Rotavirus vaccine introduction in Mexico sets precedent

When UK pharmaceuticals giant GlaxoSmithKline (GSK) launched Rotarix, a new rotavirus vaccine, in Mexico in January, it set a precedent. Spurred also by recent EU rules on drug licensing, other companies may follow suit.

The need for a rotavirus vaccine in Mexico became pressing after the only such vaccine to be launched, RotaShield was pulled from the market less than a year after its 1998 introduction when it became linked to bowel blockage or intussusception.

The recall of RotaShield, developed by US pharmaceuticals company Wyeth, held back the timetable for subsequent promising rotavirus vaccines, increasing the cost and testing period for a new product. Although the US Centers for Disease Control and Prevention (CDC) advised other countries to keep studying RotaShield, Wyeth stopped manufacturing it, making further trials impossible.

Pharmaceutical companies usually seek approval for a new product with the US Food and Drug Administration (FDA) or the EU's European Medicines Agency (EMEA) even if the product is largely needed in developing countries. This approval can, in turn, be used in other countries, particularly developing countries with less established regulatory systems.

But seeking approval with the FDA and EMEA can delay the entry of a new medicine or other pharmaceutical product in a country by up to 10 years. For rotavirus infection, where most of between 352 000 and 592 000 children who die annually of its effects live in the developing world, this could mean thousands of deaths before medication is available.

GSK said this is why it went straight to Mexican regulators, got approval in July 2004 and launched the vaccine officially in January 2005. The Mexican Ministry of Health is incorporating Rotarix into its infant immunization programme to prevent some 1000 annual deaths from rotavirus infection that occur in the country.

"We wanted to be in a country where there was a recognized medical need for the Rotarix vaccine, and we were successful in working with Mexican officials," said Patty Seif, a GSK spokeswoman based in Philadelphia. "Rotavirus isn't a big health issue in the US compared to the number of children in developing countries who are dying from rotavirus. So there was a clear medical need."

Experts say it's logical for many reasons to go into a country like Mexico first. From the company's standpoint, a drug like Rotarix has greater profit potential in a developing country because the need, and thus the market, is greater. Although rotavirus is called a 'democratic virus', one that strikes children in every country, it kills an inordinate number of children in developing countries, where there is less access to treatment for diarrhoea.

GSK's direct entrance into Mexico avoided the 10–15 years it often takes for drugs to make their way from developed countries to the poorest countries. Dr Roger Glass, chief of the Viral Gastroenteritis Unit at CDC, said that it can take even longer for such medicines to become affordable.

In December 2004 GSK filed for regulatory approval for Rotarix in the European Union and expects approval soon, said Samantha Christey, a spokesperson for GSK in Belgium.

"Rotarix has been filed in more than 30 countries worldwide," Christey told the *Bulletin*. "Rotarix will be approved in many other Latin American countries in the course of 2005." She said GSK had not sought approval for Rotarix in the US.

Some experts argue that the regulatory authorities in a country like Mexico may be less rigorous. But vaccine advocates argue that the risk criteria in developing countries are different from those in developed countries. In the US, contracting rotavirus infection — which many children under five do — is unlikely to be fatal. In a less developed country an infected child is more likely to die. They argue that in that context a smaller risk of a bowel obstruction, such as the one that took RotaShield off the market, seems a small price to save thousands of lives.

"In a place like India where about 6% of the under-five deaths of children are due to rotavirus, a vaccine would be a real lifesaver," said Glass. "If the risk [of bowel obstruction] was one in 10 000 or one in 30 000, you would save hundreds of lives in India before you would see a single intussusception event."

As developing countries strengthen their regulatory authorities, they may attract an increasing number of new drug licence applications.

"It's a strategy that will be very important in the future," said Ciro de Quadros, Director of International Programs with the Sabin Vaccine Institute, in Washington. "In the past, developing countries did not have national control authorities, [so] this could not happen."

Dr Liliana Chocarro, a WHO expert on regulatory matters, said that under new regulations in Europe the EMEA will no longer license vaccines and other medicines that will not be marketed in the 25 EU member states. She said the development could spur companies to apply for licences in the countries where the drugs will be marketed.

"Perhaps we will see this happening more and more as new vaccines targeted for developing countries come up for licensing," Chocarro said. "More vaccines may be licensed first where the countries are going to use it, not where the vaccines have been manufactured."

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Evan Simpson, spokesperson for the Rotavirus Vaccine Program (RVP), said that obtaining approval in the most developed country of a region — such as Mexico in Central America — could streamline approval in less developed countries of that region much the way US FDA approval streamlines this for other countries.

"The hope is that by introducing it in Mexico or Brazil, approval there will have a similar effect in Latin American countries as FDA approval," said Simpson, who is based in the US city of Seattle. "It's a little bit more piecemeal but hopefully a more rapid process." ■

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