



Biopharma Patent Updates

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Technical Minds. Legal Muscle.

Patents Typically Involved in Hatch-Waxman Proceedings

- Compound (including polymorphs and salts)
- Method of treatment (must be directed to the approved indication)
- Pharmaceutical compositions

Patents That Have been Involved in Biosimilar Litigations*

- Methods of treatment
- Formulations
- Methods of making
- Dosing regimens
- Purification
- Alternative patient dosing
- Biomarkers

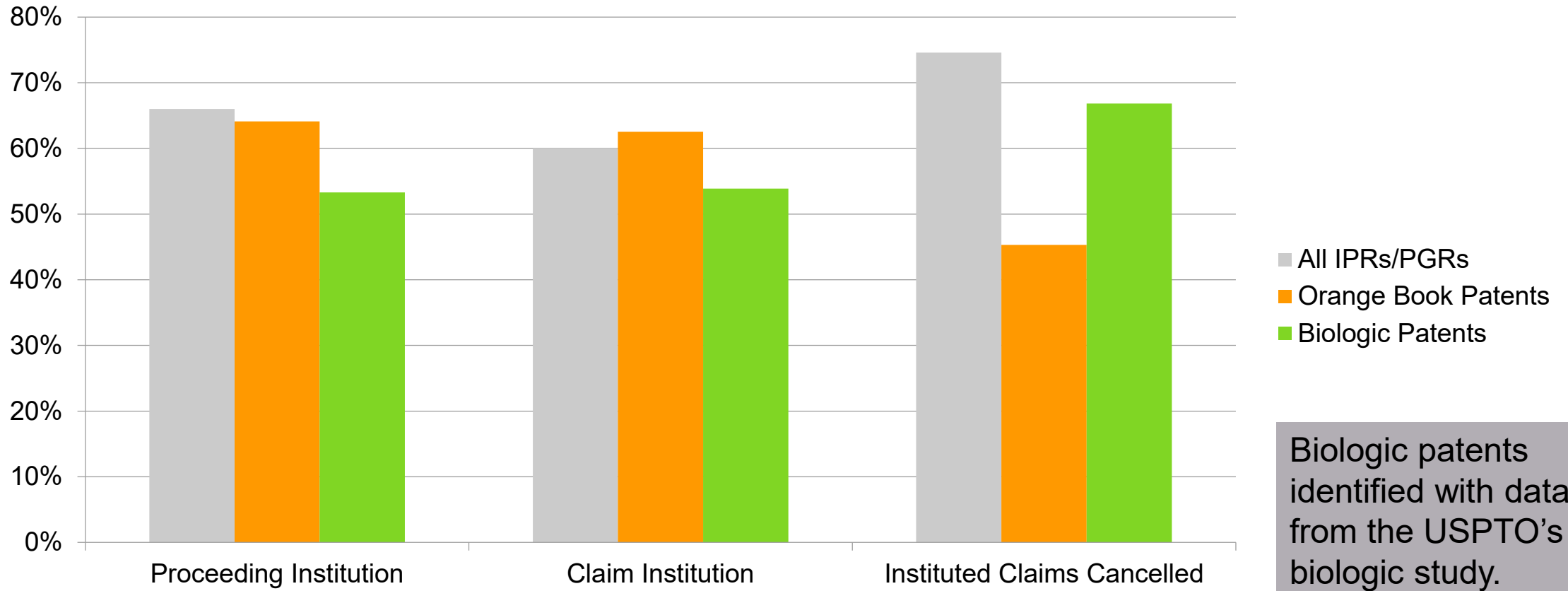
*Compiled from litigations involving biosimilars to Humira[®], Avastin[®], and Herceptin[®]

TC1600 Compared to All IPRs (Through Aug 2019)

- Institution rates in TC1600 have been slightly lower than for IPRs in general for institution decisions to date:
 - **60%** of proceedings instituted in TC1600 and **57%** of claims instituted
 - **66%** of proceedings instituted and **60%** of claims instituted for all IPRs
- When the Board reaches a Final Written Decision and decides whether the Petitioner has met its burden (not counting amended claims, settlements, request for adverse judgment, etc.):
 - The PTAB cancels **51%** of instituted claims in TC1600
 - The PTAB cancels **75%** of instituted claims in all IPRs

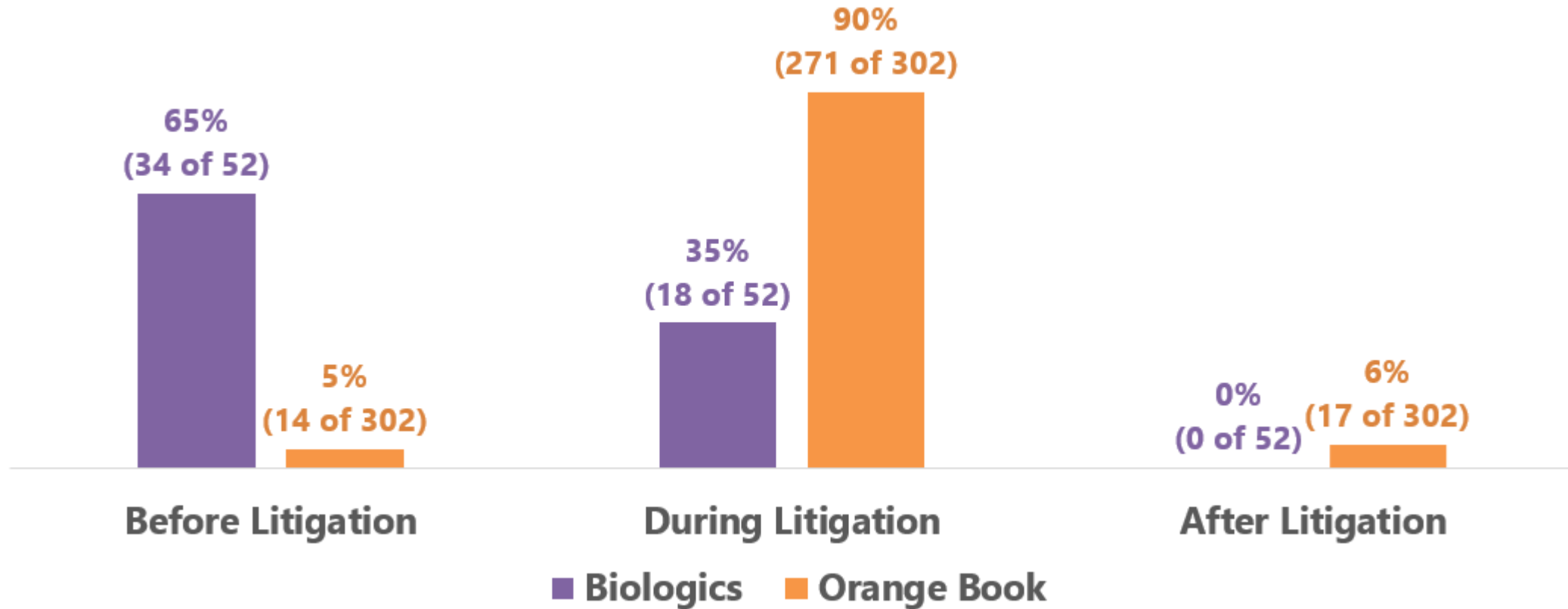
Joinder petitions and other multiple petitions filed against the same patent are included above.

Orange Book and Biologic Patent PTAB Outcomes (Through Aug 2019)



Joinder petitions and other multiple petitions filed against the same patent are included above.

When Were IPR/PGR Petitions Filed Relative to District Court Litigation?*



*From USPTO's Orange Book/patent biologic patent study and district court pharma litigation study published July 18, 2019

Pharma IPR/PGR in More Detail

- Reviewed IPRs/PGRs petitions filed on patents in Art Unit 1600 (through May 31, 2019)
- Includes patents not listed in the Orange Book or asserted in a litigation involving a biosimilar product
- Categories of patents challenged:
 - Compound Patents
 - Formulation Patents
 - Method of Treatment Patents
 - Dosage Regimen Patents
 - Process & Manufacture Patents
 - Polymorph Patents
 - Purification & Cell Line Patents

% Pharma Patents with Proceedings Instituted & % Claims Instituted/Claims Canceled

Patent Category*	% Proceedings Instituted	% Claims Instituted	% Instituted Claims Canceled
Total Patents (442)	61%	59%	51%
Compound Patents (72)	58%	65%	22%
Formulation Patents (162)	57%	57%	57%
Method of Treatment Patents (131)	68%	65%	43%
Dosage Regimen Patents (84)	60%	58%	24%
Process & Manufacture Patents (39)	68%	55%	69%
Polymorph Patents (1)	0%	0%	N/A
Purification & Cell Line Patents (17)	59%	42%	54%

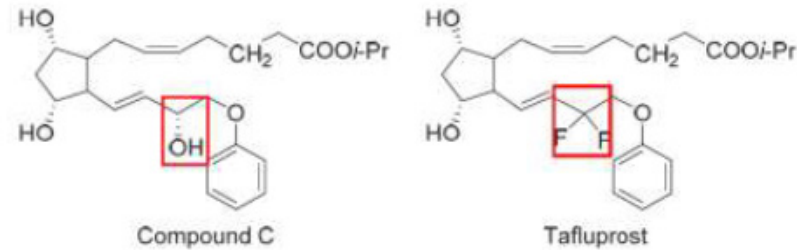
*Numbers in parenthesis are the numbers of particular patents. In our analysis, if a petition was filed challenging the validity of independent claims to different subject matter, the patent was counted for both categories (for example a patent with an independent claim to a compound and a separate independent claim to a method of treatment would be included for both categories)



Representative PTAB Decisions

Micro Labs Ltd. v. Santen Pharm. Co., Ltd., IPR2017-01434, Paper No. 53 (November 27, 2018)

- Claim to tafluprost



- Final Written Decision: Claims not shown to be unpatentable because medicinal chemistry is unpredictable, especially with respect to prostaglandins
 - PTAB assumed Compound C to be lead compound
 - Prior art Petitioner cited recognized that seemingly slight structure differences led to greatly different activity and side effects
- Takeaways:
 - PTAB will apply a lead compound analysis to an obviousness attack on compound claims
 - Should consider making “no lead compound” arguments in prosecution to set the stage for a PTAB defense
 - Consider submitting data showing “minor” changes to structure in the part of the structure that interacts with the receptor has impact on activity/toxicity

Celltrion, Inc. v. Genentech, Inc., IPR2017-01139, **Paper No. 68 (October 3, 2018)**

- Claims generally directed to a method for the treatment of a human patient diagnosed with cancer characterized by overexpression of ErbB2 receptor comprising administering to the patient an initial dose of at least approximately 5 mg/kg of an anti-ErbB2 antibody and a plurality of subsequent doses of the antibody in an amount that is approximately the same or less than the initial dose, wherein the subsequent doses are separated in time by at least two weeks.
- Final Written Decision: Claims not shown to be unpatentable because POSA would not have had a motivation to modify known **trastuzumab dosing** regimens
 - Petitioner has not explained why a POSA would apply a chemotherapy dosing strategy to trastuzumab, a targeted antibody treatment
 - Only prior art cited by Petitioner suggested increasing the period the dose is to be administered, not increasing the dose intensity
 - Prior art taught that trastuzumab should be dosed to maintain a minimum trough concentration over the entire dose interval, so POSA would not have wanted to have higher peaks and lower trough concentrations which would result from the claimed regimen
- Takeaway: Focus on how art as whole is going in different direction than invention

***Celltrion, Inc. v. Biogen, Inc.*, IPR2017-01094, Paper No. 12 (October 2, 2017)**

- Claims directed to treating subpopulation of non-Hodgkin’s Lymphoma (NHL) cancer patients, i.e. patients with bulky disease
- Institution Denied:
 - Cited prior art discloses population of NHL, which would include patients with bulky disease
 - Petitioner did not show that cited prior art discloses treating particular subpopulation
- Takeaways:
 - Prior art teaching treatment of a disease generally does not necessarily render obvious a method of treating a well-known subtype of that disease
 - Consider claims to subpopulations and disease subtypes that will appear in the product label as stand alone applications to extend product exclusivity
 - Avoid “prophetic disclosure” of long lists of disease subtypes in earlier applications

Biodelivery Sciences International, Inc. v. Aquestive Therapeutics, Inc. f/k/a Monosol RX, LLC, IPR2015-00169, Paper No. 89 (February 7, 2019)

- Claims at issue required “substantially uniform distribution” of an active component within a film layer as determined by substantially equal sized individual unit doses
- Institution denied:
 - Petitioner argued *inter alia* that prior art teaches forming a homogeneous mixture to make a film, so maintaining uniformity in the intermediate steps and in the final product would have been obvious.
 - PTAB held that prior art did not expressly or inherently describe a film having a uniform distribution of active agent
 - Petitioner and its expert did not direct PTAB to a clear or specific teaching in the prior art that the measure of “uniformity” is the same measure as that required by the claims
 - Petitioner and its expert did not direct PTAB to a clear teaching that the prior art actually satisfy the uniformity requirement of the claims
 - Prior art “at best demonstrates a degree of likelihood that [prior art’s] films would meet the standard of uniformity
 - Petitioner did not establish which particular variables would have been optimized to maintain substantial uniformity
- Takeaway: Focus on “unpredictability” in prior art and outcome is not necessarily a result of prior art

Takeaways from Decisions

- A high percentage of second and third generation patents are withstanding scrutiny at the PTAB
- Patents requiring an inherency or routine optimization basis for obviousness are surviving at a relatively high rate at the PTAB – consider filing applications, e.g., impurity profiles, dosing regimens, polymorphs (for small molecules) that have strong positions for unpredictability and/or no inherency
- PTAB generally reacts favorably to evidence establishing “unpredictability” in the field. Tends to negate routine optimization. PTAB holds petitioners to a higher standard to establish unpatentability than Examiners apply.
- Petitioners have generally been unsuccessful in establishing an “inherent” feature is in prior art -- PTAB tends to see evidence as establishing at most a probability the limitation is met, which is insufficient.
- Evaluate whether prior art directed a POSA in a different direction than that taken by the inventors
- Narrow claims may have “nexus” to establish secondary considerations to rebut Petitioner’s obviousness argument