

# ADVANCE POC Study Protocol - Testing new approaches to monitoring benefit/risk with pertussis vaccines as test case. Coverage rates of acellular and whole-cell pertussis-containing vaccines in preschool children (ADVANCE Coverage POC)

**First published:** 29/06/2016

**Last updated:** 31/03/2024

Study

Finalised

## Administrative details

### EU PAS number

EUPAS13908

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### Study ID

21742

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### DARWIN EU® study

No

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### Study countries

- Denmark
  - Italy
  - Spain
  - United Kingdom
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### Study description

The overall ADVANCE proof-of-concept (POC) question is to test the system for benefit-risk monitoring of vaccines in Europe. This will first be done by using test cases. For this POC, the following research question is used: “Has the initial benefit-risk profile in children prior to school-entry booster been maintained after the switch from whole-cell pertussis vaccines to acellular pertussis vaccines”?

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### Study status

Finalised

## Research institutions and networks

### Institutions

Department of Epidemiology Research, Statens Serum Institut

- Denmark

**First published:** 16/03/2010

**Last updated:** 24/02/2012

Institution

Outdated

EU Institution/Body/Agency

Laboratory/Research/Testing facility

ENCePP partner

## Department of Medical Informatics - Health Data Science, Erasmus Medical Center (ErasmusMC)

Netherlands

**First published:** 03/11/2022

**Last updated:** 02/05/2024

**Institution**

**Educational Institution**

**ENCePP partner**

## Fundació Institut Universitari per a la Recerca a l'Atenció Primària de Salut Jordi Gol i Gurina, IDIAPJGol

Spain

**First published:** 05/10/2012

**Last updated:** 23/05/2025

**Institution**

**Educational Institution**

**Laboratory/Research/Testing facility**

**Not-for-profit**

**ENCePP partner**

THIN UK, FISABIO Spain, BIFAP Spain, SSI Denmark

### Networks

# Accelerated development of vaccine benefit-risk collaboration in Europe (ADVANCE)

**First published:** 01/02/2024

**Last updated:** 01/02/2024

Network

## Contact details

### Study institution contact

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Study contact

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### Primary lead investigator

Hanne-Dorthe Emborg

Primary lead investigator

## Study timelines

### Date when funding contract was signed

Planned: 01/10/2013

Actual: 01/10/2013

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### Study start date

Planned: 01/06/2016

Actual: 01/06/2016

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### **Date of final study report**

Planned: 15/09/2016

Actual: 29/06/2016

## Sources of funding

- EU institutional research programme
- Pharmaceutical company and other private sector

## More details on funding

GSK, SP, NOVARTIS, SP MSD, CRUCELL, PFIZER, TAKEDA, IMI

## Study protocol

[ADVANCE POC-Coverage-Protocol.pdf](#) (1.62 MB)

## Regulatory

### **Was the study required by a regulatory body?**

No

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### **Is the study required by a Risk Management Plan (RMP)?**

Not applicable

## Methodological aspects

### Study type

### Study type list

**Study topic:**

Human medicinal product

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**Study type:**

Non-interventional study

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**Scope of the study:**

Other

**If 'other', further details on the scope of the study**

Coverage study

**Data collection methods:**

Secondary use of data

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**Main study objective:**

To estimate the coverage of pertussis-containing vaccines in children less than 6 years of age. The specific objective of this study is to assess the system capability to estimate acellular pertussis and whole-cell pertussis vaccine coverage

## Study Design

**Non-interventional study design**

Other

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**Non-interventional study design, other**

Retrospective population based cohort study

## Study drug and medical condition

**Study drug International non-proprietary name (INN) or common name**  
PERTUSSIS VACCINE

## Population studied

### **Short description of the study population**

All children registered in any of the participating databases during the study period and for whom an adequate start and end of follow-up and date of birth can be defined.

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### **Age groups**

- Infants and toddlers (28 days - 23 months)
  - Children (2 to < 12 years)
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### **Estimated number of subjects**

10000000

## Study design details

### **Outcomes**

Coverage rate overall and for wP and aP vaccines is the proportion of vaccinated children by database, birth cohort, age in months and per dose. The variability of vaccine administration is defined as the time elapsed between birth and the first dose and the time elapsed between subsequent scheduled doses. Changes of coverage rates over time will be described by general descriptive statistic.

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### **Data analysis plan**

- The coverage by age in months per birth cohort will be calculated using a Kaplan-Meier method. The proportion of vaccinated children with dose 1, 2, 3, and subsequent boosters will be calculated stratified by year of birth, type of vaccine and database.
- The change of coverage rates over time will be calculated by the difference between coverage rates and a defined threshold. Low coverage thresholds will be determined for identification of variability of interest/concern. Data-driven thresholds will be compared with set values based on coverage rates required for herd immunity. CUSUM involves the calculation of a cumulative sum (which is what makes it 'sequential'). It is designed to detect changes in the difference. It differs from Sequential Probability Ratio Test (SPRT) by always using zero function as the lower 'holding barrier'. Also, CUSUM does not require the use of the likelihood function.

## Documents

### Study results

[EUPAS13908-21740.pdf](#) (813.13 KB)

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## Data management

### ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

## Data sources

**Data source(s)**

THIN® (The Health Improvement Network®)

The Information System for Research in Primary Care (SIDIAP)

BIFAP - Base de Datos para la Investigación Farmacoepidemiológica en el  
Ámbito Público (Pharmacoepidemiological Research Database for Public Health  
Systems)

ARS Toscana

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**Data sources (types)**

[Administrative healthcare records \(e.g., claims\)](#)

[Electronic healthcare records \(EHR\)](#)

## Use of a Common Data Model (CDM)

**CDM mapping**

No

## Data quality specifications

**Check conformance**

Unknown

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**Check completeness**

Unknown

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**Check stability**

Unknown

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**Check logical consistency**

Unknown

## Data characterisation

### **Data characterisation conducted**

Unknown