

Operating Manual for the preparation and shipment of centralised biological samples for the study:

EU-SolidAct Study

**In case of problems or questions concerning the preparation and the shipment of the samples,
please contact THERADIS PHARMA:**

Email: solidact@theradispharma.com

Tel: +33 (0)4 97 02 09 39 / Fax : +33 (0)4 97 10 08 78

Contacts: Tu Van Pham (Project Leader) and the Coordination Team



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Study title: Multinational, European, Adaptive Platform trial used for new clinical trials targeting SARS-CoV-2 in short-term and other emerging infectious diseases in the longer term.

A double blind, multicentre, randomized, placebo-controlled, phase III trial to investigate the safety and efficacy of baricitinib + standard of care (SoC) compared with placebo + SoC on the occurrence of death in male and female participants aged > 18 years with severe COVID-19

The patients will be sampled for the centralised analyses at the **following visits**:

Visits	Baseline (D1)	D3	D8	D15	D22
EDTA-Plasma sample	X*	X	X	X	X
Serum sample	X*	X	X	X	X
Naso-oropharyngeal swab **	X*	X	X	X	

* Before drug intervention

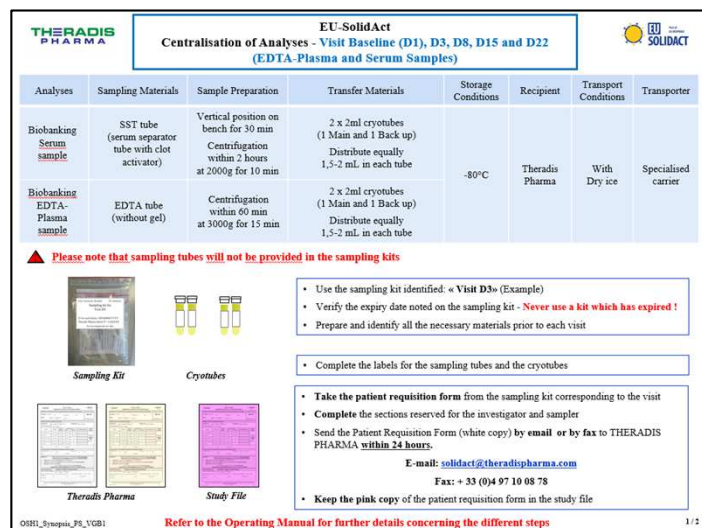
** If nasopharyngeal sample is not possible, an oropharyngeal sample is an alternative

Operating Manual



- One operating manual per site (in local language)

Synopsis



- A synopsis in English which will summarise the main steps to prepare the samples, inserted in each sampling kit

Patient Requisition Form

EU-SolidAct Study
Requisition Form (RF) for Visit D3

Investigator section: The day of the visit, complete this section and transmit the RF to the sampler

Investigator (or Delegate): Name: _____ Date: (DD/MM/YYYY) _____ Signature: _____

Patient: _____

Int. Ref.: OSH001

QR code

OSHI-DS-LAN-XXX

Sampling section: To be completed by the sampler

Date of Sampling: _____ Time of Sampling: _____

Analysis	Sampling tube	Tick if sampling is done	Tubes to be stored		Theradis Pharma section	Transport conditions & Destination
			MAIN (white copy)	BACK-UP (yellow copy)		
Biobanking Serum	SST tube	<input type="checkbox"/>	1 cryotube 2mL	1 cryotube 2mL		Transport with dry ice organised by Theradis Pharma
Biobanking Plasma	EDTA tube	<input type="checkbox"/>	1 cryotube 2mL	1 cryotube 2mL		Theradis

Name: _____ Visa: _____ Comments: _____

Processing section: To be completed by the Technician who handles the samples

Centrifugation Start Time: _____ Time of Freezing: _____

Name: _____ Visa: _____ Comments: _____

IMPORTANT Complete and immediately send the white copy to Theradis Pharma after processing samples:
Email: solidact@theradispharma.com or Fax: +33 (0)4 97 10 08 78

- White copy to be joined with the MAIN tubes sent to Theradis Pharma
- Yellow copy to be joined with the BACK-UP tubes sent to Theradis Pharma (in a separate shipment)
- Pink copy to be archived in the study file

In case of problems or questions, please contact Theradis Pharma
Email: solidact@theradispharma.com or Tel: +33 (0)4 97 02 09 39

Theradis Pharma section: Reception of samples at Theradis Pharma

Date of receipt of the samples: _____

Number of samples received: _____ Received in good condition: Yes ☐ No ☐

Received by: _____ Name: _____ Signature: _____ Date: (DD/MM/YYYY) _____

Comments: _____

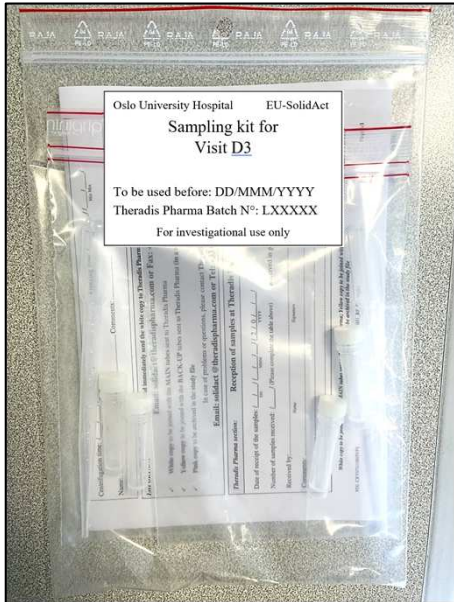
White copy to be joined with the MAIN tubes sent to Theradis Pharma; Yellow copy to be joined with the BACK-UP tubes sent to Theradis Pharma; Pink copy to be archived in the study file

FDL-CK107030505V1 OSH001_RF_D3_VGB3 Page 1/1

- One requisition form in English per patient inserted in each sampling kit
- The requisition form is a duplicate or triplicate document according to the visit
- The requisition form must be completed at the time of sampling

In case of problems regarding the material provided and for all other requests, please contact THERADIS PHARMA immediately

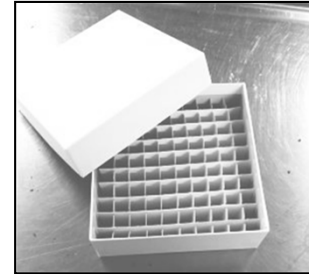
Biological Sampling Kits



Sampling kits, identified by visit:

- Serum and EDTA-Plasma samples (Biobanking)
- Naso-oro-pharyngeal swab

Cryoboxes “81 positions”



Cryoboxes for 2ml cryotubes for storage on-site and for shipment to Theradis Pharma:

- A cryobox for Main cryotubes
- A cryobox for Back-up cryotubes

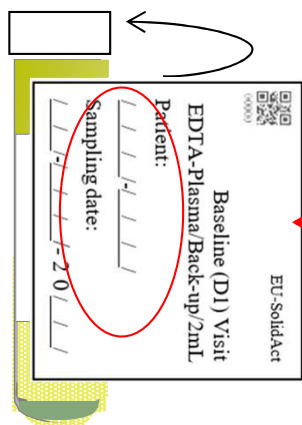


Please note that sampling tubes for Plasma and Serum will not be provided in sampling kits

In case of problems regarding the material provided and for all other logistic requests, please contact THERADIS PHARMA immediately



IMPORTANT: Prior to sampling, complete all the labels already stuck on each cryotube



Subject N° = 6 digits e.g. : / / / - / / / /
Centre N° Patient N°

Sampling Date (Collection date) = DD/MMM/YYYY e.g. : 01/APR/2021

Labels already stuck
on the cryotubes

Sampling tubes and transfer tubes details

Analyses	Visit	Sampling Material *	Sample Preparation	Transfer Material	Storage Conditions	Transport Conditions	Destination
Biobanking Serum sample	Baseline (D1), D3, D8, D15, D22	SST tube (serum separator tube with clot activator)	Vertical position on bench for 30 min Centrifugation within 2 hours at 2000g for 10 min	2 x 2ml cryotubes (1 Main and 1 Back up) Distribute equally 1,5-2 mL in each tube	-80°C	With Dry ice	THERADIS PHARMA
Biobanking EDTA-Plasma sample	Baseline (D1), D3, D8, D15, D22	EDTA tube (without gel)	Centrifugation within 60 min at 3000g for 15 min	2 x 2ml cryotubes (1 Main and 1 Back up) Distribute equally 1,5-2 mL in each tube			
Naso-oropharyngeal swab	Baseline (D1), D3, D8, D15	1 sampling flocked swab + Transport medium 3ml	NA	2x 2ml cryotubes Distribute equally 1,5 mL in each tube			

*** Please note that sampling tubes for Plasma and Serum will not be provided in sampling kits**

6 – Completion of the Patient Requisition Form for Biobanking

EU-SolidAct Study Requisition Form (RF) for Visit D3						
Investigator section: The day of the visit, complete this section and transmit the RF to the sampler					Int. Ref.: OSH001	
Investigator (or Delegate) <small>Name Date (DD/MM/YYYY) Signature</small>					QR code <small>OSH1-D3-LXXXX-XXX</small>	
Patient: <small>Centre N° Patient N°</small>						
Sampling section: To be completed by the sampler						
Date of Sampling: Time of Sampling: <small>DD MM YYYY HH Min</small>						
Analysis	Sampling tube	Tick if sampling is done	Tubes to be stored		Theradis Pharma section	Transport conditions & Destination
			MAIN (white copy)	BACK-UP (yellow copy)		
Biobanking Serum	SST tube	<input type="checkbox"/>	1 cryotube 2mL	1 cryotube 2mL		Transport with dry ice organised by Theradis Pharma → Theradis
Biobanking Plasma	EDTA tube	<input type="checkbox"/>	1 cryotube 2mL	1 cryotube 2mL		
Name: Visa: Comments:						
Processing section: To be completed by the Technician who handles the samples						
Centrifugation Start Time: Time of Freezing: <small>HH Min HH Min</small>						
Name: Visa: Comments:						
IMPORTANT Complete and immediately send the white copy to Theradis Pharma <u>after processing samples</u> : Email: solidact@theradispharma.com or Fax: +33 (0)4 97 10 08 78 <input checked="" type="checkbox"/> White copy to be joined with the MAIN tubes sent to Theradis Pharma <input checked="" type="checkbox"/> Yellow copy to be joined with the BACK-UP tubes sent to Theradis Pharma (in a separate shipment) <input checked="" type="checkbox"/> Pink copy to be archived in the study file In case of problems or questions, please contact Theradis Pharma Email: solidact@theradispharma.com or Tel: +33 (0)4 97 02 09 39						
Theradis Pharma section: Reception of samples at Theradis Pharma						
Date of receipt of the samples: <small>DD MM YYYY</small>						
Number of samples received: (Please complete the table above) Received in good condition: Yes <input type="checkbox"/> No <input type="checkbox"/>						
Received by: <small>Name Signature Date (DD/MM/YYYY)</small>						
Comments:						
<small>White copy to be joined with the MAIN tubes sent to Theradis Pharma; Yellow copy to be joined with the BACK-UP tubes sent to Theradis Pharma; Pink copy to be archived in the study file</small>						



- At the time of sampling, complete all the information required:

Investigator Section:

- Name of the Investigator
- Patient Identification
- Date and signature

Sampling Section:

- Date of Sampling
- Time of Sampling
- Name and signature of the Sampler
- Comments

Processing Section:

- Centrifugation Start Time
- Time of Freezing
- Name and signature of the Technician
- Comments

- Send the Patient Requisition Form (white copy) **by email or by fax** to THERADIS PHARMA **within 24 hours**.

Email solidact@theradispharma.com

Fax : +33 (0)4 97 10 08 78



- White copy** to be joined with the MAIN tubes sent to THERADIS PHARMA



- Yellow copy** to be joined with the BACK-UP tubes sent to THERADIS PHARMA




- Pink copy** to be archived in the study file


6 – Completion of the Patient Requisition Form for Naso-oropharyngeal samples

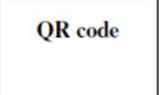



- At the time of sampling, complete all the information required:



EU-SolidAct Study
Requisition Form (RF) for Naso-oropharyngeal sample
for Visit D3



Investigator section: The day of the visit, complete this section and transmit the RF to the sampler		Int. Ref. : OSH001	
Investigator (or Delegate) <small>Name Date (DD/MM/YYYY) Signature</small>		QR code 	
Patient: <small>Centre N° Patient N°</small>		<small>OSH1-D3NOP-1Axxxx-xxx</small>	

Sampling section: To be completed by the sampler					
Date of Sampling: Time of Sampling: <small>DD MM YYYY HH Min</small>					
Please tick the box corresponding to the sample type: Nasopharyngeal sample <input type="checkbox"/> Oropharyngeal sample <input type="checkbox"/> <small>Note : The same procedure should be followed at all time points for the same patient for reproducibility.</small>					
Analysis	Sampling tube	Tick if sampling is done	Tubes to be stored	Theradis Pharma section	Transport conditions & Destination
Nasopharyngeal or Oropharyngeal swab	1 Nasopharyngeal swab + Transport medium 3mL	<input type="checkbox"/>	2 cryotubes 2mL		Transport with dry ice organised by Theradis Pharma 
Name: Visa: Comments:					
Processing section: To be completed by the Technician who handles the samples					
Time of Freezing: <small>HH Min</small>					
Name: Visa: Comments:					

IMPORTANT Complete and immediately send the white copy to Theradis Pharma after processing samples:
 Email: solidact@theradispharma.com or Fax: +33 (0)4 97 10 08 78

✓ **White copy** to be joined with the tubes sent to Theradis Pharma

✓ **Pink copy** to be archived in the study file

In case of problems or questions, please contact **Theradis Pharma**
 Email: solidact@theradispharma.com or Tel: +33 (0)4 97 02 09 39

Theradis Pharma section: Reception of samples at Theradis Pharma	
Date of receipt of the samples: <small>DD MM YYYY</small>	
Number of samples received: (Please complete the table above) Received in good condition: Yes <input type="checkbox"/> No <input type="checkbox"/>	
Received by: <small>Name Signature Date (DDMMYYYY)</small>	
Comments:	

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White copy to be joined with the tubes sent to Theradis Pharma; Pink copy to be archived in the study file

Investigator Section:

- Name of the Investigator
- Patient
- Date and signature

Sampling Section:

- Date of Sampling
- Time of Sampling
- Type of sample
- Name and signature of the Sampler
- Comments

Processing Section:

- Time of Freezing
- Name and signature of the Technician
- Comments

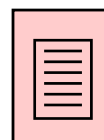
- Send the Patient Requisition Form (white copy) by email or by fax to THERADIS PHARMA **within 24 hours**.

Email solidact@theradispharma.com


Fax : +33 (0)4 97 10 08 78



- White copy** to be joined with the MAIN tubes sent to THERADIS PHARMA



- Pink copy** to be archived in the study file

THERADIS PHARMA		DATA CLARIFICATION FORM	
		DCF N°:	
SPONSOR: OSLO UNIVERSITY HOSPITAL		PROTOCOL: EU-SolidAct	
INVESTIGATOR:		CENTRE N°:	
Section reserved for Theradis Pharma:			
Date of query request (DD/MM/YYYY):		From:	
Patient N°: / / - / / Centre N° Patient N°		Visit:	
Sampling date (DD/MM/YYYY):			
MISSING DATA OR DATA TO BE CONFIRMED			
Comments:			
Section reserved for CRA and/or Investigator:			
CORRECT DATA			
Comments:			
Date: / / DD MMM YYYY		Signature:	
 Please fax immediately this completed document to Theradis Pharma +33 (0)4 97 10 08 78 Please contact us if you have any question Tel : +33 (0)4 97 02 09 39 Email : solidact@theradispharma.com			

DCF: BHO08012902V GB2 DCF_EU-SolidAct_VGB1 page 1/1

Anomalies: incorrect, missing, unreadable data on the Patient Requisition Form

- In case of discrepancies, a Data Clarification Form (DCF) will be
 - issued by THERADIS PHARMA
 - and sent by email or by fax to the centre responsible for the anomaly (copy to CRA Responsible and Sponsor)

- Immediately after receiving the DCF, please complete the “Section reserved for CRA and/or Investigator”:

- Correct data
- Any comments
- Date and signature

- Send the DCF by email or by fax to THERADIS PHARMA **within 24 hours**.

Email: solidact@theradispharma.com

Fax: +33 (0)4 97 10 08 78

- DCFs non resolved after **1 week** will be sent again by email or by fax to the centre (copy to CRA Responsible and Sponsor)

**ATTENTION !**
Important Information

- It is essential to respect the process described on the following pages for each analysis
- Check the expiry date noted on the sampling kit. **Never use a kit which has expired !**
- Use the kit corresponding to the visit
- Prepare all the material prior to each sampling. **Write the Patient N° and the sampling date** on the label stuck on each cryotube.
- Respect the sequence for sampling the tubes as described on page **12**
- Aliquoting must be done **immediately after centrifugation** using one pipet per sampling tube type
- After each sampling, place the samples in the cryobox provided and store at **-80°C until shipment**
- If a sampling kit is not usable, please send the Patient Requisition Form which is in the sampling kit by email or by fax to THERADIS PHARMA



Sequence of sampling



Tubes
SST
EDTA



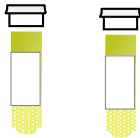
**Please note that sampling tubes pictures (on pages 13 and 14) are for reference only.
Tube and cap colours may differ depending on the manufacturers.**

Serum samples for Biobanking at: Baseline (D1), D3, D8, D15, D22 Visits

Material



SST tube
(serum separator tube
with clot activator)



2 labelled cryotubes

EU-SolidAct
Visit D3
Serum/Main/2mL

Patient: _____

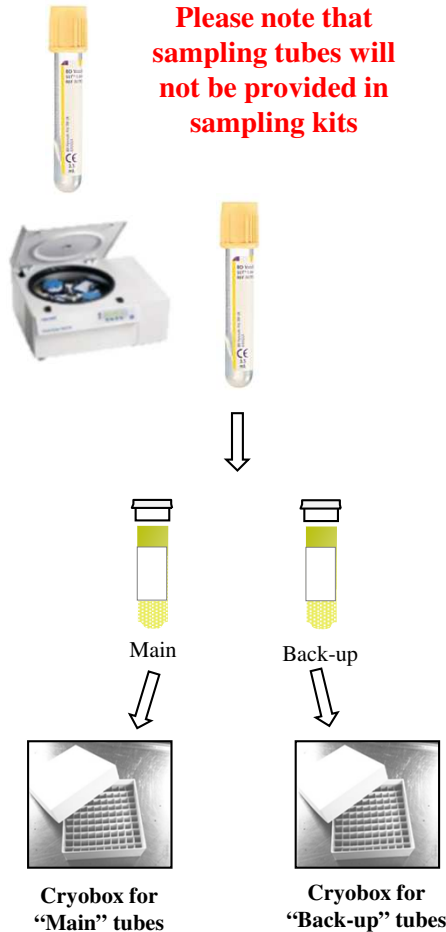
Sampling date: ____/____/____ - 20____

EU-SolidAct
Visit D3
Serum/Back-up/2mL

Patient: _____

Sampling date: ____/____/____ - 20____

Sampling, sample preparation and storage on site



Blood sampling:

- Take a blood sample using the SST tube (serum separator tube with clot activator)
- Note the time of sampling on the requisition form**

Preparation:

- Immediately after sampling, **homogenise gently by inverting 8 to 10 times** the SST tube without shaking it
- Allow the blood content of the tube to clot in the upright position at room temperature for approximately 30 minutes
- Centrifuge within 2 hours for 10 minutes at 2000g
- Immediately after centrifugation of the tube** use the pipet to distribute equally **1,5-2 mL** of serum (leave approximately 0,5 cm above the cell layer) into each of the 2 transfer tubes labelled «**Serum/Main/2mL**» and «**Serum/Back-up/2mL**»

Note: Handling of serum tubes can be grouped if blood from several patients is drawn on the same day. In the meantime, store the sampling tubes at 4°C (vertical position for the coagulation of the serum) until centrifugation. Record the time from sampling to freezing in the eCRF.

Storage:

- Immediately** place the "Main" cryotube in the cryobox identified for the study **"2ml Main cryotubes"** and the back-up cryotube in the cryobox identified for the study **"2ml Back-up cryotubes"**
- Store at -80°C** until shipment (the cryotubes should be frozen at nominal - 80°C, as soon as possible and latest within 12 hours)

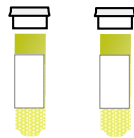
Note: Short-term freezing at -20°C for up to one week is acceptable if -80°C freezer is not available.

- Keep the **white** copy of the patient requisition form. It will be placed in the front pouch of the diagnobag at the time of shipping the Main tubes
- Keep the **yellow** copy of the patient requisition form. It will be placed in the front pouch of the diagnobag at the time of shipping the Back-up tubes
- Keep the **pink** copy of the patient requisition form in the study file



EDTA plasma samples for Biobanking at: Baseline (D1), D3, D8, D15, D22 Visits

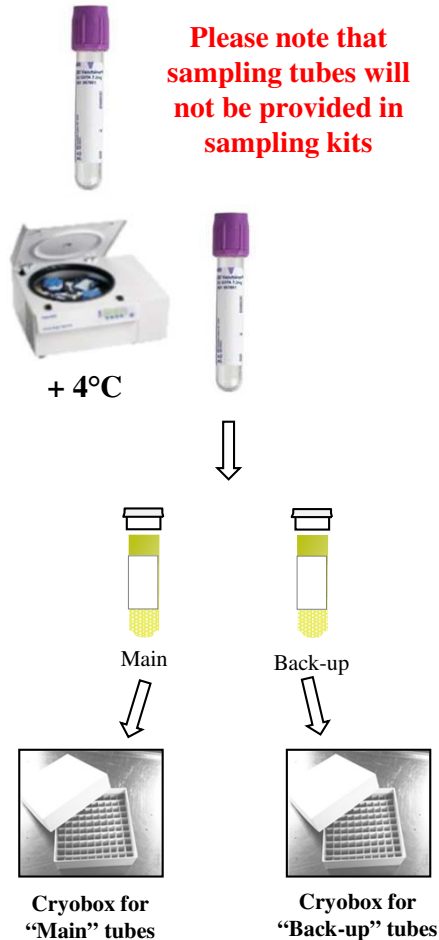
Material



EU-SolidAct
Visit D3
EDTA-Plasma/Main/2mL
Patient: _____
Sampling date: ____/____/____ - 20____/____/____

EU-SolidAct
Visit D3
EDTA-Plasma/Back-up/2mL
Patient: _____
Sampling date: ____/____/____ - 20____/____/____

Sampling, sample preparation and storage on site



Blood sampling:

- Take a blood sample using the EDTA tube (preferably without gel)
- **Note the time of sampling on the requisition form**

Preparation:

- **After sampling**, homogenise gently by inverting 8 to 10 times the EDTA tube without shaking it
- **Centrifuge** as soon as possible (preferably within 30 minutes, latest within 60 minutes) at 3000g for 15 minutes at **4° C**
- **Immediately after centrifugation of the tube** use the pipet to distribute equally **1,5-2 mL** of plasma (leave approximately 0,5 cm above the cell layer) into each of the 2 transfer tubes labelled «**EDTA-Plasma/Main/2mL**» and «**EDTA-Plasma/Back-up/2mL**»

Note: Handling of plasma tubes can be grouped if blood from several patients is drawn on the same day. In the meantime, store the sampling tubes at 4°C until centrifugation. Record the time from sampling to freezing in the eCRF

Storage:

- **Immediately** place the “Main” cryotube in the cryobox identified for the study “**2ml Main cryotubes**” and the back-up cryotube in the cryobox identified for the study “**2ml Back-up cryotubes**”
- **Store at -80°C** until shipment (the cryotubes should be frozen at nominal - 80°C, as soon as possible and latest within 12 hours)

Note: Short-term freezing at -20°C for up to one week is acceptable if -80°C freezer is not available.

- Keep the **white** copy of the patient requisition form. It will be placed in the front pouch of the diagnobag at the time of shipping the Main tubes
- Keep the **yellow** copy of the patient requisition form. It will be placed in the front pouch of the diagnobag at the time of shipping the Back-up tubes
- Keep the **pink** copy of the patient requisition form in the study file

Naso-oro-pharyngeal sample: Baseline (D1), D3, D8, D15 Visits

Material



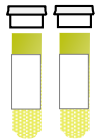
Naso-oro-pharyngeal swab +
Transport medium 3mL

EU-SolidAct
(00000)

Visit D3
NOP

Patient:
____/____/____

Sampling date:
____/____/____ - 20____/____/____



2 labelled cryotubes

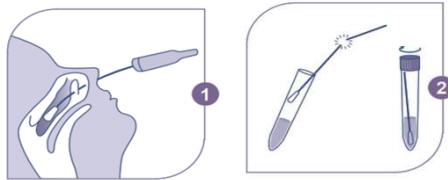
EU-SolidAct
(00000)

Visit D3
NOP/2mL

Patient:
____/____/____

Sampling date:
____/____/____ - 20____/____/____

Sampling, sample preparation and storage on site



Naso-oro-pharyngeal swab:

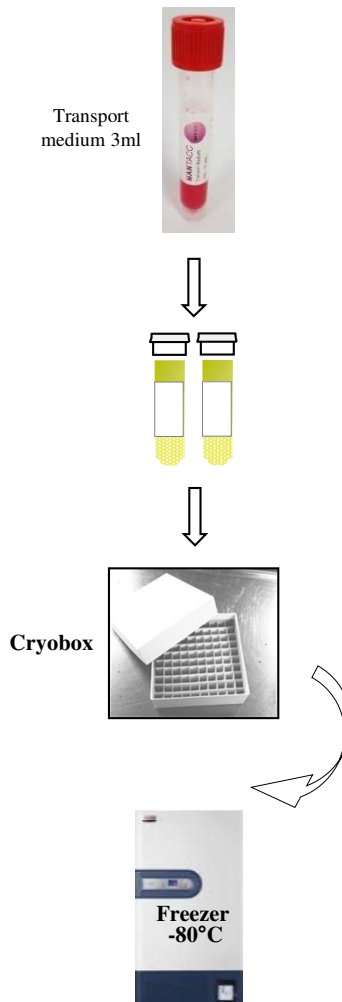
- Perform the nasopharyngeal sample with the swab provided
- Gently insert the swab along the nasal septum, just above the floor of the nasal passage, to the nasopharynx, until resistance is felt.
- Rotate the swab for 5-10 seconds to obtain cellular material.
- Break the swab into the corresponding transport medium 3mL tube and close the tube.
- **Note the sampling time on the requisition form**
- **If nasopharyngeal sample is not possible, an oropharyngeal sample is an alternative. Again, rotate the swab for 5-10 seconds.**
- The same procedure should be followed at all time points for the same patient for reproducibility.**

Preparation:

- **Immediately after sampling**, gently invert the transport medium 3mL tube 8 to 10 times without shaking it
- Then use the pipet to distribute equally approximately **1,5 mL** of the transport medium from the tube into each of the 2 transfer tubes labelled «**NOP/2mL**»

Storage:

- Then place the tubes identified «**NOP/2mL**» in the cryobox identified “**2ml Main cryotubes**”
- **Store** the cryobox **at -80° C** until shipment
- Keep the **white** copy of the patient requisition form and place it in the front pouch of the diagnobag at the time of shipping
- Keep the **pink** copy of the patient requisition form in the study file



Pick-ups will be organised by THERADIS PHARMA from Tuesday to Thursday.

3 pick-up per site are planned

Before each pick-up, THERADIS PHARMA will notify the centre by email to validate the pick-up date

Information for the pick-up of the samples:

Analyses	Cryoboxes	Destination	Frequency	Carrier	Transport conditions
Biobanking (EDTA-Plasma/Serum) Naso-oropharyngeal swab	1 to 3 cryoboxes per transport	THERADIS PHARMA (France)	3 pick-up per site: <ul style="list-style-type: none"> ○ 1 shipment for Main tubes ○ 1 shipment Main & Back Up tubes ○ 1 shipment Back-up tubes 	STARSERVICES/ TSE for France SAFETRANS or MARKEN for the other sites	With Dry ice

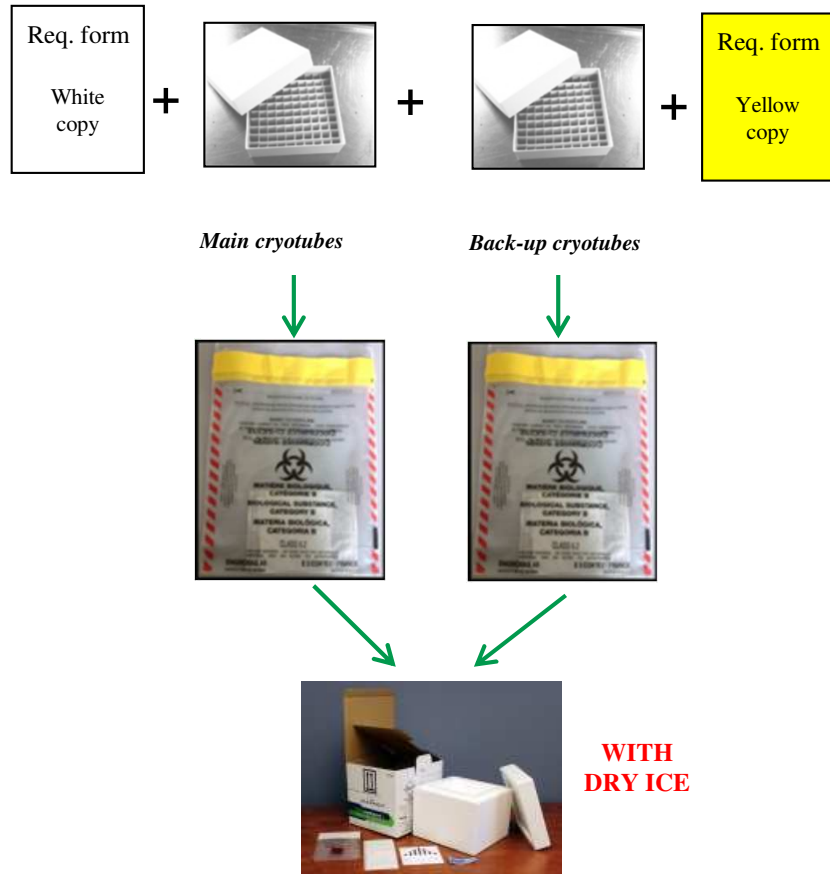
**For one patient, the main and the back-up cryotubes for a same patient must be sent separately
(two different shipments)**



**Reminder: White copy to be joined with the MAIN tubes
Yellow copy to be joined with the BACK-UP tubes**

Material brought by Safetrans, MARKEN or TSE (for France) on the day of shipment:
a transport kit, dry-ice, a diagnobag, an airwaybill

When the carrier arrives:

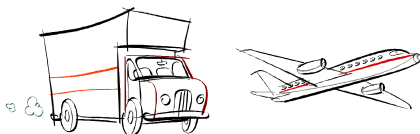


- Take the cryobox identified for the study “**2ml Main cryotubes**”
- Take the cryobox identified for the study “**2ml Back-up cryotubes**” (if applicable) of the previous patients
- Take the white and yellow copies of the patient requisition forms, completed and signed, for all the samples to be sent



For a same patient, separate shipment for main and back-up cryotubes

- Place the cryoboxes in the diagnobag provided by the carrier (**1 cryobox per diagnobag**)
- Insert the patient requisition forms in the front pouch of the diagnobag
- Give the cryoboxes to the carrier who will place it in the transport kit
- Verify that dry ice is present
- Verify the destination noted on the airwaybill stuck on the transport kit: **THERADIS PHARMA (France)**
- In case of any problems or questions, immediately contact THERADIS PHARMA
- Keep a copy of the airwaybill in the study file



On the shipping day, please make sure the carrier has brought dry ice.
Do not give the samples if there is no dry-ice