
SLW INSTITUTE
Building Extraordinary IP Assets
Emerging Tech Webinar Series Episode 04:
Patenting Vaccines: A Look Back and the Road Ahead

# Today's Presenters...

**Robin Chadwick, J.D., Ph.D.**
Principal
Schwegman Lundberg & Woessner

**Warren D. Woessner, J.D., Ph.D.**
Principal
Schwegman Lundberg & Woessner

**Monique Perdok, J.D., Ph.D.**
Principal
Schwegman Lundberg & Woessner

**Janet Embretson J.D., Ph.D.**
Principal
Schwegman Lundberg & Woessner

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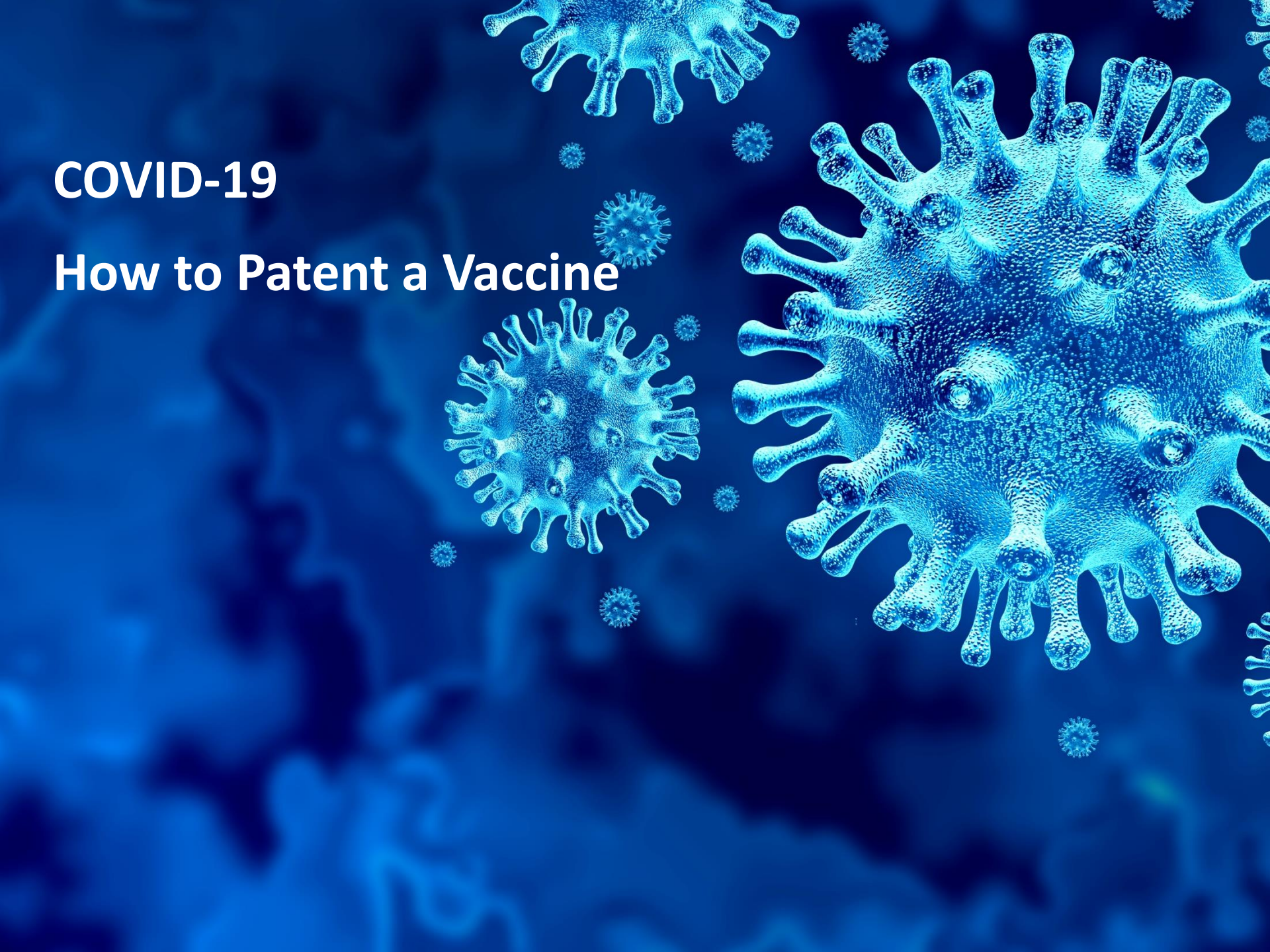
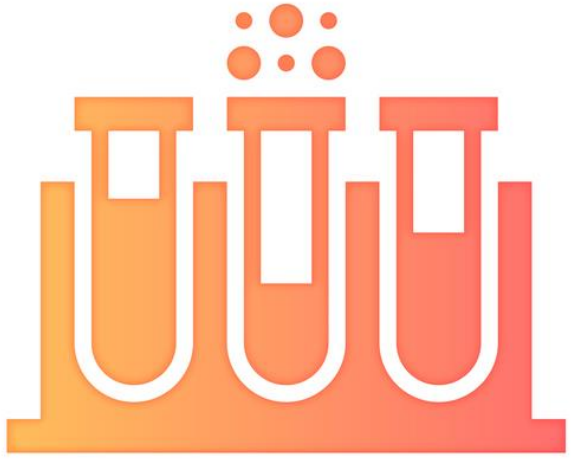
# COVID-19

# How to Patent a Vaccine



# COVID-19 is a RNA Virus/Any RNA Virus Vaccines?

- HIV (lentivirus) – No vaccine.
- Severe Acute Respiratory Syndrome (SARS) - coronavirus identified in 2003 - No vaccine.
- Poliovirus – Inactivated Vaccine used in US; Attenuated Vaccine (used in several countries).
- Influenza– yearly intramuscular inactivated vaccine or nasal spray attenuated vaccine.



# One Type of FDA-Approved Vaccine

- **Killed or Inactivated Vaccines -**

  Pathogen has been inactivated completely, e.g., by heat or chemical treatment, but is still immunogenic.

# Other Types of FDA-Approved Vaccines

**Live Attenuated Vaccines –**

Example - Pathogen is weakened by introducing mutations by serial passages in an animal host or *in vitro* culturing, but is still immunogenic.

**Subunit Vaccines –**

Immunogenic proteins or parts (capsid) isolated from the virus.

# Other Types – DNA, RNA and Vector Vaccines

- **DNA vaccines**
  - DNA plasmids express immunogenic protein(s) when injected into a subject, often with an adjuvant.
- **mRNA vaccines**
  - Inject mRNA that expresses an immunogenic protein, e.g., replicon RNA bound to a carrier like a nanoparticle.
- **Adenoviral Vector vaccines**

DNA, RNA and Adenoviral Vector Vaccines are being tested in clinical trials against COVID-19 (e.g., Inovio Pharmaceuticals, Moderna and Oxford)

# A Quick Look at the State of the Law

- Isolated human genomic DNA is a natural product and so is not patentable; neither is ssDNA (such as a primer for PCR.)
- cDNA is patentable at least if introns are removed. Natural-occurring polypeptides per se are also natural products.
- Simple “If A, then B” diagnostic claims are not patent eligible.
- They are considered simply to be the identification of a naturally occurring correlation - a natural phenomena.
- Altered reagents, such as a labelled “capture antigen” may be patent-eligible as new compounds.
- Methods of medical treatment, such as vaccination are patentable, even if the claims recite a diagnostic step.

# PTO Guidance, May 2016, Example 28

- **Claim 3:** Vaccine comprising Peptide F and a pharmaceutically acceptable carrier
- Peptide F is a Natural product, *per se* not patent eligible.
- **Patent Office / Courts:**
  - Claim 3 is not eligible for patenting.
  - A peptide + water = natural product.
  - "Yes" in step 2A of the Mayo/Alice eligibility analysis.

# PTO Guidance, May 2016, Example 28

- **Claim 4:** A vaccine comprising: Peptide F; and a pharmaceutically acceptable carrier selected from the group consisting of a cream, emulsion, gel, liposome, nanoparticle, or ointment.

- **Patent Office Guidance:**
  - Claim 4 is eligible for Patenting.
  - Claimed cream has "markedly" different structural and physical characteristics than its naturally occurring components.
  - Claim 5, which recites Peptide F + Al salt adjuvant is also patent-eligible.

# Mayo/Alice Rule - Not Well-Suited to the Natural Products Exception to Patentability

- MPEP 2106 “Subject Matter Eligibility Chart” - little guidance on analyzing compositions that are:
  - mixtures of natural products or
  - mixtures of natural product(s) with non-natural products.
- MPEP 2106.04(c)(I)(A) - If a claim is to a natural product itself, the markedly different character analysis “MDC” should be applied to the entire product.
  - Patentable example: Chakrabarty’s bacterium with two new plasmids.
  - A product made by combining multiple natural products: the MDC analysis should be applied to the nature-based composition – not to its component parts.
- Non-nature based elements are considered under Step 2C of the conventional, routine, well-understood analysis e.g. kit packaging, dosage forms.

# MPEP 2106.04(c)(II)(A) Muddies the Waters

- "When the nature-based product is a combination produced from multiple components, the closest counterpart may be the individual components of the combination." MPEP 2106.04(c)(II)(A).
  - Example: an inoculant having bacteria of species E and some bacteria of species F.
- This is an attempt to shoehorn Funk Bros. into the 2A analysis:
  - "Because there is no counterpart mixture in nature, the closest counterparts to the claimed mixture are the individual components of the mixture..."
- What happened to claim evaluation "as a whole"?

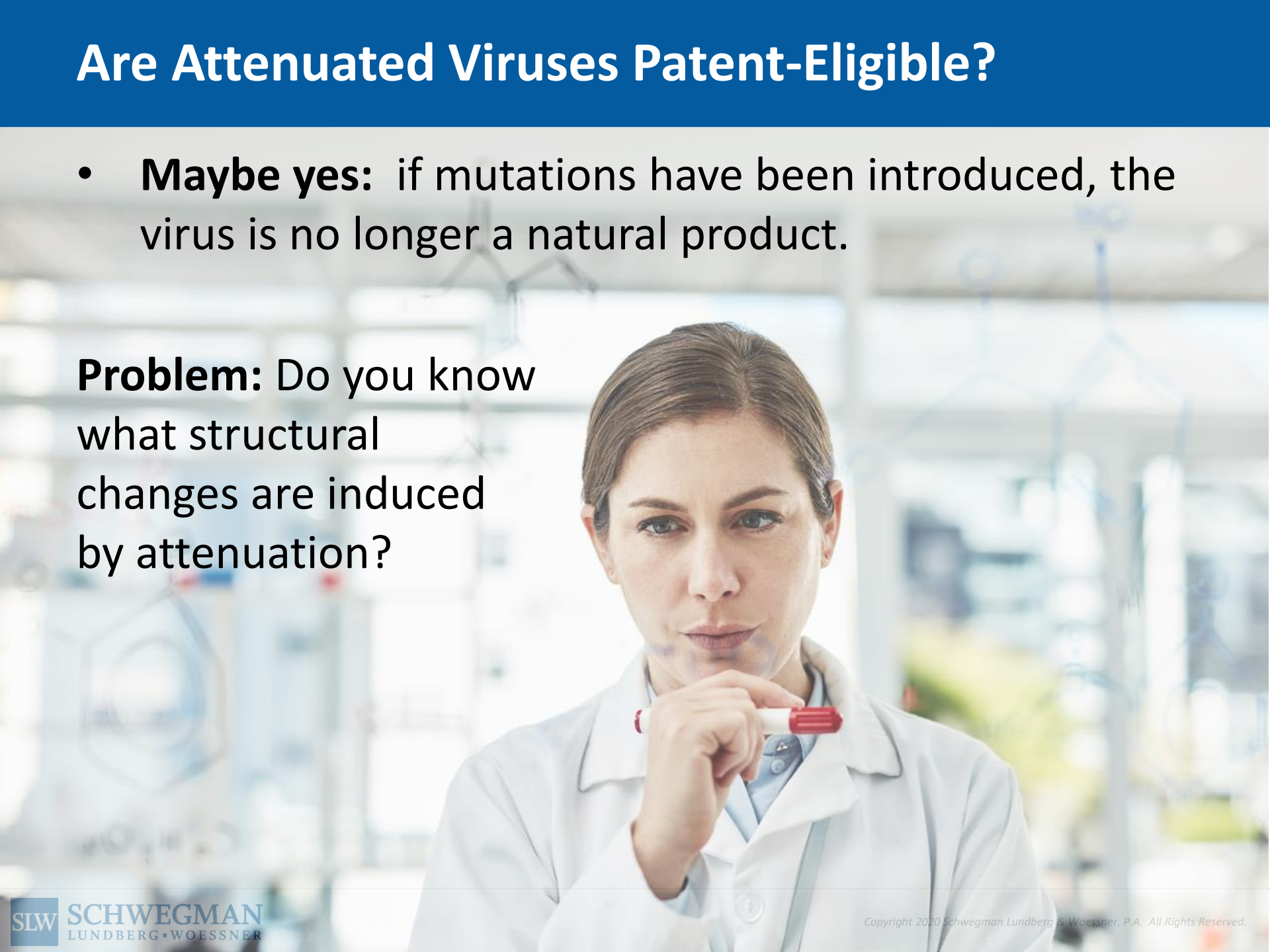
# Are “Killed” Viruses Patent-Eligible?

- **Maybe not:** without more, dead viruses are probably not eligible for patenting.
- **Maybe yes:** viruses inactivated by chemical modification (e.g., with formalin) are not natural.
- **Added ingredients?**
  – Must yield “markedly different” composition.

# Are Attenuated Viruses Patent-Eligible?

- **Maybe yes:** if mutations have been introduced, the virus is no longer a natural product.

**Problem:** Do you know what structural changes are induced by attenuation?



# Recombinant Expression Vectors Eligible?

- Expression vectors comprising immunogenic proteins are “unnatural” and probably patent-eligible.
- **Examples:**
  - “An expression vector comprising a promoter operably linked to a heterologous nucleic acid segment encoding a coronavirus spike protein with at least 95% sequence identity to SEQ ID NO:1.”
  - Ebola virus vaccine is a live, attenuated VSV vaccine that expresses an Ebola glycoprotein.
    - See, e.g., US Pat. No. 8,012,489.

# Must Describe the Invention re 35 USC § 112(a)

- **Written description requirement** –
- Patent must describe the technology sought to be patented – structurally.
- Patent must demonstrate patentee was in possession of the invention that is claimed—e.g., are there enough working examples?

# Written Description - Attenuated Vaccine

- **Claim:** A stabilized live vaccine comprising an attenuated live varicella zoster virus, and a stabilizer comprising 0.5 to 10% (w/v) of sucrose or lactose.
- **Specification:** varicella zoster are passaged 5+ times through guinea pig primary embryonic tissue cells until non-replicating.

- **Written Description problem? Probably Yes.**

# Can Written Description Problems be Fixed?

- **Does the Specification disclose attenuation structural changes / mutations?**

  **If Yes:** add the structural change(s) to the claim.

  **If No:** this could be a fatal problem.

# Can Written Description Problems be Fixed?

- **Make a deposit of the attenuated vaccine with a recognized cell depository (e.g. ATCC).**

In the US you can usually amend the specification to recite the deposit information if you include a statement at filing that a deposit is being made.

**Deposit 25 vials**

# Written Description - Structure Needed

**Claim (Original):** A peptide comprising a 7-40 amino acid surface antigen from an infectious agent and a human universal epitope.

**PTO:** The specification fails to show structures of all infectious agent antigens and of all universal epitope sequences.

- But SEQ ID NO:11 = human universal epitope

**Claim (Amended):** A peptide comprising a 7-40 amino acid surface antigen from an infectious agent and a human universal epitope having at least 95% sequence identity to SEQ ID NO:11.

# Possession – Looks Like Enablement

**Claim (Original):** A multivalent poultry vaccine consisting essentially of a recombinant herpesvirus vector containing Newcastle disease virus HN gene.

**PTO:** The specification provides examples of turkey herpesvirus as a vector. However, the specification fails to show possession of all herpesviruses as vectors.

**Claim (Amended):** A multivalent poultry vaccine consisting essentially of a recombinant turkey herpesvirus vector containing Newcastle disease virus HN gene.

# Vaccine Enablement

## Enablement

## How do you make and use a vaccine?

# “Vaccine” May Be an Enablement Problem

- **Claim (Original):** A *vaccine* for generating an immune response in an individual against Dengae virus comprising an expression vector encoding a secretable fusion protein…
- **PTO:** While being enabling for generating an immune response, the specification does not reasonably provide enablement of a *vaccine* comprising the composition.
- **Claim (Amended):** A *composition* for generating an immune response in an individual against Dengae virus comprising an expression vector encoding a secretable fusion protein…

# Undefined Cleavage Site in Viral Protein

- **(Original)** An isolated recombinant coronavirus having a genome modified to express a S protein with a residue other than glycine at position 150 in the S protein protease cleavage site.

  – Note: Cleavage makes a better coronavirus vaccine.

- **Enablement Problem:** Specification only enables two amino acids as allowing cleavage of the S protein.

- **(Amended)** An isolated recombinant coronavirus having a genome modified to express a S protein with an arginine or lysine at position 150 in the S protein protease cleavage site.

# Any Enablement Problems?

- **Example O. *Lysobacteria erythrosis* peptide claim 1:**
  A peptide having the following sequence: Ser Thr Ile Phe Leu Glu Ser Thr His Glu Asp Ile Ser Glu Ala Ser Glu.

- **Enablement okay:**
  - Specification describes how to make peptide.
  - Specification discloses how to use the peptide to make antibodies for erythrosis assays.
  - See: https://www.uspto.gov/patent/laws-and-regulations/patent-examination-policy-mpep-staff-35-usc-112-1st-para-enablement#7o

# Any Enablement Problems?

**Example O claim 3:** A method of treating a subject with erythrosis by administering the peptide of claim 1 to the host.

**Enablement Not Okay:** the specification enables the method for producing antibodies, but not for treatment of disease. Scope is too broad.

**PTO Solution:** A method of producing antibodies that recognize *Lysobacteria erythrosis* in a subject with erythrosis by administering the peptide of claim 1 to the host.

# Not All RNA Viral Species Enabled

**Claim 11:** A live, non-pathogenic vaccine for a pathogenic RNA virus, comprising a construct comprising an antigenic determinant region of the RNA virus, but no pathogenic properties.

**Problem:** Specification only provides one example of a modified Prague Avian Sarcoma Virus – the RAV-$Ac^n$ viral strain with modified env A gene.

**Solution:** recite the RAV-$Ac^n$ strain in the claim.

See, In re Wright, 999 F.2d 1557 (Fed. Cir. 1993)

# Could You Patent Other RNA Vaccines?

**Maybe – if the Specification describes:**

- RAV-Ac$^{n}$ strain Env A structural changes; and
- Structure of second RNA viral Env A protein; and
- Structural changes needed in second RNA viral Env A protein to make a second modified RNA viral strain; and
- Later show data that the second RNA viral strain can cause an immune response in a host.

**Some Enablement Problems can be solved!**

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# Thank You For Your Interest
# Questions?

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