The Role of Moderate Efficacy Vaccines in Integrated Disease Control Strategies: Introduction

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GVIRF 2014 Plenary Session 2: Regulatory and public health challenges for vaccines with modest efficacy	
Rapporteurs: Duncan Steele, BMGF and Cristina Cassetti, NIAID	
Session Outline	**Chair: David Salisbury** **Presentations:** Peter Smith, London School of Hygiene and Tropical Medicine **Discussants:** Marion Gruber, US Food and Drug Administration, Pieter Neels, Brad Gessner, Agence de Médecine Préventive
Objectives of the session	Discuss regulatory and public health issues related to authorisation and use of vaccines with modest efficacy, and with consideration of reducing disease burden (and possibly transmission) on a population basis.
Main outcome	More guidance is needed both for regulation and public health recommendations of vaccines of modest efficacy. Post-registration studies will be needed for proper benefit/risk and cost effectiveness assessments.

Peter Smith - Introduction

Statements of fact :

- All vaccines are partially efficacious (i.e. VE< 100%)
- Most vaccines in regular use have relatively high efficacy against at least some disease endpoints
- A vaccine that is licensed will not necessarily be used in public health programmes – distinction between licensing and use perhaps less clear in some LMICs?
- Vaccines with high efficacy may not be cost-effective i.e. disease is rare relative to cost of vaccine – may target vaccine to persons at high risk (e.g. rabies)
- Vaccines with modest efficacy may be cost-effective – e.g. modest impact on high incidence disease

Efficacy depends on the specificity of endpoint relative to vaccine action:

- Pneumococcal vaccine – licensing based on high efficacy against invasive disease due to serotypes in the vaccine - decisions on use may depend upon efficacy against pneumococcal pneumonia (difficult to measure) or all-cause pneumonia – against which the vaccine has low/modest efficacy
- Similar situation with respect to rotavirus vaccines.
- In public health terms, both pneumococcal and rotavirus vaccines have only modest efficacy, but against high incidence diseases.

Marion Gruber, US FDA

Regulatory Consideration for Determining Vaccine Efficacy: Summary

- No regulatory requirement for a specific VE threshold or particular endpoint, regulatory acceptance of "modest efficacy" would depend on
  - Pre-specification of endpoints and VE criteria
  - Confidence interval around the VE point estimate (esp. lower bound)
  - Severity & incidence of disease to be prevented
  - Safety profile of the candidate vaccine
  - Available alternative therapy or control measures
- Possible epidemiological modeling that suggests what "modest" levels of VE could impact public health
- Public consultation with advisory bodies
  - e.g., at planning stage for defining clinical endpoints and VE criteria
  - e.g., during review of Biologic License Application to discuss safety and efficacy data
- Approved use reflects population for which there is substantial evidence of efficacy

Summary

"The regulatory perspective and the public health perspective are different" Marion Gruber, FDA

- Regulatory:
  - Vaccine quality, safety, efficacy
  - Limited guidance on how to evaluate vaccines with limited efficacy
  - Open dialogue with manufacturers encouraged
  - Study design crucial
- Public health:
  - Cost-effectiveness and potential indirect effects may not be available at time of licensure
    - Modelling important
  - Post-introduction impact studies important
  - Communication is critical

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