**APPLICATION FORM**

**Please carefully read the Call Procedure on the** [**TRANSVAC website**](http://transvac.org/apply.html) **and ISIDORe website and the Guidelines at the end of this document before completing this Application Form.**

*TRANSVAC2 is now also offering services as part of ISIDORe, Integrated Services for Infectious Disease Outbreak Research, to support scientists and their research on epidemic- and pandemic-prone pathogens. The ISIDORe project assembles the largest and most diverse research and service-providing instrument to study infectious diseases in Europe, with expertise from structural biology to clinical trials.*

*ISIDORe brings together under the same umbrella 17 major European life sciences research infrastructures and infectious diseases networks, including to accelerate the generation of new knowledge and intervention tools to enhance Europe’s capacity for controlling (re)emerging and epidemic infectious diseases, starting with the COVID-19 pandemic.*

Instructions: This form should be completed and submitted as **a single PDF file** to transvacinfo@euvaccine.eu. If you would like to apply for more than one service at the same time (applicants are encouraged to apply for complementary services), please only submit one application form and tick the check boxes corresponding to the selected services. I*n order for your project to be accurately assessed by the evaluation panel, please contact service provider* ***before*** *the submission of this application.*

If you require any further information or experience any problems using this form, please contact transvacinfo@euvaccine.eu.

**ISIDORe details:**

|  |
| --- |
| Please indicate the ISIDORe ID number. When pre-registering in [ISIDORe website](https://isidore-project.eu/) you have been attributed an application ID number. If you do not have this number, follow the instructions at [ISIDORe website](https://isidore-project.eu/) and fill out the pre-application form visible at the bottom of each service catalogue section pages. You will receive an email with your ISIDORe ID number. |
| **ISIDORe ID number:**  |
|  |

**User-group details**

|  |
| --- |
| *Please indicate if this proposal is submitted by:* |
|  **An individual (one lead researcher)** |
|  |
| **A group (more than one lead researcher)** More than one LR may be designated on the application i.e. we can support collaborative / multi-LR applications as long as the majority of the Users work in a country other than the country where the TRANSVAC partner whose Service they wish to access is located. One LR should be identified as the main point of contact for TRANSVAC. |

|  |
| --- |
| Personal details of applicant (Principal Investigator only) |
| Family name       |
| First name       |
| Title (Please select)Mr  Mrs Dr Prof |
| Gender (Please select) Male Female Non-binary |
| Institution details |
| Name of Institution/Company      Department      Country      Legal status: UNI RES  SME PRV OTHUNI- University and other higher education organizationsRES- Public research organization (including international and public research organizations controlled by a public authority) SME- Small and medium enterprisePRV- Other Industrial and/or profit Private organizationOTH-Other organization not fitting in one of the above category |
| Job Title and Description       |
| Mailing Address      Street:      ZIP Code:      PO Box:      City:      Country:       |
| Contact Details (including international and area codes) Tel.:      Fax:      Mobile:      E-mail:       |
| **Project Acronym (max 20 characters)**      Please use a short but descriptive title and an ACRONYM (max. 20 characters) to identify your project. |
| **Project Title**      |
|  |
| **Previous application(s)** |
| Please indicate if this application previously been submitted to TRANSVAC. Or if the applicant has already benefited from other service(s) offered by TRANSVAC2. If yes, please indicate the call identifier, project title and services provided.yes; details: no |
| **Vaccine:**  Prophylactic  Therapeutic  Human Veterinary Other |
| * If Other, please specify:
 |
|  |
| **Target Disease:**       |
| * Disease (e.g. malaria, allergies, cancer, etc.)
 |
| **Other Funding**Please indicate if your institution has other funding (EC or other) for this applicationyes; details: no |
| **Contact with service provider(s)**I, hereby confirm that I have contacted a service provider and confirmed the feasibility of my study plan. yes no (*in order for your project to be accurately assessed by the evaluation panel, please contact service provider before the submission of this application. If you haven’t found accurate info on access provider contact details kindly contact* *transvacinfo@euvaccine.eu* *as early as possible in the application process*) |
| **Personal data protection**By submitting this application, I agree that my personal data included in this document will be provided to the evaluation panel for the evaluation purposes. |
|  With submission of the Application Form I declare that I have read and understood the Call Procedure and accept its terms (<https://www.transvac.org/services-application>; <https://www.transvac.org/services-application-submission>) |
|  With submission of the Application Form I agree to participate in a follow-up questionnaire that will be used for the evaluation of the socio-economic impact of the TRANSVAC2 project regardless of the call outcome |

|  |
| --- |
| Requested Access to Service infrastructure (Please tick)For scientific questions regarding a specific Service (e.g. whether a requested service matches with the actual service offered), please contact the corresponding lead scientist directly before submitting the application.  |
| **Platform Technology****VACCINE PLATFORM TECHNOLOGIES: SCREENING, EXPRESSION AND OPTIMISATION*** [**TNA 1 Cross-platform screening and optimisation services**](https://www.transvac.org/tna1-antigen-screening-optimisation)

 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). Access provider: iBET, PTFor services provided by Access provider: VetBioNet, kindly contact sascha.trapp@inrae.fr. Custom construction of nanoparticles based on respiratory syncytial virus nucleoprotein as booster for antigen presentation. Access provider: VetBioNet\_INRAE-VIM, FR Custom construction of recombinant viral proteins (e.g., SARS-Cov-2 Spike proteins) in HEK freestyle cells. Access provider: VetBioNet\_INRAE-VIM, FRCustomized construction of recombinant vaccine. Two available backbones (non-deleted or E1-deleted genomes) derived from the Manhattan vaccine strain of the canine adenovirus type 2 (CAV-2). Access provider: VetBioNet\_INRAE-VIRO, FRDesign and development of nanoparticle-based mucosal vaccine systems for SARS-CoV-2 or other respiratory pathogens. Access provider: VetBioNet\_INRAE-ISP, FRExpression (E. coli, baculovirus) and purification of SARS-CoV structural proteins for vaccination and in-vitro diagnostics. Access provider: VetBioNet\_INRAE-ISP, FR**VACCINE ADJUVANTS & FORMULATION*** [**TNA 2 Adjuvants and delivery systems**](https://www.transvac.org/tna2-vaccine-adjuvants-delivery)

Development and characterisation of vaccine formulations with liposomal  adjuvants CAF01 and CAF09b Access provider: SSI, DK  Provision of CAF01 and CAF09b adjuvants at GMP grade for use in clinical studies. Access provider: SSI, DK  Formulation development and characterisation. Access Provider: VFI, CHUpscaling of emulsion and liposome-based adjuvants from lab-scale to pilot-scale. Access Provider: VFI, CHTechnological transfer of pilot scale process; manufacturing parameters of emulsion and liposome adjuvants and manufacturing of preclinical tox batch. Access Provider: VFI, CHProvision of emulsion and liposome-based adjuvants at GMP grade for use in clinical studies. Access Provider: VFI, CHNon-GLP in vivo studies of adjuvanted formulations in a variety of species. Access Provider: VFI, CHFormulation and characterisation of vaccine candidates paired with mucosal or parenteral adjuvants. Access provider: HZI, DE**VACCINE IMMUNE MONITORING & PROFILING*** **TNA 3 Analytical services**

Systems level characterization of immune cells in human tissues (mass cytometry, FACSCanto, LSR IV, Symphony). Access providers: LUMC, UNISI, OUH, ISSIdentification and isolation of tissue immunological subsets for deep profiling of immune cell subsets and on the analysis of WGS/WES data of patients. Access providers: LUMC, IMM, IGTPLarge/Medium-scale analysis of the immune proteins. Access provider: iBET, PTEpigenetics of immune cells to study genome-wide epigenetic changes including DNA methylation, histone modifications and non-coding RNAs expression. Access provider: IDIPAZ, Access to Tissue explant models to evaluate the role of individual immune subsets in different context against infectious disease and to characterize viral isolates. Access provider: VHIRAccess to Organoids, Spheroids for Immune surveillance. Access provider: OUH, EMC BSL3Functional studies of pathogenicity of genetic variants at molecular and cellular level. Access provider: UNISI, FIMMVirus neutralization testing for human and animal sample, including SARS CoV 2. Access provider: HZI, EMC BSL3, MUG BSL3, NNK BSL3Mice, swine, cattle and poultry specific Fluidigm qPCR arrays (96/96). Access provider: INRAE-ISP, AU, UEDINImmunoprofiling in swine and poultry (polychromatic flow cytometry assays, single cell immunomics, MHC haplotyping, Luminex). Access provider: AU siRNA libraries: human, swine and poultry; sgRNA/CRISPR Cas9 knockout libraries: human, swine, cattle and poultry. Access provider: UEDINRNAseq transcriptomics, 16S NGS microbiome analysis, metabolomics (LC-MS) in livestock. Access provider: AU, ANSES-PDetection and quantification of SARS-CoV-2-specific T cells at the single cell level. Access provider: EMC BSL3T-cell cloning and expansion, determining specificity. Access provider: EMC BSL3Detection and characterization of SARS-CoV-2-specific B-cells at the clonal level. Access provider: EMC BSL3Antibody profiling to evaluate the host immune response. Access provider: EMC BSL3Virus specific immune responses, quantification of cytokines/ chemokines, surface and intracellular detection of markers/cytokines (flow cytometry) in infected biological samples. Access provider: EMC BSL3Multi-site Mass Cytometric Immuno-analysis. Access provider: INSERM-CIPHE**imaging for immune monitoring for vaccines**Development and validation of imaging probes targeting specific molecular inflammation markers or subpopulations of immune cells in surrogate infection models in vivo. Access provider: UniTO, UTU, RadboudumcBiomedical imaging technologies (PET, MRI, CT, US, optical imaging, multimodal) for monitoring the immune system. Access provider: UniTO, UTU, Radboudumc**Vaccine structural and chemical characterization*** **TNA 6 Structural Biology**

Structural characterisation of vaccine antigens in isolation or in combination with relevant ligands using X-ray methods. Access providers: DLS, CERM, EMBL HE, EMBL HH Structural characterisation of vaccine antigens in isolation or in combination with relevant ligands using Bio-SAXS, solution. Access providers: DLS, CERM, EMBL HE, EMBL Structural characterisation of vaccine antigens in isolation or in combination with relevant ligands solid state NMR technologies. Access providers: DLS, CERM, EMBL HE, EMBL Structural characterisation of vaccine antigens in isolation or in combination with relevant ligands using cryo-EM (single particle analysis). Access providers: DLS, CERM, EMBL HE, EMBLStructural characterisation of vaccine antigens in isolation or in combination with relevant ligands using cryo-ET (in combination with EuBi for correlative EM/light microscopy). Access providers: DLS, CERM, EMBL HE, EMBL Physico-chemical and in-vitro characterization of adjuvant and nanotechnology-based vaccine platforms. Access providers: JRC, IT Identification and measurement of key quality attributes of nanovaccines. Access providers: JRC, IT**VACCINE PROCESS DEVELOPMENT & PRODUCTION*** **TNA 5 GMP production Services**

 Pre-clinical GLP production services. Access provider: iBET, PTDevelopment and implementation of analytical methods for product characterization and process control and monitoring. Access provider: iBET, PT GMP Manufacturing of Starting Materials. Access provider: iBET/GenIBET, PT GMP Manufacturing of Clinical Materials. Access provider: iBET/GenIBET, PT**MODELS FOR VACCINE EFFICACY AND IMMUNOGENICITY STUDIES****Platform Animal Models**For services under the animal model platform, kindly contact sascha.trapp@inrae.fr. Vaccine efficacy studies in mice (Wild-type, K18 promoter/hACE2) Vaccine efficacy studies in hamsters Vaccine efficacy studies in ferrets Vaccine efficacy studies in non-human primates Vaccine efficacy studies in hACE2 pigs Vaccine immunogenicity studies in mice Vaccine immunogenicity studies in hamsters Vaccine immunogenicity studies in ferrets Vaccine immunogenicity studies in non-human primates Vaccine immunogenicity studies in pigs Studies of adjuvanted formulations in a variety of species**Platform Clinical Trial Support****Free services**Human clinical trial support – ECRIN, FR**Regulatory Support****Free services**Scientific advice – EATRIS, NLPreparation of Investigational New Drug (IND) application – EATRIS, NL\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**For “paid services” please contact a service provider for the information regarding cost coverage opportunities available.** |
|  |

|  |
| --- |
| List of the requested services  |
| Please list the requested “Access to Service infrastructure” (Please note that the Applicant/User group leader and the majority of the Users in the group must work in a different country than the TRANSVAC partner whose Service they wish to access). For scientific questions regarding a specific Service, please contact the corresponding lead scientist directly as indicated in the call text.  |
| 1.
 |
| Description of laboratory  |
| Please describe your laboratory and its associated facilities in relation to this application. |
|       |

|  |
| --- |
| Project description |
| **Please note that depending on the stage of development of your vaccine candidate and on the service requested to access, not all sections will need to be filled.**If you wish to add graphs or diagrams to your application, please include them directly into the text where reference is made. |
| **Abstract (max.250 words)**  |
| Please give a short description of your planned work, your main objectives, the expected outcomes and the expected impact achieved by accessing this TRANSVAC service infrastructure. |
|       |
| Gap analysis  |
| Please perform a gap analysis. Clearly state why the service is required and describe why the work cannot be performed in the applicant’s laboratory. |
| 1.
 |

|  |
| --- |
| **Objectives and goals of the project** (max. 500 words) |
| Please describe the objectives and goals of your project.  |
|       |
| **Scientific rationale** **Please read the guidelines at the end of the form for further details on the information to be provided.** |
| Biological rationale – Antigen. (max. 750 words)Please provide here available relevant information on the antigen under investigation (e.g. accessibility, protein function, *in-vivo* protection, *in-vitro* inhibition, sequence diversity, genetic analysis, sero-epidemiological data, antigenicity/immunogenicity, antigen size and solubility, pre-existing clinical data). |
|        |
| Biological rationale – Antigen. (continued) |
|  |
| Vaccine candidate rationale/validation (max. 750 words)Please provide here available relevant information on the vaccine candidate under investigation (e.g. single antigen/multi-antigen, prime-boost strategies, delivery systems, adjuvant, vectored system, synthetic antigen, antigen characterisation, antigen immunogenicity, evaluation of vaccine efficacy under conditions of natural exposure or artificial challenge).If applicable, please include evidence for compliance with GLP standards. |
|       |
| Vaccine candidate rationale/validation (continued) |
|  |
| **Methodology and associated work plan** |
| In order to select the most promising vaccine candidates you are asked in this section to provide an overview of the work plan associated with the antigen under consideration. Please indicate whether samples or materials required for the conduction of the service are readily available.  |
| Research strategy (max. 1000 words - this limit does not apply if you are requesting three or more services using a single application form): Please present here the detailed research strategy and experimental design of your project including:* Nature and form of the experiments to be performed
* Specification on the units of access required (e.g. animals, vials, formulations) in both number and nature (doses, concentration, sex of the animals etc.).
* Timelines of the experiments.
* **Clear Go/no-go criteria** for moving to the next step of your vaccine development
* If you are requesting TNA service(s) to conduct animal studies:
* It is highly recommended to contact the service provider before submission of the application to discuss the study design
* Clearly justify the necessity to test the vaccine candidate *in-vivo* and the choice of the animal species. This information is essential to obtain ethical approval from national authorities on animal experimentation and/or animal welfare bodies
* Provide statistical justifications of the number of animals (to be discussed with the service provider in advance)
* If studies in large animals are requested, evidence of previous studies in small animals will have to be separately provided (to support the request for ethical approval).
* If you are requesting TNA service(s) to conduct metabolomics studies:
* It is highly recommended to contact the service provider before submission of the application to discuss the study design and choice of metabolomics platform
* The needed sample handling and sample requirements are dependent on the biological matrix (*in vitro* (cell lysate/medium) and *in vivo* (serum/plasma/tissues/urine)) and the chosen metabolomics platforms.

If available, please include evidence for compliance with GLP standards.      |
| Development strategy (max. 1000 words): Please provide a summary of the process development strategy including toxicology studies, scale up strategy and transfer plan, if applicable.Define the key drivers and assumptions (*e.g.* product substance (active ingredient) specification and final product specifications, yield/cost, chosen scale of development, chosen scale of purity, ability to scale up, robustness, number of clinical batches, and number of doses (total and per batch)).Toxicology strategy (*e.g.* vaccine reactogenicity or toxicity, adjuvant tested alone and/or in multiple species for novel adjuvants).      |
| Analytical development (max. 750 words): Please provide a summary of the analytical development strategy. This should include key drivers and assumptions or rate-limiting factors: assays, equipment costs, anticipated complexity of methods (potency test, quality control tests, functional tests etc.) test development, stability testing, validation, optimisation strategy).      |
| Clinical development (max. 750 words): If applicable, please list the executive summary of the clinical development plan.      |
| Intellectual property: Please provide here in detail available information on intellectual property of the antigen, delivery system, etc.       |
| **Expected outcomes and impact of the project (max. 750 words)** |
| Describe the expected outcomes and the impact of your project in relation to the topic in question (scientific, economic, social, etc.). Mention the steps that will be needed to bring about these impacts. Mention any assumptions and external factors that may determine whether the impacts will be achieved.Clearly state why the data generated through the requested services is needed and indicate the next development steps (with Go/No-go criteria) based on generated data. |
|       |

|  |
| --- |
| Publications  |
| Please list here your publications relevant to this application (maximum 5) with author/s, title, full reference and date. |
| 1.
 |
| 1.
 |
| 1.
 |
| 1.
 |

|  |
| --- |
| **Ethical considerations – obligatory to all applicants** |
| Please complete the ethics table and provide any relevant ethical, scientific, and regulatory approvals (particularly for the use of clinical samples). |
| 1.
 |
| **Reasons for animal use - obligatory for applicants requesting animal studies**Alternatives to using animals must be investigated and used wherever possible\*. The TRANSVAC SEAC ad USP must be informed of alternatives that exist and why these cannot be used.\* [*https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex%3A32010L0063*](https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex%3A32010L0063) |
| **Study design/Number of animals - obligatory for applicants requesting animal studies**It should clearly be explained why the number of animals has been chosen. Too few animals (resulting in statistically insignificant data) may be as much of a problem as too many animals (in terms of wastage of the use of animals). |

|  |  |
| --- | --- |
| **Humans** |  |
| 1. Does your research involve human participants?
 | Yes No |
| 1. Are they volunteers for social or human sciences research?
 | Yes No |
| 1. Are they persons unable to give informed consent?
 | Yes No |
| 1. Are they vulnerable individuals or groups?
 | Yes No |
| 1. Are they children/ minors?
 | Yes No |
| 1. Are they patients?
 | Yes No |
| 1. Are they healthy volunteers for medical studies?
 | Yes No |
| 1. Does your research involve physical interventions on the study participants?
 | Yes No |
| 1. Does it involve invasive techniques?
 | Yes No |
| 1. Does it involve collection of biological samples?
 | Yes No |
| **Human cells/tissues** |  |
| 1. Does your research involve human cells or tissues?
 | Yes No |
| 1. Are they available commercially?
 | Yes No |
| 1. Are they obtained within this project?
 | Yes No |
| 1. Are they obtained from another project, laboratory or institution?
 | Yes No |
| 1. Are they obtained from a biobank?
 | Yes No |
| **Personal data** |  |
| 1. Does your research involve personal data collection and/or processing?
 | Yes No |
| 1. Does it involve the collection and/or processing of sensitive personal data

(e.g.: health, sexual lifestyle, ethnicity, political opinion, religious or philosophicalconviction)? | Yes No |
| 1. Does it involve processing of genetic information?
 | Yes No |
| 1. Does it involve tracking or observation of participants?
 | Yes No |
| 1. Does your research involve further processing of previously collected personal data (secondary use)?
 | Yes No |
| **Non-European Union (EU) countries**  |  |
| 1. In which non-EU countries will the research take place?
 | Yes No |
| 1. Do the research related activities undertaken in these countries raise potential ethics issues?
 | Yes No |
| 1. Do you plan to use local resources (e.g. animal and/or human tissue samples, genetic material, live animals, human remains, materials of historical value, endangered fauna or flora samples, etc.)?
 | Yes No |
| 1. Do you plan to import any material – including personal data – from non-EU countries into the EU?
 | Yes No |
| 1. Do you plan to export any material – including personal data – from the EU into non-EU countries?
 | Yes No |
| 1. If your research involves low and/or middle-income countries, are benefits sharing actions planned?
 | Yes No |
| 1. Could the situation in the country put the individuals taking part in the research at risk?
 | Yes No |
| **Environment & Health and Safety** |  |
| 1. Does your research involve the use of elements that may cause harm to the environment, to animals or plants?
 | Yes No |
| 1. Does your research deal with endangered fauna and/or flora and/or protected areas?
 | Yes No |
| 1. Does your research involve the use of elements that may cause harm to humans, including research staff?
 | Yes No |
| **Dual use, civil applications, misuse** | Yes No |
| 1. Does your research involve dual-use items in the sense of Regulations 428/2009, or other items for which an authorisation is required?
 | Yes No |
| 1. Could your research raise concerns regarding the exclusive focus on civil applications?
 | Yes No |
| 1. Does your research have the potential for misuse of research results?
 | Yes No |
| **Human embryos, foetuses** |  |
| 1. Does your research involve Human Embryonic Stem Cells (hESCs)?
 | Yes No |
| 1. Will they be directly derived from embryos within this project?
 | Yes No |
| 1. Does your research involve the use of human embryos?
 | Yes No |
| 1. Are they previously established cells lines?
 | Yes No |
| 1. Does your research involve the use of human foetal tissues/cells?
 | Yes No |
| 1. Does your research involve the use of human embryos?
 | Yes No |
| 1. Can you confirm that your research will not destroy those embryos?
 | Yes No |
| 1. Does your research involve the use of human foetal tissues / cells?
 | Yes No |
| **Security** |  |
| 1. Will your project involve activities or results raising security issues?
 | Yes No |
| 1. Will your project involve 'EU-classified information' as background or results
 | Yes No |
| Are there any other ethics issues that should be taken into consideration? Please specify in the ethics self-assessment attachment | Yes No |

|  |
| --- |
| **Training** |
| In certain circumstances TRANSVAC can also offer training to a user accessing an infrastructure.Please indicate if you or your group members wish to receive training in the concerned infrastructure. In case you apply for more than once service with this application form, please indicate the infrastructures for which you would like to receive training. |
|  |

|  |
| --- |
| **Other TRANSVAC2 Support** |
| Did you know TRANSVAC2 also grants access to a [database](https://www.transvac.org/databases-biobank-sample-sharing) of the types of sample collections (*i.e.,* animal study derived products (sera, tissues etc.), mainly involving a biohazard level 3 or 4 for mice, NHP and farm animals)? Yes NoIf not, would you consider using it? Please refer why: |
|  |
| Did you know TRANSVAC2 also provides free [training modules](https://www.transvac.org/training) in applied and fundamental vaccinology?Yes No |

# Guidelines for completing the TRANSVAC Transnational Access Project description

# Project description

For the purpose of this application, *project* refers to the tasks, experiments or investigation which you are planning to carry out at a TRANSVAC infrastructure.

The project description should clearly summarise the aim of the project, the scientific background, and the overall methodological approaches (including statistics where appropriate) proposed to solve the main scientific problems. Please also include details about possible local participation (if any) and a summary of expected results. More information about evaluation and selection criteria can be found in the call text.

For a competitive evaluation it is important that the description of the objectives and the methodological approach can be easily evaluated. These should be clearly structured.

**Scientific rationale:**

* 1. **Biological rationale – Antigen**
		1. Accessibility

e.g. antigen location/abundance

Protein targets of antibody need to be accessible, for example by virtue of surface location. This can be in part predicted by bioinformatics and confirmed by antibody reactivity.

* + 1. Protein function

An immune response that disrupts the specific function of a protein of a pathogen could be very important in preventing its replication or pathology.

* + 1. In vivo protection

e.g. correlates of protection. Immunisation and challenge studies in primates, rodents or other animal models. Passive immunisation with mono-specific Ab may implicate antigen

* + 1. *In vitro* inhibition

e.g. growth inhibition assay, antigen specific assays, processing assays.

* + 1. Diversity

e.g. sequence and antigen diversity (minimal sequence variation)

Sequence diversity may be extensive, e.g. due to point mutations or variation in repetitive sequences. Some proteins occur in essentially two forms. Some antigens are highly conserved. The functional significance of diversity and its importance in antigenic diversity is presently unclear.

* + 1. Genetic analysis

The product of an essential gene is probably a good target. However non-essential genes (e.g. members of a family) may also be important.

Transfection e.g. inability to knock out corresponding gene due to lethality.

* + 1. Sero-epidemiological data

Studies carried out in human populations to study the immune response to the particular antigen under conditions of natural infection e.g. association between specific antibodies in an exposed donor population and reduced risk of infection or disease.

* + 1. Antigenicity/Immunogenicity

The response to an antigen that is ‘seen’ during an infection may be boosted by further natural infection e.g. reactivity with antibodies or cells of naturally exposed or artificially challenged donors.

* + 1. Antigen size and solubility

Large and multidomain membrane spanning proteins are difficult to express well in a heterologous host e.g. small soluble proteins are easier to replicate as recombinant proteins.

* + 1. Pre-existing clinical data

Data on immunogenicity and vaccine efficacy when possible are very useful in developing better products e.g. some proteins have already been investigated in human subjects.

* 1. **Vaccine candidate Rationale/Validation**
1. Single antigen/multi-antigen approaches

e.g. a single subunit protein or combination of antigens.

1. Prime-boost strategies

e.g. combination of different delivery processes.

1. Delivery systems

e.g. antigen with adjuvant, vectored system, attenuated pathogen.

Recombinant proteins can be delivered via virus-like particles wherever possible to enhance immunogenicity prior to addition of adjuvant.

1. Adjuvant

e.g. data from rodent models, vaccine tolerance, strong antigen-specific T- and B-cell responses in majority of volunteers.

1. Vectored system

e.g. DNA, virus, bacterium (e.g. biological rational, e.g. strong antigen-specific T- and B-cell responses in majority of volunteers, data from rodent models, presence of pre-existing antibodies, vaccine is well tolerated replication competence/attenuation antigen capacity, single/multiple genes, antigen location in host cells, vector yields and stability).

Be aware of state of development of vectors for other diseases to avoid developing same vector and to learn from results with other disease targets. Please detail your knowledge about other vaccines using the same vectors (in development or already marketed).

1. Synthetic antigen
* Either as peptide/recombinant antigen or in vectored system
* Codon optimisation and exact sequence including any modifications (including non-natural amino acids in peptide), exogenous sequences (e.g. tags) to be expressed
* Choice of expression vector and host (e.g. bacterium, yeast, other eukaryote)
* Antigen expression level
* Growth and genetic stability
* Fermentation and downstream purification (e.g. precipitation, chromatography)
* Antigen purity and stability
* Monomer/aggregation state
* Fusion partners with virus-like particles facilitate purification because of large size - readily separated from contaminating proteins.
1. Antigen characterisation
* Reducing/non-reducing conditions (e.g. purity by SDS-page/HPLC (reverse phase, ion exchange, size exclusion))
* Contaminants (DNA, protein, metals, endotoxin)
* Identity (N-terminal sequence analysis, amino acid analysis, Ellman’s test for cystines)
* Conformation: secondary/tertiary structure/posttranslational modifications (biophysical characterisation: circular dichroism, mass spectrometry, NMR Spectroscopy etc.)
* Antigenicity (e.g. ELISA, reactivity with mAbs)
* Antigen-specific criteria, e.g. red cell binding.
1. Antigen immunogenicity
* Immunogenicity of antigen using most rational immune assay should be included in antigen characterisation to monitor changes in antigen immunogenicity during process development
* Immunogenicity in animal models (mice and rabbits) e.g. production of specific antibodies (Western blot, ELISA, immunoprecipitation, immunofluorescence assay etc.)
* Induction of T-cells that recognise specific antigens/produce cytokines, ELISpot
* Functional activity
* Antigen-specific assays e.g. inhibition of processing, inhibition of binding
* Responses relative to standards.
1. Evaluation of vaccine efficacy under conditions of natural exposure or artificial challenge
* Separate into two categories - there is a big difference between efficacy (preliminary, qualitative) in challenge models vs natural exposure
* Preclinical data for regulatory filing
* Ethical, scientific and regulatory approval for clinical trials
* Show tolerability and safety in first in-human clinical trial, immunogenicity and protection from artificial challenge
* Show safety and efficacy in target population

**TNAs offering animal studies**

Please note that if a proposal is selected by the TRANSVAC2 consortium, the animal experiments will still require approval by the respective local ethics committee (from the country where the experiments are to be conducted). If this approval is not granted, the TRANSVAC2 consortium cannot be deemed responsible, and the applicant cannot make any claim for compensation.