Reports of leaking syringes provided by GlaxoSmithKline

Update to York Region health care providers as of April 4, 2018

GlaxoSmithKline (GSK) has received reports of leaking syringes for some GSK vaccines, potentially causing under-dosing for some clients. GSK has provided the Public Health Agency of Canada and York Region Public Health with information regarding these reports.

The leakage of some vaccine syringes was reported to occur either during the preparation of the vaccine or its administration, at the connection of the syringe tip and the needle hub. This type of leakage creates a risk of under-dosing, potentially leaving clients inadequately protected from the disease(s). The leakage is associated with ceramic-coated tip syringes of the following vaccines: Boostrix, Boostrix-Polio, Infanrix-Ipv, Infanrix-Ipv+Hib, Infanrix-Hexa, Twinrix (adult and pediatric), Havrix and Typherix.

Please see the attached report from GSK for additional details on reports of leaking syringes, including pictures of the syringe type affected. If under-dosing is suspected, health care providers should use their clinical judgement based on the information provided in the memo from GSK.

If you have any questions or encounter any product issues with publicly-funded vaccines, report it to York Region Public Health at **1-877-464-9675 ext. 74033**. For more information on immunization in York Region, visit our healthcare professionals' website at york.ca/healthprofessionals.

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IMPORTANT INFORMATION

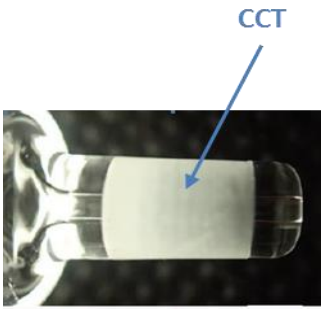
Related to reports of leaking syringes for some GlaxoSmithKline (GSK) vaccines

GSK is providing the Public Health Agency of Canada (PHAC) with this important information related to reports of leaking syringes for some GSK vaccines. The following summary provides the reason for reports of leaking syringes, the medical safety assessment completed by GSK and options for dosing recommendations (based on CDC, PHE and WHO guidances) when leakage is reported. The information provided is considered confidential and is not intended for further distribution beyond the agreed dissemination by PHAC.

Background:

GSK has received complaints about leakage from the syringes of some of its vaccines. The leakage occurred either during the preparation of the vaccine or its administration. The leakage was at the connection of the syringe tip and the needle hub and is associated with the ceramic-coated tip (CCT) syringes (see Picture 1) distributed by GSK Canada (and which are supplied to GSK by two different syringe suppliers). The rate of complaints received by GSK in Canada between January 2016 and September 2017 is 0.0097 % (i.e., 97 reports of leakage for every 1 million doses distributed).

**Leakage as referred to in this information letter is a small droplet expelled at the connection between the needle and the syringe during preparation or injection (see Picture 2). This small droplet is estimated to be only a very small percentage of the total vaccine dose.*



Picture 1: CCT syringe

Picture 2: Syringe with a needle affixed

After GSK's thorough investigation, the syringe suppliers have introduced corrective and preventative actions to stop such leakage. GSK will continue to follow-up on the implementation of the corrective and preventative actions and assess their effectiveness.

The vaccines involved are BOOSTRIX, BOOSTRIX-POLIO, INFANRIX-IPV, INFANRIX-IPV+HIB, INFANRIX-HEXA, TWINRIX (adult and pediatric), HAVRIX and TYPHERIX.

The clinical risk associated with this type of leakage is the possibility of under-dosing, potentially leaving individuals inadequately protected from disease. Most of the affected vaccines are given in multiple doses (2-3 priming doses plus booster) to achieve anticipated levels of protection. As very few syringes are affected, any leakage is unlikely to be clinically relevant when the full course of the vaccine has been given. GSK therefore concluded that the balance between benefit and risk strongly favours continuing vaccination with the available syringes.

Medical and safety assessment:

The leakage does not compromise the integrity of the syringe before usage and does not affect the vaccine's sterility.

The efficacy, immunogenicity and safety profiles for GSK's vaccines are derived from clinical trials on participants who received the standard vaccine dose. Data on administration of lower antigen content are available for HAVRIX.[1-2] Administration of half the antigen dose of HAVRIX does not suggest an impact on seroprotection or seropositivity. The probability of the leakage resulting in an underdose of half of the antigen content is very low. Therefore, any underdose related to leaking CCT syringes is not expected to have an impact on seroprotection/seropositivity.

For TWINRIX, although no dose-range studies are available, the immune response to the two antigens in the TWINRIX vaccine was demonstrated to be at least as good as that after vaccination with the monovalent vaccines [3], HAVRIX and ENGERIX , for which data on administration of lower antigen content are available.

For the other impacted vaccines, as there are no dose-range studies, GSK cannot assess the likely impact of an underdose on seroprotection/seropositivity. However, most of the potentially affected vaccines are given in multiple doses to produce a full immune response (2-3 priming doses plus booster). In the course of a vaccination series to an individual, it is highly unlikely that each dose will be administered with a leaking syringe. In addition, some of these vaccines have to be reconstituted, a process that inevitably results in the loss of a certain amount (droplets) depending on the reconstitution technique. Based on long-term pharmacovigilance data, GSK has no indication of vaccine failure (lack of efficacy) due to the loss during reconstitution.

GSK recommendations to Healthcare Providers:

It is expected that if leakage volume were to be substantial enough to potentially reduce efficacy, the leakage would be visible and therefore detected by the healthcare professional injecting the vaccine.

In case the healthcare professional detects leakage in any of the scenarios described herein, the healthcare professional should report this to GSK.

There are two possible scenarios for visible leakage reports:

A. Leakage during reconstitution of lyophilized vaccines: GSK recommends discarding the leaking syringe.

B. Leakage during injection: the healthcare professional can decide whether to revaccinate individuals who have received less than the standard dose. According to available data for vaccines after overdosage including INFANRIX-IPV, INFANRIX-IPV+HIB, BOOSTRIX, BOOSTRIX-POLIO, and TWINRIX [4-10], the reported adverse events were similar to those reported with the standard dose administration. For underdosing, the following US Centers for Disease Control and Prevention (CDC), the United Kingdom Public Health England (PHE) and the World Health Organization (WHO) recommendations may be considered.

- US CDC guidelines recommend that "any vaccination using less than the standard dose should not be counted, and the person should be revaccinated according to age unless serologic testing indicates that an adequate response has developed. If a partial dose of a parenteral vaccine is administered because of syringe or needle leakage, the dose should be repeated." [11]
- United Kingdom PHE recommends that "where vaccines are administered to patients at less than the recommended dose, vaccination will need to be repeated because the doses that patients received may not be sufficient to evoke a full immune response. Vaccination should ideally be repeated on the same day. If it is not possible to repeat the vaccine on the same day, live vaccines should be repeated following a minimum interval of four weeks since the incorrect dose. Inactivated vaccines should be repeated as soon as possible." [12]
- According to WHO in its 2015 recommendations for interrupted or delayed schedules it is advised for DTP combination, measles, rabies, mumps and varicella vaccines "to resume the schedule without repeating the previous dose, however the booster dose should always be given." [13]

The full product monographs can be found at www.gsk.ca or by contacting the sponsor, GlaxoSmithKline Inc. at: 1-800-387-7374 or cacsu@gsk.com.

References:

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(3) Van Damme P, Van Herck K. A review of the efficacy, immunogenicity and tolerability of a combined hepatitis A and B vaccine, Expert Rev.
(4) GDS INFANRIX-IPV+HIB version 012.
(5) GDS INFANRIX-HB-IPV+HIB version 015
(6) (https://www.medicines.org.uk/emc/medicine/14555)
(7) GDS BOOSTRIX Version 009.
(8) BOOSTRIX-IPV SmPC- https://www.medicines.org.uk/emc/medicine/28679
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(11) CDC, accessible at: http://www.cdc.gov/vaccines/pubs/pinkbook/vac-admin.html#nonstandard Last accessed: 06/Feb/2017.
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(13) WHO recommendations for interrupted or delayed immunization schedules – summary of WHO position papers, update 27 February 2015 accessible: http://www.who.int/immunization/policy/Immunization_routine_table3.pdf?ua=1 Last accessed: 06/Feb/2017