



## 101034339 – PROMISE

### Preparing for RSV Immunisation and Surveillance in Europe

#### WP3 –Clinical validation studies

# D3.6 Samples will be ready for shipment to WP4 partners with optimal conditions for storage and shipment

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## Table of contents

Table of contents.....	2
Definitions .....	3
Abbreviations .....	4
Publishable summary .....	5
1. Introduction.....	6
2. Methods.....	7
3. Results.....	8
4. Conclusion and next steps .....	9
ANNEXES.....	10
ANNEX I. PROMISE sample detail and location file .....	10
ANNEX II. PROMISE sample shipment file .....	11

## Definitions

- **Participants** of the PROMISE Consortium are referred to herein according to the following acronyms:
  1. **UEDIN.** The University of Edinburgh (United Kingdom)
  2. **UMCU.** Universitair Medisch Centrum Utrecht (Netherlands)
  3. **UA.** Universiteit Antwerpen (Belgium)
  4. **Imperial.** Imperial College of Science, Technology and Medicine (United Kingdom)
  5. **UOXF.** The Chancellor, Masters and Scholars of the University of Oxford (United Kingdom)
  6. **THL.** Terveysten Ja Hyvinvoinnin Laitos (Finland)
  7. **RIVM.** Rijksinstituut voor Volksgezondheid en Milieu (Netherlands)
  8. **NIVEL.** Stichting Nedelands Instituut voor Onderzoek van de Gezondheidszorg (Netherlands)
  9. **TUCH.** Varsinais-Suomen Sairaanhoidopiirin Kuntayhtymä (Finland)
  10. **TEAMIT.** TEAM IT Research, S.L. (Spain)
  11. **ReSViNET.** Stichting Resvinet (Netherlands)
  12. **SSI.** Statens Serum Institut (Denmark)
  13. **SERGAS.** Servizo Galego de Saúde (Spain)
  14. **PENTA.** Fondazione PENTA - For the treatment and care of children with HIV and related diseases - ONLUS (Italy)
  15. **FISABIO.** Fundación para el Fomento de la Investigación Sanitaria y Biomédica de la Comunitat Valenciana (Spain)
  16. **MLU.** Martin-Luther-Universitaet Halle-Wittenberg (Germany)
  17. **SP.** Sanofi Pasteur, S.A. (France)
  18. **GSK.** GlaxoSmithKline Biologicals, S.A. (Belgium)
  19. **JANSSEN.** Janssen Pharmaceutica, N.V. (Belgium)
  20. **Novavax.** Novavax, Inc. (United States)
  21. **Pfizer.** Pfizer Limited (United Kingdom)
  22. **AZ.** AstraZeneca AB (Sweden)
  
- **Grant Agreement.** (including its annexes and any amendments) The agreement signed between the beneficiaries of the action and the IMI2 JU for the undertaking of the PROMISE project (Grant Agreement No. 101034339).
- **Project.** The sum of all activities carried out in the framework of the Grant Agreement.
- **Work plan.** Schedule of tasks, deliverables, efforts, dates, and responsibilities corresponding to the work to be carried out, as specified in Annex I to the Grant Agreement.
- **Consortium.** The PROMISE Consortium, comprising the above-mentioned participants.
- **Consortium Agreement.** The agreement concluded amongst PROMISE participants for the implementation of the Grant Agreement. The agreement shall not affect the parties' obligations to the Community and/or to one another arising from the Grant Agreement.

## Abbreviations

<b>Acronym / Abbreviation</b>	<b>Meaning</b>
<b>UMC Utrecht</b>	University Medical Center Utrecht
<b>WP</b>	Work Package
<b>RESCEU</b>	Respiratory Syncytial virus Consortium in Europe

## Publishable summary

The PROMISE case-control validation study (study 2) is a prospective monocenter study conducted at UMC Utrecht. The main objective of this study is to validate biomarkers for severity of RSV disease in infants identified in the RESCEU infant studies. The study started in November 2021. Until now biological samples and clinical information have been collected from 102 previously healthy infants (<1 year of age) sub-divided into the following groups:

- Hospitalized, ventilated infants with RSV infection (N=22)
- Hospitalized, non-ventilated infants with RSV infection (N=24)
- Medically attended, non-hospitalized infants with RSV infection (N=27)
- Healthy infants without respiratory tract infection (N=29)

All samples collected to date are available for shipment to analyzing centers. Samples are stored in the UMCU biobank under optimal conditions and a detailed sample identifier and locator file is in place. A sample shipment list has been developed and contains all the necessary sample information. Shipments will be organized by the recipient in close collaboration with UMCU and will be done by a certified courier under optimal conditions. The first shipments will be initiated in May 2023.

## 1. Introduction

In the PROMISE infant case-control validation study samples were collected with the aim to validate the biomarkers pre-identified from the RESCEU infant case-control study as part of Work Package (WP) 4 activities. WP4 is the Biomarker identification validation WP and will analyse samples collected in the case-control biomarker validation study conducted by WP3, the clinical validation studies WP. This study maintains a similar design to the RESCEU infant case-control study (protocol RESCEU infant case-control study described in Jefferies et al, JID 2020, doi: 10.1093/infdis/jiaa239).

## 2. Methods

The monocenter case-control validation study is being conducted at UMC Utrecht and will provide biological samples for the PROMISE biobank (for analysis in WP4) with the objective to validate biomarkers of severe disease and of sequelae in infants after RSV infection identified in the RESCEU case-control study.

The aim is to prospectively collect biological samples and clinical information from 160 previously healthy infants (<1 year of age) sub-divided into the following 4 groups:

- Hospitalized, ventilated infants with RSV infection (N=40)
- Hospitalized, non-ventilated infants with RSV infection (N=40)
- Medically attended, non-hospitalized, infants with RSV infection (N=40)
- Healthy infants without respiratory tract infection (N=40)

Blood, stool, buccal, urine and nasopharyngeal samples (and bronchial samples if ventilated) will be obtained from all infants at presentation and for RSV-positive infants also in convalescence 6-8 weeks later. Clinical symptoms will be collected from medical charts and parents will be asked to fill out a questionnaire at inclusion and a symptom diary for 14 days (only if RSV-positive). Families will be followed up with yearly questionnaires until the end of the study to document the long-term sequelae following RSV infection in the first year of life (see D3.1 for study protocol).

All samples will be stored in the UMCU biobank under optimal storage conditions.

### 3. Results

The study started in November 2021. Up to now 102 infants have been recruited with an even distribution across the 4 subgroups:

- Hospitalized, ventilated infants with RSV infection (N=22)
- Hospitalized, non-ventilated infants with RSV infection (N=24)
- Medically attended, non-hospitalized infants with RSV infection (N=27)
- Healthy infants without respiratory tract infection (N=29)

Additional sample size calculations with recently available results of the RESCEU infant biomarker study, indicated that a sample size of at least 20 per group is expected to be sufficiently informative for the validation of the most important pre-identified biomarkers. Based on this the intention is to not extend the study for another RSV season (decision to be finalised during the GAM4 in May 2023). All samples collected until now are available for shipment to analyzing centers. The first shipments will be initiated in May 2023.

All collected samples are stored in the UMCU biobank. A detailed sample identifier and locator file has been developed based on the RESCEU sample files (see Annex I) and will also be integrated in the virtual sample tracking tool/dashboard which is currently being developed within WP5 (Task 5.6, Data Management and visualization).

The information in this file is non-identifiable and contains the following information:

- study ID
- sample type, volume
- date of collection and type of visit
- actual location
- any other information

In addition, a sample shipment list has been developed based on the RESCEU sample shipment list (Annex II). This file contains the necessary information about the samples which will be shipped and the contact details of the originating and recipient sites.

During the WP4 meetings sample logistics have been discussed and further details about shipment date, information needed, shipment conditions and contact details of the courier will be discussed with the individual sites. All sample shipments will be organized by the recipient of the samples. Sample transport will be done by a certified courier under optimal conditions.

## 4. Conclusion and next steps

All collected samples are stored in the UMCU biobank under optimal conditions. Samples are ready for shipment to WP4 partners on request. All samples are identifiable through a detailed sample detail and location file. For each shipment a sample shipment file will be created with the necessary sample and shipment information. The receiving partner will organize the shipment. First sample shipments are expected to be initiated in May 2023.



