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Questions and answers on the detection of unexpected viral DNA in live attenuated vaccines

Outcome of a procedure under Article 5(3) of Regulation (EC) 726/2004[1]

The European Medicines Agency has completed a review of the impact of the detection of DNA fragments from viral agents in some live attenuated vaccines using a new testing method. The Agency's Committee for Medicinal Products for Human Use (CHMP) has concluded that the presence of unexpected viral DNA in these vaccines does not pose a risk to public health.

What are live attenuated vaccines?

Live attenuated vaccines are vaccines that contain viruses that are 'alive' but that have been 'attenuated' (weakened) so that they do not cause the disease. Live attenuated vaccines that have been authorised in the European Union (EU) include vaccines to protect against polio, measles, mumps and rubella, and gastroenteritis (diarrhoea and vomiting) caused by rotavirus infection.

Why were these vaccines reviewed?

The review of live attenuated vaccines was triggered by the publication of an article in March 2010[2], which reported the discovery of viral DNA fragments in different live attenuated vaccines. A research team in the United States of America had carried out a systematic test for 'adventitious' (unexpected) and 'endogenous' (originating from the cells used to prepare the vaccines) viruses in a number of live attenuated vaccines using a new technique called 'metagenomics'. This is a high-tech method that is not routinely used for testing vaccines. Unexpected viral DNA from porcine circovirus (PCV, a virus commonly found in meat and other foods) was detected in rotavirus vaccines.

Consequently, on 13 April 2010, the Agency's Executive Director asked the CHMP to give its scientific opinion on the potential consequences of these findings for public health and, more generally, on the possible use of new techniques for detecting endogenous and adventitious viruses in vaccines, and the need for developing guidance on the testing of vaccines as well as other biological products.

[1] Article 5(3) of Regulation (EC) 726/2004, opinion on any scientific matter concerning the evaluation of medicinal products for human use.
[2] Viral Nucleic Acids in Live-Attenuated Vaccines: Detection of Minority Variants and an Adventitious Virus. Victoria JG, Wang C, Jones MS, Jaing C, McLoughlin K, Gardner S and Delwart EL. *J Virol. 2010 Jun;84(12)*. http://jvi.asm.org/cgi/content/short/84/12/6033

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Which data has the CHMP reviewed?

The CHMP has reviewed all relevant published literature on endogenous and adventitious agents in medicinal products and their associated risks. It also looked at all available guidelines on testing for viral agents in vaccines and biological products. A group of European experts on metagenomics, quality control of biologics and virology was convened to provide advice.

What are the conclusions of the CHMP?

Based on the evaluation of the currently available data and the scientific discussion within the Committee, the CHMP concluded that, because the PCV found in rotavirus vaccines does not cause disease in humans, there is no risk to public health.

The most likely cause of the unexpected presence of the viral DNA was found to be 'porcine trypsin' (pig-derived material used to produce the vaccines). The Committee recommended that guidance on this reagent should be developed.

Metagenomic testing appears to be a valuable method for detection of a broad range of unexpected and unknown viral agents, but it does not provide information on viral activity. Given its novelty and absence of standardisation, the CHMP concluded that this method may be used as an additional tool to current standard testing, but that any unexpected findings will need to be evaluated on a case-by-case basis and lead to an appropriate benefit-risk assessment.

What will happen next?

Several meetings are planned on the testing of biological products, and cooperation with the European Directorate for the Quality of Medicines (EDQM) and international partners such as the World Health Organisation (WHO) and the US Food and Drug Administration (FDA) is sought to set up a common approach.