

ADVANCE POC I Benefit-Risk pillar – testing new approaches to monitoring benefit/risk with pertussis vaccines as test case:  
benefit-risk analysis of pertussis vaccines in pre-school children comparing whole-cell and acellular formulations in the post-marketing setting

**First published:** 06/07/2016

**Last updated:** 02/07/2024

Study

Finalised

## Administrative details

**EU PAS number**

EUPAS13978

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**Study ID**

31237

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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?” The objectives of this specific benefit-risk modelling exercise, which focuses on testing methods for benefit-risk analysis with pertussis vaccines as test case, are the following: 1. To analyze the benefit-risk balance of pertussis-containing vaccines in children comparing wP and aP formulations at the time of the switch from wP to aP adopting a public health perspective (historical benefit-risk) 2. To investigate the impact of (1) statistical uncertainty in benefit and risk estimates as obtained from the literature, clinical trials, observational databases (uncertainty analyses), (2) differences in preferences and (3) subjective model choices (scenario analyses). 3. To identify the benefit and risk criteria that would most likely modify the benefit-risk balance in case they would change over time (i.e. the pivotal parameters). 4. To assess the feasibility of (retrospectively) monitoring the benefit-risk balance of pertussis-containing vaccines over time (this to mimic prospective monitoring) 5. To re-analyze the benefit-risk balance of pertussis-containing vaccines in children comparing wP and aP formulations from a public health perspective using all currently available evidence (current assessment).

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## Study status

Finalised

## Research institutions and networks

## Institutions

### P95 Clinical and Epidemiology Services

-  Belgium
-  Colombia
-  Netherlands
-  South Africa
-  Thailand
-  United States

**First published:** 07/11/2022

**Last updated:** 21/02/2025

**Institution**

**Laboratory/Research/Testing facility**

**Non-Pharmaceutical company**

**ENCePP partner**

## 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**

Kaat Bollaerts

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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**Data analysis start date**

Planned: 01/09/2016

Actual: 01/09/2016

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**Date of interim report, if expected**

Actual: 30/04/2017

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**Date of final study report**

Planned: 01/02/2017

Actual: 30/07/2017

## Sources of funding

- EU institutional research programme

## More details on funding

IMI

## Study protocol

[ADVANCE\\_POCI\\_BRprotocol.pdf](#) (1.38 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:**

Disease /health condition  
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**

Benefit-risk modeling

**Data collection methods:**

Secondary use of data

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**Main study objective:**

1. Analyze the benefit-risk of pertussis vaccines in children comparing wP and aP at the time of switch from wP to aP (historical)  
2. Investigate the impact of uncertainty in benefits, risks and preferences  
3. Identify the criteria that most likely modify the benefit-risk  
4. Assess the feasibility of monitoring benefit-risk over time  
5. Re-analyze the benefit-risk using currently available evidence

## Study Design

**Non-interventional study design**

Other

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**Non-interventional study design, other**

Cohort state transition model, Multi-criteria decision analysis (MCDA)

## Study drug and medical condition

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

PERTUSSIS VACCINE

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### **Medical condition to be studied**

Injection related reaction

Somnolence

Crying

Convulsion in childhood

Lip swelling

Pertussis

## Population studied

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

Children from birth until their school-entry pertussis booster if any (4th or 5th dose) within all eligible ADVANCE databases.

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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**

1

## Study design details

### **Outcomes**

Exposure of interest: any whole-cell and acellular pertussis-containing vaccines and their doses in the vaccine schedule  
Outcomes: Injection site reactions, fever, somnolence, persistent crying, generalized convulsive seizures, HHE, extensive limb swelling, pertussis, pertussis related death

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### **Data analysis plan**

The benefit-risk assessments will be carried out following the Multi-Criteria Decision Analyses (MCDA) methodology. MCDA is a quantitative methodology for appraising alternatives on individual, often conflicting criteria and combining them into one overall appraisal, through incorporating elicited preferences (weights). The preferences will be elicited using MCDA-swing weighting. In addition, several sensitivity analyses will be conducted to investigate the impact of uncertainty in the benefits, risks and preference estimations on the overall benefit-risk balance. A state transition model will be build to generate the effects table, which will be used for the MCDA swing weighting.

## Documents

### **Study results**

[D5.6\\_ExecSummaryEU-PAS.pdf](#) (1.07 MB)

[D5.7\\_ADVANCEPOC12\\_reportv1.11\\_reviewed.pdf](#) (1.79 MB)

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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 sources (types)

[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

No