Global Advisory Committee on Vaccine Safety (GACVS)

Report from the December 2016 meeting

World Health Organization

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

***Asturias EJ, et al. Contributions and challenges for worldwide vaccine safety: The Global Advisory Committee on Vaccine Safety at 15 years. Vaccine 2016; 34(29)**

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
  - Evalutated 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 1/5th 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

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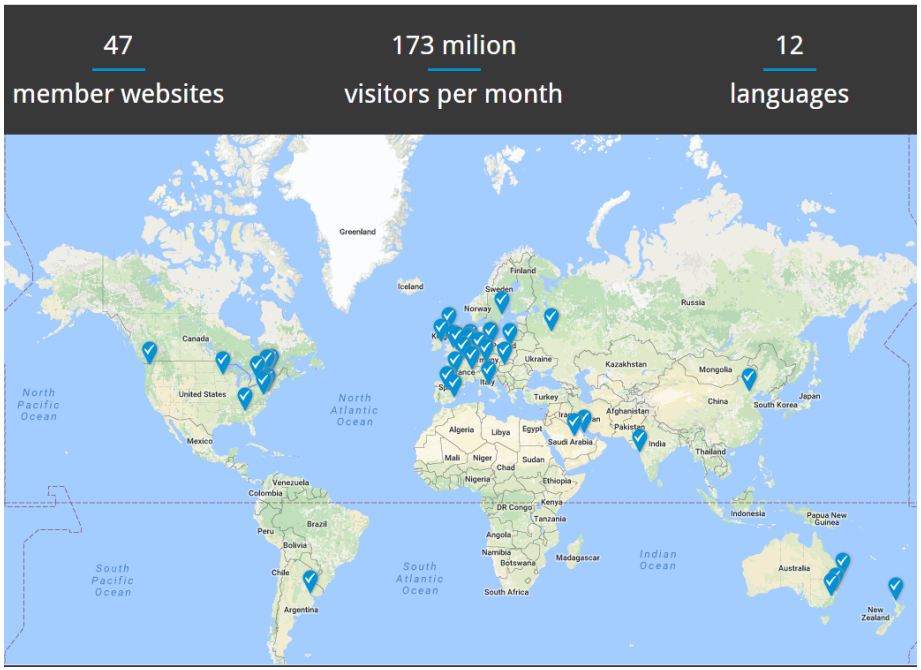
The Vaccine Safety Net



- 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

World Health Organization

Outcome of a meeting of members

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

- 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

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