

# INTERNATIONAL STANDARDS, BEST PRACTICES, RECOMMENDATIONS AND MINIMUM REQUIREMENTS FOR ISIDORe WORK PACKAGES PROVIDING INFECTIOUS DISEASE RESEARCH SERVICES

In this section an overview of all infectious disease research services offered by ISIDORe service partners, a general overview of relevant international standards and scientific recommendations as well as specific minimum requirements for each service provider to use their services is presented.

**Table 5: Overview list of relevant international standards, best practices and scientific recommendations per ISIDORe WP**

International standards, best practices, scientific recommendations as well as minimum requirements for the use of the ISIDORe services are listed, if available (although the intention was to be comprehensive, we make no claim to completeness).

Work package	Services	International standards / best practices / scientific recommendations
	<b>General</b>	<ul style="list-style-type: none"> <li>- Specific standards data quality</li> <li>- ISO/TS 8000-1:2022- Part 1: Overview</li> <li>- ISO 8000-2:2020 - Part 2: Vocabulary</li> <li>- ISO 8000-100:2016 - Part 100: Master data: Exchange of characteristic data: Overview</li> </ul>

- ISO 8000-110:2021 - Master data: Exchange of characteristic data: Syntax, semantic encoding, and conformance to data specification
- ISO 8000-120:2016 - Part 120: Master data: Exchange of characteristic data: Provenance
- ISO 8000-130:2016 - Part 130: Master data: Exchange of characteristic data: Accuracy
- ISO 8000-140:2016 - Part 140: Master data: Exchange of characteristic data: Completeness
- ISO 8000-150:2022 - Part 150: Data quality management: Roles and responsibilities
- ISO 8000-8:2015 - Part 8: Information and data quality: Concepts and measuring
- ISO 8000-61:2016 - Part 61: Data quality management: Process reference model
- Specific standards information technology
- ISO/IEC 2382:2015 - Information technology – Vocabulary
- FAIR principles of European Commission
- European Commission, Directorate-General for Research and Innovation, Turning FAIR into reality – Final report and action plan from the European Commission expert group on FAIR data, Publications Office, 2018, <https://data.europa.eu/doi/10.2777/1524>
- FAIR principles

		<ul style="list-style-type: none"> <li>- Wilkinson et al. (2016), "The FAIR Guiding Principles for scientific data management and stewardship", Scientific Data 3, 9p. DOI:10.1038/sdata.2016.18 <a href="https://www.nature.com/articles/sdata201618">https://www.nature.com/articles/sdata201618</a>; <a href="https://www.go-fair.org/fair-principles/">https://www.go-fair.org/fair-principles/</a></li> <li>- Holub et al. (2018), "Enhancing Reuse of Data and Biological Material in Medical Research: From FAIR to FAIR-Health." Biopreserv Biobank. 16(2):97-105. DOI: 10.1089/bio.2017.0110.</li> </ul>
<p><b>WP9</b></p>	<p><b>Provision of services for structural biology:</b></p> <p><b>General</b></p>	<p><b>Light Microscopy:</b></p> <ul style="list-style-type: none"> <li>- BS ISO 8036:2015-06-30 Microscopes. Immersion liquids for light microscopy</li> <li>- BS ISO 10934:2020-08-27 - Microscopes. Vocabulary for light microscopy</li> <li>- BS ISO 19056-3:2022-02-23 - Microscopes. Definition and measurement of illumination properties. Incident light fluorescence microscopy with incoherent light sources</li> </ul> <p><b>Human imaging:</b></p> <p>Protein:</p> <ul style="list-style-type: none"> <li>- <b>P4EU</b> - Quality Control of purified protein – Best practice recommendations <a href="https://p4eu.org/P4EU-Inhalt/uploads/2018/04/Extended-guideline-7.pdf">https://p4eu.org/P4EU-Inhalt/uploads/2018/04/Extended-guideline-7.pdf</a></li> </ul>
	<ul style="list-style-type: none"> <li>- <b>INSTRUCT-BE_Nanobodies4INSTRUCT:</b> Nanobody discovery</li> <li>- <b>INSTRUCT-CZ_CEITEC:</b> Biomolecular Interactions and Crystallisation; Cryo-electron microscopy (cryo-</li> </ul>	<p><b>Nanobiotechnology:</b> ISO 45001:2018 Occupational health and safety management systems - Requirements with guidance for use</p>

<p>EM) and tomography; Nuclear Magnetic Resonance Techniques (NMR); Proteomics</p>	<p><b>Cryo-EM:</b> local Safety-Sheets, Best practice documents</p> <p><b>NMR, Proteomics:</b> not specified</p> <p><b>BIC:</b> Proclamation on chemical compounds; quality requirements are discussed on case-to-case basis</p> <p>There are many limits that differ for each individual technique available within offered services. The limits are also affected by the nature of the sample and level of information that is about to be gathered during the experiment.</p>
<ul style="list-style-type: none"> <li>- <b>INSTRUCT-CZ_BIOCEV:</b> Biophysical techniques, Crystallization of Proteins and Nucleic Acids; Structural Mass Spectrometry (MS); Diffraction Techniques; Molecular target pipeline (Complete pipeline from sequence to full characterisation and diffraction screening)</li> </ul>	
<ul style="list-style-type: none"> <li>- <b>INSTRUCT-EMBL_HD:</b> Cryo-EM single particle analysis, cryo-Electron Tomography, and Cryo-Correlative Light and EM</li> <li>- <b>INSTRUCT-EMBL_HH:</b> Sample preparation and characterization, beamlines and data analysis for MX and BioSAXS.</li> <li>- <b>INSTRUCT-EMBL_GR:</b> Crystallography pipelines for fast characterization of new variants and other targets; CrystalDirect Fragment screening for rapid characterization of target compound complexes in support of drug design and Med. Chem. optimization and drug re-purposing.</li> </ul>	<p><b>Cryo-EM:</b></p> <ul style="list-style-type: none"> <li>- Provision of service for BSL1 and BSL2 biospecimens of which the handling has approved by EMBL internal Health and Safety Office</li> <li>- For life imaging of BSL2 specimen, only plastic (no glass) ibidi chambers may be used</li> <li>- Prior to the service a risk assessment form must be filled</li> </ul>
<ul style="list-style-type: none"> <li>- <b>GUF:</b> NMR of viral proteins, RNA, ligand-protein and ligand-RNA complexes</li> </ul>	

- **INSTRUCT-ES\_I2PC:** EM Image Processing, including structural flexibility analysis

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- **INSTRUCT-FI\_UOULU:** X-ray crystallography including data management, crystallization, data collection
- **INSTRUCT-FI\_UEF:** Analysis of single viral proteins and binding to drugs and antibodies using native MS (FT-ICR and TIMS-QTOF)
- **INSTRUCT-FI\_UH:** Biophysical characterization of complexes using field flow fractionation and centrifugation; EM and Image Processing; NMR sample preparation with segmental labelling, screening of samples, data collection; Single cell MS and proteomics; Fragment screening approaches

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- **INSTRUCT-FR1\_IGBMC:** Macromolecular crystallography (Crystallisation; test and characterization by RX); cryo-EM; FIB/SEM with operator; Super resolution cell imaging; Protein production in mammalian cells, insect cells and bacteria
- **INSTRUCT-FR2\_IBS-ISBG:** CryoEM - structural characterisation of viruses and their proteins; NMR - structural and dynamic characterisation of viral targets, in isolation and in complex with viral and host factors

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- **INSTRUCT-IL\_ISPC:** Protein production in mammalian cells, insect cells and bacteria; crystallography

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- **INSTRUCT-IT\_CERM:** Atomic level characterization and/or interactions (IDP, proteins, nucleic acids);

<p>Quality assurance via NMR (HOS of vaccines, antibodies, antigens/adjuvants), Fast fingerprinting/profiling via NMR metabolomics on blood (serum, plasma) and urine; Fragment-screening by NMR; druggability</p>	<p>Not specified</p>
<ul style="list-style-type: none"> <li>- <b>INSTRUCT-NL_NKI:</b> Integrated biophysics for sample characterisation and crystallisation; Expression/Purification of viral proteins and complexes for structural studies; Scaling up of monoclonal antibodies from hybridoma cells; Integrated biochemistry and biophysics instrumentation, screening or hit and lead validation; HP automated refinement of crystallographic protein structures, ligand and fragment screening</li> <li>- <b>INSTRUCT-NL_NeCEN:</b> CryoEM including, sample preparation and sample screening, Aquilos sample milling, Krios data collection and image processing</li> <li>- <b>INSTRUCT-NL_Bijvoet Centre:</b> Structural proteomics MS, including structural analysis of viral particles; Plasma proteome profiling, including monitoring of viral and immune response proteins; NMR-based structural biology, including structural analysis of viral proteins; NMR-based screening, including screening of protein-drug interactions</li> </ul>	<p>Not specified</p>
<ul style="list-style-type: none"> <li>- <b>SAS:</b> Structural analysis of glycans by NMR and MS</li> </ul>	<p>Not specified</p>
<ul style="list-style-type: none"> <li>- <b>INSTRUCT-UK_Astbury Centre:</b> cryo-EM; NMR; MS</li> </ul>	<p>Not specified</p>
<ul style="list-style-type: none"> <li>- <b>INSTRUCT-UK_Diamond:</b> EM; XChem Fragment Screening; X-ray Diffraction and Bio-SAXS</li> </ul>	<p>Not specified</p>

- **INSTRUCT-UK\_RFI:** Rapid selection of nanobodies by in vitro screening/affinity maturation complementary to VIB nanobodies by immunisation
- **INSTRUCT-UK\_OPIC:** 3D Structure analysis using electron cryo-EM and tomography

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**Provision of imaging services**

- <https://www.eurobioimaging.eu/>
  - <https://www.eurobioimaging-interim.eu/>
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- **Sofia BioImaging Node - Advanced Light Microscopy Node:** High-speed live cell imaging, laser ablation, proteinprotein interactions
  - <http://dnarepair.bas.bg/eurobioimaging.bg/site/>
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- **Advanced Light and Electron Microscopy Node Prague CZ:** Volume Electron microscopy, correlative light & electron microscopy, Super-resolution microscopy, label-free imaging
  - <https://www.czech-bioimaging.cz/euro-bi/>
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- **European Molecular Biology Laboratory:** Euro-BioImaging EMBL-Node: Previous work on SARS-CoV2 effect on cell physiology with electron microscopy, High-throughput microscopy, Lightsheet imaging, super-resolution microscopy, correlative light & electron microscopy, protein dynamics, image data analysis
  - <https://www.embl.org/>
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- **Finnish Advanced Light Microscopy Node:** High-throughput screening including on organoids, super-

resolution microscopy, correlative light & electron microscopy, mesoscopic imaging, label-free imaging

- <https://www.bioimaging.fi/finnish-advanced-light-microscopy-node-new-website/>

- **French BioImaging Node:** Unique panel of equipment in biosafety levels II and III, research on virus life-cycle in infected cells, electron microscopy, super-resolution imaging, protein dynamics, image data analysis

- <https://france-bioimaging.org/>

- **Hungarian ALM and MI Node:** Protein dynamics, functional imaging, multi-photon imaging

- <https://www.eurobioimaging.eu/nodes/cellular-imaging-hungary>

- **Advanced Light Microscopy Italian Node:** Super-resolution microscopy, correlative light & electron microscopy, elemental imaging, functional imaging

- <https://www.eurobioimaging-interim.eu/almin.html>

- **Molecular Imaging Italian Node:** MRI, PET, SPECT, Imaging Probes, CT, ultrasound imaging applied to animal models of human pathologies

- <http://www.mmmi.unito.it/>

- **Phase Contrast Imaging Flagship Node Trieste:** Phase Contrast Imaging, previously used to evaluate COVID-19 patient lung samples

- <https://www.eurobioimaging.eu/nodes/phase-contrast-imaging-flagship-node-trieste>



- **Challenges Framework Node:** Image Analysis algorithms, AI and machine learning approaches
- <https://grand-challenge.org/>

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- **Correlative Light Microscopy Dutch Flagship Node:** Correlative light & electron microscopy, research projects on infectious diseases, viruses, and immunology
- <https://www.eurobioimaging-interim.eu/clmdfn.html>

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- **High Throughput Microscopy Dutch Flagship Node:** High-throughput microscopy, whole-genome RNAi screens, image data analysis
- <https://www.eurobioimaging.eu/nodes/high-throughput-microscopy-dutch-flagship-node>

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- **Preclinical Imaging Centre (PRIME) - Molecular Imaging Dutch Node:** Multimodal imaging of small animals, MRI, PET, CT, SPECT, multi-photon imaging, ultrasound imaging, SPF/DMII unit allowing work with certain viruses
- <https://www.radboudumc.nl/Research/Organisation/ofresearch/Departments/cdl/PRIME/Pages/default.aspx>

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- **Population Imaging Flagship Node Rotterdam:** Imaging in large, prospective epidemiological studies, data and image archiving and analysis
- <https://populationimaging.eu/>

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- **NorMIC Oslo - Advanced Light Microscopy Node Oslo:** Super-resolution microscopy, fast live-cell

imaging, electron microscopy, focus on immune cells and intra-cellular dynamics

- <https://www.mn.uio.no/ibv/english/research/infrastructure/facilities/life-science/imaging/normic/index.html>

- **Finnish Biomedical Imaging Node:** PET, MRI, MEG, optical intravital imaging, tracers/probes, wide range of animal models as well as systems for patients

- <https://eurobioimaging.fi/FiBI/>

- **Austria BioImaging:** Correlative imaging pipelines combining biological and biomedical imaging, body donor facility, large animal research facilities, super-resolution, image analysis

- <https://austrian-bioimaging.at/>

- **Portugal PPBI:** Biosafety level II imaging facilities, Electron microscopy, mesoscopic multimodal imaging, superresolution imaging, screening, image data analysis

- <https://www.ppbi.pt/joomla30/>

- **INRAE-IERP, INRAE-APEX, UEDIN:** Rodents, livestock and wildlife species: super-resolution confocal, multiphoton microscopy, high content and light sheet microscopy, scanning and transmission electron microscopy, mass spectrometry imaging, STORM/Airyscan, IVIS Spectrum in vivo imaging, histopathology (ECVP certified)

- [https://www6.jouy.inrae.fr/ierp\\_eng/IERP-Unit](https://www6.jouy.inrae.fr/ierp_eng/IERP-Unit)

- [https://www6.angers-nantes.inrae.fr/panther\\_eng/News-events/APEX](https://www6.angers-nantes.inrae.fr/panther_eng/News-events/APEX)

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#### Provision of services for metagenomics and transcriptomics data

- **APHP/HMN:** "Shotgun metagenomics" (ISO 15189 accredited)

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#### Provision of analytical vector services

- **INFRAVEC:** insect disease vector research, advice and guidance, genomics and analytical services on arthropod disease vectors, including vector sequencing, genotyping, insecticide resistance, genome editing, functional genomics and bioinformatics
- **UG, POLOGGB, IMPERIAL, MPIIB, FORTH, INSA BSL3:**
  - o Analysis of insecticide resistance (metabolic analysis for novel insecticide synergists, electron microscopic analysis of cuticle thickness).
  - o Vector genotyping and vector Illumina/Nanopore sequencing services with or without bioinformatics support for whole RNA transcriptome, genome and amplicons, metagenomics, virome, small RNA, long read DNA sequencing.
  - o Vector functional genomic analysis by custom gene silencing in Aedes with infection by Zika, chikungunya, dengue; or Anopheles with infection by Plasmodium falciparum.

**FORTH:** appropriate storage of samples to retain quality for nucleic acid determinations

	<ul style="list-style-type: none"> <li>○ Vector custom genome editing in Anopheles by CRISPR/Cas9 mutagenesis or PiggyBac element transgenesis.</li> </ul>	
<p><b>WP10</b></p>	<p><b>General</b></p>	<p>Medicinal chemistry</p> <ul style="list-style-type: none"> <li>- Purity requirements for synthetic compounds (&gt;90% pure by NMR/HPLC)</li> </ul> <p>Common operational standards EU-OPENSREEN:  <a href="https://www.eu-openscreen.eu/fileadmin/user_upload/newsroom_and_downloads/210203_EU-OS HTS_QC_General_Guidelines_v2.1.pdf">https://www.eu-openscreen.eu/fileadmin/user_upload/newsroom_and_downloads/210203_EU-OS HTS_QC_General_Guidelines_v2.1.pdf</a></p>
	<p><b>Provision of access to the small molecule discovery platform</b></p> <ul style="list-style-type: none"> <li>- <b>MEDI, HZI, SIN, IMTM, ITMP, IBCH-PAS, KUL:</b> Assay development</li> <li>- <b>MEDI, HZI, SIN, IMTM, ITMP, UH, IBCH-PAS, KUL:</b> High-throughput screening services</li> <li>- <b>EU-OS, UiO, ITMP:</b> Access to libraries of compounds</li> <li>- <b>MEDI, HZI, SIN, UH, IBCH PAS, ITMP:</b> Hit validation and hit profiling</li> </ul>	<p><b>IBCH-PAS:</b></p> <p><b>Formal requirements</b> - After the decision that genetically modified material and cells will go to us in a given project. We must submit/obtain consent (for work with GMM or GMO) from the Minister of the Environment, because the work will be carried out by us.</p> <p>Quality requirements - Cat. I or II GMM or GMO (according to the Ministry's classification and assessment of the degree of risk to people and the environment prepared by the researcher) and standard transfer documents.</p> <p><b>Cells:</b> Our standard quality requirement for newly received cell lines is that we run the cell culture for a minimum of 2 weeks. After this period, we collect the cell culture media and run a PCR test which allows one to detect the presence of mycoplasma. If the result is negative, we can start to perform experiments with the cells. If the result is positive, however, we do not attempt to eliminate the infection. When it comes to overall requirements, we require the cells to be in good condition and proliferate well. Cells should be shipped to us frozen in vials on dry</p>

ice. The concentration of cells in the vials should be minimum 1 mln cells/per vial. The concentration might be also higher than 1 mln, however, this is dependent on the cell line. In addition, we require information about the name of the cell line, passage number and the concentration of cells in vials provide to us.

**Protein samples:** Regarding the requirements for these samples, we require high purity products (powder, lyophilisate, solution) of known concentration (or units of activity) and exact composition description (if it contains, for example, any stabilizers). If samples are delivered in several aliquots, they should be comparable with each other (best if they were derived from one batch). Samples should be delivered frozen in vials on dry ice (if needed). We should know the temperature at which we can store the delivered samples and the approximate stability.

**RNA samples:** we require a high purity product in the form of a lyophilisate or solution. In solution form, the samples should be RNase free and their concentration as high as possible. If the sample contains any additional components, we should have a description of them. Samples should be delivered frozen in vials on dry ice (if needed).

**Assay Development:**

**For cell lines** we overall need 2-3 vials with the proper concentration of cells (minimum 1 mln/per vial) to start the cell culture and to culture sufficient amount of cells which is needed for specific types of experiments. This number of vials is sufficient for performing cell-based screening tests for 5000 compounds in the 384-well plate format. For performing tests for higher number of

compounds (e.g. 100k) we would need higher amounts of vials.

**In the case of proteins**, the amount required depends on the assay type and / or activity of the protein. Ideally, one batch (or many similar batches) of delivered probes should be enough for assay development, assay transfer and automation and all stages of screening process (primary screening, confirmatory screening and IC/EC 50 measurements) assuming an additional sample excess of approximately 20%. For 100k compounds screening, the amount of sample needed is about 10 times higher than for 5k compounds screening.

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**Provision of access to the Hit to Lead /Candidate development platforms:**

- **LIOS, FMP-FVP, CSIC, DTU, IBB-PAN, MEDI:**  
medicinal chemistry, in vitro early safety and toxicity profiling, compound bio profiling in animal tissues

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**Provision of access to the antibody discovery platform**

- **IRB, IBB-PAN, MSCNRIO, MUW:**
    - o cell clones after immunization of animals, and from convalescent patient samples, antibody cloning and characterisation in binding assays with viral/bacterial antigens, antibody neutralization assays, high throughput viral phenotypic assays (KUL), lower throughput infection assays with mutant strains of SARS-CoV-2 using lentiviral based pseudovirus infection models
    - o Nanobody library construction from llamas, phage display, identification and validation of
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specificities, protein overexpression and purification.

**Antibody characterization**

- **IRB, IBB-PAN, MSCNRIO, MUW, JRC:** Recombinant production and purification, humanization of mouse, llama or other animal-derived antibodies, kinetic characterization, low throughput neutralization assays also with mutated Spike protein with/without exogenous ACE2 or TMPRSS2 expression on cell surface; stability and aggregation assays, class switching, epitope mapping, engineering for increased stability, solubility, modulation of complement engagement, multi specific constructs; 3D structural analysis of antibody-antigen complexes with experimentally guided computational simulations.

**Microfluidic devices**

- **BRFAA, BF, JR, JRC:** Test of infections with different virus variants, Test of patient's immunity against different virus variants
- **JRC:** Characterization of in-vitro diagnostic devices and sensing platforms with analytical techniques

**Access to SARS-CoV 2 ex vivo models**

WP11

- **INIA, ANSES-P, APHA, INRAE-IVPC, INRAE-VIM, WBVR, FLI, EDI-IVI, AU, MRI, IP, AMU, UL, INMI, RIVM, IZSVE, EMC BSL3, MUG BSL3, KUL BSL3:** SARS-CoV-2 infection studies in 2D and 3D ex vivo models

**Access to ex vivo models for other respiratory viruses including influenza viruses and other coronaviruses:**

- **INRAE-ISP, APHA, EDI-IVI, WBVR, AU, FLI, UEDIN, IP, INMI, RIVM, IZSVE, EMC BSL3, INSERM BSL4:** Human and animal influenza viruses infection studies in 2D and 3D ex vivo models.
- **INRAE-ISP, FLI, EDI-IVI, AU, IP, INMI, RIVM, IZSVE, EMC BSL3, MUG BSL3, KUL BSL3:** Non SARS CoV 2 coronaviruses infection studies in 2D and 3D ex vivo models

**Access to ex vivo models for RG4 pathogens:**

- **INSERM BSL4, FOHM BSL4, NNK BSL4, FLI, INMI:** Includes filoviruses (Ebola and Marburg virus), old and new world arenaviruses (Lassa, Machupo, Guanarito, Junin virus), Crimean Congo Haemorrhagic Fever virus, henipavirus (Hendra and Nipah virus) infection studies in 2D and 3D ex vivo models

**2D cellular models:**

- **INRAE-ISP, ISX, ANSES-P, AU, INIA, AMU, IP, UL, INMI, RIVM, IZSVE, MUG BSL3, EMC BSL3, INSERM BSL4, FOHM BSL4, NNK BSL4:** Immortalized cell lines for infection studies
- **AU, EDI-IVI, ANSES-P, UEDIN, FLI, INRAE-ISP, INRAE-IVPC, MUG BSL3, EMC BSL3, FOHM BSL4, NNK BSL4:** primary cells from various tissues



- **INIA:** Mesenchymal stem cells
- **INRAE-ISP, EDI-IVI, UEDIN, EMC BLS3, KUL BSL3, MUG BSL3:** Well differentiated and/or polarized cell systems including Air Liquid Interphase (ALI) cell cultures
- **UEDIN, IP, APHA, INRAE ISP, ISX:** Engineered cell lines and primary cells, e.g. cells modified by targeted and genome-scale gene silencing activation or mutagenesis (siRNAs or sgRNA, CRISPR/Cas9) and reporter cells for infection, for vector competence and for monitoring cellular responses and signalling pathways

**3D cellular models derived from different tissues or organs:**

- **EDI-IVI, INRAE-IVPC, INRAE-ISP, UEDIN, MUG BSL3, EMC BSL3:** Organoids
- **EMC BSL3:** 3D vessel-on-chip
- **WBVR, APHA, EDI-IVI, INRAE-ISP, EMC BSL3:** Precision-cut tissue slices cultures
- **INRAE-ISP, APHA, EDI-IVI, ANSES-P, UEDIN, AMU:** Organotypic cultures (including explants, enteroids)
- **APHA, ANSES-P, UEDIN:** in ovo infection models (embryonated SPF chicken eggs)
- **INRAE-VIM, CCMAR:** Zebrafish embryo and early larvae as screening models

WP12

**Provision of state-of-the art services for Immune Monitoring and Profiling**

- **LUMC, UNISI, OUH, ISS:** Systems level characterization of immune cells in human tissues (mass cytometry, FACSCanto, LSR IV, Symphony)
- **LUMC, IMM, IGTP:** Identification and isolation of tissue immunological subsets for deep profiling of immune cell subsets and on the analysis of WGS/WES data of patients
- **iBET:** Large/Medium-scale analysis of the immune proteins
- **IDIPAZ:** Epigenetics of immune cells to study genome-wide epigenetic changes including DNA methylation, histone modifications and non-coding RNAs expression
- **VHIR:** Access to Tissue explant models to evaluate the role of individual immune subsets in different context against infectious disease and to characterize viral isolates
- **OUH, EMC BSL3:** Access to Organoids, Spheroids for Immune surveillance
- **UNISI, FIMM:** Functional studies of pathogenicity of genetic variants at molecular and cellular level
- **HZI, EMC BSL3, MUG BSL3, NNK BSL3:** Virus neutralization testing for human and animal sample, including SARS CoV 2
- **INRAE-ISP, AU, UEDIN:** Mouse, swine, cattle and poultry specific Fluidigm qPCR arrays (96/96)

- **AU:** Immunoprofiling in swine and poultry (polychromatic flow cytometry assays, single cell immunomics, MHC haplotyping, Luminex)
- **UEDIN:** siRNA libraries: human, swine and poultry; sgRNA/CRISPR Cas9 knockout libraries: human, swine, cattle and poultry
- **AU, ANSES-P:** RNAseq transcriptomics, 16S NGS microbiome analysis, metabolomics (LC-MS) in livestock
- **EMC BSL3:** Detection and quantification of SARS-CoV-2-specific T cells at the single cell level; T-cell cloning and expansion, determining specificity; Detection and characterization of SARS-CoV-2-specific B-cells at the clonal level; Antibody profiling to evaluate the host immune response; Virus specific immune responses, quantification of cytokines/ chemokines, surface and intracellular detection of markers/cytokines (flow cytometry) in infected biological samples

#### **Provision of imaging services**

- **UniTO, UTU, Radboudumc:** Access to Mass Cytometry Imaging (MCI), PET-CT, PET-MRI, US modalities for studies of the immune system response against infectious diseases. Test imaging-based immunodiagnostics on precision mouse models for infectious diseases including PET, MRI, CT, US, optical imaging.

#### **Provision of Multi-site Immuno-analysis of Infectious Samples**

- **CIPHE:** metal tag detection by mass cytometry

<b>WP13</b>	<p>Provision of services that are specifically needed in the field of vaccine development (GLP and GMP production, access to adjuvants and formulation services)</p> <ul style="list-style-type: none"><li>- <b>iBET:</b><ul style="list-style-type: none"><li>○ Cross platform screening and optimization (pre-clinical) with access to vaccine platform technologies (including proteins, viral like particles, viral vectors) and expression systems (including mammalian and insect cells).</li><li>○ Pre-clinical GLP production services</li><li>○ Development and implementation of analytical methods for product characterization and process control and monitoring.</li></ul></li><li>- <b>SSI:</b><ul style="list-style-type: none"><li>○ Development and characterisation of vaccine formulations with liposomal adjuvants CAF01 and CAF09b</li><li>○ Provision of CAF01 and CAF09b adjuvants at GMP grade for use in clinical studies</li></ul></li><li>- <b>VFI:</b><ul style="list-style-type: none"><li>○ Formulation development and characterization</li><li>○ Upscaling of emulsion and liposome-based adjuvants from lab-scale to pilot-scale</li><li>○ Technological transfer of pilot scale process; manufacturing parameters of emulsion and liposome adjuvants and manufacturing of preclinical tox batch</li></ul></li></ul>
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- Provision of emulsion and liposome-based adjuvants at GMP grade for use in clinical studies

- Non-GLP in vivo studies of adjuvanted formulations in a variety of species

- **HZI:**

- Formulation and characterisation of vaccine candidates paired with mucosal or parenteral adjuvants

- **iBET/GeniBET:**

- GMP Manufacturing of Starting Materials
- GMP Manufacturing of Clinical Materials