**APPLICATION FORM**

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

Instructions: This form should be completed and submitted as a single PDF file to [transvacinfo@euvaccine.eu](mailto: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](mailto:transvacinfo@euvaccine.eu).

**User-group details**

|  |
| --- |
| *Please indicate if this proposal is submitted by:* |
| **An individual** |
|  |
| **A group** |

|  |
| --- |
| Personal details of applicant (Principal Investigator only) |
| Family name |
| First name |
| Title (Please select)Mr Ms  Mrs Dr Prof |
| Gender (Please select) Male Female |
| Institution details |
| Name of Institution/Company  Department  Country  Legal status: UNI RES  SME PRV OTH  UNI- university and other higher education organizations  RES- public research organization (including international and public research organizations controlled by a public authority)  SME- Small and medium enterprise  PRV- other Industrial and/or profit Private organization  OTH-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) |
| * Has this application previously been submitted to TRANSVAC? If yes, please indicate the call identifier. * Has the applicant already benefited from other service(s) offered by TRANSVAC2? |
|  |
| **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 application  yes; 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*) |
| **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>) |

|  |
| --- |
| 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**  **Free services**   * **TNA 1 Cross-platform screening and optimisation services**   Single protein expression in *Nicotiana* – IME, DE  Mammalian and insect cells (transient and constitutive) expression   platforms – iBET, PT  Cross-platform expression screening (bacterial, plant, eukaryotic) – IME, DE; iBET, PT  Construction of commensal bacterial strains displaying selected antigens –   UNISI, IT  Expression of vaccine antigens in Adenovirus and MVA vectors – UOXF, UK   * **TNA 2 Adjuvants and delivery systems**   Adjuvant and formulation services – VFI, UK  Development and characterisation of vaccine formulations with liposomal   adjuvants CAF01 and CAF09b – SSI, DK  Formulation and characterisation of candidate antigens paired with   mucosal adjuvants – HZI, DE  Formulation of antigens in LPS adjuvants – ITV, NL   * **TNA 3 Analytical services**   Single compound analysis (structural integrity, purity, binding) – IME, DE  SPR-analytics (kinetic binding parameters, CFCA) – IME, DE  Flow-cytometry for antigen-specific polyfunctional T-cell response – CEA, F  (Semi) quantitative proteome analysis based on mass spectrometry – ITV, NL  Cell-based reporter assays for characterisation of innate immune receptor induced signalling cascades – BPRC, NL   * **TNA 4 Pre-clinical GLP production services**   Preclinical GLP production services in yeast (*Pichia pastoris*) and/or plant   (*Nicotiana*) expression platforms – IME, DE  Preclinical GLP production services in mammalian and/or insect cells (transient and constitutive) expression platforms – iBET, PT  Production of pre-GMP grade MVA vector(s) expressing antigen(s) of interest  – UOXF, UK   * **TNA 6 Structural Biology**   X-ray methods – INSTRUCT (Diamond, UK)  NMR Spectroscopy – INSTRUCT (CERM/CIRMMP, IT)  cryo-Electron Microscopy – INSTRUCT (OPIC/eBIC, UK)  Nanobody production – INSTRUCT (VIB, BE)  X-Chem fragment screening – INSTRUCT (Diamond, UK)  **Paid services**   * **TNA 5 GMP production Services**   GMP production of recombinant vaccine candidates for clinical trials   phase I/II – SSI, DK  GMP production services – GEN, PT  **Platform Immunocorrelates and Systems Biology**  **Free services**  Next-generation sequencing and data analysis – Bioaster, FR  Mass cytometry and multidimensional data analysis – CEA, FR  Metabolomics profile – LU, NL  Mathematical modelling – UNISI, IT  Mathematical modelling – ETHZ, CH *(service not available in current call)*  Multiplex cytokine/chemokines analysis – UNISI, IT  Next-generation sequencing – UNISI, IT  Metabolomics Imaging by Mass Spectrometry, for in-situ adjuvant/antigen   tracking and inflammation monitoring – Bioaster, FR  Computational analysis of multiparametric flow cytometry data – UNISI, IT  Longitudinal statistical analysis – Bioaster, FR  **Platform Animal Models**  **Free services**  Immunogenicity and efficacy studies in mice – HZI, DE  Immunogenicity and efficacy studies in mice – SSI, DK  *In-vivo* assessment of kinetics and biodistribution profile of vaccine(s) by   optical and/or simultaneous evaluation of induced host immune response   *in vivo* (using specific probes) and *in vitro* (cytometry analysis) – Bioaster, FR  Immunogenicity and efficacy studies in mice, chickens, pigs, ruminants and   ferrets – IRTA, SP (please check availability with provider)  Antigen tracking, immunogenicity, challenge and efficacy studies in pigs,   ruminants and other farm animals – INRA, FR (please check availability with   provider)  Immunogenicity and challenge studies in ferrets – PHE, UK (please check   availability with provider)  Immunogenicity studies in non-human primates – BPRC, NL  *In-vivo* imaging in NHPs at different levels of containment – CEA, FR (please check availability with provider)  **Paid services**  Preclinical NHP model of Bordetella pertussis infection – CEA, FR  Preclinical NHP model of influenza or RSV infection – CEA, FR  **Platform Clinical Trial Support**  **Free services**  Human clinical trial support – ECRIN, FR  **Regulatory Support**  **Free services**  Scientific advice – EATRIS, NL/EVI, DE  Preparation of Investigational New Drug (IND) application – EATRIS, NL/EVI,   DE  \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_  **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. |
|  |
| Description of laboratory |
| Please describe your laboratory and its associated facilities in relation to this application. |
|  |
| Publications |
| Please list here your publications relevant to this application (maximum 5) with author/s, title, full reference and date. |
|  |
|  |
|  |
|  |

|  |
| --- |
| 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. |
|  |
| **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. |
| 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. |
| **Objectives and goals of the project** (max. 500 words) |
| Please describe the objectives and goals of your project. |
|  |
| **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. |
|  |
| **Ethical considerations - obligatory** |
| **Please complete the ethics table and provide any relevant ethical, scientific and regulatory approvals (particularly for the use of clinical samples).** |
|  |

|  |  |
| --- | --- |
| **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 philosophical  conviction)? | 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. |
|  |

# 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).

Since same vector cannot be used for two diseases, need to 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.