Global Advisory Committee on Vaccine Safety (GACVS)

Report on GACVS meeting

December 2011

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Influenza A(H1N1)2009

- Association of Pandemrix with narcolepsy/cataplexy in Finland and Sweden
  - European Medicine Agency concluded that "benefits of Pandemrix continue to outweigh its risks (…) in people <20 years of age only if recommended seasonal vaccine is not available"
  - Additional epidemiological studies are still in progress in Europe and Canada
  - Immunological and animal model studies to help elucidate the biological mechanism of the observed association are in progress

Influenza A(H1N1)2009

- Other studies:
  - Possible increase in risk of Guillain-Barré (USA) not yet replicated elsewhere
  - Possible association with other clinical syndromes did not identify major safety concerns
- Immunization in pregnancy:
  - An observational cohort study in Canada and data from birth and infant health registry in the United States did not point to any safety concerns related to pandemic vaccines among women during gestation or their offspring
  - Additional data expected as other studies are completed

Influenza A(H1N1)2009 GACVS conclusions

- Need to elucidate the possible biological mechanism for an association between Pandemrix and narcolepsy/ cataplexy
  - Role of the adjuvant?
- If confirmed, the risk of GBS observed in the USA would be much lower than that observed in 1976 during the swine influenza vaccination campaign
- For other signals reported, GACVS noted that the sample size or methodology of these studies might not have been optimal for establishing causal relations

Rotavirus vaccines and intussusception

- 2009 SAGE recommendations for current rotavirus vaccines:
  - First dose be administered between 6-15 weeks of age
  - Last dose be administered before 32 weeks of age
- Delays in timing of vaccination are noted in many countries, in particular in countries with high rates of rotavirus-associated infant mortality
- Risk of intussusception documented after use of Rotarix (Australia and Mexico) and RotaTeq (Australia)

Rotavirus vaccines and intussusception

- In studies where a risk was found, 4- to 6-fold increases in risk are clustered within the first week after the first dose
- This compares to 30-fold risk during the same time period with Rotashield
- A risk–benefit analysis predicts that use of current rotavirus vaccines without age restriction would prevent an additional 49 500 (range: 35 000–67 000) rotavirus deaths while potentially causing about 300 (range: 180–400) excess intussusception deaths, compared with the current age-restricted strategy

Rotavirus vaccines and intussusception GACVS conclusions

- 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
- Levels of risk observed are substantially less than those observed with the previous vaccine, Rotashield
- The benefits of rotavirus vaccination without age restriction would greatly exceed the risks, particularly in developing countries with moderate and high mortality from rotavirus disease
- Active surveillance of intussusception in countries that plan to introduce rotavirus vaccines should be seriously considered

Vaccine safety in pregnancy and lactation

- Policy formulation regarding vaccination during pregnancy is challenging because of limited evidence available
- SAGE requested GACVS to provide guidance on the safety of vaccines used among pregnant and lactating women
- Issues under discussion:
  - Framework for addressing the safety of vaccines in pregnancy and lactation
  - Feasibility of assessing safety of vaccines in pregnancy and lactation during the vaccine development process
  - Additional opportunities for generating post licensure data
  - Possible role for WHO to help harmonize practices vaccine package labeling

Vaccine safety in pregnancy and lactation GACVS approach

- GACVS recognizes the need to address safety issues related to the use of vaccines during pregnancy and lactation
- GACVS proposes to review available evidence for selected vaccines
- We will also consider including methodological points for planning and analysis of clinical trials and postmarketing studies

Global network for post marketing surveillance and AEFI monitoring

- WHO-led pilot project aimed at enhancing the monitoring, reporting and sharing of vaccine safety data for countries introducing new prequalified vaccines
- Reporting of AEFI to a central database (Vigibase) located at the WHO Collaborating Center for international drug monitoring
- A dictionary for prequalified vaccines has been developed to determine the components of vaccines that could be implicated in serious or relevant adverse events

Global network
GACVS conclusions

- GACVS recognized the limited value of spontaneous reports to determine vaccine safety profiles
- Nevertheless, spontaneous reports of AEFI are important to generate signals and can inform the design and conduct of epidemiologic studies
- GACVS also acknowledges the importance of a global database for all drugs and vaccines to allow countries, regions, and investigators to detect global vaccine safety signals that could go unrecognized at a country level
- GACVS also emphasized the need for strengthening AEFI surveillance systems at country and regional levels to improve the current reporting of safety signals following immunization

GVS Blueprint implementation

- Terms of reference for the management of the **Global Vaccine Safety Initiative** were presented
- Structure designed to deliver the programmatic changes required of the GVSI and will align its efforts with those of other WHO advisory groups
- In supporting the GVSI, GACVS has a role in development of safety communication plans, development of internationally harmonized tools, and provision of international expert advice
- GACVS could also have a role in prioritization of GVSI activities and review and guide any demonstration surveillance projects

GVS Blueprint implementation

- WHO and its partners should lead the Blueprint implementation
- GVSI should be aligned with other related WHO capacity-building efforts
- SAGE suggested that a mechanism be developed to enable prioritization of both activities and countries in the implementation of the Blueprint
- SAGE invited the GAVI Alliance and other partners to support this implementation

Next GACVS meeting: 6-7 June 2012

Specific issues

- Shancol safety profile
- Thiomersal safety
- Aluminum in vaccines

General issues

- Causality classification scheme for serious AEFI
- Immunization in pregnancy
- Core data for vaccine safety monitoring