

Intellectual Property in Precision Medicine

Arti K. Rai, Elvin R. Latty Professor; Founding Director,
Center for Innovation Policy, Duke Law School



(with Colleen Chien)

Supreme Court “Section 101” decisions

- *Mayo v. Prometheus* (2012)
- *CLS Bank v. Alice* (2014)
- Step 1: Does the patent claim encompass: law of nature; product of nature; abstract idea
- Step 2: If so, does it have an “inventive concept” or “additional elements” that go beyond unpatentable law of nature, product of nature, abstract idea

The View from Lawyers

Since 2012, a series of U.S. Supreme Court decisions...have left innovators in the biotechnology and software industries unable to secure patent protections for many of their inventions. Since patents play a critical role in driving innovation, these decisions have potentially far-reaching implications for the U.S. economy.



IPWatchdog®

PLI
PRACTISING LAW INSTITUTE
Taught by John White & Gene Q

Topics

Inventors

Tech

Events

Politics

Jobs



The Supreme Court's Section 101 Jurisprudence: Dangers for the Innovation Economy



By Gene Quinn
December 1, 2016

[Print Article](#)



PATENT ELIGIBLE SUBJECT MATTER:
REPORT ON VIEWS AND
RECOMMENDATIONS FROM THE PUBLIC

United States Patent and Trademark Office

July 2017

A majority [of participants] recommended legislative change. A call for legislation **was particularly strong from the life sciences industry** but also had many supporters from computer-related industries. According to these participants, **the Court's precedent is having such a harmful impact on innovation and business development that a legislative solution is critical.**

[PATENT BLOG](#) [JOBS](#)

PATENTLYO

[ETHICS](#) [JOURNAL](#)

The Need for Legislative Reform: The Berkeley Section 101 Workshop

© October 10, 2017  [Dennis Crouch](#)

Assessing the Need for Legislative Reform of Patent Eligibility in the Mayo/Alice Era: Final Report of the Berkeley Center for Law & Technology Section 101 Workshop [[Read the Full Report](#)]

By Jeffrey A. Lefstin, Peter S. Menell, and David O. Taylor

Over the past five years, the Supreme Court has embarked upon a drastic and far-reaching experiment in patent eligibility standards. Since the founding era, the nation's patent statutes have afforded patent protection to technological innovations and practical applications of scientific discoveries. However, the Supreme Court's 2012 decision in *Mayo Collaborative Services v. Prometheus Laboratories* imposed a new limitation on the scope of the patent system: that a useful application of a scientific discovery is ineligible for patent protection unless the inventor also claims an "inventive" application of the discovery. The following year, the Court ruled that discoveries of the location and sequence of DNA compositions that are useful in diagnosing diseases are ineligible for patent protection. And in its 2014 *Alice Corp. v. CLS Bank International*

The current state of patent eligibility jurisprudence is indefensible

Patently-O Authors

Dennis Crouch
Associate Professor, University of Missouri School of Law

SSRN Articles

Jason Rantanen
Professor, University of Iowa College of Law

SSRN Articles

Occasional guest posts by IP practitioners and academics

Popular Tags

[Abstract Idea](#)

[Administrative Law](#) [Affirmed](#)

nearly all of the conferees recognized that **this state of the law poses serious concerns for bioscience research and development**

Also . . .

- Regulatory uncertainty
- Reimbursement challenges

Motivating Question

How have Court decisions, other uncertainty affected patenting behavior and other metrics?

Caveats

- 1) Metrics not (necessarily) the same as innovation
- 2) Because of regulatory, reimbursement complications in time frame, cannot make causal claims regarding impact of Court decisions
- 3) Various time lags

Metrics

Patent app counts (and
patent scope) (treatment
vs control)

SEC “Biomarker”

FDA Approvals

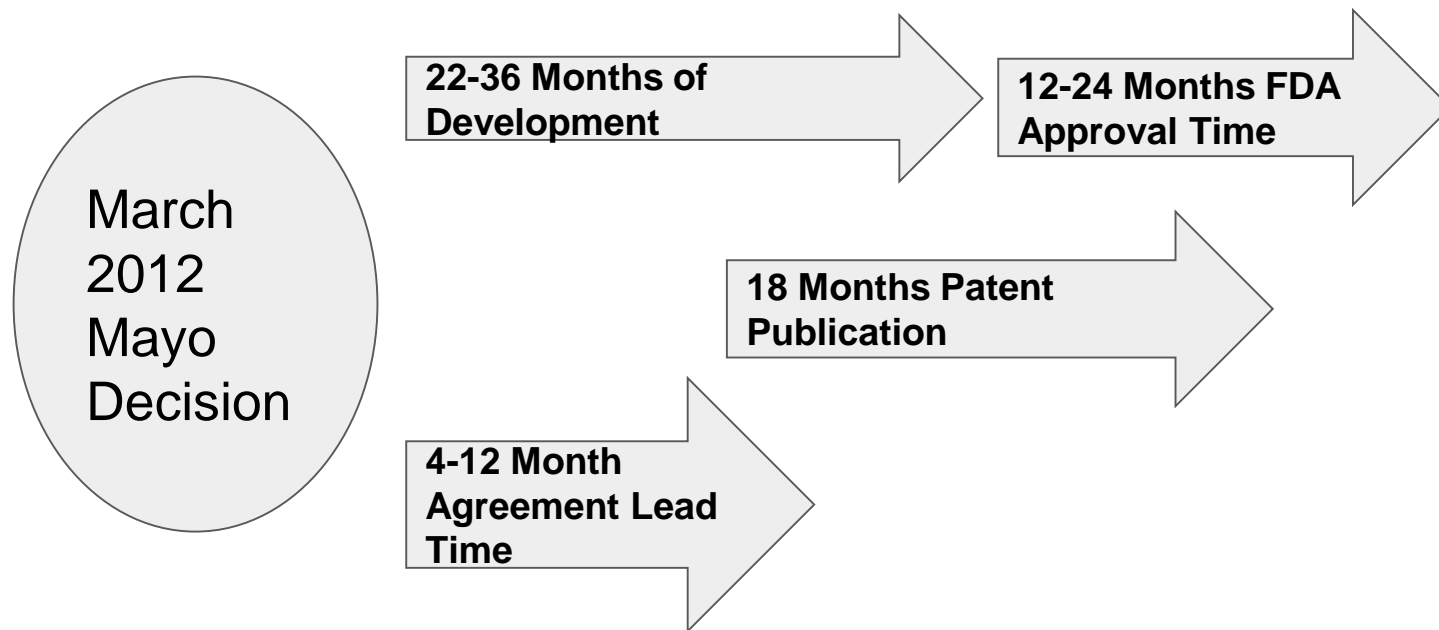
“Med Dx” CPCs (biomarker *correlated* to medically relevant utility)

- G01N2800: Detection or diagnosis of diseases (not including disease caused by micro-organisms where the micro-organism is detected); G01N33/569 (detection of bacteria, viruses); G01N33/571 (detection of venereal disease); G01N33/574 (cancer detection)
- C12Q1/6883 and C12Q1/6886 (using nucleic acids to test for disease) (biggest category; 96% true positive)
- C12Q2600/106, 112, and 118 (short nucleic acid sequences used for characterizing disease)

“Control” CPCs (TC 1600 generally)

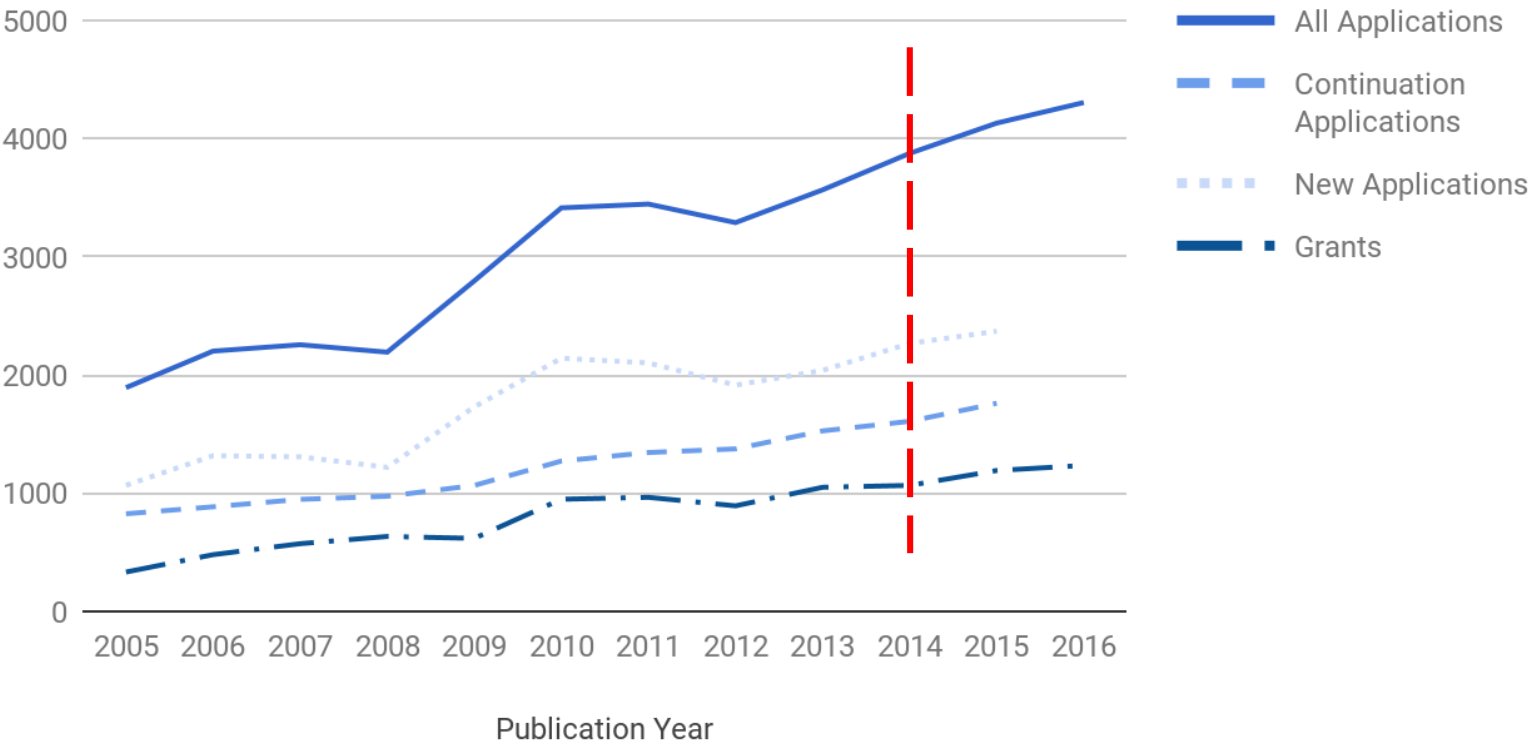
Focus on impact of *Mayo*

Assuming immediate impact, how soon would we see impact?



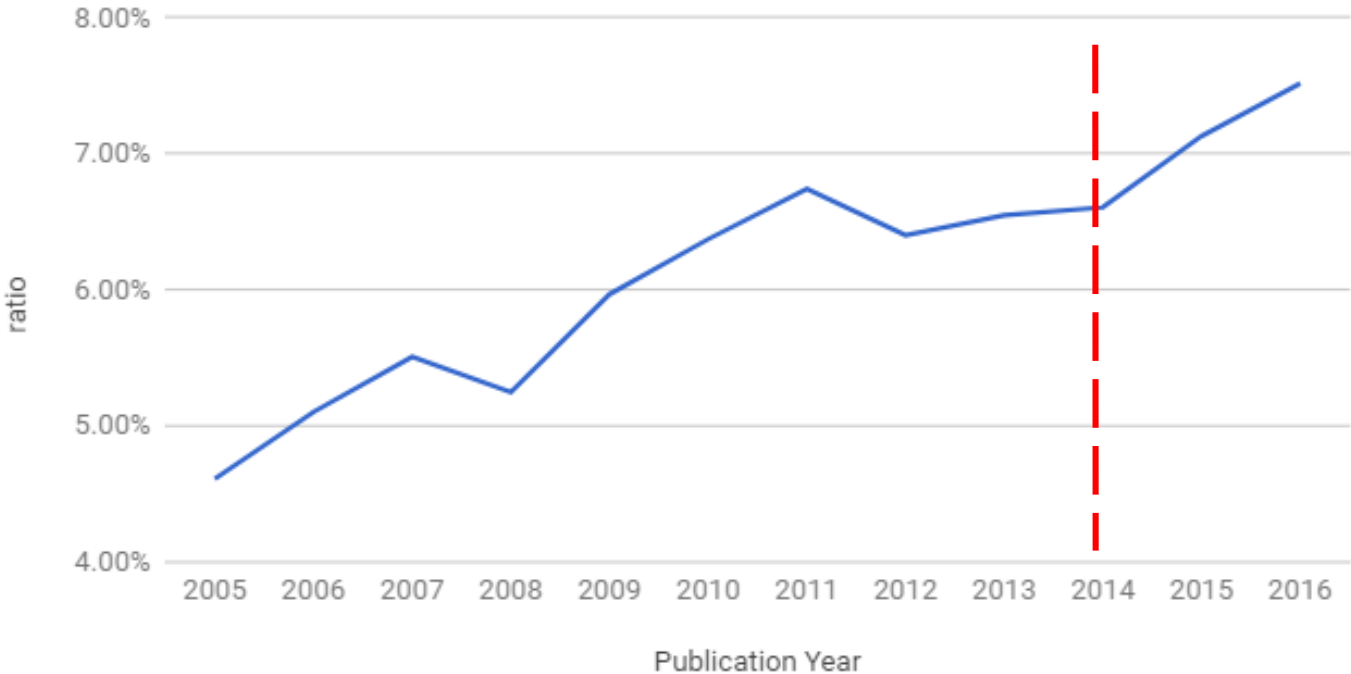
No absolute decline in US Med Dx apps

Fig. 1: US Diagnostic Patent Applications and Grants



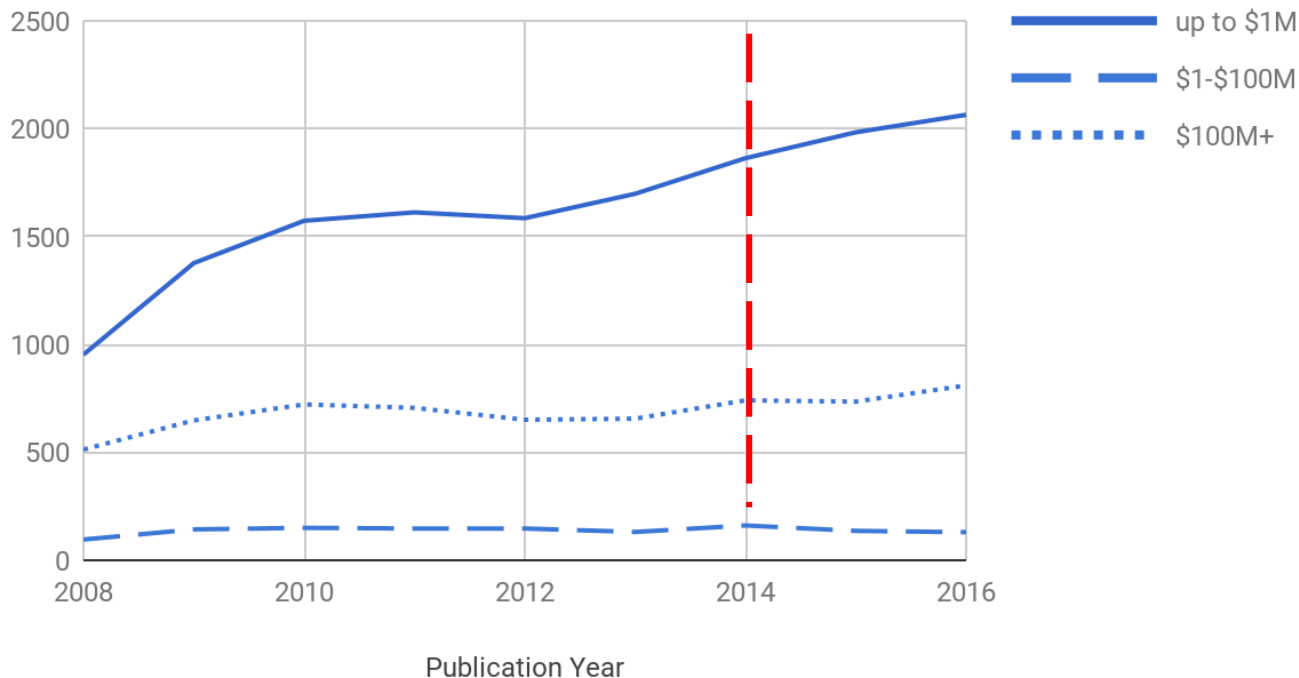
No relative decline in US Med Dx apps (vs. TC1600)

Fig. 2: US Diagnostic as a Share of All TC1600 (Biotechnology) Patent Applications



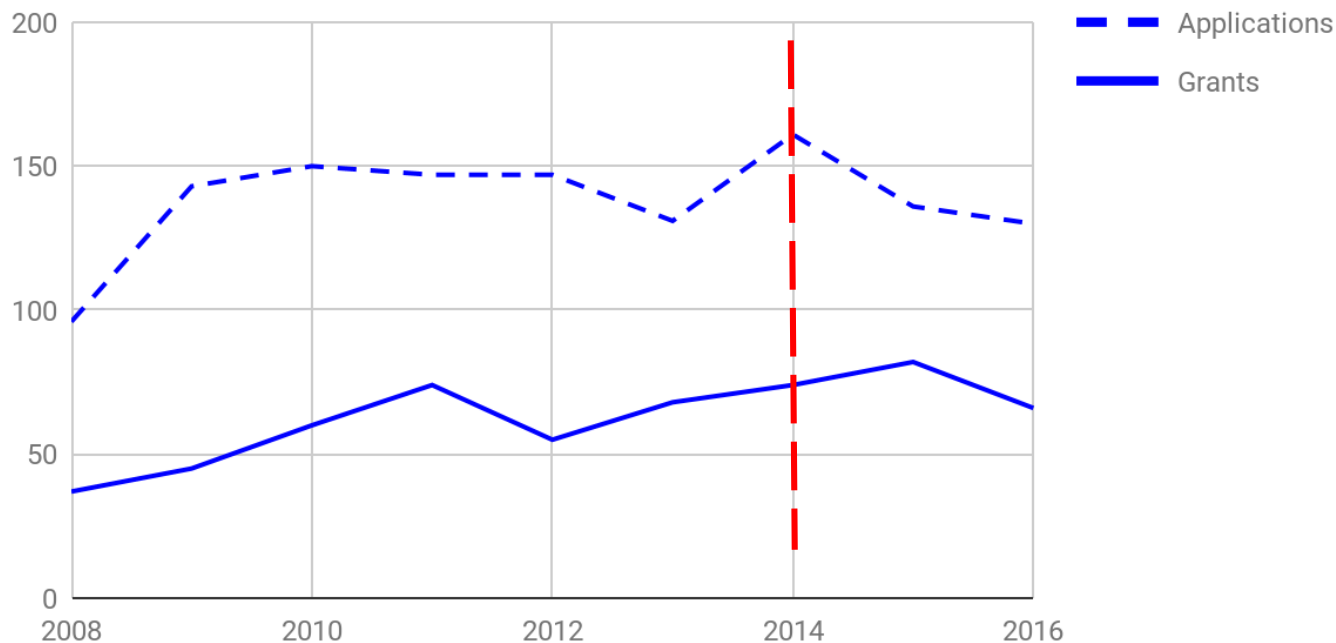
However growth has been uneven across segments... while filings by nonprofits and large companies have grown...

Fig. 3: US Diagnostic Patent Applications by Revenue



Firms with \$1M-\$100M in revenue have experienced uneven growth/slight declines

Fig. 4: US Diagnostic Patent Applications and Grants of Firms with \$1M-\$100M in Revenue



Has the scope of US protection **narrowed**, relative to the EPO?

Measure narrowing through longer claims

US8906625 (“genes involved in estrogen metabolism”)

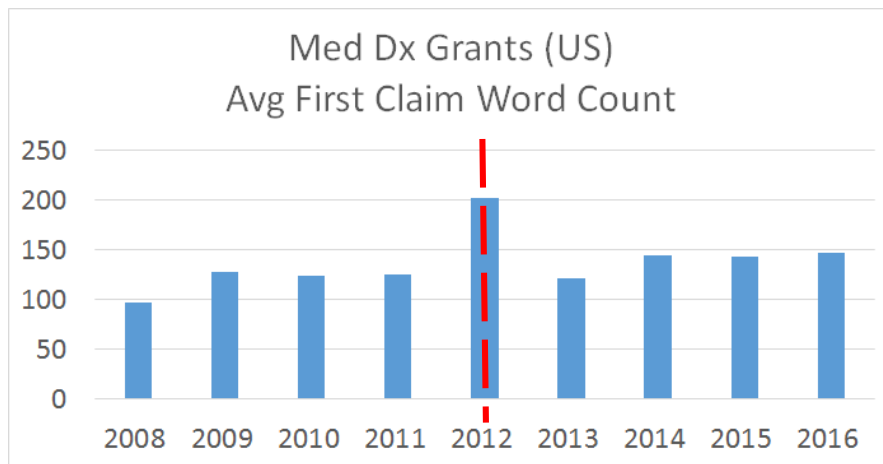
-
- | | |
|---|--|
| <p>1. A method of predicting the likelihood of cancer recurrence for a human subject diagnosed with breast cancer, comprising: assaying a level of an RNA transcript of voltage-dependent anion channel 1 (VDAC1) in a tumor sample obtained from said subject using a primer comprising a nucleotide sequence selected from SEQ ID NO:334 and SEQ ID NO:335; normalizing the level of an RNA transcript of VDAC1 against the expression level of one or more reference genes to obtain a normalized expression level of VDAC1; using the normalized expression level of VDAC1 to generate information comprising a prediction of cancer recurrence for said subject, wherein the normalized expression level of VDAC1 is positively correlated with an increased likelihood of cancer recurrence.</p> | <ul style="list-style-type: none">• Filed in 2010• Bolded language overcame <i>Mayo</i> rejection (“examiner comments”) |
|---|--|
-

US8765383 (“methods of predicting cancer risk using gene expression in premalignant tissue”)

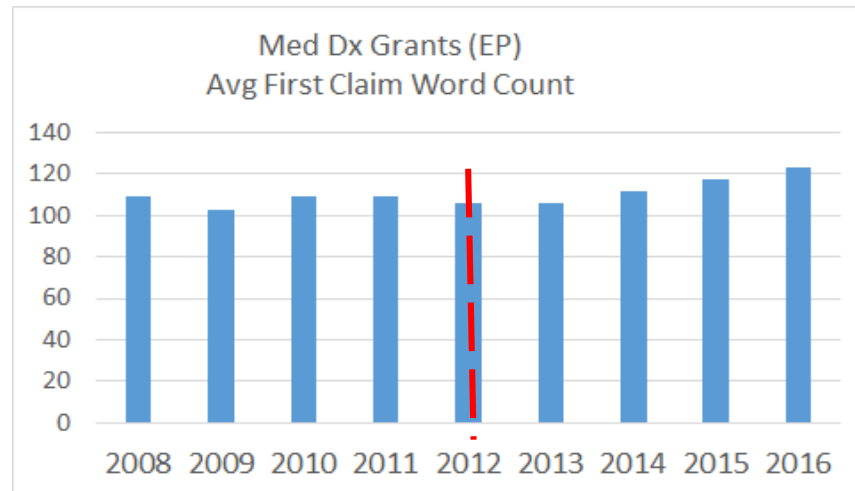
1. A method for determining cancer risk for a human patient, comprising: **analyzing a sequence of BRAF in a tissue sample obtained from a premalignant lesion from the lower gastrointestinal (GI) tract of the patient to detect a V600E mutation**; measuring a level of an RNA transcript of DUSP6, or its expression product, in the tissue sample; normalizing the level of the RNA transcript of DUSP6, or its expression product, against an expression level of at least one reference gene, to obtain a normalized expression level of DUSP6, comparing the normalized expression level of DUSP6 from the patient to the normalized expression level of DUSP6 in a population with no cancer; and determining that the patient has an increased cancer risk if the normalized expression level of DUSP6 from the patient is increased, or that the patient has a decreased cancer risk if the normalized expression level of DUSP6 from the patient is decreased.
-
- Bolded language overcame *Mayo* rejection
 - *European counterpart* (intention to grant announced) (EP2417271)
 - For EPO, limitation of “sequence of BRAF from biological sample to detect a V600E mutation” introduced in dependent claim ONLY

Finding: Avg 1st claim length has increased in the PTO and EPO (more in PTO)

Issued Patent Avg 1st Claim Length



18% increase since 2011



13% increase since 2011

Has the scope of US protection **narrowed**, relative to the EPO and the pre-treatment period?

Both EPO and US issued claim lengths are growing; US claim length has grown more than EPO claim length

Is it easier to get a Dx patent in Europe than in the US now?

No clear evidence

Abandonment/withdrawal rates among the European twin within the pair is higher than the abandonment/withdrawal rate among the US twin. However time effects make the sample size too small to draw strong conclusions.

How has 101 caselaw impacted US prosecution rel to EPO prosecution?

Preliminary results based on case study of 10 resolved cases in the EPO and USPTO, 7 with 101 rejections

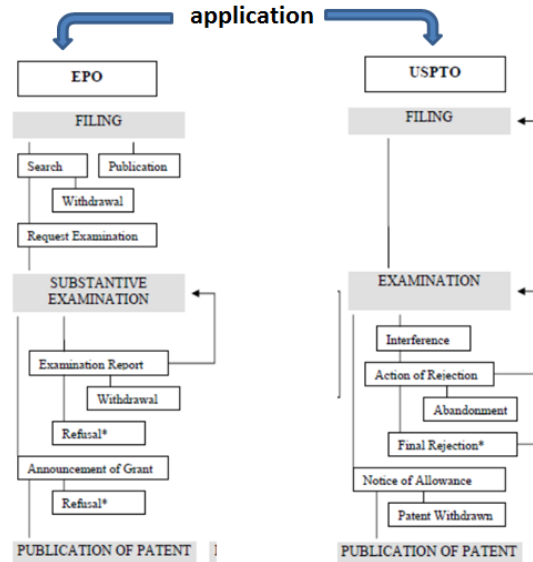
EPO outcome re 7

- 4 grants
- 3 withdrawals, bases:

--- 53(c) (subject matter)*

--- inventive step

--- novelty + unity of invention

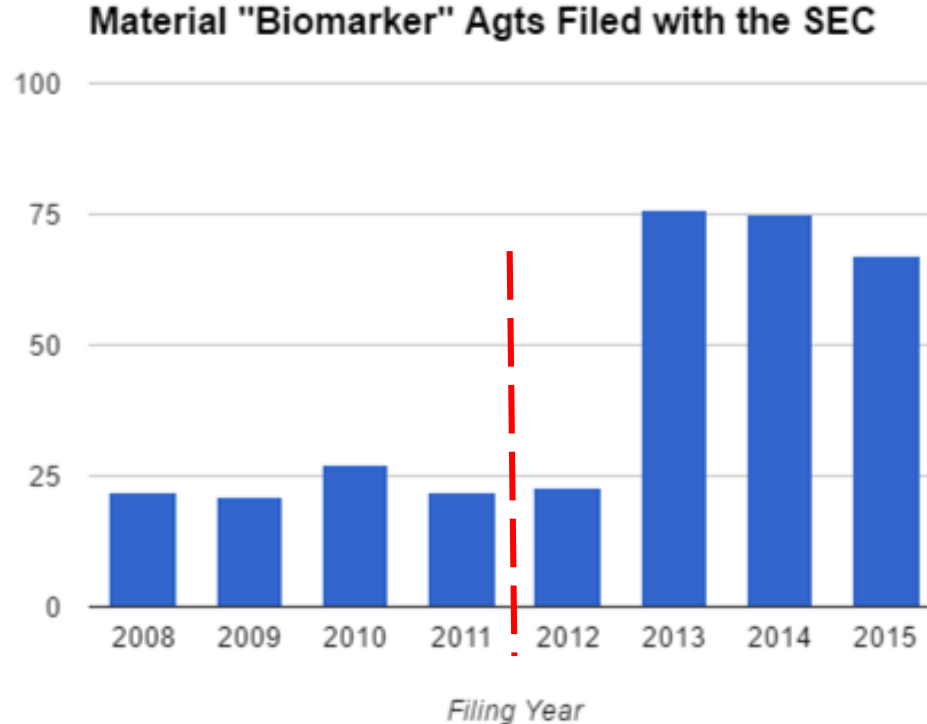


USPTO outcome re 7

- 5 grants
- 2 withdrawals (based on 101)

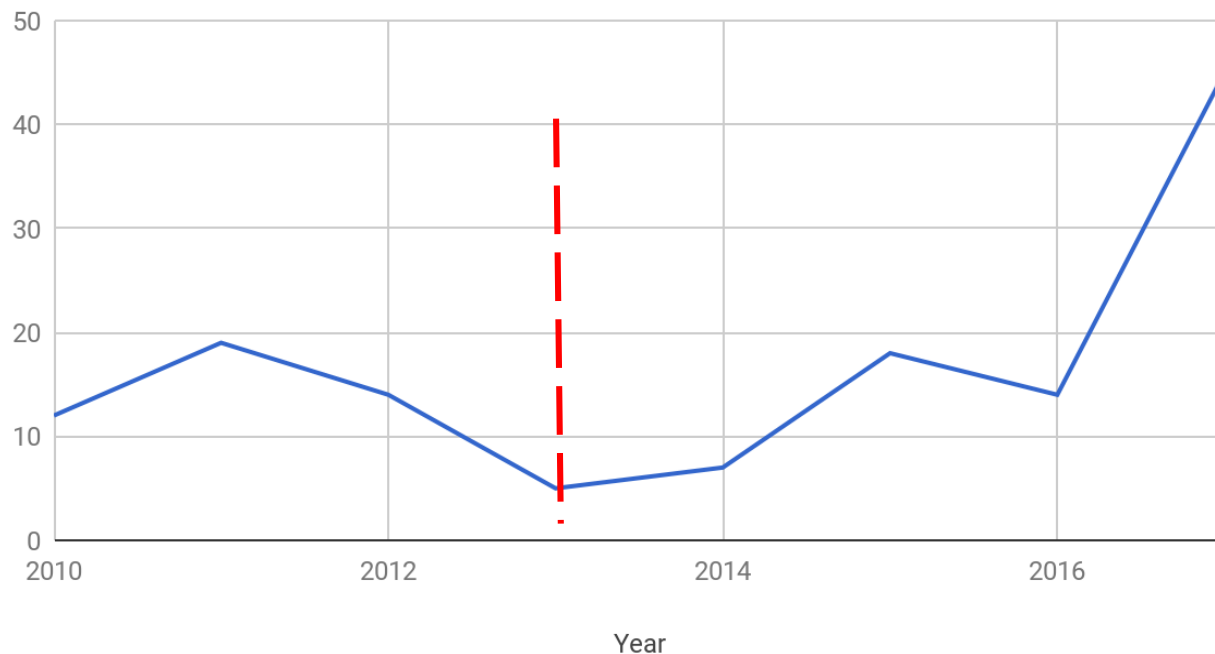
Has there been a **decline** in innovation, measured by material transactions?

Has there been a **decline** in innovation, measured by material transactions?



Has there been a **decline** in innovation, measured by material FDA Approvals?

Fig 7A: FDA Device "Diagnostic" Approvals - All



Has there been a **decline** in innovation, measured by material transactions or approvals?

No clear evidence

Recorded “biomarker” transaction and approvals are up.

Tentative Conclusions

- Large firms, nonprofits continue to file
- Some decline for smaller firms
- Scope has narrowed more in US than EU
- Unclear if it's easier to get patent in EU
- Biomarker agreements, approvals up (but lag problem for approvals)