



# American College of Pediatricians

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## Patient Information Handout Series

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### Origin and Production of Vaccines in the United States

To make an informed decision regarding the use of vaccines for their children, parents need to know details regarding the vaccine's risks and benefits, as well as its origin and production. When vaccines are developed, it is necessary to use animal or human products. The production of some vaccines involves the use of human cell cultures originally obtained years ago from electively aborted fetuses. It is important to note, however, the vaccines listed below were developed using material descended from previously aborted fetuses, and their use today does not require additional fetal tissue from on-going, additional human abortions.<sup>1</sup>

In the United States, there are five common vaccines in use that are manufactured using human tissue cultures originally derived from aborted fetuses: Rubella (German measles), Chickenpox (and Zoster or shingles caused by the same virus), Hepatitis A, Rabies, and Polio.

#### Rubella

The rubella (German measles) vaccine that is available in the United States is produced from a virus recovered in 1964 from the tissue of an aborted child with congenital rubella infection.<sup>2</sup> That virus was then grown in tissue culture derived from the lungs of another human fetus aborted in 1966, and the material harvested was developed into the rubella vaccine currently used.<sup>3,4</sup> In the US, this rubella vaccine is only available as a combination vaccine containing the measles and the mumps vaccine, which are not manufactured using fetal cell cultures. It is supplied by Merck Pharmaceutical as the MMR vaccine.<sup>5</sup> The ProQuad vaccine contains this MMR vaccine in combination with Varivax, a chickenpox vaccine. There is currently no alternative rubella vaccine in the United States. A different rubella vaccine made from rubella virus from the throat of an infected child and cultured in rabbit kidney cells is used in Japan (Takahashi strain)<sup>6</sup> and also comes combined with measles and mumps vaccine, but is not approved by the FDA for use in the US.

Rubella (German Measles) is not dangerous to young children, but it can be devastating to unborn babies during the first trimester. Infants born to mothers infected with rubella early in pregnancy are often born blind, deaf, with severe heart defects, and/or developmentally delayed. The vaccine was developed primarily to protect women of childbearing age before they become pregnant. Measles is highly contagious and causes high fever, eye infection, severe congestion and cough, and frequently secondary pneumonia that can be fatal. It can also cause chronic infectious encephalitis (infection of the brain) resulting in permanent brain damage or death. Mumps not only causes painful swelling of the salivary glands, but can cause pancreatitis, meningitis, and painful infection of the testes which can result in the inability to father children.

#### Chickenpox

There is currently only one vaccine against chickenpox: *Varivax* by Merck, which is grown in human fetal cell cultures.<sup>5</sup> There are currently no alternatives to Merck's *Varivax* and *Zostavax*<sup>5</sup> (used to prevent shingles which is a reactivation of the chickenpox virus in previously infected individuals), but GlaxoSmithKline (GSK) is developing a shingles vaccine using hamster cells called *Shingrix*.<sup>7,8,9</sup>

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Failure to vaccinate your child against chickenpox leaves him/her susceptible to the disease. Because there is currently less circulating chickenpox virus in the community due to widespread use of the vaccine, unvaccinated children may not be exposed to the disease for many years. Older chickenpox sufferers have more severe cases and a much higher death rate. People infected with chickenpox also risk passing their infection to children or adults with weakened immune systems from cancer, AIDS, chronic disease, or to those who take anti-rejection drugs after organ transplants. Such immunosuppressed people are at special risk for death from severe, disseminated chickenpox infection.

## Hepatitis A

There are currently at least three vaccines available in the US to protect children and adults from hepatitis A, and all are manufactured in a cell line derived from an aborted human fetus. *Havrix* by GSK<sup>10</sup> and *Vaqta* by Merck<sup>5</sup> are different brands of just hepatitis A vaccine, and *Twinrix* by GSK<sup>10</sup> is a combination vaccine against both hepatitis A and hepatitis B. There are currently no alternatives to the hepatitis A vaccine in the United States for long-term protection against the disease. Gamma globulin shots provide short-term protection lasting only a few months. A different hepatitis A vaccine, *Aimugen*, is in use in Asia and Europe. *Aimugen* is made from monkey kidney cell cultures rather than human fetal tissue.<sup>11</sup>

Failure to vaccinate leaves a child susceptible to hepatitis A, which can spread rapidly among household members and causes mild “flu-like” symptoms, jaundice, nausea, abdominal pain and diarrhea. Some children and adults with hepatitis A require hospitalization, and rarely it can (mainly in adults) be fatal. The Centers for Disease Control (CDC) recommends that all children be given 2 doses of hepatitis A vaccine: the first at 1-2 years of age, and the second at least 6 months later. Of note, the hepatitis B vaccine is recommended for all infants and is not made using any human fetal tissue.<sup>5, 10</sup>

## Rabies

In the United States the rabies vaccine, *Imovax* by Sanofi Pasteur (SP), grown in human fetal cell cultures,<sup>12</sup> is used for individuals at high risk of exposure to rabid animals, or for individuals who have had high-risk exposures to possibly rabid animals. In the United States an alternative to the *Imovax* vaccination, *RabAvert* by GSK,<sup>13</sup> is produced using hen eggs. However, intermittently either *Imovax* or *RabAvert* is in short supply and unavailable and only one brand may be available in adequate time from the local health department or emergency room.

Rabies is a virus usually spread by an animal bite. Failure to vaccinate an individual bitten by a rabid animal almost always results in death. Very few persons are known to have survived a rabies infection.

## Polio

In the United States, the single ingredient inactivated polio vaccines (IPV, *IPOL* by SP)<sup>12</sup> given by injection is not manufactured using aborted human tissue. The monkey kidney cell culture-grown IPV is also used in GSK’s combination vaccines *Pediarix*<sup>10</sup> (given at ages 2–18 months) and *Kinrix*<sup>10</sup> (given at age 4 years). But two other combination vaccines by SP, *Pentacel*<sup>12</sup> and *Quadracel*,<sup>12</sup> do contain inactivated polio vaccine manufactured in aborted human tissue.

Immunization against polio is critical to a child since the disease can cause permanent physical deformity, disability, and even death though there are hopes that the disease may soon be eliminated worldwide.<sup>13</sup>

## Conclusion

Immunization prevents serious illnesses and saves lives. The American College of Pediatricians urges parents and patients with further questions about these vaccines to have a discussion with their pediatrician.

Updated: July 2017

## References to Supplemental Information on Vaccine Origins

- <sup>1</sup> Fibroblast from Skin, Lung. Coriell Institute. On Coriell website at: [https://catalog.coriell.org/0/Sections/Search/Sample\\_Detail.aspx?Ref=AG05965-C&PgId=166](https://catalog.coriell.org/0/Sections/Search/Sample_Detail.aspx?Ref=AG05965-C&PgId=166), accessed June 25, 2017.
- <sup>2</sup> Plotkin SA, Cornfield D, and Ingalls TH Studies of immunization with living rubella virus: trials in children with a strain cultured from an aborted fetus. *American Journal Diseases of Children*, Vol. 110, Oct. 1965 381-389.
- <sup>3</sup> Wadman, M, Medical Research: Cell Division. *Nature*, Vol. 498, June 2013, <http://www.nature.com/news/medical-research-cell-division-1.13273>, accessed June 25, 2017.
- <sup>4</sup> Bo Ma, Li-Fang He, Yi-Li Zhang, et al. Characteristics and viral propagation properties of a new human diploid cell line, wavax-2, and its suitability as a candidate cell substrate for vaccine production, *Hum Vaccin Immunother*, 2015 Apr; 11(4): 998–1009. Published online 2015 Mar 24. Accessed June 25, 2017.
- <sup>5</sup> Information on sources of vaccines made by Merck is found in the Prescriber Information (package inserts) found on the Merck website, MerckVaccines.com, <https://www.merckvaccines.com/Products/Pages/vaccine-Prescribing-Information>, accessed June 25, 2017. Merck vaccines include Gardasil, MMR, PedvaxHIB, Pneumovax, ProQuad, Recombivax HB, RotaTeq, Vaqta, Varivax, and Zostavax.
- <sup>6</sup> Shishido A, Ohtawara M, Development of attenuated rubella virus vaccines in Japan. *J Med Sci Biol Japan* 1976 Oct;29(5):227-53, <https://www.ncbi.nlm.nih.gov/pubmed/827627>.
- <sup>7</sup> Leroux-Roels I, Leroux-Roels G, Clement F, et al. , A phase 1/2 clinical trial evaluating safety and immunogenicity of a varicella zoster glycoprotein e subunit vaccine candidate in young and older adults. *J Infect Dis*. 2012 Oct;206(8):1280-90.
- <sup>8</sup> GSK's candidate shingles vaccine shows high efficacy against shingles and its complications in adults aged 70 years and over in phase III study published in *NEJM*, September 14, 2016, London, UK, <http://www.londonstockexchange.com/exchange/news/market-news/market-news-detail/GSK/12966505.html>, accessed June 25, 2017.
- <sup>9</sup> Haumont M, Jacquet A, Massar M, et al. Purification, characterization and immunogenicity of recombinant varicella-zoster virus glycoprotein gE secreted by Chinese hamster ovary cells. *Virus Res*. 1996 Feb;40(2):199-204.
- <sup>10</sup> Information on sources of vaccines made by GSK is found in the Prescriber Information (package inserts) available on the GSK website, GSKDirect.com, <https://www.gskdirect.com/gsk/en/USD/RootCategory/c/1>, accessed June 25, 2017. GSK vaccines include Bexsero, Boostrix, Engerix, Fluvarix, Flulaval, Havrix, Hiberix, Infarix, Kinrix, Menveo, Pediarix, RabAvert, Rotarix, and Twinrix.
- <sup>11</sup> Atsuko Totsuka and Yasuo Moritsugu, Hepatitis A Vaccine Development in Japan, *Viral Hepatitis and Liver Disease* (1994). pp 509-513, Department of Viral Disease and Vaccine Control, National Institute of Health, Tokyo, 208 Japan accessed on June 25, 2017 at [https://link.springer.com/chapter/10.1007/978-4-431-68255-4\\_132](https://link.springer.com/chapter/10.1007/978-4-431-68255-4_132)
- <sup>12</sup> Information on sources of some vaccines made by Sanofi-Pasteur (SP) is found in the Prescribing Information (package inserts) available at the SP website [VaccineShoppe.com](http://VaccineShoppe.com) <https://www.vaccineshoppe.com/index.cfm?fa=resources.product&product=Imovax> (Adacel, Fluzone, Imovax Rabies, Menactra, Quadracel, and TENIVAC) accessed June 25, 2017. Package inserts for other Sanofi-Pasteur vaccines are available as follows: Pentacel <https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM109810.pdf> accessed June 25, 2017; IPOL (inactivated polio used in US) <https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM133479.pdf> accessed June 25, 2017; Daptacel <http://druginserts.com/lib/other/meds/daptacel/page/2/>, accessed June 25, 2017; ActHIB [http://vaccines.procon.org/sourcefiles/ActHib\\_package\\_insert.pdf](http://vaccines.procon.org/sourcefiles/ActHib_package_insert.pdf) accessed June 25, 2017; DT <http://druginserts.com/lib/other/meds/diphtheria-and-tetanus-toxoids-adsorbed/> accessed June 25, 2017; Typhim <http://druginserts.com/lib/other/meds/typhim-vi-1/> accessed June 25, 2017; and YF Yellow fever <https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM142831.pdf> accessed June 25, 2017. SP also makes oral polio vaccine used abroad.
- <sup>13</sup> Polio: Global Eradication Initiative. <http://polioeradication.org/> accessed June 26, 2017.