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Information on leaking syringes of various GSK vaccines

The following products are affected: **BOOSTRIX, BOOSTRIX Polio, ENGERIX-B 20, ENGERIX-B 10, HAVRIX 720, HAVRIX 1440, INFANRIX Hexa (DTPa-HepB-IPV+Hib), INFANRIX DTPa-IPV+Hib, INFANRIX DTPa-IPV, PRIORIX, PRIORIX Tetra, TWINRIX 720/20, VARILRIX**

Summary

• During vaccine preparation (reconstitution) or administration, leakages from syringes have occurred with certain GSK vaccines (escape of fluid between the syringe and needle, see Figure 1).

• The frequency of leaking syringes, calculated on the basis of complaint rates in Switzerland, is 5.53 in 100,000 distributed vaccine doses.

• The sterility of the vaccine is not adversely affected by the syringe leakages.

• The escape of fairly large quantities of vaccine from a leaking syringe could, in theory, result in under-dosing and hence reduce the protection afforded by vaccination. However, an analysis of GSK's pharmacovigilance data has shown no evidence that the observed syringe leakages have resulted in vaccination failure or other safety concerns for vaccinated individuals.

• **If a leakage occurs during the reconstitution of lyophilised vaccines, the affected syringe should be discarded.**

• **If leakage is observed during the administration of a vaccine, the doctor must decide whether the individual concerned should be revaccinated. The potential benefit of increasing vaccination protection by administering a second full dose should be weighed against the risk of the adverse events due to a repeated administration. Preparation-specific decision-making guidelines can be found below under *Information on potential under-dosing / over-dosing.***

• Doctors are asked to report complaints about product quality, medication errors and suspected adverse reactions. For reports of adverse drug reactions (ADRs), Swissmedic recommends the use of the reporting portal developed for this purpose. This portal, which is known as the Electronic Vigilance System (EIViS), can be used to submit ADRs directly or by downloading an xml file. All the necessary information can be found at www.swissmedic.ch > *Market surveillance > Pharmacovigilance*

Background on the occurrence of leaking syringes

Since July 2015, GSK has received an increasing number of reports of leaking vaccine syringes with a ceramic-coated tip (CCT syringes) (escape of fluid between the syringe and needle during use, see Figure 1). This is attributable to unsolvable technical problems during syringe manufacture.

The syringe leakage occurs when the plunger is pressed down during the injection / reconstitution (pressure build-up); given the absence of any leakage problems before use, there are no sterility concerns.

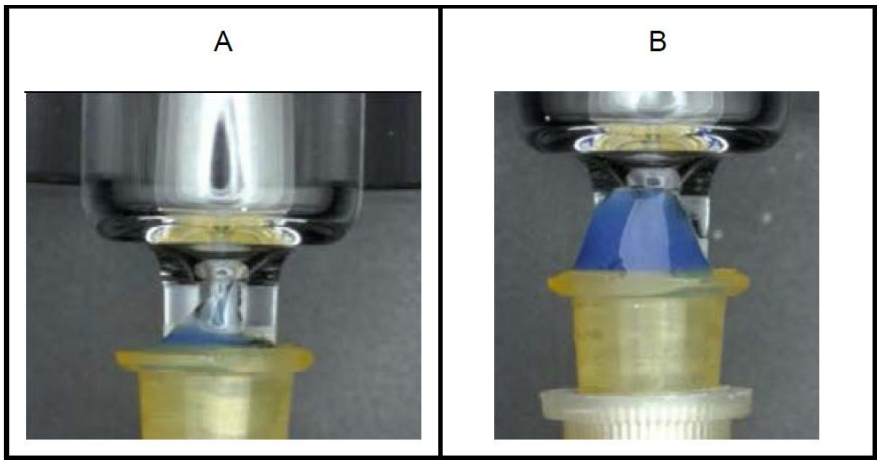

Figure 1: Examples of different volume losses (blue area)

Based on the literature data, investigations by the syringe supplier and practical testing, the volume losses can range from approximately 10µl (photo A) to 50 µl (photo B).

An extreme case with a falling droplet would potentially lead to a volume loss of 100µl or more.

Corrective actions:

GSK has been continuously evaluating and implementing corrective actions, in cooperation with the syringe suppliers, since receiving the first defect reports. These have been discussed with the Swiss Agency for Therapeutic Products, Swissmedic, which has also carried out its own laboratory investigations on the syringes. The checks during manufacture of the syringes were greatly intensified during 2017, and improved syringes have been used during preparation of the vaccines since January 2018. As a result, the proportion of syringes prone to defects will progressively decline. A complete switchover to the improved syringes will be achieved by the end of 2019.

Information on potential under-dosing

Relevant data on the administration of lower antigen doses relating to the vaccines **Havrix** and **Engerix** (1, 2) indicate that the administration of half the usual antigen dose does not affect seroprotection / seropositivity. Since the probability of a leaking syringe resulting in the vaccinated individual receiving half the required dose is very low, no impact on the seroprotection / seropositivity afforded by these vaccines is expected.

Although no dose-range studies are available for **Twinrix**, the immune response to the two antigens in the Twinrix vaccine was demonstrated to be at least comparable with that observed after vaccination with the monovalent vaccines Havrix and Engerix (2), for which data on the administration of lower antigen quantities are available.

No statements can be made about the possible impact of under-dosing with any of the **other affected vaccines**. However, for vaccines given in a multi-dose schedule (2-3 priming doses plus booster), it is highly unlikely that each dose will be administered with a leaking syringe (risk reduction).

Information on potential over-dosing

Regarding a potential risk of over-dosing in case of revaccination, according to the available data for Infanrix, Infanrix-IPV+Hib, Boostrix, Boostrix Polio and Twinrix, the reported adverse events are comparable with those reported after the administration of a standard dose.

Contact for additional information

Further information can be obtained, if necessary, from GSK Customer Service:

Medical queries: Tel. 031 862 21 11 or swiss.info@gsk.com

Quality-related queries: Tel. 031 862 21 11 or swiss.complaints@gsk.com

For all other queries: Tel. 031 862 21 21 or swiss.customerservice@gsk.com

Sources quoted:

(1) Innis B, Snitbhan R, Kunasol P et al., J. Protection Against Hepatitis A by an Inactivated Vaccine JAMA. 1994;271(17):1328-1334.

(2) Van Damme P, Van Herck K. A review of the efficacy, immunogenicity and tolerability of a combined hepatitis A and B vaccine, Expert Rev. 2004 Jun;3(3):249-67.