The Benefits of Japanese Patent Law System Over those of the US in the Pharmaceutical Area

What can we do to maximize the benefits?

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“Long Long Time Ago”

- **Poor Prosecution**
  - Slow, Claim scope narrow if granted at all, claim types not sufficient

- **Weak Enforcement**
  - Court proceedings took forever; Infringement/damages hard to prove; Damages minimal

Regarding Enforcement:

October 1994 – US Commissioner of Patents Bruce Lehman:

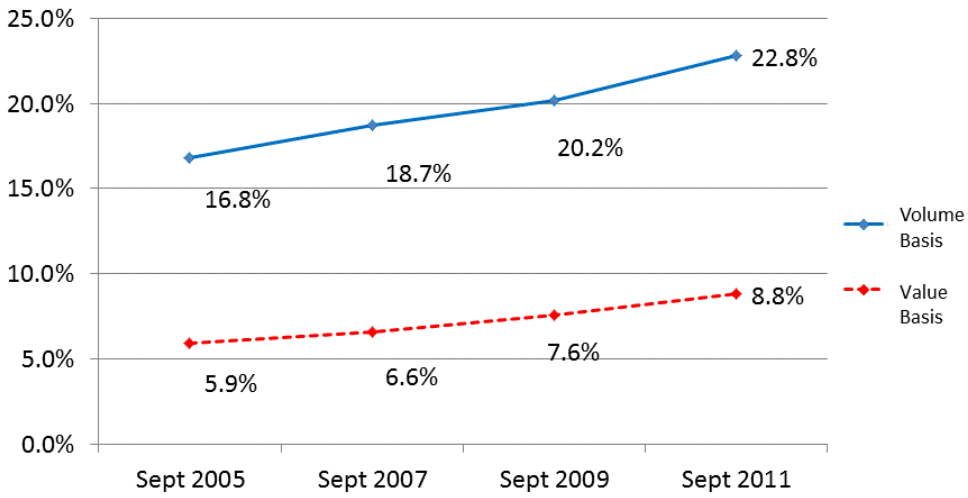
“…the relative nonlitigiousness of Japanese society tends to minimize the importance of enforcement...US citizens holding Japanese patents should be able to rely on those patents more than their US patents…”

Circa late 1990’s, JPO Commissioner Tekashi Isayama admitted:

“The Japanese market is dishonorably regarded as ‘lenient towards infringement’. It is sometimes said that one may as well infringe whatever patents he likes in Japan, because court proceedings are slow and compensation insignificant”
(taken from Mr Shusaku Yamamoto’s post)

Trends in the Market Share of Generic Drugs

Unit of measurement : %



Source: Survey by the Ministry of Health, Labour and Welfare

- Aging population and attendant increase in healthcare cost, Japanese government started to aggressively promote the use of generic drug since 2007
- More numbers:
  - Sept 2016 – about 60% (by volume)
  - Japanese government wants to increase the use to 80% in fiscal year 2018-2020!
- Patents are the only effective tools available to prevent the entry of generics
  - Unlike in prior to 2007, opportunity cost of "not getting things right" in Japan could be enormous

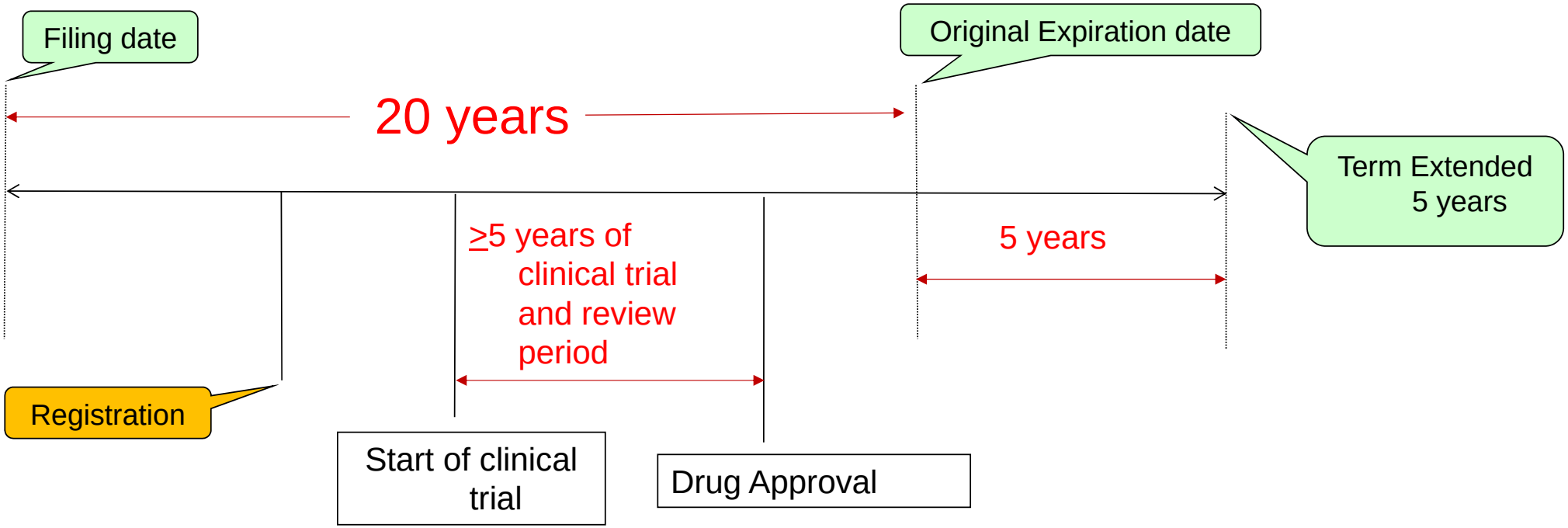
Comparison Between US v Japanese Patent Term Extension System

- Both in Japan and US, if a drug undergoes clinical trial and review period, the patent which covers the drug can be extended up to 5 years.
  - However, overall the Japanese system can offer better protection

- Japanese Patent Law Article 67 (2): Where there is a period during which the patented invention is unable to be worked because approvals [is needed]… to ensure the safety [of pharmaceuticals]…, patent right may be extended … by a period not exceeding 5 years.
  - Another improvement: Recent amendment to JP Patent Law took away requirement for at least two years of clinical trial

- US Patent Law 35 USC § 156: Up to five years of extension for (1) ½ of IND (Investigational New Drug) period and full review period; but (2) total period of remaining patent term including the extension cannot exceed 14 years from approval; and (3) only one patent extension for one product (active ingredient).

Outline of the Japanese PTE system



- HUMIRA – Abbvie product (9 indications) – 2015 worldwide sale $12.5 billion (ex-US about $4.5 billion)
- Even one day of PTE could make huge difference in revenue

Japanese PTE system is overall more favorable!

Japan

- Full 5 years – if clinical trial period + review period are 5 years or more (and patent registration occurs before these periods)
- Allows multiple PTEs for same active ingredient directed to e.g. new formulation, dosage, use, etc.
- Same patent can be extended multiple times covering different approved active ingredient

US

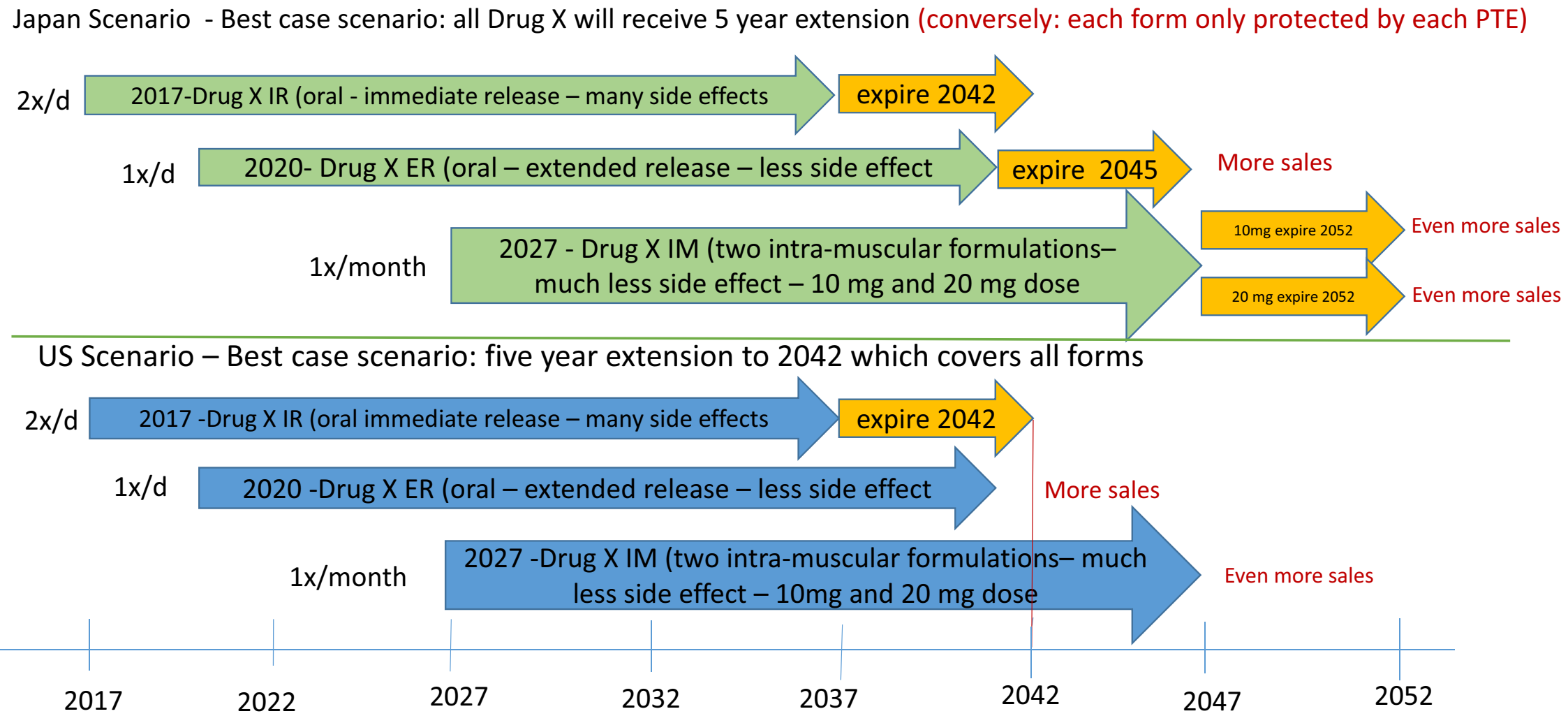
- Even if in Japan get 5 years, US could be under 5 years
  - ½ of IND period
  - 14 year cap from approval
- Allows only one PTE per active ingredient
- No extension for the patent already extended once even if it covers different approved active ingredients

HUMIRA JP patents - multiple and longer extensions

- In US, base case expired and many companies including Amgen filed for biosimilar applications
- In Japan, Kyowa Hakko/Fujifilm developing Humira biosimilar

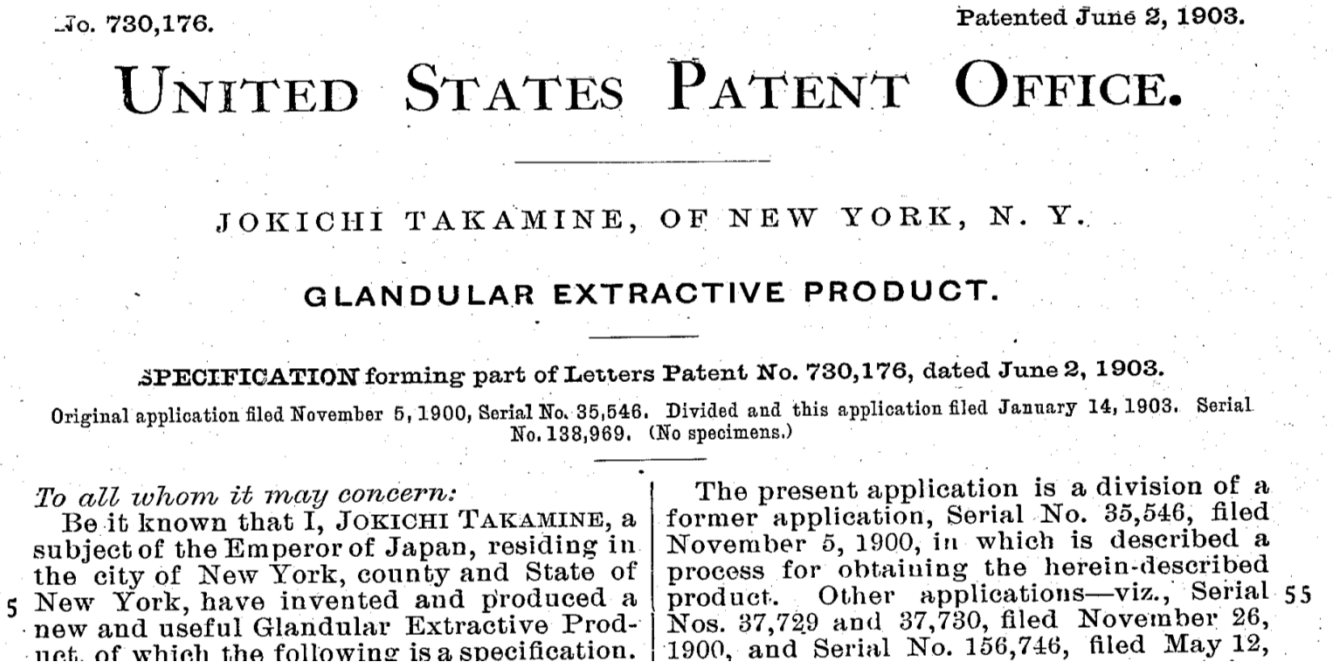
One patent family	Normal expiration	No of Extensions /patent	Actual latest expiration
US6090382 (base case)	2/09/2016	One (no other patents extended)	12/31/2016 (326 days)
JP Counterparts			
JP3861118	2/10/2017	7	8/20/2021
JP4404181	2/10/2017	9	9/10/2020
JP4890997	2/10/2017	2	8/1/2018
JP5422501	2/10/2017	None (recently granted)	2/10/2017
JP56899902	2/10/2017	None (recently granted)	2/10/2017
JP5759526	2/10/2017	None (recently granted)	2/10/2017
JP5951056	2/10/2017	None (recently granted)	2/10/2017

Comparison of Exclusivities US v Japan
Hypothetical Anti-arthritic Drug X's (all same active ingredient)



Current Risks Affecting Pharmaceutical, Diagnostic, and Nutraceutical Companies in the US

- Since 19th century, US patent office has granted patents on “products” found in nature isolated by man
- US730176 - adrenaline “practically free from…associated gland tissue” (issued 1903)



No. 730,176. Patented June 2, 1903.

UNITED STATES PATENT OFFICE.

JOKICHI TAKAMINE, OF NEW YORK, N. Y.

GLANDULAR EXTRACTIVE PRODUCT.

SPECIFICATION forming part of Letters Patent No. 730,176, dated June 2, 1903.

Original application filed November 5, 1900, Serial No. 35,546. Divided and this application filed January 14, 1903. Serial No. 138,969. (No specimens.)

To all whom it may concern:

Be it known that I, JOKICHI TAKAMINE, a subject of the Emperor of Japan, residing in the city of New York, county and State of New York, have invented and produced a new and useful Glandular Extractive Product, of which the following is a specification.

The present application is a division of a former application, Serial No. 35,546, filed November 5, 1900, in which is described a process for obtaining the herein-described product. Other applications—viz., Serial Nos. 37,729 and 37,730, filed November 26, 1900, and Serial No. 156,746, filed May 12,

- US2449866 – claim 13: streptomycin (issued 1948)

Current Risks Affecting Pharmaceutical Industry, Diagnostic, and Nutraceutical Companies in the US

- USPTO also issued patents on diagnostic methods for human diseases

- But dramatic changes started to occur since early 2010 following:
  - *Mayo v Prometheus* (method of adjusting drug dosage; Supreme Court, 2012);
  - *AMP v Myriad (human genes;* Supreme Court, 2013)
  - *Sequenom v Ariosa* (genetic diagnostics; CAFC 2015, *cert denied*)

  - Uncertainties on patent eligibility on potential important pharmaceutical assets
    - Proteins, antibiotics, and other pharmaceutically active agents found in nature
    - Diagnostics methods for predicting and diagnosing diseases

      - The enforceability of already issued patents not clear
      - Impacting in-licensing, patent filings and maintenance activities

AMP v Myriad – Patentability of Genes

- U of Utah located and isolated BRAC1/2 genes, and discovered mutated forms are associated with ovarian and breast cancer.

- Filed patents on isolated DNA encoding BRAC1/2 (mutated and wildtype) genes, which Myriad licensed

- U.S. 5747282 for BRCA 1
    1. An isolated DNA coding for a BRCA1 polypeptide…set forth in SEQ ID NO:2.
    5. An isolated DNA having at least 15 nucleotides of the DNA of claim 1.

- U.S. 5837492 for BRCA 2 (also US5693473)
    1. An isolated DNA molecule coding for a BRCA2 polypeptide...set forth in SEQ ID NO:2.
    6. An isolated DNA molecule coding for a mutated form of the BRCA2 polypeptide set forth in SEQ ID NO:2, wherein said mutated form of the BRCA2 polypeptide is associated with susceptibility to cancer.

Patent Eligibility

35 U.S.C. § 101 INVENTIONS PATENTABLE

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter….. may obtain a patent…

- But courts have always maintained "judicial exceptions" of (a) pure laws of nature, (b) natural phenomenon, and (c) abstract idea not patentable themselves, but their application patentable.

Supreme Court in *Myriad*

"A naturally occurring DNA… is a product of nature and not patent eligible merely because it has been isolated…."

- BRCA1/2 genes are "law of nature"
- Isolated DNA is not a patentable subject matter under § 101, unless it is significantly different from found in nature. (adopted the analysis of *Mayo*)
  - cDNA is patentable because it not naturally occurring

Examination Guidelines JP vs US

USPTO Interim Guidance on Subject Matter Eligibility

- Dec 2014, Nature–Based Product Examination Guideline (also see May 2016 Life Science Examples)
  - Antibiotic L (protein) – not patent eligible
  - Purified antibiotic L – patent eligible (when purified takes different form)
  - “Purified Amazonic acid” – not patent eligible

Japanese Patent Law

- Article 29 (1),… an invention that is industrially applicable may be entitled to… a patent....
- Article 2, paragraph 1 defines invention as "the highly advanced creation of technical ideas by which a law of nature is utilized".

Japanese Examination Guideline

- Invention does not include simple “natural law” or “simple observation” (same as US)
- But invention include chemical products, micro-organisms, etc. which are isolated by man from nature
  - DNA patent eligible so long as function known and having utility (2000 Examination Guideline)

- Japanese “Myriad Counterparts” lived their lives peacefully
  - In 2015, FALCO (Kyoto company) took exclusive license from Myriad, and conducting BRCA1/2 tests in Japan
  - Japanese gene patents and natural products patents still useful

What about Diagnostics Patents?

- US6033857 (BRCA2) – CAFC ruled not patent eligible
  - Claim 2. A method of diagnosing a predisposition for breast cancer…[by] comparing … BRAC2 from a subject [to] the wildtype… wherein alteration…indicates a predisposition to said cancer

- JP3399539 (BRCA1) (lived its life fullest to 2015)
  - Claim 1 – A method to identify the presence of breast and ovarian cancer gene in an individual by comparing BRCA1 gene from the individual to that of the wildtype wherein alteration indicates the presence of the cancer gene

- JPO Examination Guideline (effective Oct 2015) – patent eligible
  - Example 5: A method of examining the susceptibility…to hypertension by determining the type of base …in X gene…and comparing…with standard

So What is with Diagnostics Patents?

- Until recently, fetal chromosomal abnormalities detected by highly invasive amniocentesis and villus chorionic assays involving high risk to the fetus.
- Inventors found presence cell free fetal DNA (cffDNA) in mother's blood and developed innovative non-invasive method of detecting cffDNA to do prenatal genetic tests. Filed patent (US625840) assigned to ISIS.
- Sequenom commercialized MATERNIT21® under license from ISIS using cffDNA detection; Ariosa launched competing method named HARMONY™
- In *Ariosa v Sequenom* (Fed Circuit 2015) [Also Inter Partes Review attack]
  - CAFC ruled that certain methods claimed in US6258540 patent ineligible
    - Claim1. (1) Amplifying paternally inherited DNA from plasma or serum from pregnant female; and (2) detecting the presence of such DNA of fetal origin
- Sequenom could not block entry of HARMONY™. Now at least three players using this method in US.

Reasons behind CAFC's decision

- Claims are directed to natural phenomenon (of paternally inherited cffDNA being present in maternal blood/serum), and recited steps of amplifying and detecting are routine methods

- Applied analysis of *Mayo*
  - First determine if claim is directed to "judicial exceptions" (i.e. law of nature, natural phenomenon, or abstract ideas), if so, determine if significantly more is added to the claim.
  - Judge Dyke in denying hearing "en banc" said the claims might be patentable if "narrow in scope" otherwise they are overbroad
    - Narrower the claim, the invention will be designed around

- JP4245666 – Claim 1 substantially identical to US claim still alive, and clinical trial on the technology started 2016 in Japan

Another Attack under § 101

- In 2017, the District of Delaware would have addressed Merck's § 101 challenge (BMS/Ono v Merck) to three "Honjo patents" for methods of treating cancers using anti-PD1 antibodies
  - eg US9067999
    1. A method of treating a lung cancer comprising administering a composition comprising a human or humanized anti-PD-1 monoclonal antibody…

- In April 2016, Delaware court accepted Merck's argument that the claims were directed to the natural phenomenon of using T cells to activate the immune system, thereby satisfying the first prong of § 101 analysis under *Mayo*
  - Second prong of whether claims "add enough" beyond the natural phenomenon would have been addressed in early 2017
- Update
  - Oct 24, 2016, Ono sued Merck for infringement under counterparts JP4409430 and JP5159730 having substantially the same claims as the US claims
  - Jan 20, 2017, Merck and Ono/BMS settled in US/EP/Japan for high royalty.
    - Japanese patents also contributed to extraction of royalties !!