SAGE discussion and statement in relation with the IPV supply situation

10 March 2016

BACKGROUND

In February and March 2016, the two main IPV suppliers (i.e. Bilthoven Biologicals and Sanofi Pasteur) informed WHO/UNICEF that they will substantially reduce or delay the quantities of IPV supplied in 2016 and 2017, due to technical challenges in scaling up IPV bulk production and the associated quality control testing and releases. This has created significant delays in IPV introduction and shortages of supply in many countries.

SAGE POLIO WG DISCUSIONS

The SAGE WG closely reviewed the IPV supply situation during a conference call held on 3 March 2016 as well as via email in response to the further details provided on 7 March 2016.

While the SAGE WG expressed concern that the shortage may cause serious disruption in many countries, it unanimously reaffirmed that the public health risks associated with the continued use of the type 2 component contained in tOPV outweigh the risks of new VDPV2 emergence after the global withdrawal of OPV type 2, even in countries where IPV introduction will be further delayed. It furthermore noted that a global stockpile of mOPV2 is available for emergency response in case of cVDPV2 emergence.

It reaffirmed that countries should proceed with the switch as scheduled during the period 17 April to 1 May 2016.

The SAGE WG also reviewed evidence available on the administration of fractional, intradermal (ID) IPV. Recent studies from Bangladesh[1] and Cuba[2] demonstrate that the immunogenicity of two fractional doses of IPV (0.1 ml) administered through the intra dermal route are superior to one full dose (0.5 ml) administered through the intra muscular route. In Cuba, two fractional doses of IPV given intradermally at 4 and 8 month induced 98% seroconversion rate against type 2, in comparison to 63% seroconversion conferred by one full dose administered intra-muscularly at 4 months. Similarly, in Bangladesh, two fractional doses of IPV administered intradermally at 6 and 14 weeks in induced 81% seroconversion against type 2 versus 39% with one full dose of IPV administered intra-muscularly at 6 weeks. The seroconversion rate reported following two fractional doses at 6 and 14 weeks (i.e. 81%) in Bangladesh is higher than the seroconversion following one full dose of IPV given at 14 weeks (73%) reported from a subsequent trial, conducted by the same investigators, in a similar study population in Bangladesh, using the same laboratory (Anand A. Unpublished data, 2016). In both studies, two fractional doses induced substantially higher antibody titres (16- to 32-fold higher) against type 2 than one full dose (and two fractional doses at 6 and 14 weeks in Bangladesh induced higher antibody titres than one full dose at 14 weeks in the follow-on study [10-fold higher]). The WG concluded that the proposed schedule of two fractional IPV doses can induce equal or better immunity than the one full-dose schedule.

Related developments

Based on these data and ongoing IPV shortage, the updated WHO position paper on polio vaccine (to be published on 25 March 2016) reaffirmed the previously stated potential alternative of using a fractional dose of IPV via the ID route and states that, in order to ensure that all eligible infants receive IPV, countries could consider instituting a 2-dose fractional dose schedule which is dose-sparing and results in better immunogenicity than a single full dose of IPV.

In March 2016, the India Expert Advisory Group (IEAG) recommended to the Ministry of Health and Family Welfare that 6-7 states in India should introduce a schedule of two fractional doses of IPV to be administered at 6 and 14 weeks of age[3].

SAGE Position

During its 2nd preparatory teleconference for the April SAGE meeting, SAGE discussed the above.
SAGE fully concurs with the WG conclusions:

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[1] Anand A et al. Early priming with inactivated poliovirus vaccine (IPV) and intradermal fractional dose IPV administered by a microneedle device: A randomized controlled trial. Vaccine. 2015 27;33:6816-22

[2] Resik S et al. Priming after a fractional dose of inactivated poliovirus vaccine. N Engl J Med 2013;368: 416-24.

[3] India Expert Advisory Group for Polio Eradication. Delhi, India, 26 February 2016. Conclusion and Recommendations http://www.who.int/immunization/diseases/poliomyelitis/endgame_objective2/inactivated_polio_vaccine/planning/en/

- SAGE re-affirms its October 2015 conclusion that the Switch should proceed in April 2016, even with the recent decline in IPV supply
- SAGE recommends that countries consider adopting a two fractional doses IPV schedule (e.g. at 6 and 14 weeks for early protection), as mentioned in the upcoming WHO Polio Position Paper
- SAGE recommends that countries which are considering introducing a fractional dose schedule should ensure that health workers capacity to administer ID injection is assessed and strengthened.