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Hot Topics in Bio Practice
Hot Topics in Chemical Practice

Gerald M. Murphy, Jr.

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HOT TOPICS IN BIO PRACTICE

- STATUTORY SUBJECT MATTER – PTO Interim Guidance and *In re BRCA* litigation
- WRITTEN DESCRIPTION – *Abbvie v. Janssen*

What is a “Law of Nature” – PTO Guidance

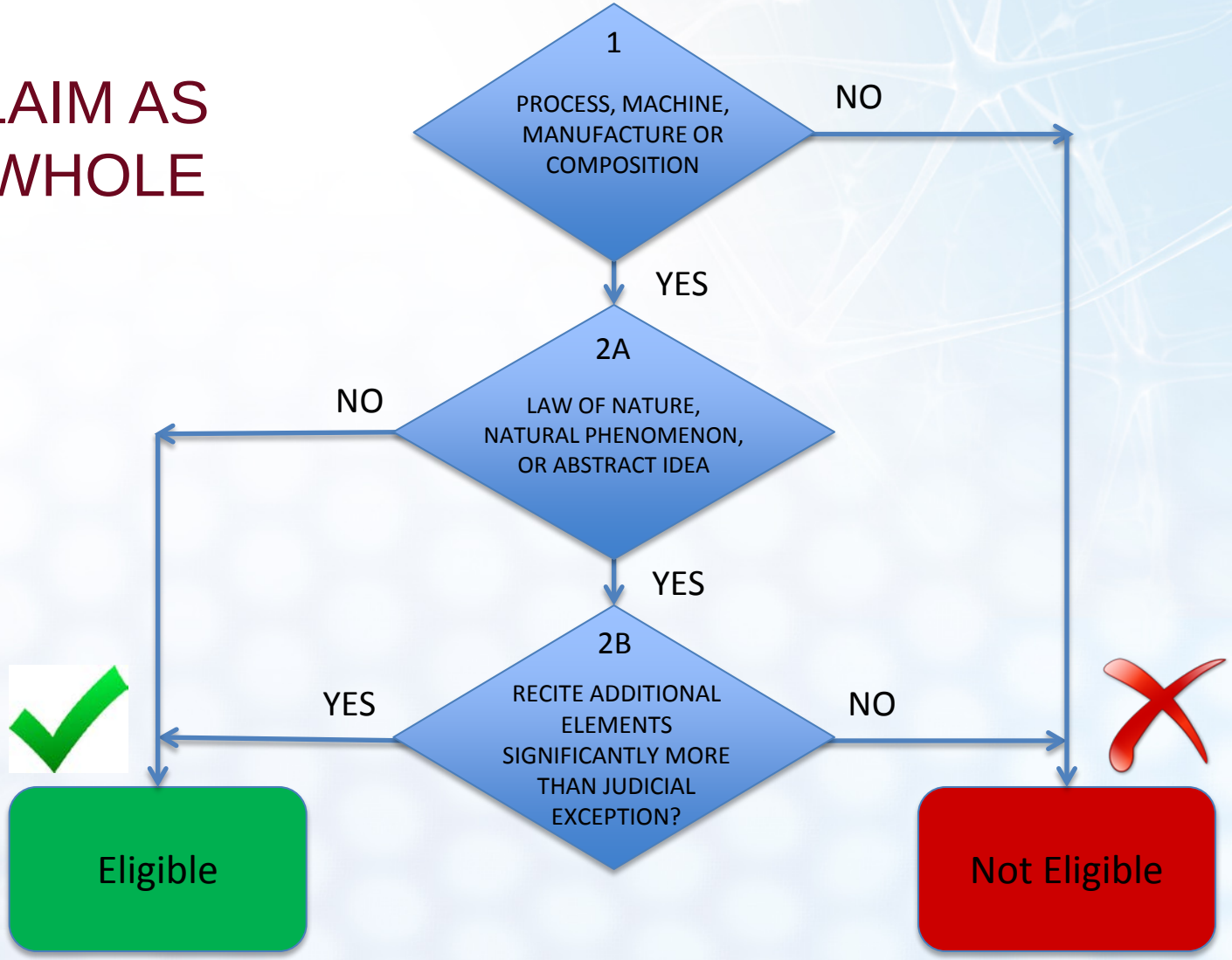
- PTO Guidance and Examples issued Dec. 15, 2014

http://www.uspto.gov/patents/law/exam/examguide.jsp

- New analysis and new Examples
- PTO is seeking comments until mid-March 2015

Two-Part Analysis for Judicial Exceptions

CLAIM AS A WHOLE



Natural Materials

- Ex 2: **Pomelo juice + added preservative**: Yes
- Ex 3: **Amazonic acid**
  - Purified – No
  - Comp. with additive, new use – Yes
- Ex 4: **Purified Proteins** –
  - Yes, if purified form protein yields new physical form (crystal) or if differently glycosylated
- Ex 8: **Antibodies to new bacterial protein**

  "Human ab": Yes, if humans not previously infected

  Other "new" antibodies: Yes

Living Organisms/Materials

- Ex 5: **Bacterium with two plasmids**, yes
- Ex 6: "**Mixture" of two bacteria**
  - **Yes**, if do not occur naturally together and if the mixture has new property (ability to infect legumes)
- Ex 7: Yes, if modified structure (*Myriad*)
- Ex 9: **Human pacemaker cells,** they exist in nature in combination with other cells and materials

  No, if **just purified** or **just put in container**

  Yes, if new marker or in **biocompatible 3D scaffold**

Food

- Ex 10: **New combination of old bacteria with new properties for making yogurt**
- **Individual bacteria are in nature**
  - Separate purified bacteria not patentable.
  - "**Kit**": **No**, not "mixed" in the kit.
  - "**starter culture**" – a mixture of the two bacteria: **Yes**, new properties when mixed together.

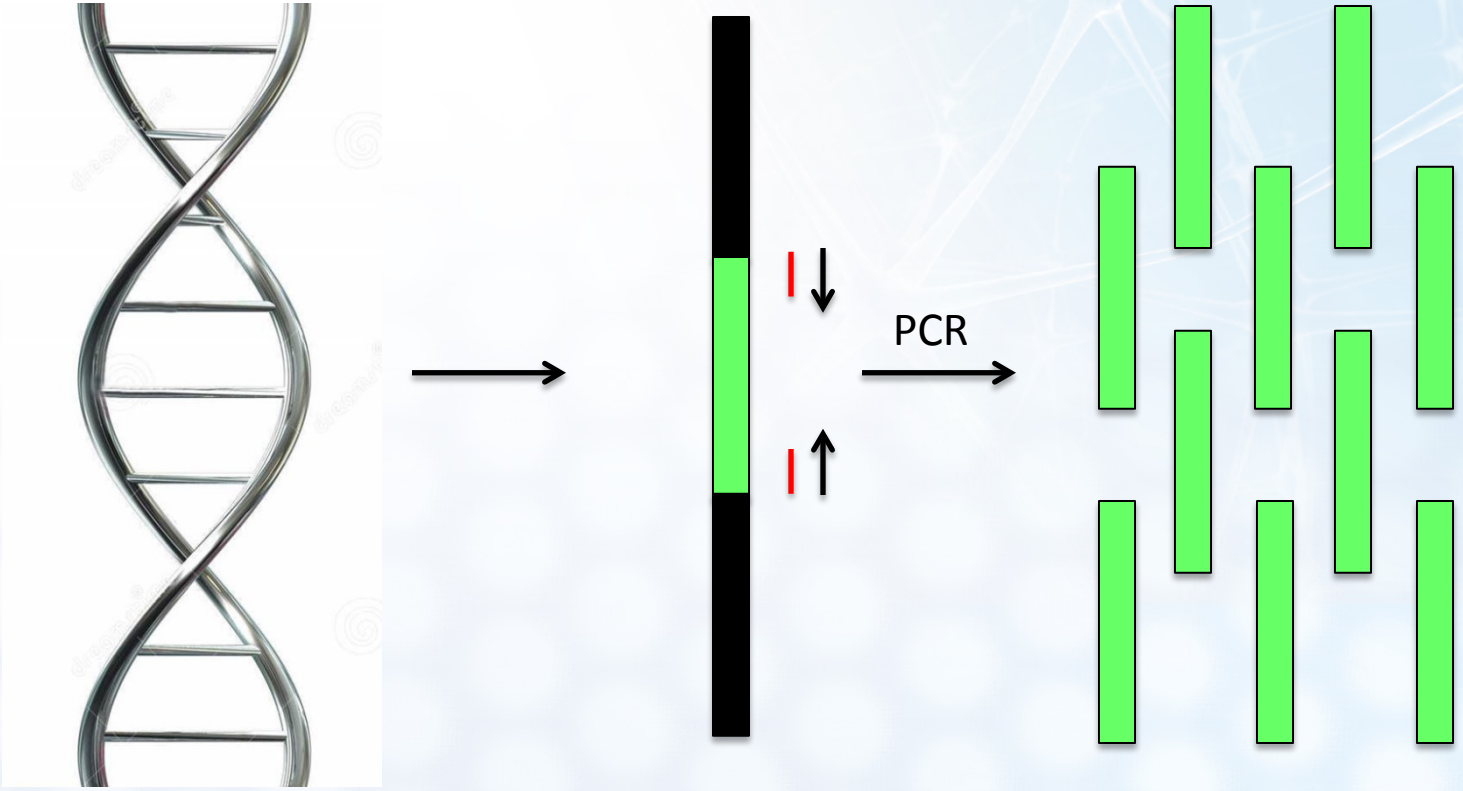
Conclusions from PTO Guidance

- “Mixture” of individually ineligible materials may be eligible if new properties
- Mere “combination” of ineligible materials not patentable, sort of like agreggration of elements?
- “Small” chemical modification may render natural product patentable

In re BRCA Litigation (Fed. Cir. Dec 2015)

- Claims previously considered by Supreme Court
  - 1.Primers – not patentable.
  - 2.Method involving comparing wild-type sequences with patient's sequences – not patentable.

WHAT IS THE FUNCTION OF PRIMERS?



NEW PRIMER

- A pair of single-stranded DNA primers for determining … derived from chromosome 17q, wherein PCR results in DNA of the BRACA1 gene.
- “single-stranded” not enough – no explanation.
- Mere synthetic replication not enough (like Dolly)
- Some different “functions” not enough, both primers and natural DNA have ability to bind DNA

NEW METHOD CLAIMS

- Claims 7 and 8 claim methods for screening sample comprising “comparing” sequences from sample with wild-type. Regarding “comparing” step, see prior *Myriad* Fed. Cir. decision.
- The claims do not “do significantly more than simply describe natural relations”, citing *Mayo* (US 2012)
- Also, claims recite “abstract ideas”.
- Claim 8 also recites “amplifying” & “sequencing”.
- Number of possible comparisons unlimited

CLAIM 8

- Claim 8 also recites “amplifying” DNA in sample and “sequencing” amplified DNA.
- “nothing more than spell out what practitioners already knew using routine, ordinary techniques”.
- Prior S. Ct. opinion suggested cl. 21, which listed “predisposing mutations”, might be patentable.
- But, claims 7 and 8 are broader and more abstract.

CONCLUSIONS ON 101 ELIGIBILITY

- Mere “kit” or “combination” not patentable.
- Are “mixtures” from PTO Guidance still patentable? Maybe if new properties of mixture?
- Broad claims to diagnostic method not patentable if based on discovery of genetic markers.
- Combination of primers not patentable.
- Are method claim directed to analysis or testing of specific mutations patentable? If yes, how many mutations can you cover and still be patentable?

Abbvie v. Janssen (Fed. Cir. July 2014)

- For written description support of a humanized monoclonal antibody – need representative species throughout the claim.
- Need sufficient number of species and sufficient variety within the species.
- This case illustrates how insufficient variety of species can cause broad claim to be invalid.

CLAIMS

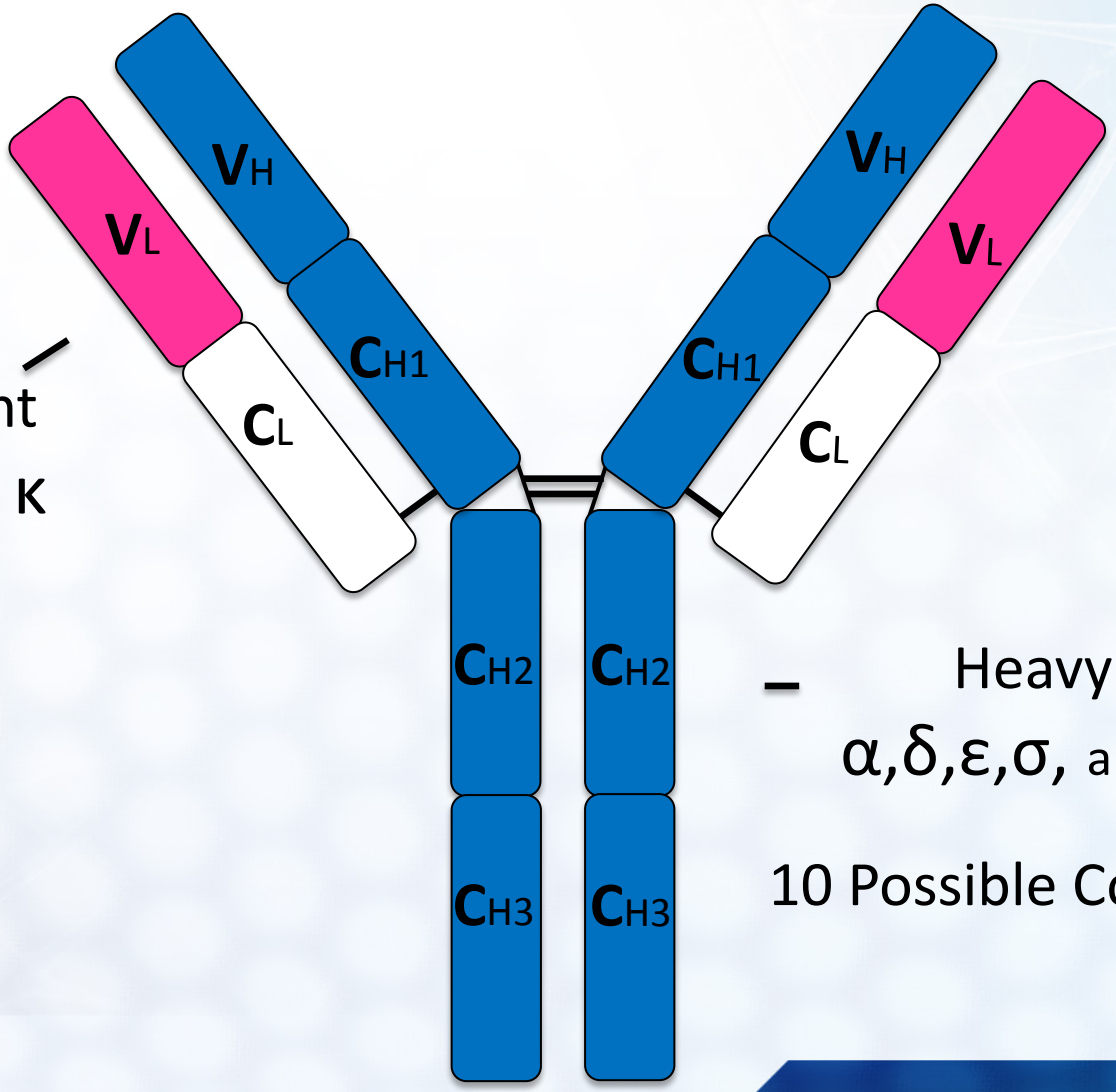
- USP 6,914,128

29. A neutralizing isolated human antibody that binds to human IL-12 with a K_{off} rate constant of $1x\mathbf{10}^{-2}s^{-1}$ or less…

- USP 7,504,485

11.A pharmaceutical composition … isolated human antibody … capable of binding to an epitope of the p40 subunit of IL-12 with a Kd of … or a K_{off} of …

ANTIBODY STRUCTURE



Light
λ & κ

Heavy
α,δ,ε,σ, and μ

10 Possible Combinations

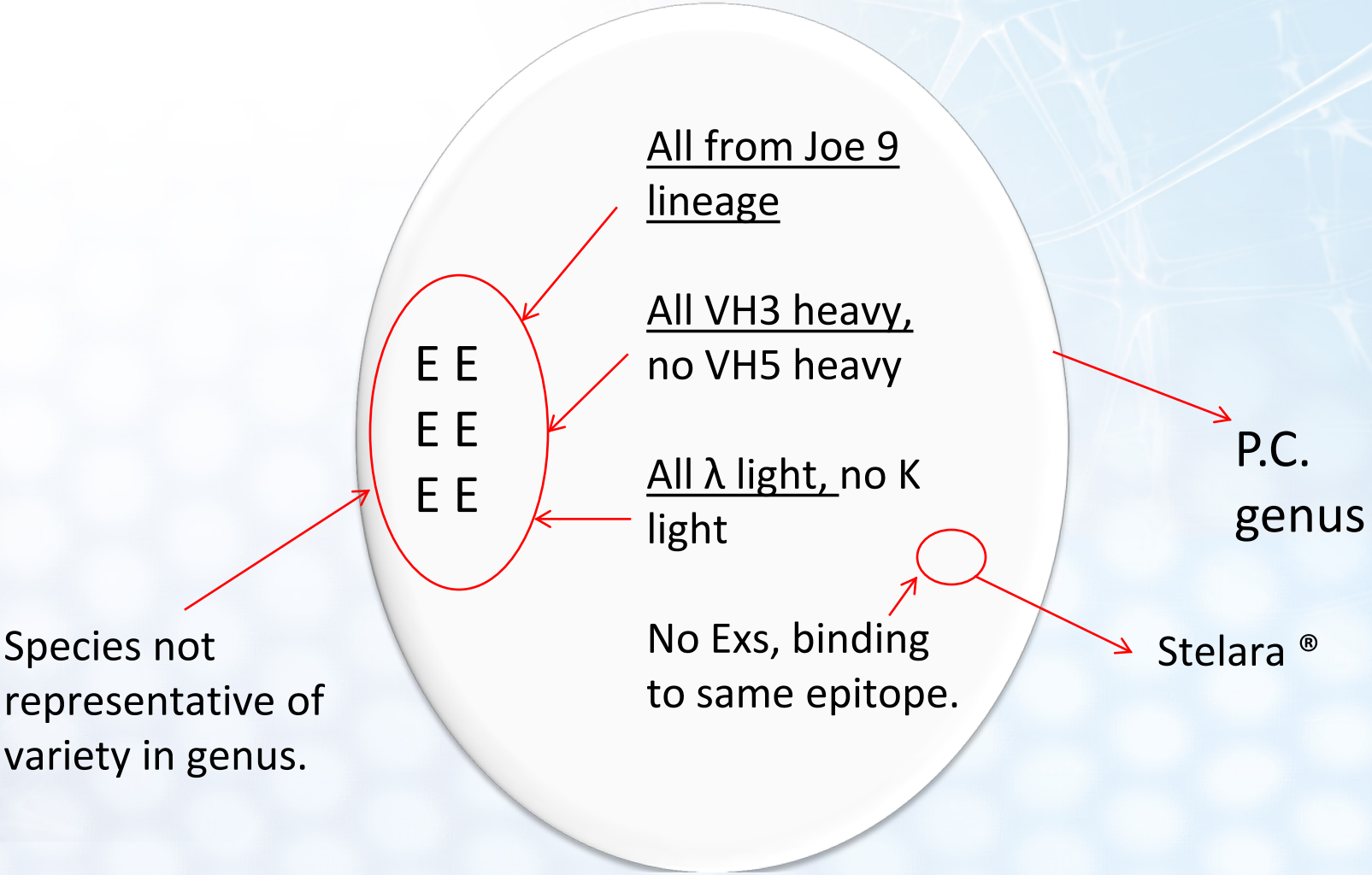
Joe-9 Antibody

- Joe-9 antibody identified through screening
- Y61 - Mutations introduced to increase binding
- >200 antibodies made by site-directed mutagenesis of Y61 that differ by only one amino acid and share 99.5% sequence similarity in variable region.
- J695 – significant increase in IL-2 neutralization and binding

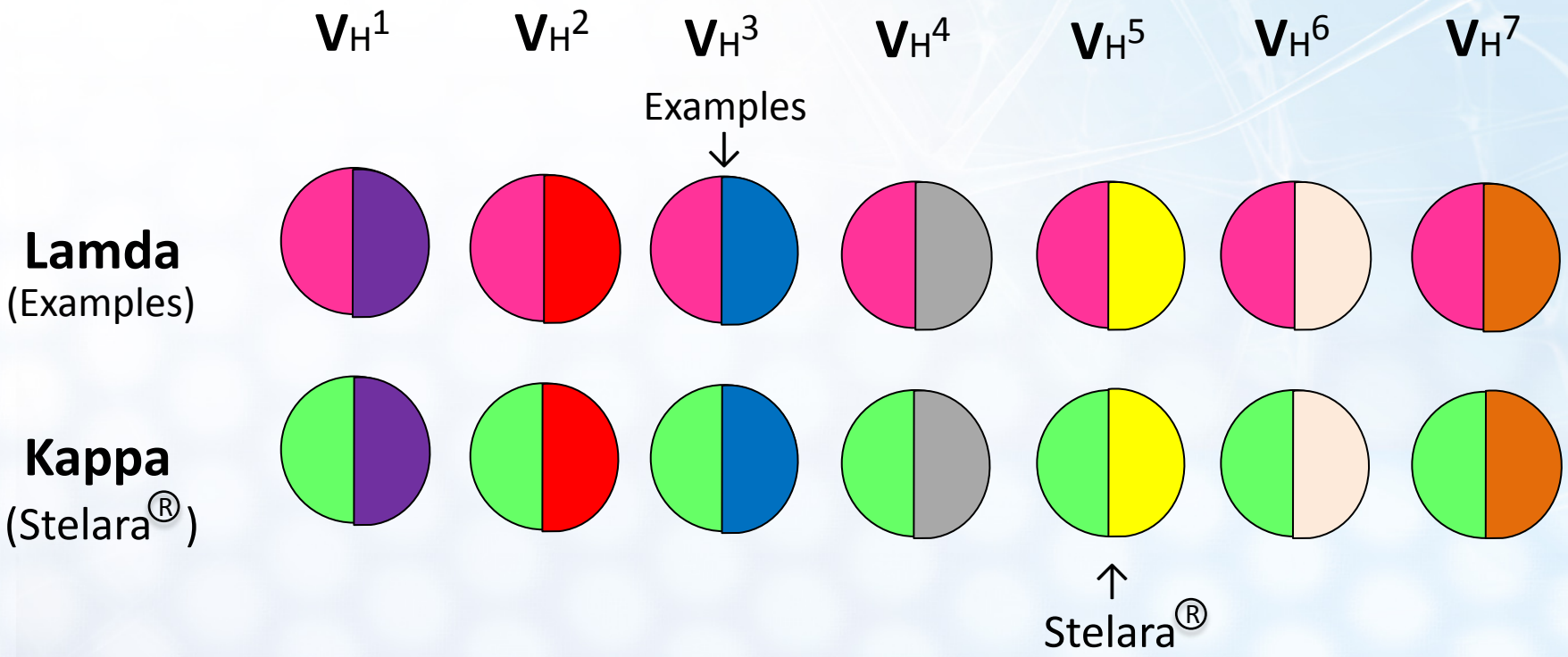
Stelara®, J695 & Joe-9

	Stelara	J695	Joe-9
Sequence Similarity	50%	90%	90%
CDR Length	Different	Identical	Identical
Epitope Binding Site	Side Binder	Bottom Binder	Bottom Binder
V_H Family	V_H5	V_H3	V_H3
Light Chain Type	Kappa	Lambda	Lambda

CLAIMS VERSUS DISCLOSURE



14 Combinations



What Did Abbvie Really Invent?

- What did Abbvie Really Invent?
  - 200 Examples of λ/VH3 antibodies
  - High homology to Joe 9

How to support broader claim?

- 2 or 3 examples each of various combinations of light chains and VH1-7 domains.
- More variation in variable region?
- What would have happened if infringer was using same λ/VH3-type of antibody? Would jury have been as sympathetic to the argument?

JURY VERDICT

- Invalid – Written Description
- Invalid – Enablement
- Invalid – Obvious
- Basically, claims broader than supporting disclosure as to definition of antibodies-- and also obvious.

FEDERAL CIRCUIT OPINION

- AbbVie argued that the disclosed antibodies reflect variation over full range of claimed K*off* rate.
- AbbVie's expert conceded patents do not disclose structural features common to members of genus.
- AbbVie admitted antibodies with 80% sequence similarity to J695 could bind to different antigens.
- In unpredictable fields, need correlation between structure and function to support functional claims.
- AbbVie only had a "research plan" for other antibodies.

Take Home Lessons

- You cannot patent what you have not “invented”.
- For biotech inventions, may need large number of examples and variety with respect to all important aspects of the invention.
- For humanized antibodies, may need working Examples of different “types” of antibodies with different basic structures.
- Present different claims emphasizing different features, e.g., structure, function, sequence, types.

Fed. Cir. Claim is Like Fence Around Land