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Regulatory and public health challenges for vaccines inducing modest efficacy

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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

Criteria to license?

- A vaccine that is “safe” and shows high efficacy against a primary endpoint is likely to be licensed
- Regulators are not used to being presented with vaccines which have low or modest efficacy against primary endpoint
- Decisions on licensing do not take account of the cost of the product
- What criteria would regulators use to license a vaccine with low/modest efficacy vaccine against primary endpoint – safe and better than water, but how much better than water?

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.

Suppose efficacy is modest against primary endpoint:

- First generation malaria vaccines will have only modest efficacy against clinical malaria
- Would the licensing situation be any different if we could identify strains of malaria against which the vaccine gave high efficacy and others against which there was no efficacy (akin to serotypes in pneumococcal vaccines), so that overall the protection against malaria was modest?
- Is the licensing situation different according to the mode of vaccine action (e.g. modest protection to all vaccinated vs. high protection to some and little or no protection to others)?

Will modest efficacy vaccines erode public confidence?

- Public expect vaccines to prevent disease (e.g. measles). Would a vaccine that prevents only some disease (an effect that may be difficult for an individual to perceive) erode confidence in vaccination programmes?
- Probably an unfounded fear, given the experience already with pneumococcal and rotavirus vaccines, which have modest efficacy against the endpoints of most public (health) interest.