

Presence of material from PCV-1 in ROTARIX® (*Rotavirus Vaccine, Live attenuated*)

GSK STATEMENT

GlaxoSmithKline (GSK) has notified regulatory authorities worldwide, including the TGA in Australia, of the presence of material from a virus called porcine circovirus (PCV-1) in its oral rotavirus vaccine, Rotarix®.

The name 'porcine' refers to the fact that this virus can infect pigs **but it is important to emphasise it is not itself of animal origin**. It is commonly found in swine herds and therefore is present in every day meat products and is frequently eaten with no resulting disease or illness. There is no evidence that PCV-1 can infect or cause disease in humans.

GSK will continue to supply Rotarix while the balance of benefits and risks remains positive.

The TGA has reviewed all information provided by GSK and concluded that: "Clinical trials data and extensive experience to date have demonstrated that Rotarix is effective in preventing infection with rotavirus and is well tolerated in babies."

In addition, they have stated that "scheduled vaccination with Rotarix should proceed as normal, and parents should contact their doctor if they have concerns about immunisation of their baby with Rotarix."

The TGA is convening an expert panel to provide further advice on this matter and GSK will continue to update the TGA with all new information as it becomes available.

"The TGA will provide additional advice regarding its careful scientific risk assessment as soon as it is completed. Based on current evidence and pending further expert review the TGA does not consider this constitutes a threat to public health"

For full details of the TGA statement visit <http://www.tga.gov.au/alerts/medicines/rotarix.htm>

The European Medicines Agency (EMA) and the World Health Organization (WHO) issued statements today confirming that the presence of the material from PCV-1 does not suggest any change to the positive balance of benefits and risks of the vaccine and have not recommended any change to the way that healthcare practitioners in Europe and the developing world use Rotarix.

The US Food and Drug Administration (FDA) similarly has issued a statement confirming that there is no evidence that this finding poses a safety risk based on the excellent safety profile of Rotarix and evidence

that PCV-1 is a known virus that does not multiply in humans and is not known to cause illness in humans. Rotarix has been produced according to standards reviewed and approved by regulatory authorities at the time of licensure.

Notwithstanding the above, based on initial findings communicated by the Company and as a precautionary measure, the FDA is recommending that US clinicians and public health professionals temporarily suspend the use of the GSK vaccine.

The extensive safety record of Rotarix is based on global clinical data from the largest vaccine clinical trial programme conducted by GSK, enrolling more than 90,000 participants in Europe, Latin America, Asia, Africa and the US. Retrospective testing of Rotarix, using recently developed techniques, has confirmed that material from PCV-1 has been present since the initial stages of the vaccine's development in the cell bank and rotavirus seeds used as base production material. Therefore any potential impact on the safety of the vaccine through the presence of material from PCV-1 has been extensively studied in infants. These trials involved testing and monitoring of participants for up to 3 years.

Q & A

Q1. What is PCV-1?

A1. PCV-1 is a porcine circovirus. The name 'porcine' refers to the fact that this virus can infect pigs **but it is important to stress that PCV-1 is NOT itself of animal origin.**

According to global scientific literature, PCV-1 is a known virus that does not infect or multiply in humans and is not known to cause illness in humans.^{1,2} It is a virus commonly found in swine herds including in Australia, and therefore is present in every day meat products and is frequently eaten with no resulting disease or illness.

Q2. Does the presence of PCV-1 material in Rotarix pose a safety issue?

A2. The TGA has reviewed all information provided by GSK and reached the conclusion that "Clinical trial data and extensive experience to date have demonstrated that Rotarix is effective in preventing infection with rotavirus and is well tolerated in babies."

In addition they have stated scheduled vaccination with Rotarix should proceed as normal , , and parents should contact their doctor if they have concerns about immunisation of their baby with Rotarix."

GSK continues to provide all new information to the TGA as it becomes available and the TGA review of this information is ongoing: "The TGA will provide additional advice regarding its careful scientific risk assessment as soon as it is completed. Based on

current evidence and pending further expert review the TGA does not consider this constitutes a threat to public health”

FDA and EMEA have issue statements confirming that there is no evidence that this finding poses a safety risk and based on the extensive safety profile of Rotarix and evidence that PCV-1 is a known virus that does not multiply in humans and is not known to cause illness in humans. Rotarix has been produced according to standards reviewed and approved by regulatory authorities at the time of licensure.

The extensive safety record of Rotarix is based on global clinical data from the largest vaccine clinical trial programme conducted by GSK, enrolling more than 90,000 participants in Europe, Latin America, Asia, Africa and the US. Retrospective testing of Rotarix, using recently developed techniques, has confirmed that material from PCV-1 has been present since the initial stages of the vaccine’s development in the cell bank and rotavirus seeds used as base production material. Therefore any potential impact on the safety of the vaccine through the presence of material from PCV-1 has been extensively studied in infants. These trials involved testing and monitoring of participants for up to 3 years.

Q3. How was material from PCV-1 detected in Rotarix?

A3. The material was first detected following work done by a research team in the US using a novel technique for looking for viruses. This team then shared their findings with GSK. After being notified, GSK conducted additional tests which confirmed the findings. GSK has confirmed that the material is present in the finished Rotarix vaccine as well as in the cell bank and seed from which the vaccine is derived.

Once GSK had corroboration of the results shared by the independent research team, it immediately shared the available data and information with regulatory agencies worldwide in those markets where Rotarix is licensed.

Q4. What routine testing does GSK undertake for its vaccines?

A4. GSK Biologicals has over fifty years of experience of research and development in producing complex high quality vaccines. Vaccine research, development and production require careful compliance with appropriately strict quality standards.

In addition to being monitored through extensive manufacturing quality assurance and quality control programs, GSK vaccines undergo extensive clinical development programs during which the safety of the vaccines are carefully monitored. GSK continues to monitor the safety of its vaccines after they are approved by regulatory authorities through various surveillance mechanisms. These data and information generated through these various systems and mechanisms enable GSK to continuously monitor the safety profile of its vaccines.

Q5 When did the presence of PCV-1 occur in the development of Rotarix?

A5. Retrospective testing of Rotarix, using recently developed techniques, has confirmed that material from PCV-1 is present in the cell bank and virus seeds used as base production material as of the initial development of the vaccine in the 1990's.

Cell banks serve as the manufacturing starting point for the development of many vaccines. These cell banks - which are certified by regulatory authorities - are used to multiply the virus which will be contained in the vaccine.

Further investigations are underway to determine why the PCV-1 DNA is found in the vaccine.

The extensive safety record of Rotarix is based on global clinical data from the largest vaccine clinical trial programme conducted by GSK, enrolling more than 90,000 participants in Europe, Latin America, Asia, Africa and the US. Retrospective testing of Rotarix, using recently developed techniques, has confirmed that material from PCV-1 has been present since the initial stages of the vaccine's development in the cell bank and rotavirus seeds used as base production material. Therefore any potential impact on the safety of the vaccine through the presence of material from PCV-1 has been extensively studied in infants. These trials involved testing and monitoring of participants for up to 3 years.

Q6. Could PCV-1 be present in other GSK vaccines? Is GSK testing for this?

A6. At this stage, no material from PCV-1 has been detected in any other final vaccine product. However, this is still under investigation and further testing is being conducted to confirm these preliminary findings.

Q7. Have traces of PCV-1 DNA been found in each batch of Rotarix?

A7. GSK has reviewed the manufacturing process for Rotarix and can confirm that material from PCV-1 is present in a number of manufacturing steps for Rotarix production and also in the lots we have so far tested. Therefore we expect material from PCV-1 to be present in all batches of the vaccine.

Q8. The FDA has decided the administration of Rotarix should be put on hold. So why is this not the case in Australia?

A8. The statement issued on March 22 by the US Food and Drug Administration (FDA) confirms that "there is no evidence at this time that this finding poses a safety risk" and the "excellent safety profile" of Rotarix. In addition, the European Medicines Agency (EMA) and the World Health Organization (WHO) have issued statements confirming that the presence of the material from PCV-1 does not suggest any change to the positive balance of benefits and risks of the vaccine and have not

recommended any change to the way that healthcare practitioners in Europe and the developing world use Rotarix. Moreover, the EMEA's Committee for Medicinal Products for Human Use (CHMP), after considering the data showing the presence of the material from the PCV-1 virus concluded that the presence of the material does not present a public health threat.

The TGA has reviewed all information provided by GSK and reached the conclusion that "Clinical trials data and extensive experience to date have demonstrated that Rotarix is effective in preventing infection with rotavirus and is well tolerated in babies."

In addition they have stated scheduled vaccination with Rotarix should proceed as normal ,, and parents should contact their doctor if they have concerns about immunisation of their baby with Rotarix."

GSK continues to provide all new information to the TGA as it becomes available and the TGA review of this information is ongoing: "The TGA will provide additional advice regarding its careful scientific risk assessment as soon as it is completed. Based on current evidence and pending further expert review the TGA does not consider this constitutes a threat to public health"

Q9. While the investigations and review by the regulatory authorities are ongoing is GSK going to recall Rotarix?

A9. No. GSK will continue to supply Rotarix while the balance of benefits and risks remains positive. Continued availability of rotavirus vaccine remains important from a public health perspective to address the disease burden associated with rotavirus.

The TGA has reviewed all information provided by GSK and reached the conclusion that "Clinical trials data and extensive experience to date have demonstrated that Rotarix is effective in preventing infection with rotavirus and is well tolerated in babies."

In addition they have stated scheduled vaccination with Rotarix should proceed as normal , and parents should contact their doctor if they have concerns about immunisation of their baby with Rotarix."

GSK continues to provide all new information to the TGA as it becomes available and the TGA review of this information is ongoing: "The TGA will provide additional advice regarding its careful scientific risk assessment as soon as it is completed. Based on current evidence and pending further expert review the TGA does not consider this constitutes a threat to public health"

Q10, Has Rotarix been recalled in other countries?

A.10 The situation with respect to regulatory agencies worldwide is continuously evolving as new information becomes available. Both the FDA and the EMA have found no evidence of a risk to human health at this time.

In Australia The TGA has reviewed all information provided by GSK and reached the conclusion that "Clinical trials data and extensive experience to date have demonstrated that Rotarix is effective in preventing infection with rotavirus and is well tolerated in babies."

In addition they have stated "Individual vaccination programs that have commenced should continue, and parents should contact their doctor if they have concerns about immunisation of their baby with Rotarix."

GSK continues to provide all new information to the TGA as it becomes available and the TGA review of this information is ongoing: "The TGA will provide additional advice regarding its careful scientific risk assessment as soon as it is completed. Based on current evidence and pending further expert review the TGA does not consider this constitutes a threat to public health"

Q11. At this time, what is the advice to healthcare professionals administering Rotarix OR parents of those babies who have received or are about to receive the vaccine?

A11. GSK will continue to supply Rotarix while the balance of benefits and risks remains positive. The TGA has reviewed all information provided by GSK and reached the conclusion that "Clinical trials data and extensive experience to date have demonstrated that Rotarix is effective in preventing infection with rotavirus and is well tolerated in babies."

In addition they have stated scheduled vaccination with Rotarix should proceed as normal , and parents should contact their doctor if they have concerns about immunisation of their baby with Rotarix."

Having reviewed the information and data submitted by GlaxoSmithKline as well as information available regarding PCV-1 from the world's literature, the European Medicines Agency (EMA) and the World Health Organization (WHO) issued statements today confirming that the presence of the material from PCV-1 does not suggest any change to the positive balance of benefits and risks of the vaccine and have not recommended any change to the way that healthcare practitioners in Europe and the developing world use Rotarix. Moreover, the EMA's Committee for Medicinal Products for Human Use (CHMP), after considering the data showing the presence of the material from the PCV-1 virus concluded that the presence of the material does not present a public health threat.

The FDA also has made clear in its statement that there is no evidence at this time that the presence of the material from PCV-1 in Rotarix poses a safety risk.

The extensive safety record of Rotarix is based on global clinical data from the largest vaccine clinical trial programme conducted by GSK, enrolling more than 90,000 participants in Europe, Latin America, Asia, Africa and the US. Retrospective testing of Rotarix, using recently developed techniques, has confirmed that material from PCV-1 has been present since the initial stages of the vaccine's development in the cell bank and rotavirus seeds used as base production material. Therefore any potential impact on the safety of the vaccine through the presence of material from PCV-1 has been extensively studied in infants. These trials involved testing and monitoring of participants for up to 3 years.

Q12. Can Rotavirus vaccines be used interchangeably?

A.12 GSK has no clinical data on Rotavirus vaccine interchangeability and cannot make any recommendation on this question. Please refer to the factsheet from the National Centre for Immunisation Research and Surveillance (NCIRS) for guidance. <http://www.ncirs.usyd.edu.au/immunisation/fact-sheets/rotavirus-fact-sheet.pdf>

Q13. What further action will GSK be taking for Rotarix?

A13. GSK is now reviewing how best to replace, in a timely way, the cell bank and virus seeds used as base production material. In the meantime, and in accordance with the regulators, the company will continue to manufacture Rotarix to the existing approved production methods to ensure no disruption to supply of the vaccine.

Q14. Has PCV-2 been found in the vaccine?

A14. PCV-2 is a different virus. Investigations conducted to date have not revealed the presence of material from PCV-2. GSK will continue to conduct tests for material from PCV-1 and PCV-2 as part of its ongoing investigations.

There is no evidence that PCV-2 is a virus that is harmful in humans.^{1,2}

Q15. Isn't Rotarix a human-derived vaccine? Does this mean no animal-based products are involved in the manufacturing or production of the vaccine?

A15. In some instances, the development and manufacturing of vaccines does involve steps which use materials from animal-based sources. This is common practice in the manufacturing of vaccines and is conducted in-line with the appropriate guidelines set out by the regulatory authorities.

These animal-based products are inactivated and/or removed from the final vaccine. GSK remains consistent and transparent in its scientific communication with regulatory authorities regarding the formulation and production processes for all of its all vaccines.

Rotarix GSK's rotavirus vaccine does not contain any material of animal origin. It is manufactured according to standards as reviewed and approved by regulatory authorities at the time of licensure.

Q16. Do other companies manufacture their vaccines in this way?

A16. GSK cannot comment on the manufacturing processes used by other companies.

It is common practice to use animal-based products in the manufacturing of vaccines and this is conducted in-line with the appropriate guidelines set out by the regulatory authorities.

Q17. Has PCV-1 been detected in rotavirus vaccines made by other manufacturers?

Q17. GSK cannot comment on rotavirus vaccines manufactured by other companies and any enquiries should be referred directly to the relevant manufacturer.

References

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More information

Health care professionals seeking additional information are invited to contact GSK Medical Information on 1800 033 109.

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