Global Advisory Committee on Vaccine Safety (GACVS)

World Health Organization

Report from the June 2017 meeting

Topics discussed in June

- Safety monitoring of the RTS,S vaccine pilot implementation programme
- Safety update of BCG vaccine
- Safety update of HPV vaccines
- Template for reviewing the safety profile of new vaccines

Safety monitoring of the RTS,S vaccine pilot implementation programme

- GACVS has followed the development of RTS,S
  - With EMA (article 58): WHO recommending further evaluation
    - 4-dose schedule, impact on all-cause mortality, excess cases of meningitis and cerebral malaria
- Proposal calls for pilot implementations in areas of moderate to high transmission (Ghana, Kenya, Malawi)
- GACVS was updated on designs of the pilot programmes
  - Introduction through the national EPI in districts/counties
  - Regulatory approval for pilot introduction and Risk Management Plan from GSK
  - State of routine vaccine pharmacovigilance in the pilot countries
  - The proposed safety data flow, and
  - Proposal to set up a Programme Safety Committee.

Safety monitoring of the RTS,S vaccine pilot implementation programme

Conclusions/Recommendations

- Strengthening routine pharmacovigilance ahead of pilot introductions
- Supported training, logistics, criteria for readiness, including
  - Minimum 10 annual AEFI reports/100 000 surviving infants
  - Functional AEFI committees + resourced investigation teams + safety communication plans
  - An EPI focal point to oversee reporting and training
- Identification of Adverse Events of Special Interest assessable by active surveillance
  - Based on routine program and theoretical RTS,S concerns, and established baseline data
- Establish a Programme Safety Committee (PSC) for overall evaluation
  - Including a joint dataset for review by the PSC, and updates to countries and to GACVS – who will continue providing support

Safety update of BCG vaccine

Notes, Conclusions and Recommendations

- Reviewed in preparation for an updated WHO position paper and safety information sheet (previous ones in 2004 and 2007)
  - BCG vaccines remain important despite a small number pre-qualified
  - Effective in infants but variable, leading to varied BCG policies
- Safety profile is well-established, however
  - Reactogenicity influenced by strain, age administered, immune status, manufacturing changes and revaccination – often hard to predict
- A recent systematic review noted limitations in available safety data, but was underway at the time of the meeting. Information still sought:
  - Strain-specific reactogenicity including variations within the same manufacturing process
  - Differences in rates between newborns, late- and post-neonatal periods
  - HIV and non-HIV affected infants

Safety update of HPV vaccines

- GACVS has reviewed safety data over 6 prior meetings
  - Last to SAGE in 2016 (autoimmune disease, POTS, update on Japan)
- Since that update, further data from Denmark, the UK and the US
  - GBS: large self-controlled case-series study in the UK, studies in the US
  - Complex regional pain syndrome (CRPS), postural orthostatic tachycardia syndrome (POTS), premature ovarian insufficiency, primary ovarian failure, and risk of venous thromboembolism
  - Obstetric, birth, congenital anomalies: cohort studies in Denmark, US
- CRPS and POTS continue to be presented as case reports
  - Diverse symptoms make assessment difficult
  - New data from Japan: events in girls > boys, both vaccinated & unvaccinated
- GACVS presented with a review of that included data on 74,000
  - Good quality RCTs and cohort studies
  - No difference in rates of selected serious events

Safety update of HPV vaccines

Conclusions/Recommendations

- Over 270 million doses of HPV vaccine have been distributed
  - Safety studies: several million persons, wide range of outcomes
  - Despite this: attention focused on spurious case reports/allegations
- Negative impact has affected coverage, limiting effectiveness
  - Japan: has been seeing increased mortality from cervical cancer, now likely to continue
  - Countries with programs: reporting decreases in pre-cancerous lesions
- GACVS found no events of concern based on large, quality studies.
  - New data at the June meeting strengthened the position
  - With all data collection, artefacts may be observed, posing challenges
  - Better access to summaries of safety information important to assist decision-making

Template for reviewing the safety profile of new vaccines

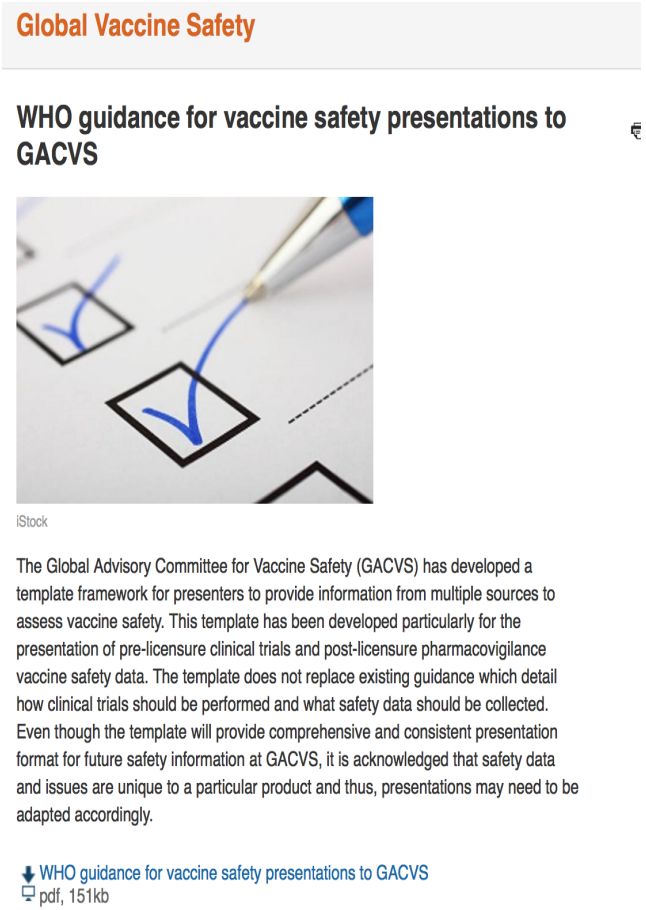
- GACVS evaluates evidence from multiple sources
  - Presentations to GACVS vary in quantity and quality of information
  - The review of GACVS recommended standardization to facilitate assessment and increase efficiency
- Guidance developed to provide presenters with a framework
  - Including essential information GACVS requires to assess safety
    - Section 1: Presenters/conflicts of interest/product development/characteristics.
    - Section 2: Integrated Summary of Safety.
    - Section 3: Pre-licensure clinical trials.
    - Section 4: Methodology and results from post-licensure trials, surveillance studies
    - Section 5: Plans for future post-marketing studies or pharmacovigilance activities
    - Section 6: Supporting material, references, product labels, etc.
- Includes timelines for submitting material and review prior meetings
- Presenters encouraged to liaise with the WHO/GACVS while developing content

Template for reviewing the safety profile of new vaccines

World Health Organization

Conclusions

- The template was revised and is now posted on the GACVS website
- The template and guidance document to be piloted by presenters for the December meeting



Global Vaccine Safety

WHO guidance for vaccine safety presentations to GACVS

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The Global Advisory Committee for Vaccine Safety (GACVS) has developed a template framework for presenters to provide information from multiple sources to assess vaccine safety. This template has been developed particularly for the presentation of pre-licensure clinical trials and post-licensure pharmacovigilance vaccine safety data. The template does not replace existing guidance which detail how clinical trials should be performed and what safety data should be collected. Even though the template will provide comprehensive and consistent presentation format for future safety information at GACVS, it is acknowledged that safety data and issues are unique to a particular product and thus, presentations may need to be adapted accordingly.

WHO guidance for vaccine safety presentations to GACVS
pdf, 151kb

Proposed topics for December, 2017

- RTS,S vaccine pilot updates
- Vigilance of vaccines administered during pregnancy
- Rotavirus vaccine safety
- Guidance on immunization triggered stress responses
- AEFI causality assessment – inter-rater study