

Update on CBER Activities on Porcine Circovirus in Rotavirus Vaccines

ADVISORY Committee on Immunization Practices
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FDA/CBER/OVRR

Background

- February 2010, GlaxoSmithKline Biologicals (GSK) informed by a UCSF investigator of DNA sequences of PCV-1 detected in 2 batches of Rotarix®
 - GSK initiated experiments to confirm results, and conduct further investigations
 - Tests confirmed the presence of PCV-1 DNA in Rotarix at all stages of the production process
- GSK informed FDA of the detection of PCV-1 DNA fragments in Rotarix® and in harvests (but not final product) of IPV (inactivated poliovirus)-containing vaccines that were produced in a related cell bank

Background (cont'd)

- CBER testing confirmed presence of PCV-1 DNA in Rotarix®.
- On March 22, 2010, FDA recommended temporary suspension of use of Rotarix vaccine as precautionary measure as CBER gathers additional information.
- Although testing by Victoria et al. did not find PCV1 DNA sequences in Merck's rotavirus vaccine (RotaTeq), CBER embarked on testing RotaTeq and recommended Merck to do the same.
- FDA subsequently notified by Merck that preliminary studies identified fragments of DNA from porcine circovirus type 1 and type 2 (PCV1 and PCV2) in RotaTeq vaccine.

CBER Lab Response

- Confirmed presence of PCV-1 DNA in Rotarix
 - Including complete virus genomes
- Showed that PCV-1 DNA in Rotarix is particle-associated
- Showed that PCV1 virus in Rotarix can infect swine cells in culture
- Confirmed PCV1 and PCV2 DNA fragments in Rotateq
 - To date no detection of full length PCV genomes
 - To date no infectious virus (tested in cell culture) found
 - Studies are ongoing

Porcine Circoviruses

- PCV-1 and PCV-2 are small viruses containing a single strand of circular DNA.
- PCV-1 is ubiquitous in pigs and found in pork products
- PCV's are not known to cause disease in humans.
- No evidence at this time that PCV or PCV DNA in US licensed vaccines poses a safety risk.
- To date, no serious or unexpected safety signals in post-market surveillance of Rotarix or RotaTeq.
- GSK's preliminary serology studies did not show antibody response to PCV-1 among recipients of Rotarix, suggesting PCV-1 did not infect vaccine recipients

CBER and Manufacturers' results

Vaccine	CBER	Manufacturer
Rotarix (GSK)	PCV-1 DNA in product	PCV-1 DNA in product, bulks, seeds, cells
	Particle-associated near full length PCV1 DNA in product	
	Infectious PCV1 in cell culture	Infectious PCV-1 in cell culture
IPV containing vaccines (GSK)	Pending	Preliminary data: No PCV-1 seroresponse among vaccine recipients PCV-1 DNA in harvest, seeds, cells, but not in bulks or final container
Rotateq (Merck)	Particle-associated PCV-2 DNA fragments in harvest; PCV-1 and PCV-2 DNA fragments in final container	PCV-1 and PCV-2 DNA in harvest, PCV DNA in final container

FDA U.S. Food and Drug Administration

VRBPAC 7 May 2010

- Considered the substantial safety record of the vaccines known to contain PCV
- Considered benefit of vaccines to outweigh theoretical risks from the presence (or potential presence) of PCV
- Discussed the importance of transparency & providing information to public
- Recommended taking steps to remove PCV's from products

FDA U.S. Food and Drug Administration

New technologies for virus detection

- VRBPAC also discussed new genomic techniques that may increase the likelihood of finding additional viruses, virus-like sequences in vaccines
- If found, potential risk from such viruses or sequences may be difficult to assess
- Introduction of these techniques in a regulatory setting will require standardization & development of approaches to confirm findings

FDA U.S. Food and Drug Administration

Subsequent and Ongoing FDA Actions

- Recommendation to suspend Rotarix use reversed
- Continued testing at CBER
- Discussions with manufacturers re:
 - Further testing
 - Labeling
 - Removal of PCV from product
- Discussions on implications of new genomic techniques in regulatory setting

FDA U.S. Food and Drug Administration

Acknowledgment

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 Rose Tiernan, MD
 Douglas Pratt, MD
 Lewis Schrage, MD
 Loris McVitti, PhD

Christine Uhlenhaut, PhD
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