

# QUESTION 1

**Rotavirus vaccines efficacy & effectiveness is lower in settings with high under five mortality**

**# of doses:** limited evidence suggest that giving 3 doses of RV1 may be superior to a 2 dose schedule.

**additional evidence is required** – some studies ongoing

**age at administration:** limited evidence to assess the effect of different ages at administration on key outcomes.

**co-administration:** available evidence suggests that there are no differences in efficacy after a full course of RV is administered alone or concomitantly with other childhood vaccines

# QUESTION 2

**Trade-offs exist when considering various schedule options**  
**Model estimates include large uncertainties**

	Median (5 <sup>th</sup> and 95 <sup>th</sup> percentiles)	
	Rotavirus Deaths Averted	Associated Intussusception Deaths
<b>Restricted</b>	<b>156,100</b> (110,100 to 201,800)	<b>288</b> (99 to 688)*
<b>No age restriction</b>	<b>199,200</b> (140,700 to 255,400)	<b>605</b> (310 to 1,133)*
<b>No age restriction (vs. age restriction)</b>	<b>43,100</b> additional rotavirus deaths averted (30,600 to 53,500)	<b>317</b> additional IS deaths associated (211 to 445)

# Potential advantages of removing age restriction

**Increased number of children vaccinated and greater number of deaths averted**

- in some LMICs countries only **60%** of children receive the 1<sup>st</sup> dose of DTP by **15 weeks** of age and,
- only **50%** of the children received the 3rd dose of DTP by **32 weeks** of age.

**Logistically easier to implement**

- with DTP contacts
- In many developing countries, as many as **80% of infants are reached by outreach services.**

# Potential disadvantages of removing age restriction

## **Potential to increase the number of intussusception cases and deaths**

- Limited evidence whether there would be increased risk of intussusception including deaths

There may be less emphasis in on timeliness of vaccination for rotavirus and other vaccines

Potential negative impact on rotavirus vaccine and overall immunization programme

- May be difficult to communicate and develop messages, if there are different recommendations in various countries in regards to age limitations
- Potential legal issues linked to off label use.

# Conclusions (1)

Most participants concurred that SAGE members should **consider a recommendation to remove the age restrictions** currently guiding the administration of the 1<sup>st</sup> and last dose of rotavirus vaccines.

# Conclusions (2)

This decision should be communicated to countries together with:

- a clear and simple description of the **extent and robustness of the evidence**,
- a clear statement on the **potential benefits and risks involved**,
- guidance to assess the **trade-offs involved** in such recommendation and,
- with a reminder on the need for **enhancing post marketing surveillance** efforts

# Conclusions (3)

Participants emphasized the importance of country level **NITAGs** in selecting the most appropriate schedule for their country

- **independent assessment** of whether the estimated benefits in that country outweigh the potential risks.
- **transparency with the public** regarding the risks and benefits of the selected rotavirus vaccination schedule

# GACVS, Dec 2011

... available data suggest that both Rotarix and RotaTeq continue to exhibit **a good safety profile, but may be associated with an increased (up to 6-fold) risk of intussusception after the first dose** of vaccine in some populations. ..

...the levels of risk observed are substantially less than those observed with the previous vaccine, Rotashield. ..

... GACVS reiterates that **the benefits of rotavirus vaccination to all infants, without age restriction, would greatly exceed the risks**, particularly in developing countries with moderate and high mortality from rotavirus disease.



# IPAC, Sept 2011

IPAC stressed the need of appropriate health worker training to accompany rotavirus introduction.

A sub group was formed to assist with RV training guidance. Case scenarios with which the health worker could be confronted, and potential training solutions.

1. unknown birth date,
2. no availability of EPI card,
3. health worker doubts on age based on infant's appearance,
4. suspected intussusceptions,
5. contraindications,
6. spitting
7. regurgitation of dose,
8. mishandling when opening the tube.

# Conclusions (4)

Given the data on the disease epidemiology and despite the somewhat lower immunogenicity observed in young infants, the 1<sup>st</sup> dose should be administered at 6 weeks of age or as soon thereafter as possible

- impact of the rotavirus vaccination programme depends on **timely achievement of high coverage with each of the rotavirus vaccine doses.**
  - especially in LICs, where rotavirus disease peaks around **26-30 weeks** of age and where rotavirus related mortality in infants is high

# Conclusions (5)

Preliminary immunogenicity data suggest that there could be **merit in further assessing the potential benefits** (e.g. greater seroconversion rates) of a 3<sup>rd</sup> dose of RV1 (Rotarix™)

- the currently available evidence is **insufficient to assess the clinical benefits** of an additional dose of RV1. On-going studies will provide additional information by 2013.
- need to define **what type of evidence** will be required to inform global policy and, weigh the **cost versus benefit** of adding a third dose of RV1.

# Research Priorities

**Especially in high mortality settings in Africa and Asia**

## **SAFETY - INTUSSUSCEPTION**

- Background risk rates of intussusception by age
- Safety of rotavirus vaccines when administered to infants at various ages
- Potential impact of rotavirus vaccine in reducing the risk of intussusception.

## **EPIDEMIOLOGY**

- Epidemiology of rotavirus disease (finely stratified by age especially in infants and young children)

## **IMPACT**

- Actual age at vaccination & coverage achieved with each dose by age in weeks
- Impact and cost-effectiveness of alternative strategies to improve timeliness.
- Head to head comparisons on the effectiveness of rotavirus vaccines depending on timing of doses and the number of doses given

# SUMMARY

Based on all this evidence, the *ad hoc* Expert Group on Rotavirus Vaccines recommends that SAGE should consider lifting the current global age restrictions for rotavirus vaccines