Global Advisory Committee on Vaccine Safety (GACVS)

Report from the December 2016 meeting
Topics Discussed in December

- Narcolepsy and 2009 pH1N1 influenza vaccines: new data
- Typhoid vaccines
- Yellow fever vaccine: use of fractional dose
- Recommendations arising from “The GACVS at 15 years” *
- Vaccine Safety Net: Follow up to a meeting of members

New data on narcolepsy

- Previous GACVS reviews: June 2013 and December 2015
  - “Consistent evidence” in Europe of increased risk following Pandemrix

- Meeting reviewed additional studies/evidence
  - Early results from SOMNIA (Systematic Observational Method for Narcolepsy and Influenza Immunization Assessment)
  - Cases of narcolepsy in South Korea following unadjuvanted vaccines

- SOMNIA: included ASO3 and MF59 adjuvanted vaccines
  - 13 study sites in 9 countries: Canada, Argentina, Netherlands, Spain, Switzerland, China, Taiwan, and Denmark, Sweden and UK

- Case reports from South Korea following unadjuvanted vaccine
Conclusions/Recommendations

- Results: new data consistent with current information
  - New evidence on Focetria (MF59) – elevated risk (non-significant) only in children only in restricted period analysis
  - No other substantial associations found except in Sweden (already known)
  - No increased risk for Arepanrix (a previous study did find risk of 1/million doses)

- GACVS reassured that with the exception of Pandemrix in a few countries, no other substantial association between use of p2009H1N1 vaccines and narcolepsy has been identified

- Need remains to elucidate the precise mechanism

- GACVS noted that additional data may yet become available from extended follow-up of existing studies
Typhoid vaccines

- Current vaccines include live attenuated Ty21a (oral) and Vi (PS)
  - Used for over 3 decades with good safety profile
  - Moderate effectiveness in children

- ViPS conjugate vaccines:
  - A Vi-rEPA conjugated vaccine evaluated in Vietnam showed good efficacy
  - Two Vi-TT conjugated vaccines from India (Peda Typh and Typbar-TCV).

- Safety data on Typbar
  - Evaluated in 1000 subjects pre-licensure
  - No safety signals from clinical evaluation of 970 subjects postlicensure
  - Based on 3 million doses of Typbar-TCV in the private market, no serious adverse events reported from 3,000 case reports analyzed.
Conclusions/Recommendations

- GACVS noted the limitations to the available data
  - No new signals of serious events identified with any existing vaccine
  - Difficult to make a recommendation for new vaccines (eg. to SAGE) given limited data

- Need for further safety monitoring through post-marketing surveillance and planned large effectiveness studies
  - Noted that a larger study underway and look forward to results
Yellow fever vaccine fractional doses

- Existing use of vaccine: generally safe, life long protection
- Outbreak of yellow fever in 2016 in sub-Saharan Africa
  - Mass campaign in Angola, DRC and Uganda: 31 million vaccinated
- Global shortage of vaccine necessitated use of fractional dose with intradermal administration

- Mass campaign in Kinshasa with ~7.5M receiving 1/5\textsuperscript{th} dose (0.1 ml)
  - Safety monitored with several approaches: spontaneous reporting, community surveys, alerts for serious cases
  - Profile of adverse events from fraction doses were similar to full dose

- GACVS met to discuss surveillance of AEFI in DRC, particularly regarding fractional dosing
Conclusions/Recommendations

- GACVS recommended use of Brighton case definitions and better ascertainment of yellow fever cases as vaccine-related vs wild-type
  - Including more detailed review of potential programmatic errors given fractional dosing

- Given the current shortage in vaccine and eventual need to expand use of fractionated dose GACVS urged DRC to conduct a detailed analysis of its AEFI reports
Review of GACVS at 15 years*:
Conclusions/Recommendations

Discussion around strengthening operations and outreach

- Capacity for systematic review / need for presentation standards
  - Improve the quality of evidence presented to GACVS
  - Template for presenting safety data from clinical trials and early post-licensure surveillance (to be reviewed at June 17 meeting)

- Increase dissemination of GACVS output, focus on LMICs
  - New e-newsletter disseminated to > 3800 stakeholders
  - Consideration for social media, releases as with SAGE

- GACVS as an advocate/facilitator: bridge gaps in safety capacity globally
  - Use the Global Vaccine Safety Initiative (GVSI)
  - Convene Member States to discuss vaccine safety with GACVS and to identify priorities at all levels, from local to regional

The Vaccine Safety Net

- WHO initiative to facilitate access to reliable information on the safety of vaccines via the Internet through quality standards
  - GACVS previously endorsed revised evaluation criteria
- Established 2003 at the request of stakeholders to help counter increasingly unbalanced and misleading information on the Internet
- Members presented with:
  - New visual identity
  - Web portal in development
  - Proposed web analytics project
  - Opportunity to help shape VSN and develop vision/mission
Outcome of a meeting of members

- Strengthened links between members
- VSN mission and objectives reinforced
- Advisory Group to be established
- Public and Member portal welcomed
- A VSN visual identity endorsed
- Agreement to participate in a web analytics project and future collaborations

November 2016: VSN members meet for the first time in over 10 years!

GACVS members noted the work undertaken in developing the VSN and emphasizing the value of international collaboration
Topics for June 2017

- Templates for safety presentations to GACVS
- Malaria vaccine pilots in 2018
- Update on HPV vaccines
- BCG vaccines: systematic review