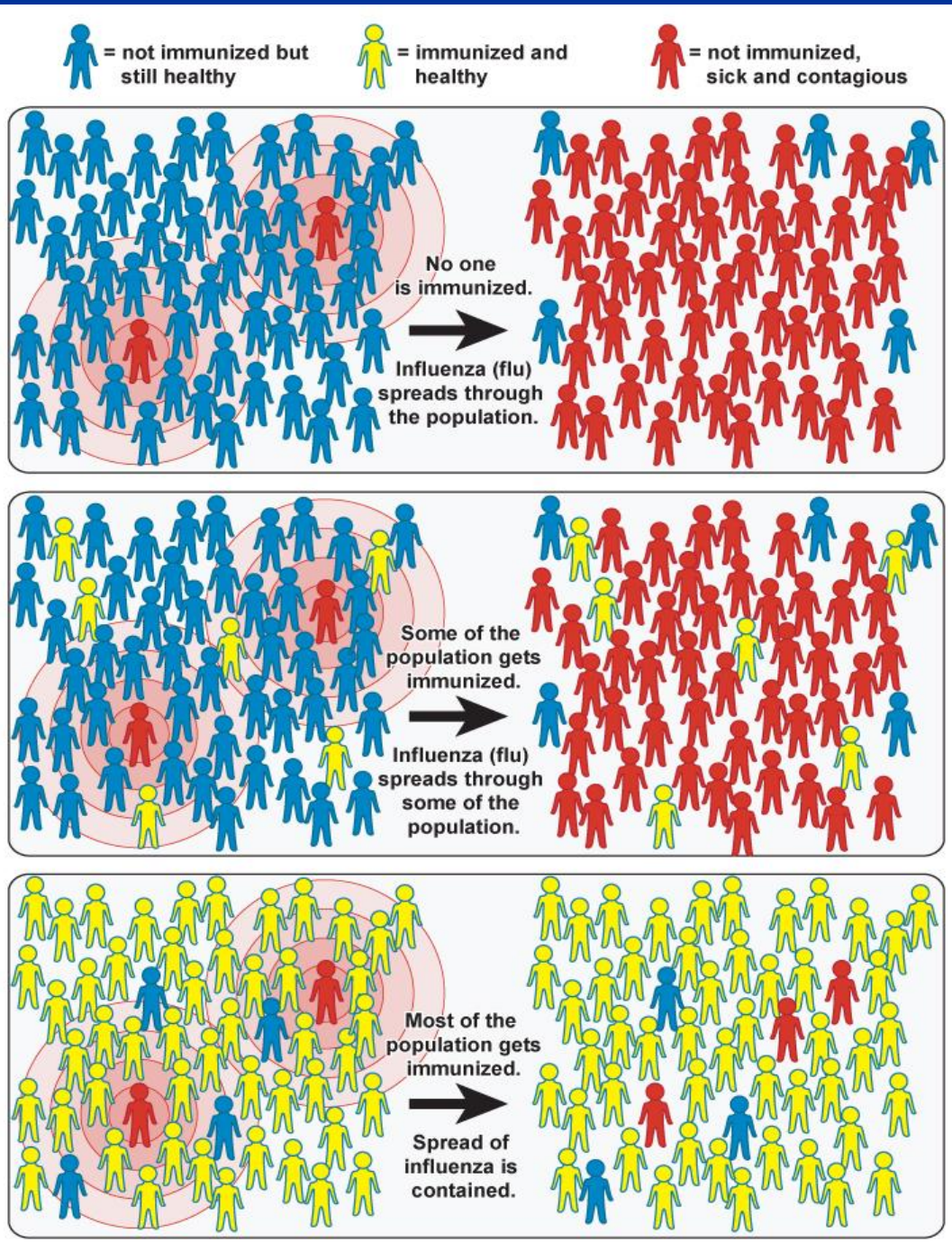
EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

The European regulators agenda to foster prevention and immunisation

Pr. Guido Rasi, EMA Executive Director

- “Historical vaccines”
- “Recurrent vaccines”
- “Emergency vaccines”

"Herd effect"



Community Immunity" by National Institutes of Health (NIH) - National Institutes of Health (NIH). Licensed under Public domain via Wikimedia Commons"

Current clinical requirements for vaccine approval (EMEA/CHMP/VWP/164653/2005)

a) Immunogenicity studies (dose-finding studies, determination of primary vaccination schedule, persistence of protection and timing of booster doses)

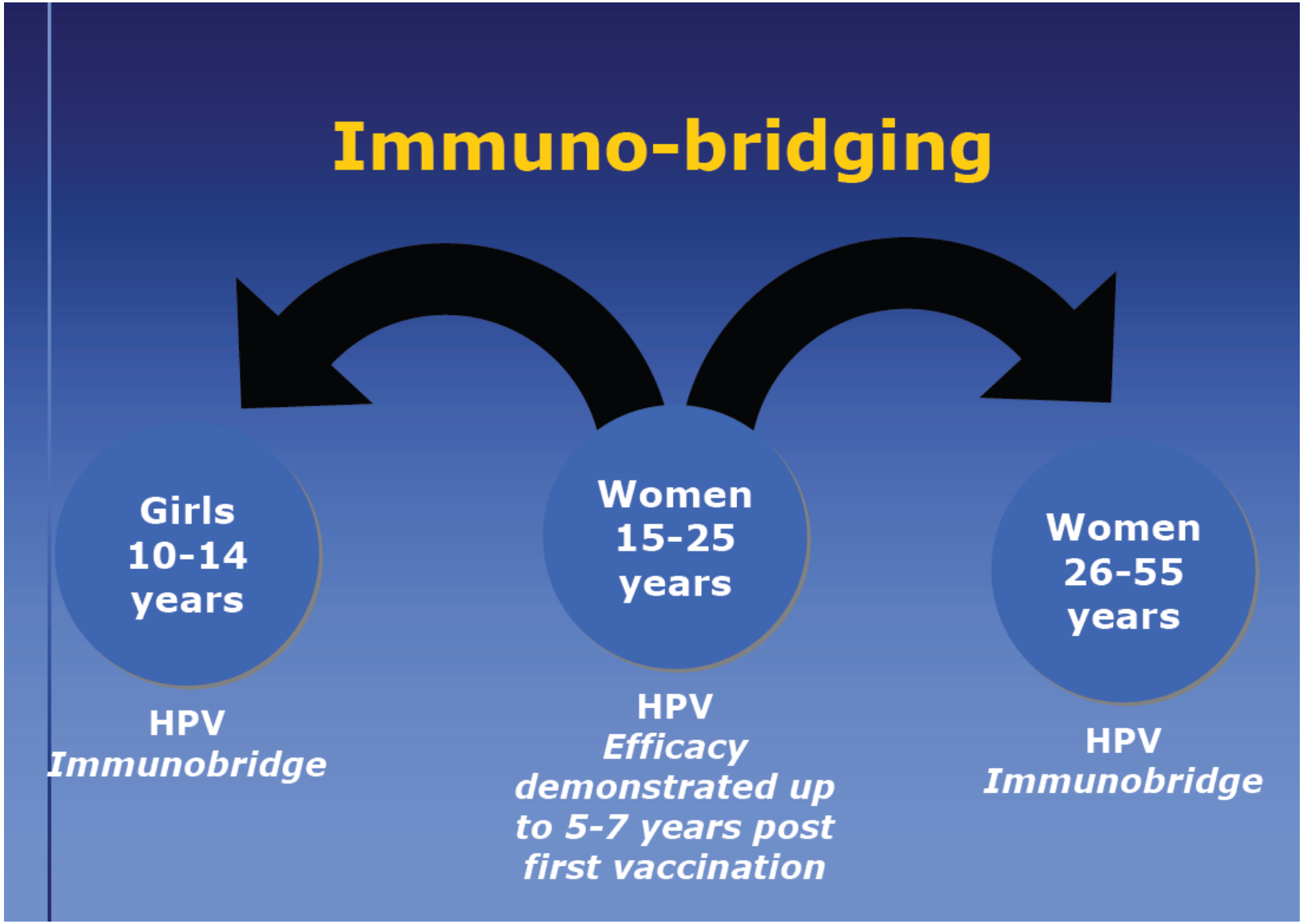
b) Efficacy studies (to evaluate the protective efficacy of a vaccine) and effectiveness studies (to evaluate effectiveness post-authorisation)

Current clinical requirements for vaccine approval (EMEA/CHMP/VWP/164653/2005)

- Safety studies (in principle 3000 individuals in the proposed age range, AEs occurring with frequency between 1/100 – 1/1000)
- Special considerations:
  - immune interference (more than one antigen or concomitant administration of vaccines);
  - cross reacting immune responses;
  - lot-to-lot consistency studies;
  - bridging studies (to extrapolate efficacy based on immunogenicity data from one population to another or for additional schedules) → can only be conducted in case a **Correlate for Protection** (CoP) exists.

Protective Efficacy Studies

- **Not necessary**: if well-established Immune Correlates of Protection (DTaP-IPV-HB-Hib vaccines: e.g. Hexacima, Hexyon, Infanrix Hexa)
- **Necessary** (if feasible) if vaccine is new and no ICP (e.g. first Hib; PnC: Prevenar; rotavirus: Rotarix, Rotateq; HPV: Gardasil, Silgard, Cervarix)
- Subsequent vaccines may be licensed based on **comparative immunogenicity**, e.g. extended 10- and 13-valent PnC (Prevenar 13, Synflorix)



EXAMPLE: Gardasil, Cervarix

EMA committed to support vaccines development by providing *clearer and up to date scientific* guidelines

Discussions on how to facilitate and accelerate vaccine development by ***investigating scientific and regulatory strength of alternatives*** to large and costly randomised clinical trials: e.g. human challenge studies

Post-authorisation activities

- Continuous monitoring of B/R of vaccines also reinforced by the new legal tools (Pharmacovigilance Legislation)
- Several post-authorisation issues such as e.g. PCV1 and narcolepsy
- Importance of long-term studies and effectiveness studies for vaccine approved on surrogate endpoints

Importance of Vaccine Effectiveness

- Measures vaccine efficacy in actual use so encompasses any herd effect
- Informative even when pre-licensure efficacy data exist
- Requires accurate data on vaccine coverage and disease surveillance
- Not truly feasible in many parts of world
- Needs collaboration with Public Health Authorities

Safety

- General approach as for all medicines
- Local /systemic AEs proactively sought
- PSURs routine for all new vaccines
- Special safety studies may be required post-authorisation (PASS)
- Intermittent issues will always arise
- Need to prevent loss of public confidence

EBOLA
options for vaccine development

- RCT
- Pre-clinical studies
- Immunogenicity/innovative CT design

Ebola: EMA activities

- Creation of an ad hoc expert group: EMA scientific committee and working party members with relevant experience in vaccines, infectious diseases, preclinical and clinical trial design, paediatric aspects, quality of biological medicinal products
- Early interactions with manufacturers for rapid scientific advice
- Discussions with EC, HSC, ECDC
- FDA, HC, WHO on available treatments/vaccines and clinical trial design

Regulatory pathways for Ebola vaccines

- GSK ChAd vectored vaccine and Newlinks rVSV vectored vaccine are the most advanced, i.e. now in Phase I
- Assessing evidence from safety and immunogenicity studies for possible options for early approval
- Efficacy studies planned in Western Africa pending evaluation of feasibility
- Size of safety database and current knowledge with similar constructs
- Handling of uncertainties and post-approval studies as needed

Vaccines cannot afford a failure!