VACCINES AVAILABLE AND SYSTEMS FOR USAGE IN THE FIELD

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Disclaimer

- No vaccine type or manufacturer is being endorsed
- References are not exhaustive and are mostly provided where data are new or otherwise limited

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Definitions: Protection and Efficacious

- Maintain animal health and minimize production losses
  - No mortality or morbidity
- Reduce virus spread/onward transmission
  - Reduce shed titers 100X or more
- Reduce public health risk
  - e.g., vaccination of ducks for H5N1

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Technical Considerations: Good quality vaccine

- Has an adequate antigenic load to induce immunity
- Contains an antigen which is:
  - Antigenically closely related to the field strain (and the field strain is monitored for antigenic drift)
  - Sufficiently immunogenic

  → Autogenous vaccines work well if adequately immunogenic
- Contains a sufficient antigenic load
- Effective adjuvant
- Administered effectively to birds

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Technical Considerations: Antigen selection/optimization

- Matching:
  - Antigenic cartography
  - Protective epitopes
  - Programs to monitor antigenic variants
- Breadth of response:
  - Mixing antigens: Prime/boost with different vaccines
  - Computationally optimized broadly reactive antigen (COBRA) induces a broader response (Bertran, Vaccine 2021)
- Immunogenicity:
  - Adjuvants

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Technical Considerations: Adjuvants

- Inactivated vaccines must be adjuvanted
- Most evaluation work has been done in chickens
- Many mineral oil-based adjuvants are commercially available
- Novel/experimental adjuvants for poultry:
  - Interleukins, Rig-I ligands, poly I:C, chitosan, *B. subtilis* spores, novel mineral oil formulations

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Vaccine availability

- No technical barriers to producing vaccines
  - Supply of sufficient quantities of suitable vaccine
    - Stockpiles/vaccine banks
      - Which antigen?
  - Production considerations (logistical considerations)
  - Regulatory considerations
  - Licensing
  - Production

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Vaccine platforms: Inactivated vaccines

- Chemically inactivated whole virus, adjuvanted oil emulsion
  - 95.5% of all AIV vaccine use by dose (Swayne, Rev Sci Tech 2011).
- Effective in numerous species
  - Most efficacy data have been produced with chickens and turkeys
  - Limited data with other species: Pekin Ducks, Domestic geese, indicate broad efficacy. (Rudolf, Rev Sci Tech 2009; Kilany, PLOS ONE 2016; Pantin-Jackwood, Av Dis 2019)
  - Efficacious for many species, could potentially protect zoo birds, endangered species in addition to poultry
    - Data lacking on non-poultry species

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Vaccine platforms: Inactivated vaccines

- Primarily induces humoral immunity
- Requires:
  - Strain that replicates to high titers in eggs
  - Low pathogenic cleavage site
- Inactivated vaccines relatively expensive to administer
- Regulatory withdrawal time for meat birds in some countries
- Inactivated vectored APMV-1
  - Bi-valent AIV – NDV with HA insert

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Vaccine platforms: Vectored Vaccines

- Induce cellular immunity
- Licensing varies by country
- May be affected by prior exposure or maternally derived antibody (MDA) to the vector or AIV insert
- Some vectors species specific
- Proteins not altered by chemical inactivation
- Egg-free production
  - Logistics and mutations
- Subunit vaccines
  - Allow for antigen updates (can be affected by regulations)
  - Applicable to some DIVA strategies

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Vaccine platforms: Common vectors and sub-unit vaccines

- Replicating Vectors
  - Herpes virus of turkeys (HVT)
  - Fowlpox virus (FPV)
  - Avian paramyxovirus type-1 (APMV-1) Newcastle disease vaccines
- Non-replicating vectors
  - Alphavirus virus-like particles (VLP)
  - Baculovirus VLP
  - Inactivated APMV-1
- Nucleic acid
  - Self amplifying-RNA (sa-RNA)
  - DNA & mRNA

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Vaccine platforms: Herpes virus of turkeys (HVT)

- Stable well characterized vector
- Induces cellular immunity
  - Can tolerate antigenic variation better than inactivated vaccines
  - Immunity not fully inhibited by AIV MDA (Bertran, Vaccine 2018)
- Can be mass applied to chickens (*in ovo*)
- Immunity can be enhanced when used as a priming vaccination
- Efficacious for chickens and turkeys

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Vaccine platforms: Herpes virus of turkeys (HVT)

- Pekin ducks (*Anas platyrhinchos domesticus*)
  - Vector does not replicate sufficiently, and protection is poor (Pantin-Jackwood, Av Dis 2016; Palya, Av Dis 2016)
- Muscovy ducks (*Cairina moschata*) and Mule ducks
  - Vector replicates better and confers some protection (Kilany, PLOS ONE 2016; Palya, Av Dis 2016)
- Domestic geese (*Anser anser*)
  - Vector replicated better than other waterfowl, but less than chickens (Palya, Av Dis 2016)

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Vaccine platforms: Duck enteritis virus

- Herpesvirus which causes an important disease in domestic ducks that is controlled by vaccination
- Disease from H5 HPAIV in ducks varies by strain, duck age and duck species.
  - Can reduce shed titers and virus spread
- Has been shown to be efficacious in domestic ducks and chickens (reduced mortality and virus shed) (Liu, J. Virol 2011; Liu, Antiviral Res. 2013; Chen, Vaccine 2019)

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Vaccine platforms: Fowlpox virus (FPV)

- One of the oldest vaccine vectors for poultry (Taylor, Vaccine 1988)
- Administration primarily by wing-web stab
- Not fully inhibited by FPV MDA
- Limited host range: Most efficacious in Chickens
  - Has been shown to work in Pekin and Muscovy ducks with inactivated vaccines booster (Steensels, Vaccine, 2009; Niqueux, Vaccine 2013;)
- Best as a live prime in chicks

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Vaccine platforms: Avian paramyxovirus type-1 (APMV-1) Newcastle disease vectored vaccines

- Used in Mexico and China
- Can be mass applied – spray, water
- Induces mucosal and cellular immunity
- Most data from chickens and turkeys, but may be able to protect other avian species
- Interference from APMV-1 MDA (Bertran, Vaccine 2018) or exposure to widely used live ND vaccines limit application
  - Live prime vaccine after MDA wane or naïve chicks

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Vaccine platforms: Alphavirus virus-like particle

- Non-replicating vector, virus-like particles without packaging machinery
- Multiple doses can be used (does not interfere with itself)
- Data are much more limited than older vaccines, but appears to be efficacious in numerous species:
  - Chickens (Bertran, Vaccine 2017; Ladman, Av Path, 2019)
  - Turkeys (Santos, Vaccine 2017; Kapczynski, Vet Imm 2017)
  - Pekin ducks (Pantin-Jackwood, Av Dis 2019)
- Licensed in US

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Vaccine platforms: Baculovirus based vaccines

- Native antigen presentation
- Immunostimulatory
- Multiple doses can be used
- Virus-like particles
- Purified protein
  - Quadrivalent vaccines for seasonal influenza (Arunachalam, NPJ Vaccines 2021)
- Bivalent LPAIV vaccine immunogenic in chickens (Sun, Front Imm 2022)
- Bivalent HPAIV vaccine protective in chickens (Hu, Front Vet Sci 2021)
- Intranasal and oral administration has been protective in mice (Kumar, PLOS ONE, 2013; Basak, PLOS ONE 2020)

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Vaccine platforms: Self amplifying-RNA (sa-RNA)

- Viral (non-segmented, positive sense ssRNA, e.g., alphavirus) replicase drives amplification of RNA and subsequent translation of the antigen
- More efficient than DNA or mRNA
  - Lower dose vs mRNA vaccine (1/64) was protective for mice challenged with influenza (Vogel, Gene & Cell Ther. 2017)
- May be encapsulated for better stability

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THANK YOU FOR YOUR ATTENTION

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