COVID-19 Conversations

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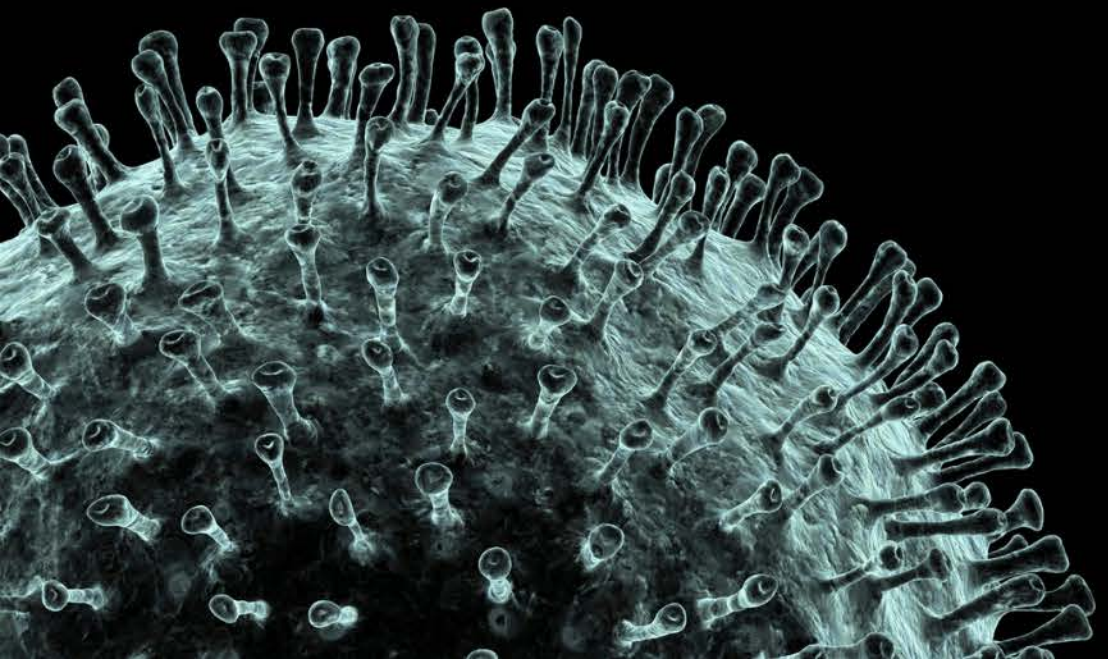

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Authorization & Licensure of Vaccines to Prevent COVID-19

NAM-APHA Webinar on COVID-19 vaccines

November 18, 2020

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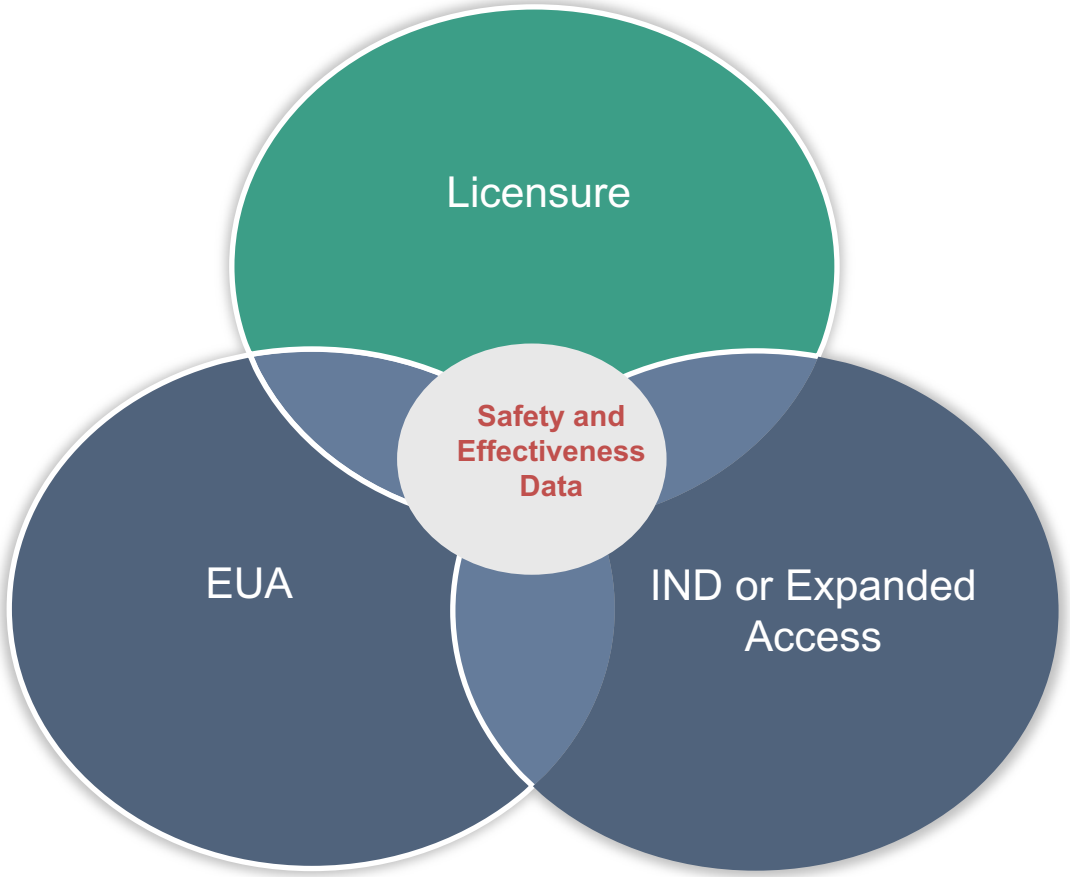
COVID-19 Vaccine Development and FDA Regulatory Activities

- Development, authorization and licensure of vaccines against COVID-19 are critical to mitigate the current SARS-CoV-2 pandemic and to prevent future disease outbreaks
- **FDA must ensure that vaccines that are approved or authorized under EUA are supported by adequate scientific and clinical data**
- FDA is facilitating COVID-19 vaccine development by
  - Providing expedited reviews of CMC information, preclinical and clinical protocols and clinical trials data
  - Providing timely advice and guidance to sponsors to expedite proceeding to Phase 3 clinical trials
  - Directing efforts at generating adequate data to support access to investigational COVID-19 vaccines

US Regulatory Framework for making COVID-19 Vaccines available



Considerations for COVID-19 Vaccines

- COVID-19 vaccines will be widely deployed and administered to millions of individuals, including healthy people
- Public expectation that COVID-19 vaccines will be safe and effective
  - low tolerance for vaccine-associated risks
- **COVID-19 vaccines that are licensed in the US or authorized under EUA must meet applicable legal requirements**
  - **FDA will apply the same standards to grant a biologics license for a COVID-19 vaccine as for other preventive vaccines**
- Vaccine development can be expedited; however, there needs to be sufficient time to accrue adequate manufacturing, safety and effectiveness data to support potential widespread use of these vaccines

COVID-19 Vaccines: Development Strategy & Data Required to Support Licensure

- Manufacturing process to ensure product quality and consistency
- CMC and facility data: compliance with cGMPs requirements
- Nonclinical data
  - Non clinical safety & immunogenicity studies
  - Address the potential for vaccine-induced enhanced respiratory disease
- Clinical data adequate to support the proposed indication and use
  - Efficacy and safety
    - Clinical endpoint that assesses for direct evidence of protection against SARS-CoV-2 infection or disease
      - VE point estimate of ≥50% vs. placebo, with an appropriately alpha-adjusted confidence interval lower bound >30%
    - Characterization of the immune response
- Post-licensure pharmacovigilance plan

Emergency Use Authorization

- An Emergency Use Authorization (EUA) may be issued only after several statutory requirements are met (section 564 of the FD&C Act (21 U.S.C. 360bbb-2))
- Issuance of an EUA requires a determination that the known and potential benefits of the **investigational** product outweigh its known and potential risks
- Use of an **investigational** COVID-19 vaccine under an EUA is not subject to informed consent requirements but vaccine recipients need to be provided a fact sheet that describes
  - the investigational nature of the product
  - the known and potential benefits and risks
  - available alternatives
  - option to refuse vaccination

Emergency Use Authorization (cont.)

- An EUA for a COVID-19 vaccine may allow for rapid and widespread deployment for administration of the investigational vaccine to millions of individuals, including healthy people
- Issuance of an EUA for an investigational COVID-19 vaccine would require
  - Adequate manufacturing information to ensure the product's quality and consistency
  - A determination that the benefits outweigh its risks based on data from at least one well-designed Phase 3 clinical trial demonstrating safety and efficacy
- Any assessment regarding an EUA would be made on a case-by-case basis considering the proposed target population, the product characteristics, preclinical and human clinical data, and the totality of the available scientific evidence relevant to the product

Data to Support COVID-19 Vaccine EUA

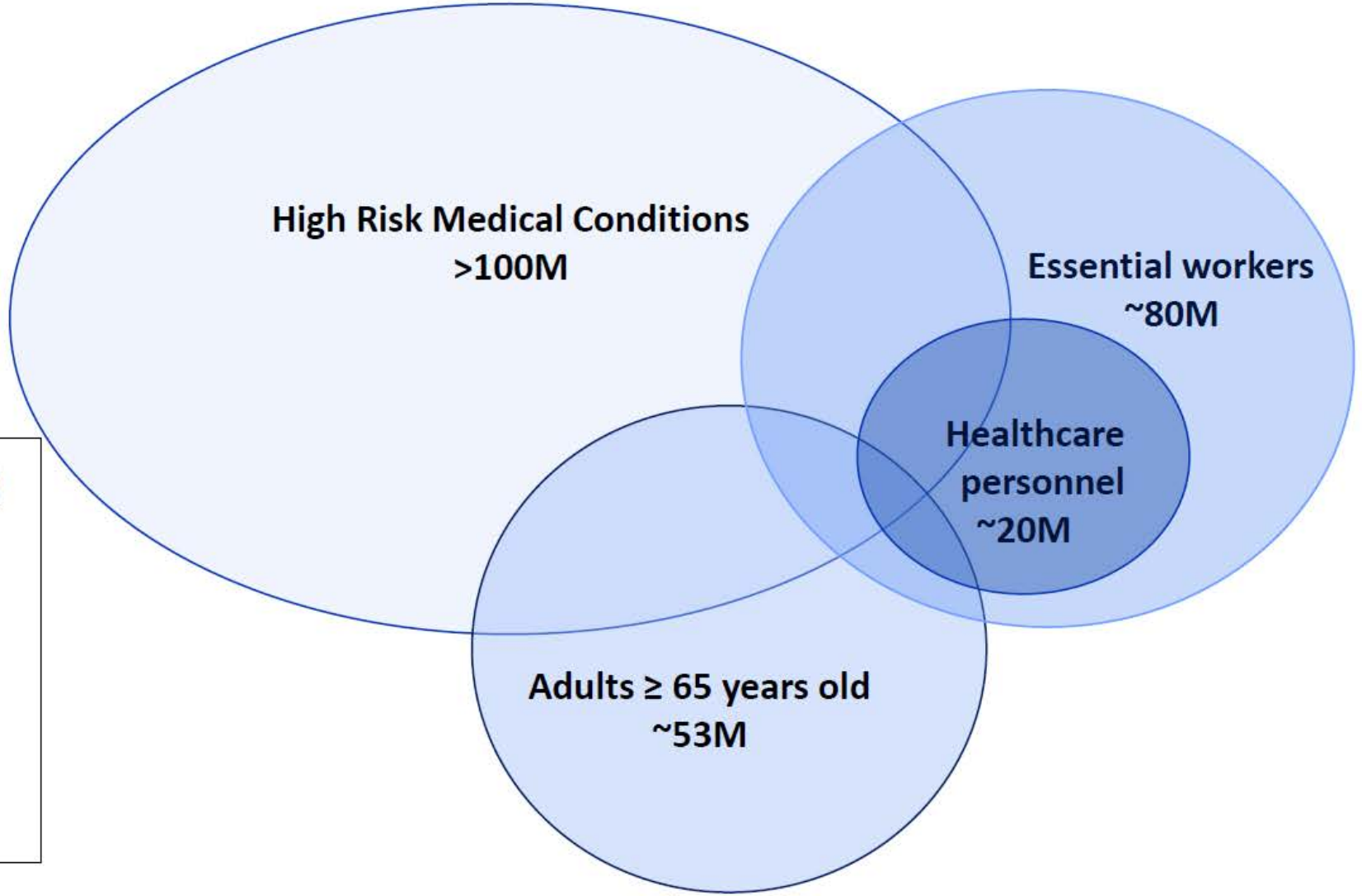
- EUA request for a COVID-19 vaccine may follow a case-driven interim analysis from one or more clinical trials
- To support a favorable benefit/risk determination, taking into account widespread deployment to millions of individuals, vaccine effectiveness should be supported by:
  - Clinical endpoint that assesses for direct evidence of protection against SARS-CoV-2 infection or disease
  - VE point estimate of ≥50% vs. placebo, with an appropriately alpha-adjusted confidence interval lower bound >30%
- In addition to passive safety follow-up an EUA request for a COVID-19 vaccine should include a plan for active safety follow-up of persons vaccinated under the EUA
  - Including but not necessarily limited to deaths, hospitalizations, and other serious or clinically significant AEs
  - To inform ongoing benefit/risk assessments for continuation of the EUA

FDA Guidance for Industry: COVID-19 Vaccines

Development & Licensure of Vaccines to Prevent COVID-19 (June 2020)
Emergency Use Authorization for Vaccines to Prevent COVID-19 (October 2020)

- Reflects advice the FDA has been providing to vaccine developers
- Describes the agency's current recommendations regarding the data needed to support issuance of an EUA for vaccines to prevent COVID-19

Possible groups for Phase 1 vaccination



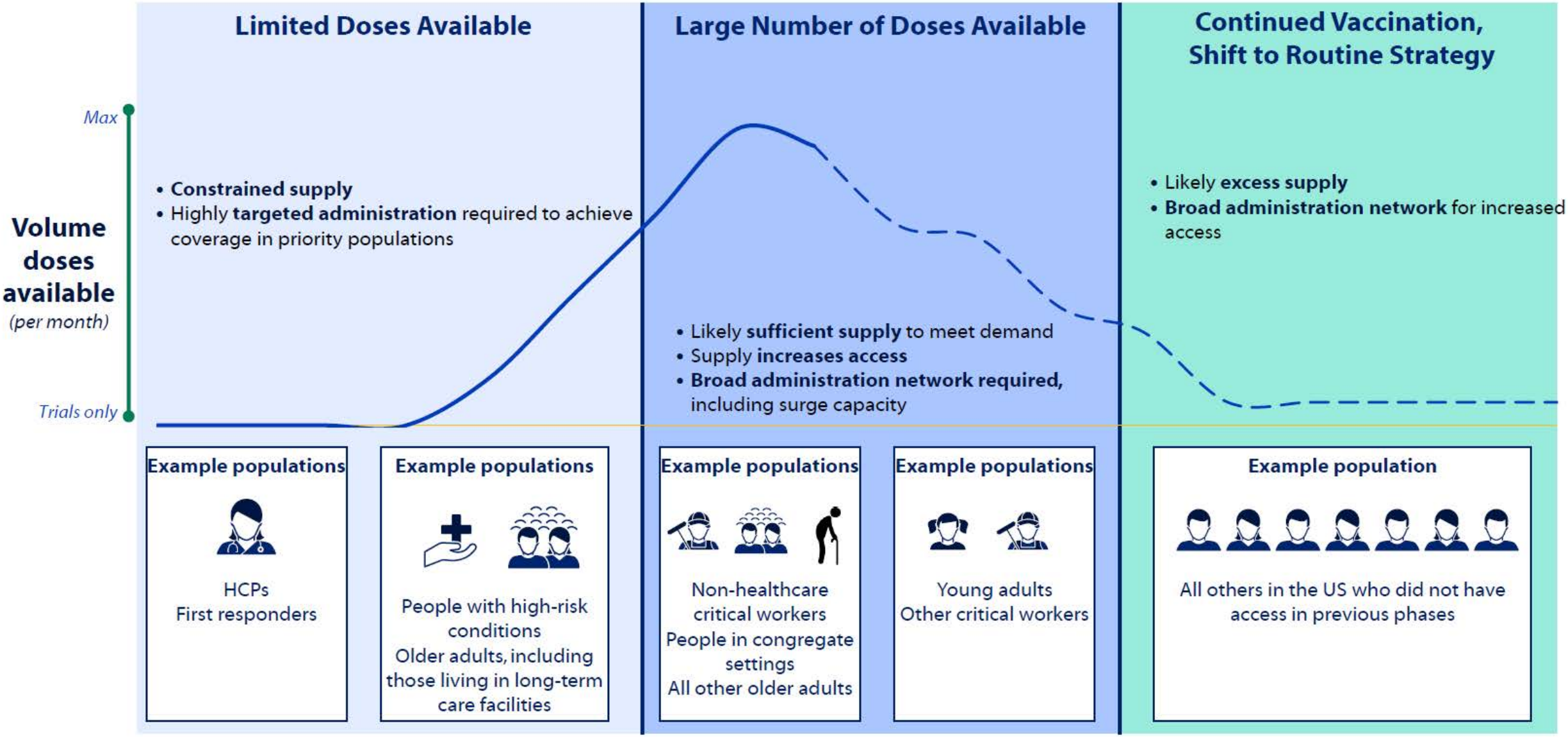
From prior ACIP Discussions:

Phase 1a:
-HCP

Phase 1b:
-Essential Workers
-High Risk Med Conditions
-Adults ≥ 65 years old

Illustrative scenario for planning purposes; will be adapted based on clinical / manufacturing information on all OWS candidates & vaccine prioritization

Distribution will adjust as volume of vaccine doses increases



Illustrative example populations; final prioritization to be decided by ACIP

ACIP Pathway to Recommendation