

## Circovirus and impact of temporary withdrawal of rotavirus vaccines in Spain

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The Spanish Medicines and Health Products Agency (AEMPS) did not authorize the release of new batches of rotavirus vaccines onto the Spanish market since March 29 (Rotarix<sup>®</sup>) and June 10 (RotaTeq<sup>®</sup>), 2010, respectively, due to problems of good manufacturing practice (GMP). On November 4, 2010, AEMPS again allowed the release of batches of the RotaTeq<sup>®</sup> vaccine. Until March 2010, the average vaccination coverage against rotavirus in Spain had reached 40%. We have tried to estimate the impact of the temporary withdrawal of these vaccines from the Spanish market in terms of disease burden and associated costs. During the five months in which neither of the rotavirus vaccines was distributed in Spanish pharmacies, 84,450 children were not vaccinated against rotavirus and remain at risk, leading to a total avoidable cost between 1,901,498 and 2,172,941 euros. The impact of the temporary withdrawal of rotavirus vaccines in Spain may have been outstanding. The influence of this event in rotavirus vaccination trust may have been even more important.

At the beginning of 2010 DNA fragments of a porcine circovirus 1 (PCV-1) were detected in the monovalent rotavirus vaccine, Rotarix<sup>®</sup> (GlaxoSmithKline), and later also of PCV-1 and PCV-2 in the RotaTeq<sup>®</sup> (MSD) vaccine. These viruses are frequently found in meat and other products for normal human consumption and have not been shown to cause

disease in humans. Although the World Health Organization (WHO) and the European Medicines Agency (EMA) did not recommend discontinuation of vaccination against rotavirus because of its positive risk—benefit ratio, the Spanish Medicines and Health Products Agency (AEMPS) did not authorize the release of new batches of Rotarix<sup>®</sup> and RotaTeq<sup>®</sup> vaccines onto the Spanish market since March 29 and June 10, 2010, respectively, due to problems of good manufacturing practice (GMP), until research on this issue was complete.<sup>1</sup> On November 4, 2010, AEMPS again allowed the release of batches of the RotaTeq<sup>®</sup> vaccine having checked that it only had fragments of the DNA of the porcine virus (and thereby met the GMP standards), so that currently there are only restrictions on the marketing of the Rotarix<sup>®</sup> vaccine.<sup>1</sup> Until March 2010, the average vaccination coverage against rotavirus in Spain in terms of dose distribution data (BMI and census data) had reached 40%. Furthermore, the first data reported on the effectiveness of the vaccine in Spain were consistent with this coverage and with the data reported for other countries.<sup>2</sup>

### Discussion

We believed it was important to estimate the impact of the temporary withdrawal of these vaccines from the Spanish market in terms of disease burden and associated costs. According to the National Statistics Institute (INE) the birth cohort in 2010

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**Table 1.** Avoidable impact estimate if rotavirus vaccination had not been interrupted in Spain

	Estimated vaccine coverage 5%	Estimated vaccine coverage 0%
Total number of acute gastroenteritis episodes due to rotavirus	<b>2,541</b>	<b>2,904</b>
No. of hospitalizations	<b>434</b>	<b>497</b>
No. of visits to the ER	<b>1264</b>	<b>1444</b>
No. of visits to the paediatrician	<b>1465</b>	<b>1674</b>
Indirect medical costs	<b>494,546 euros</b>	<b>565,196 euros</b>
Direct medical costs	<b>1,406,952 euros</b>	<b>1,607,745 euros</b>
<b>Total avoidable costs</b>	<b>1,901,498 euros</b>	<b>2,172,941 euros</b>

Two vaccine coverage scenarios are assumed (0 to 5%) during the months of suspension of release of new vaccine lots.

in Spain was 506,700 children.<sup>3</sup> The incidence of rotavirus disease and the number of requests for primary care treatment in Spain is estimated at 38 cases per 1,000 infants under 1 year,<sup>4</sup> with hospitalizations at 6.5 per 1,000 <5 year, emergency care at 18.9 per 1,000 <5 year, and visits to health centers at 21.9 per 1,000 <5 year.<sup>5,6</sup> The average indirect cost of an episode of acute gastroenteritis caused by rotavirus is 194.6 euros (2010 update).<sup>6</sup> The direct medical cost is funded by the health service and according to the REVEAL study in Spain the average direct medical cost is estimated at 549 euros.<sup>7</sup> We have supposed a vaccine efficacy of 90.5% in patients who have received at least one dose of the vaccine and that vaccination coverage in Spain was 40%.<sup>8</sup> We have assumed that during the five months since the suspension of release of new batches of rotavirus vaccines, the coverage achieved during those months could have been between 0% and 5%, taking into account that some pharmacies still had stocks of these vaccines available during this period. We have also alleged that all children just before the suspension and after the resumption of vaccination are correctly and fully vaccinated against rotavirus. We have not taken into consideration the potential benefits of vaccination against rotavirus through herd immunity.

Based on these assumptions we can estimate that during the five months in which neither of the rotavirus vaccines was distributed in Spanish pharmacies, 84,450 children were not vaccinated against rotavirus and remain at risk, leading to a total avoidable cost between 1,901,498 and

2,172,941 euros (Table 1). Our estimates only take into account the impact of the disease and the costs, and do not discount the price of the vaccines. In spite of this, it is also probable that the temporary withdrawal of the vaccine has had an even greater negative effect on professional and public confidence in the rotavirus vaccine in particular and other vaccines in general. It will be important to check this and measure the actual impact. Public health decisions are often complex and carefully weighed before its implementation, but should be better coordinated with the corresponding regulatory agency and all the related institutions and health care providers. Otherwise the impact may be negative, the consequences irreversible, and the trust in the institutions and the health professionals can result seriously damaged.

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#### Potential Conflicts of Interest

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All conceived the study and equally contributed to the final result. All authors read and approved the final manuscript.

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