For SAGE discussion

Potential guidance to countries on vaccines for the mercury-treaty negotiations

Information already provided by WHO on the use of thiomersal in human vaccines

- The amount of mercury involved with thiomersal use in vaccines is very small compared to other sources of mercury
- There is no evidence that suggests a possible health hazard with the amounts of thiomersal currently used in human vaccines
- WHO recommends multi-dose vaccine vials for routine immunization programmes in many countries because they are safe and effective, they limit the required storage capacity and help reduce vaccine costs
- Alternative presentations would incur significantly higher costs in manufacturing procedures and new regulatory approvals, thereby limiting the ability to offer affordable vaccines

Potential additional guidance to countries

- Replacement of thiomersal with an alternative preservative may affect final formulation and will be viewed by regulatory authorities as a new product that requires registration in each jurisdiction of the world where the product will be used

- New product development will be unpredictable since:
  - there are no clear alternative candidate preservatives for the near-or mid-term and not all options perform equally with existing vaccines
  - alternative preservatives may interact with the components of the vaccine and removal of thiomersal may impact vaccine performance and vaccine safety
  - lack of incentive to reformulate current low cost vaccines (TT, DTwP, hep B)

Potential additional guidance to countries

- Removal of thiomersal and switch to single-use vials affects manufacturing capacity; has significant cold chain, storage, and waste management implications; increases health care workload; and with very large increases in cost
- There is a risk that some products (if reformulation/development with alternative preservatives or with no preservatives is required) will become unavailable
- There is a high risk of serious disruption to routine immunization programmes and mass immunization campaigns if multi-dose vials (currently thiomersal-preserved) are not available
  - the consequences will be a predictable and sizable increase in mortality, for very limited environmental impact

Additional considerations

Risks to vaccine access during treaty negotiations

- Political considerations in one country have resulted in a decision to ban thiomersal-containing vaccines without appropriate technical planning on alternative supply options
- Supply interruptions may result if similar policy decisions are made in other countries
- Solution: strong advocacy in countries using thiomersal preserved vaccines, based on
  - the WHO position and SAGE conclusions
  - expert impact assessments collated for the April 3-4 meeting

Risks to vaccine access after the treaty is ratified

(even if vaccines are excluded from the scope of the treaty)

- There is, globally, a single source supplier of pharmaceutical-grade thiomersal, accounting for 70% of it's business

- annual output in 1992 was 10,000 kg; by 2011 this had fallen to 2,434 kg. In addition, over the same period, the price of Thiomersal has also changed from $3,500 per kg to about $1,000 per kg

- Environmental regulatory requirements on import and export of thiomersal will likely increase, creating potential problems with availability of raw materials for vaccine manufacture

- Vaccine manufacturers will face increased environmental regulatory burden to adequately manage and protect (workers and the environment) against accidental exposure to/spillages of thiomersal during vaccine production

- Solutions:
  - (a) consider measures to support thiomersal supply and,
  - (b) proactive work with regulators and manufacturers on environmental protection measures for working with thiomersal

Future work

- In the long term, as an insurance policy to ensure availability of multidose vaccines, further work should be stimulated, recognizing

  - there is, currently, little or no academic or regulatory research on alternative preservatives

  - there is little or no operational research to evaluate the relationship between the criteria for antimicrobial tests for preservatives and the safety of multi-dose vaccines when used with current immunization practices

  - that these efforts will be difficult and may not be successful

- Solution: investment and focused effort to identify (a) additional preservatives, and (b) preferred product presentations for multi-dose formulations with or without preservatives