Analysis of suspected batch AC20B199AA of Infanrix-IPV® vaccine

Introduction and background

In The Netherlands, the DPT-polio vaccine Infanrix-IPV® is given to children at age of approximately 4 years as part of the Netherlands Immunisation Programme (NIP). About 92% of children at this age are given this vaccine.

In October 2012 the manufacturer GlaxoSmithKline (GSK) initiated a recall of a specific batch of Infanrix-IPV®. Internal investigations by GSK identified a potential contamination of batch AC20B199AA. During production an intermediate product had been in a room that was later found to be contaminated with a bacterium. All batch release tests had passed successfully according to prespecified criteria. All required tests were negative with regard to the potential contamination.
This batch was in use in several countries. However, GSK decided to exclude any potential risk, and recalled the product. This recall was the consequence of recently sharpened internal rules within the company and was not based on current European quality guidelines.
GSK notified the RIVM at the end of Friday 5 October 2012. On Monday 8 October 2012, the RIVM send emergency messages to all health care workers implementing the NIP not to use this specific batch of Infanrix-IPV® anymore. Later all remaining product has been recovered by the RIVM.

Lareb was asked to investigate whether there was any indication that the suspected batch of the product had been contaminated.

Methods of investigation

The potential health problems associated with a suspected product contamination were defined. Injection of a contaminated vaccine would lead to signs and symptoms of infection, at the injection site and/or generalized complaints. However, such complaints partly resemble that from the usual inflammation-based reactogenicity associated with this vaccine, which is indeed known to occur after this particular vaccine. In the case of an infected vaccine such complaints are expected to be more severe and longer lasting, and moreover requiring antibiotic therapy and/or hospitalisation.

Lareb performed a staged analysis:
1. At the moment of onset of the recall, the primary impression based on the reports in the previous 3 months was that no apparent health problem had occurred. Based on previous reports no unusually more severe pattern had surfaced. This primary and subjective impression was followed by a more detailed analysis.
2. A case review was done of all reports related to the suspected batch received so far, with special attention for the potential health problems mentioned above. In this case review no abnormal or suspect pattern of reported side effects were found, for instance no cases of hospitalisation because of local infections at the site of administration.
3. A more in depth analysis was done, to find abnormal batch-specific reporting patterns. All reports related to Infanrix-IPV® were studied at batch level. Reporting Odds Ratio's (ROR) were calculated with a stratified approach, using the scheme below:

		reports with reaction	
		suspected reactions	all other reactions
reports with drug	suspected drug	a	b
	all other drugs	c	d

a = suspected batch of suspected vaccine with suspected reactions/profile
b = suspected batch of suspected vaccine with all other reactions
c = all other batches of suspected vaccine with suspected reactions/profile
d = all other batches of suspected vaccine with all other reactions
NB groups c and d contain also reports after Infanrix-IPV of which the batch number is unknown.

For the present analysis we included as
- suspected vaccine: all batches of Infanrix-IPV® used from 2007 including the suspected batch: AC20B199AA. This was a total of 1258 reports.
- suspected reactions: we used multiple profiles (1 t/m 4) of reactions coded in MedDRA® compatible with:
  (1): reactogenicity of pandemic influenza vaccine (this profile was used earlier in 2009-2010).
  (2): infections (reactions from the complete MedDRA® System Organ Class).
  (3): local reactogenicity (injection site reactogenicity).
  (4): systemic reactogenicity (including terms like Anaphylactic reaction, Angioedema, etc).
  Profiles (3) and (4) were made using all terms for local (injection site) reactogenicity and systemic reactogenicity that had been used at Lareb since the year 1995.

In the analysis using profile (1) all recent reports received after Infanrix-IPV® fulfilled this profile, and almost no reports had reactions that were not part of the profile. This indicated that the used profile (1) was not specific enough. Therefore we developed the more applicable profiles (2), (3) and (4).

Results
At the moment of analysis Lareb had received a total of 1258 reports of reactions after Infanrix-IPV®, including 70 reports regarding the suspected batch. The remaining 1188 reports could also include reports of the suspected batch, of which the batch number could not be retrieved. In about 40% of the reports regarding Infanrix-IPV® the batch number was not known.
The RIVM dictates that Lareb is only allowed to retrieve the batch number upon approval of the patient or the parents of the patient. It was however considered unlikely that proportions of suspected and not suspected reactions would differ between vaccines with known versus unknown batch number. The suspected batch had been given to about 50.000 children, the remainder of 20.000 doses had been recalled. Of the other batches used the numbers of doses was not known at the moment of analysis. Therefore we were not able to calculate incidences of reactogenicity per batch.
The analysis of reports using the infection profile (2), local reactogenicity profile (3) and systemic reactogenicity (4), or both profiles (3) and (4) combined, showed comparable ROR values for all batches. Thus, the suspected batch AC20B199AA showed no deviant ROR values in any of the analyses.

Discussion and conclusion

Lareb was able to study reports regarding this specific suspected batch at a short note, i.e. within a few days. This preview was followed by more specific queries of the Lareb database.

Lareb did not find indications that the pattern of reported reactions after the suspected batch suggested a potential contamination of this batch. The pattern of reported reactions of the suspected batch was not different from that of the other batches. All batches had similar levels of reactogenicity. The suspicion of contamination of the specific batch could not be confirmed.

This signal has been raised on May 2013. It is possible that in the meantime other information became available. For the latest information please refer to the website of the MEB www.cbgmeb.nl/cbg/en/default.htm or the responsible marketing authorization holder(s).