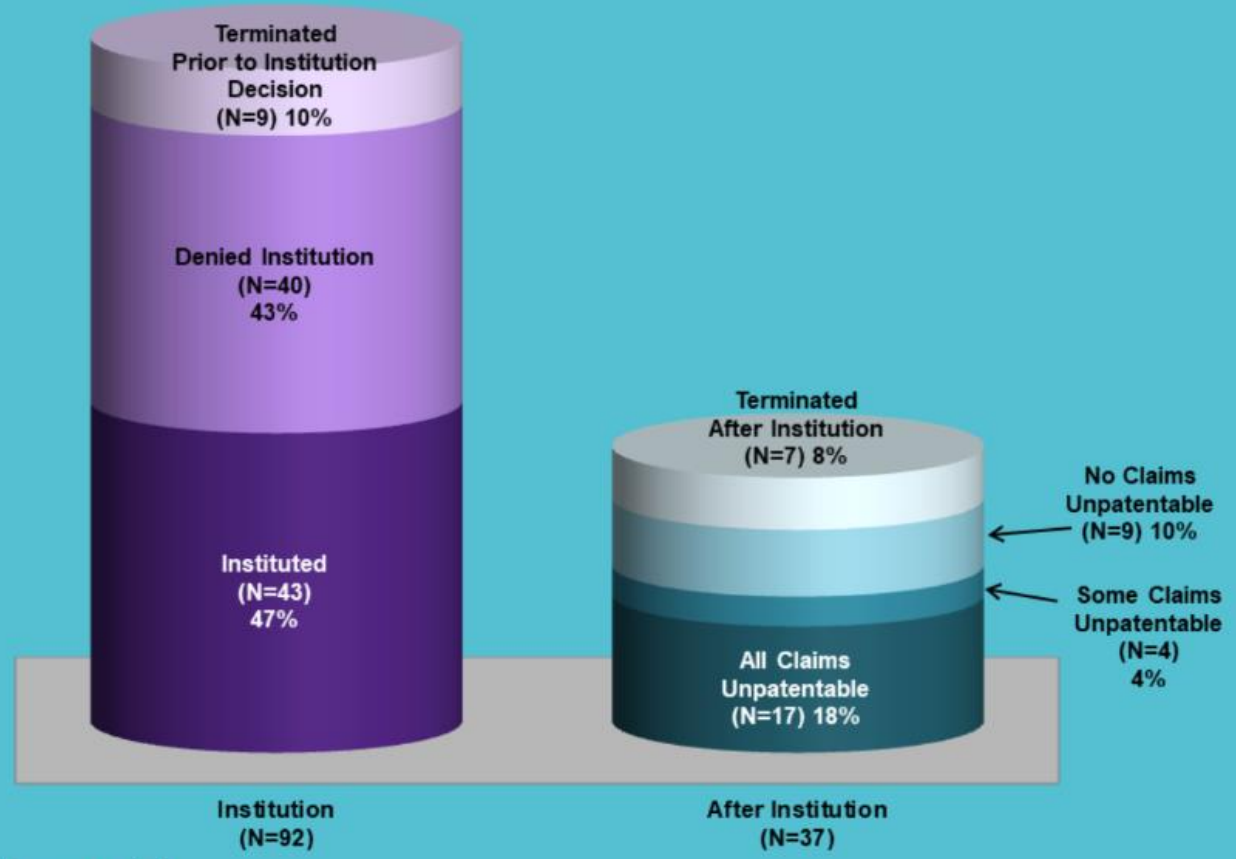
AIA Petitions filed as of February 15, 2019 (IPR, PGR, CBM, DER)



Status of Biosimilar IPRs



Biosimilar-Related IPRs: Institution and Final Written Decision Outcomes



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As of Jan. 31, 2019

Claims challenged in multiple petitions are counted in each petition.

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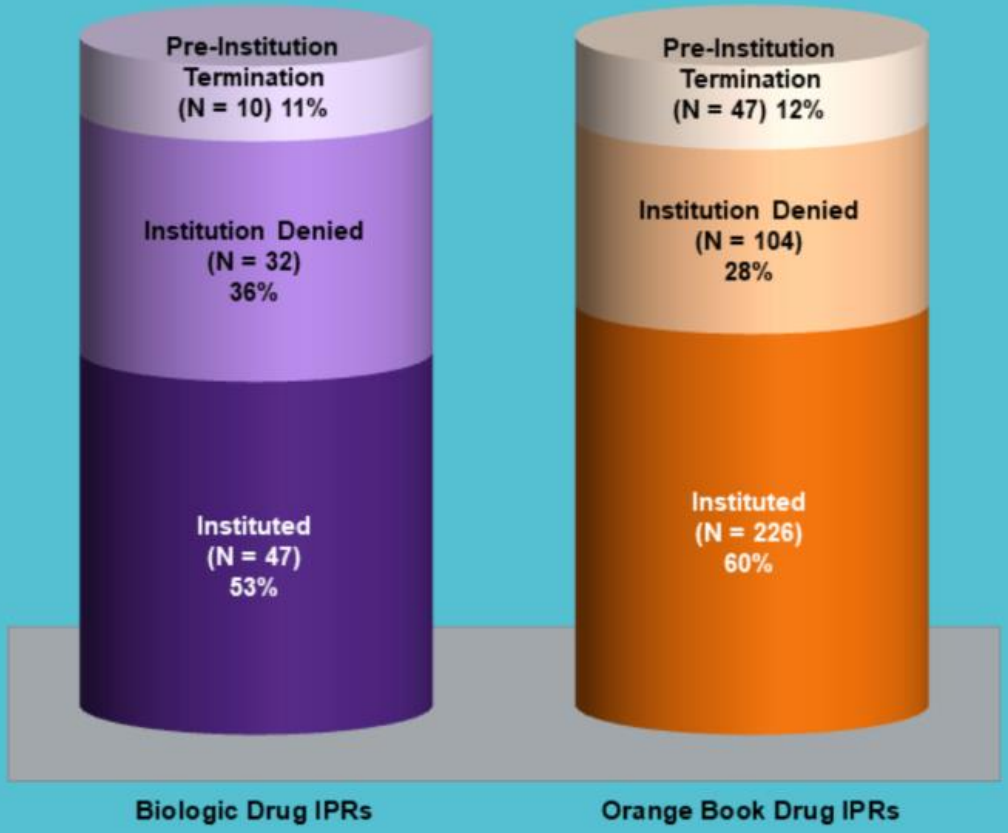
Institution Outcomes: Biologic and Orange Book Drug IPRs



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As of Mar. 31, 2018

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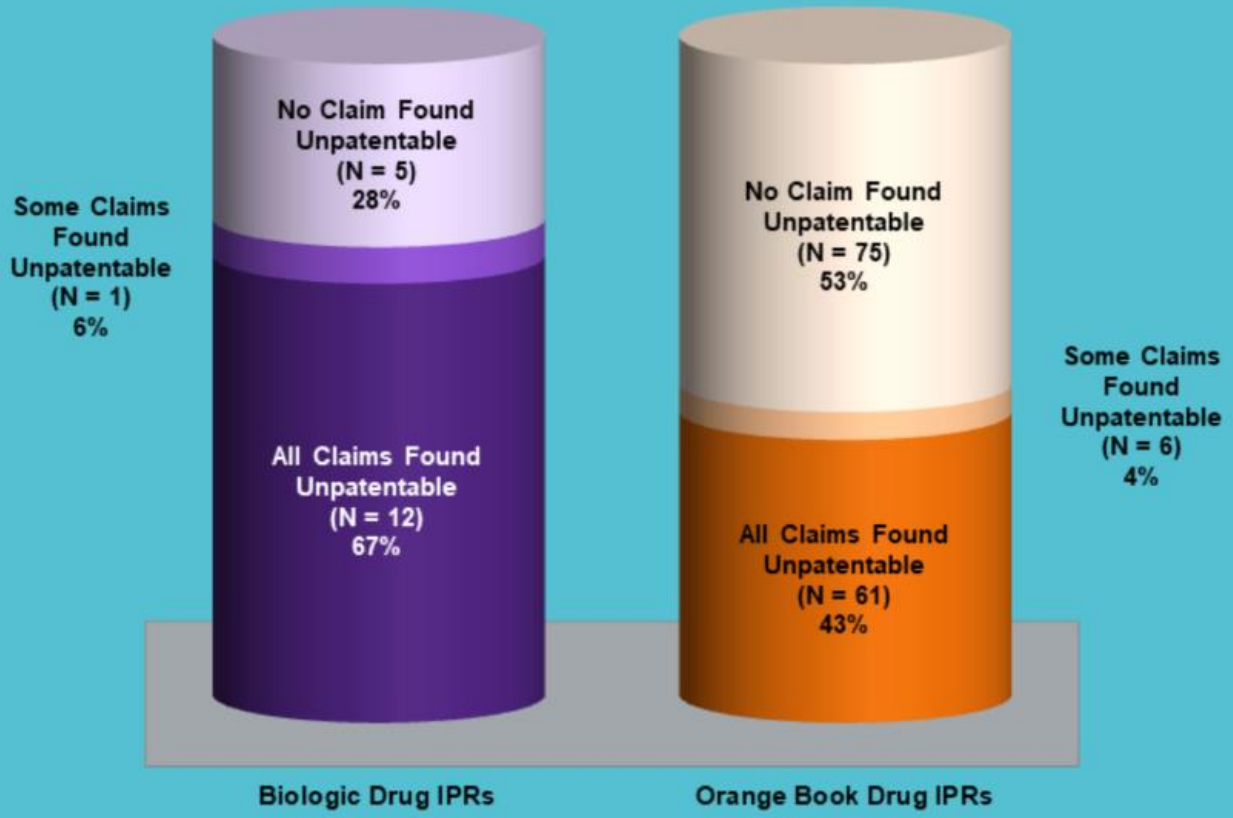
FWD Outcomes: Biologic and Orange Book Drug IPRs



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As of Mar. 31, 2018

*Considering IPR2017-00826 and IPR2017-01008 as one IPR, and IPR2017-00827 and IPR2017-01009 as one IPR.

Biologics post-grant proceedings

- **Most proceedings attack the follow-on patents**
  - About 50% challenging method of treatment patents
    - Most vulnerable to prior art attacks
    - Patents with label claims may pose obstacles to biosimilar applicants
  - About 25% challenging formulation patents
  - About 13% challenging composition of matter patents
  - About 12% challenging methods of manufacture

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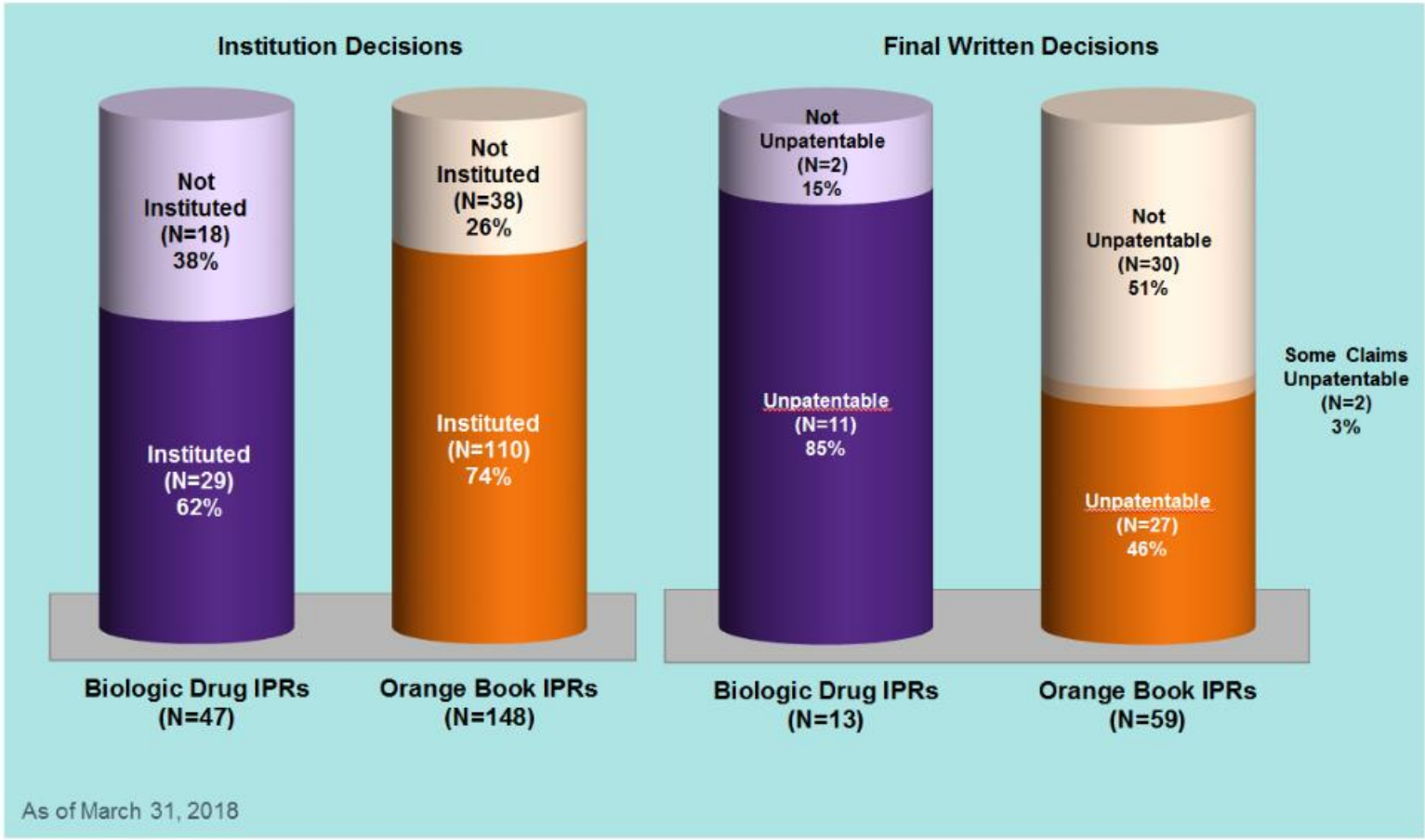
Method of Treatment Claim Challenges



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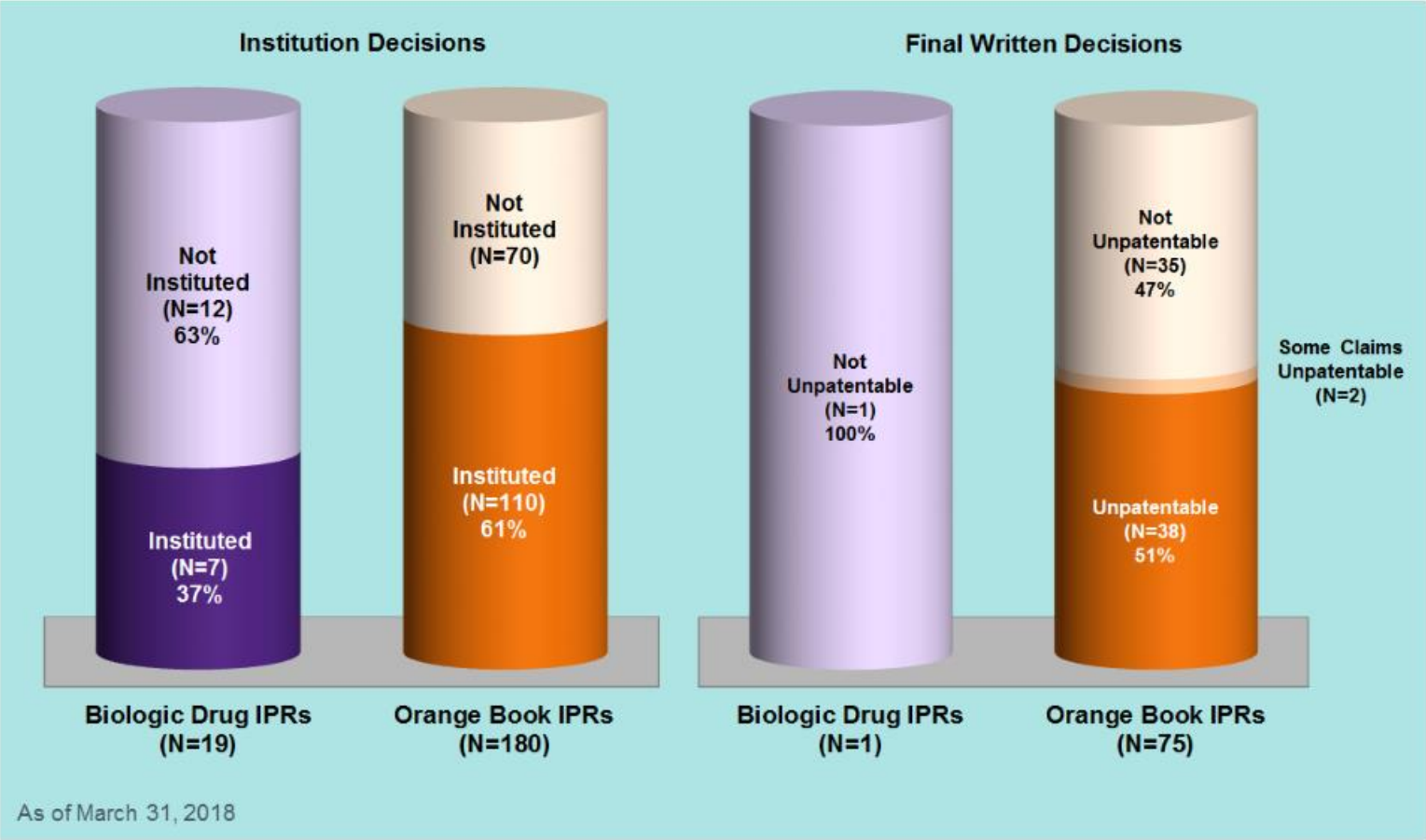
Formulation Claim Challenges



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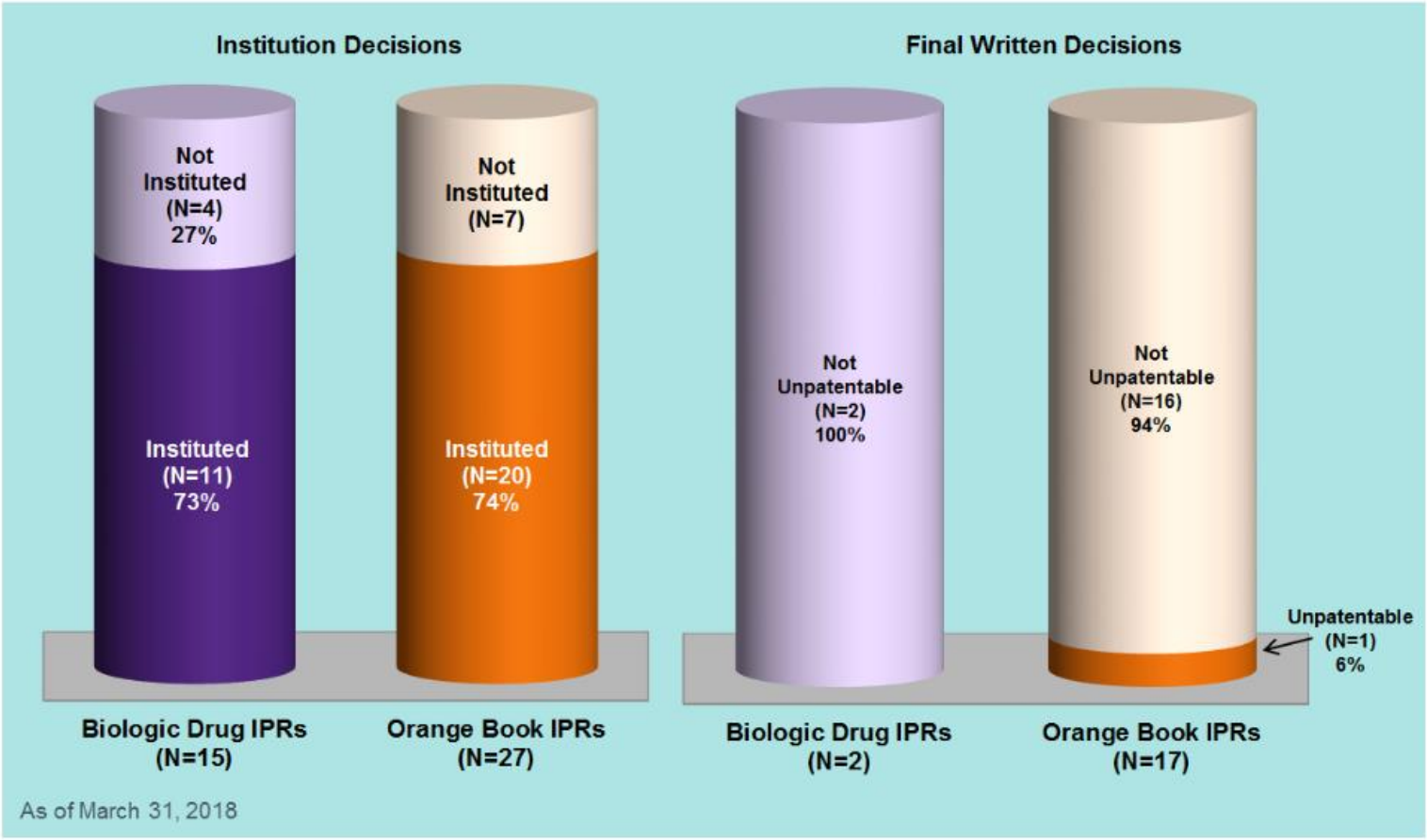
Composition of Matter Claim Challenges



Petitioner considerations

- IPR or PGR vs litigation?
  - Estoppel (no §112 challenges in IPRs)
  - Technical knowledge - PTAB panel has at least one judge knowledgeable in technical field
  - Speed of resolution
  - Discovery
- When to file IPRs?
  - Before aBLA approval? How far in advance of approval?
  - Within 12 months after suit?
- File own petition or request joinder?

Patent Owner Considerations

- File a preliminary response?
- With declaration evidence?
- Request discovery for RPI or privity issues?
- When and whether to present secondary considerations? How to show nexus?

Recent developments

- Standing – *Momenta v BMS*, compared to *Altaire v. Paragon*
- SAS/estoppel
- Pilot program for motions to amend
- New claim construction standard
- “Printed publications” in view of GoPro v. Contour IP Holding

Momenta Pharmaceuticals v. Bristol-Myers Squibb, Appeal No. 2017-1694 (Fed. Cir. Feb 7 2019)

- Federal Circuit dismissed Momenta's appeal
- When Momenta filed its IPR petition in 2015, it was developing a biosimilar of Bristol-Myers Squibb's Orencia®. The PTAB decided the challenged claims were not unpatentable, and Momenta appealed.
- Momenta terminated its Orencia® biosimilar program in Dec 2018 but retained possible future royalties. The Federal Circuit held there was no case or controversy without "concrete plans" to develop a potentially infringing drug product. *Accord Phigenix v ImmunoGen*, 845 F.3d 1168 (Fed. Cir. 2017) (possible future economic interest does not confer standing)
- Contrast the situation in *Altaire Pharmaceuticals v. Paragon Bioteck*, 889 F.3d 1274 (Fed. Cir. 2018), where the court held that Altaire had standing because of "imminent" and "concrete" injury. Altaire said it planned to file an ANDA and testified to the imminence of an infringement suit.

SAS Institute v. Iancu
200 L.Ed.2d 695 (Apr 2018)

- 5-4 majority of the Supreme Court significantly changed PTAB practice
- In the past, the PTAB believed it had discretion to institute IPR on a claim-by-claim, ground-by-ground basis and therefore could issue final written decisions on only part of the IPR petition.
- Many district courts took the position that estoppel did not apply to the non-instituted grounds.
- Supreme Court held that the AIA statute does not authorize the PTAB to "partially" institute an IPR petition, so the PTAB must review and decide all of the challenged claims if it chooses to institute an IPR.
- *All grounds of an instituted IPR must be decided.*

Pilot program for motions to amend
Request for comments, 83 FR 54319 (Oct 29 2018)

- Within 6 weeks of IPR institution, Patent Owner may file a motion to amend its claims
- Petitioner has 6 weeks to file its opposition
- PTAB will issue a preliminary, nonbinding decision within 1 month.
  - If likely to be denied
    - Patent Owner may revise its motion to amend, or it may reply to the preliminary decision
    - Petitioner may respond to either
    - If motion to amend was revised, Patent Owner reply and Petitioner sur-reply are permitted
  - If likely to be granted
    - Petitioner may file a reply to the preliminary decision
    - Patent Owner may file a sur-reply

PTAB changes claim construction standard Final Rule, 83 FR 51340 (Oct 11 2018)

- The final rule replaces the "broadest reasonable interpretation" standard previously used at the Patent Office with the federal court claim construction standard that is used to construe a claim in a civil action under 35 U.S.C. § 282(b), as articulated in *Phillips v. AWH Corp.*, 415 F.3d 1303 (Fed. Cir. 2005) (en banc).
- The same claim construction standard will be used for proposed substitute claims in a motion to amend.
- The PTAB will consider any prior claim construction made in a proceeding in district court, or the ITC, if that is timely made of record.
- The rule applies to IPR, PGR, and CBM petitions filed on or after November 13, 2018.

GoPro, Inc. v. Contour IP Holding LLC (Fed. Cir. Nov 1, 2018)

- GoPro distributed a catalog at trade shows for action sports vehicles
- PTAB held it was not a printed publication because the show was a dealer show, and persons of ordinary skill would not be interested in it because it was not an academic or camera industry conference.
- Federal Circuit *reversed*, holding that GoPro had shown its catalog was a printed publication. There was testimony that there were over 150 vendors, 1,000 attendees, and that GoPro displayed and distributed hundreds of copies of the catalog without restriction
- "the standard for public accessibility is one of 'reasonable diligence' [] to locate the information by 'interested members of the *relevant* public."

Thank you

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