This procurement receives funding under the European Union's Horizon 2020 research and innovation programme under the grant agreement No 874719. The EU is however not participating as a contracting authority in this procurement

PCP REQUEST FOR TENDERS

Instand-NGS4P— Integrated and Standardized NGS Workflows for Personalised Therapy

Project number: 874719

Medizinische Universität of Graz
(MUG – Coordinator and lead procurer – AT)

University of Florence
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(CLB – FR, coordinating ERN on adult rare cancers)

Summary

This PCP Request for Tenders document should be read in conjunction with other documents associated with this Pre-Commercial Procurement (PCP). All the documents for this PCP are available on the Instand-NGS4P website (https://www.instandngs4p.eu/). With this document, interested legal entities are invited to submit a tender for the provision of research and development (R&D) services and the further award of phase contracts in this PCP project, with the aim to develop new, beyond state-of-the-art solutions for integrated and standardized workflows for NGS diagnostics of common and rare cancers in adult and children as outlined in the chapter 2 of this RFT document that also contains details on background, challenges and expected outcome of the project.

The Medizinische Universität Graz, Graz, Austria (MUG) will be the Lead Procurer acting in the name of and on behalf of a consortium of 7 procuring partners who are Università degli Studi di Firenze (UNIFI), Florence, Italy; Erasmus Universitair Medisch Centrum Rotterdam (EMC), Rotterdam, Netherlands; St. Anna Kinderkrebsforschung GmbH (CCRI GmbH), Vienna, Austria; Università Degli Studi di Milano-Bicocca (UNIMIB), Milan, Italy; University Clinic of Schleswig-Holstein (UKSH), Kiel, Germany Centre Leon Berard (CLB), Lyon, France.

Tender Documents:

Request for Tender

Framework Agreement

Specific Contract Phase 1

Tender Submission Forms (Annex A General Submission Form, Annex B Technical Submission Form, Annex C Financial Submission Form, Annex D Form for Exclusion Criteria, Annex E Form for Selection Criteria, Annex F Form for On/Off Criteria)

TERMS/ACRONYMS DEFINITIONS

Background: Any intellectual property rights, data, software, know-how or information, whatever its form or nature (tangible or intangible), including any attached rights such as intellectual property rights ('background IPRs') that is held by any Buyers Group member or the Supplier prior to the award of the Framework Agreement, which is needed to perform the R&D Services or exploit the Results of the PCP.

Buyers Group: The group of procurers that contribute to the procurement budget.

Contractor: A natural or legal person, who acts on its own behalf or in the name and on behalf of the other members of group of tenderers, with whom the "Framework Agreement" has been concluded.

Fair and reasonable market conditions: Appropriate conditions, including financial terms or royalty-free conditions, taking into account the specific circumstances of the request for access (for example, the actual or potential value of the Results or Pre-existing rights to which access is requested and/or the scope, duration or other characteristics of the exploitation envisaged).

Feasibility: Expertise and capacities to execute the R&D Services by the Tenderer

Foreground Intellectual Property: Any intellectual property created by either party as a result of their involvement in the Instand-NGS4P Framework Agreement.

Framework Agreement: The contract between the Lead Procurer and the Supplier concerning the delivery of the R&D services under this PCP, covering Phases 1 through 3.

Generated in the PCP Project: Generated in activities described in the PCP Framework Agreement or Specific Contracts.

Innovation: Innovative upgrade towards complete workflows and standardization rather than full *de novo* developments (depending on the Lots). Clear progress beyond current products should be achieved. The proposed solution can build on existing technologies or applications, but progress *beyond* the current State of the Art should be achieved.

Integration into complete workflow: Interoperability and compatibility of solutions developed as a result of the R&D Services for different Lots and within individual Lots.

Intellectual Property: patents, inventions (whether or not patentable or capable of registration), trademarks, service marks, copyrights, topography rights, software, design rights and Database rights, (whether or not any of them are registered or registerable and including applications for registration, renewal or extension of any of them), trade secrets and rights of confidence, trade or business names and domain names and all rights or forms of protection of a similar nature which have an equivalent effect to any of them which may now or in the future exist anywhere in the world.

Lead Procurer: MUG in the role of representative of the other Procurers pursuant to this Agreement.

Performance: Analytical performance including metrological traceability

Request for Tenders: The Instand-NGS4P invitation to tender on the basis of which the Tenders for the award of the Framework Agreement and the Specific Contract for Phase 1 are submitted, and the subsequently issued invitations to tender for the Phase 2 and Phase 3.

R&D Service: Research and development services including tasks, deliverables and milestones performed by the Contractor and as set out in the Technical Offer and the Request for Tender document for the specific phases.

Results (i.e. foreground): Any tangible or intangible output, such as data, knowledge or information, that is generated in the PCP Project, whatever its form or nature, whether or not it can be protected, as well as any rights attached to it, including Intellectual Property Rights.

Solution Provider: A company or institution that performs research and develops solutions needed to address the challenges related to integrated and standardized NGS workflows.

Specific Contract: The Contract for each phase of the R&D services under the Framework Agreement to be concluded between the Lead Procurer and the Supplier in addition to the Framework Agreement.

Standardization: Compliance to applicable international standards (see Instand-NGS4P website for list of relevant standards).

Subcontractor. A subcontractor is a third party contributing to the provision of the services referred to in the procurement contract.

Tender: The formal and commercial bid/offer submitted by the Tenderer on the basis of the Tender Documents.

Tender Documents: All documents issued or published by the Lead Procurer as part of the PCP process and made available on the Instand-NGS4P project website, including - without limitation - the TED Contract Notice, the Request for Tender, the Framework Agreement, annexes or attachments there to, and any schedules.

Tenderer: A company or consortium that is going to or has already submitted a tender but has not yet been awarded a contract to execute the R&D Services.

Usability: According to ISO 9241-11:2018, usability is the extent to which a product can be used by specified users to achieve specific goals with effectiveness, efficiency and satisfaction in a specified context of use**.**

User Needs: Minimal and desirable needs (clinical and patients' needs) as defined by the Buyers and refined on basis of the feedback of the OMC.

Value for Money: The most advantageous combination of cost (Price) and quality of the R&D Services (the extent that award criteria are addressed, performance, standardization, integration in the whole workflow and usability).

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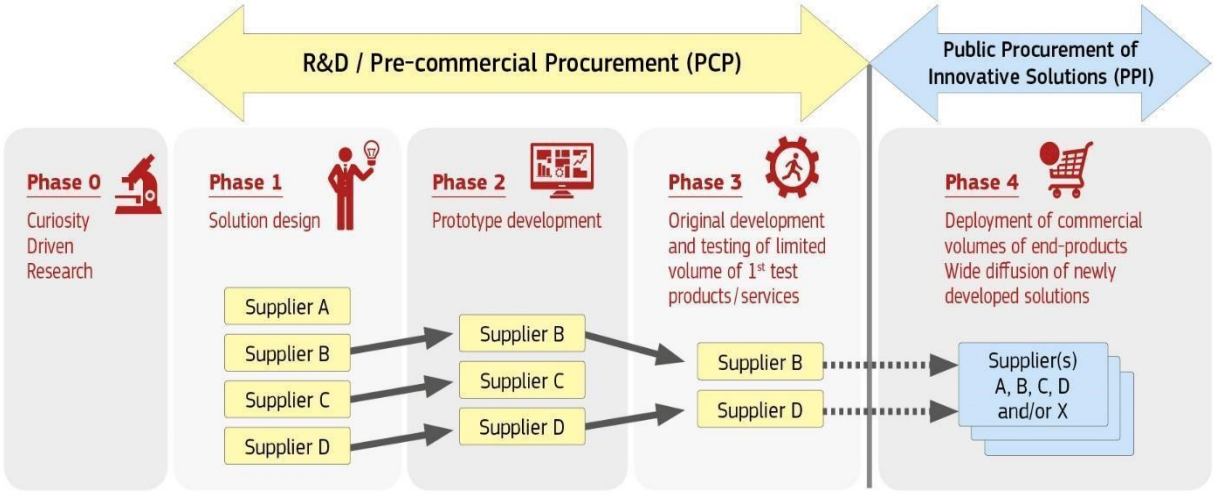
1. General context & background

This procurement is a **pre-commercial procurement (PCP)**.

PCP means that public procurers challenge innovative players on the market, via an open, transparent and competitive process, to develop new solutions for a technologically demanding mid- to long-term challenge that is in the public interest and requires new R&D Services (Figure 1).

Figure 1: Overview on the various phases of a PCP Project



PCP is characterised by the following **features**:

1.1 Competitive development in phases to identify the solutions offering the best value for money

PCP targets situations that require radical innovation or R&D and for which there are typically no solutions on or close to the market yet. Different competing providers may have different ideas for solutions to the problem. As R&D is yet to take place, there is not yet any proof as to which of these potential alternative solutions would best meet customers' needs.

PCP therefore awards R&D contracts to a number of competing Contractors at the same time, in order to compare different approaches to solving the problem. It thus offers innovators an opportunity to show how well their solution compares with others. It also allows a first customer test reference to be obtained from countries of the procurers that will test the solutions.

The R&D Service is split into **3 phases** (solution design, prototyping, original development and testing of a limited set of 'first' products or services) (Figure 1). Evaluations after each phase progressively

identify the solutions that offer the best value for money and meet the customers' needs. This phased approach allows successful contractors to improve their offers for the next phase based on lessons learnt and feedback from Procurers in the previous phase. Using a phased approach with gradually growing contract sizes per phase also makes it easier for smaller companies to participate in the PCP and enables SMEs to grow their business step-by-step with each phase.

Depending on the outcome of the PCP, Procurers may or may not decide to follow-up the PCP with a public procurement to deploy the innovative solutions (PPI) after completion of the PCP.

1.2 Public procurement of R&D services

PCP addresses mid- to long-term public procurement needs for which either no commercially stable solutions yet exist on the market, or existing solutions exhibit structural shortcomings that it requires further R&D Service to resolve. PCP is a way for Procurers to trigger the market to develop new solutions that address these shortcomings. PCP focuses on specific identified needs and provides customer feedback to businesses from the early stages of R&D. This improves the likelihood of commercial exploitation of the newly developed solutions.

PCP is explained in the PCP communication COM/2007/799 and the associated staff working document SEC/2007/1668. The R&D Services can cover research and development activities ranging from solution exploration and design, to prototyping, right through to the original development of a limited set of 'first' products or services in the form of a test series. Original development of a first product or service may include limited production or supply in order to incorporate the results of field-testing and demonstrate that the product or service is suitable for production or supply in quantity to acceptable quality standards. R&D Services do not include quantity production or supply to establish the commercial viability or to recover R&D costs.[1] It also excludes commercial development activities such as incremental adaptations or routine or periodic changes to existing products, services, production lines, processes or other operations in progress, even if such changes may constitute improvements.

1.3 Open, transparent, non-discriminatory approach - No large-scale deployments

PCP is open to all operators on equal terms, regardless of the size, geographical location or governance structure. There is, however, a place of performance requirement that they must perform a predefined minimum percentage of the contracted R&D Services in EU Member States or Horizon 2020 associated countries.

Any subsequent public procurement of innovative solutions (PPI), for the supply of commercial volumes of the solutions, will be carried out under a separate procurement procedure. Providers that

[1] See also Article XV(1)(e) WTO GPA 1994 and the Article XIII(1)(f) of the revised WTO GPA 2014.

did not take part in this PCP (or were not chosen to go through as far as the last phase) will thus still be able to compete on an equal basis in any subsequent procurement looking for contractors to provide a solution on a commercial scale.

1.4 Sharing of IPR-related risks and benefits under market conditions

PCP procures R&D Services at market price, thus providing Contractors with a transparent, competitive and reliable source of financing for the early stages of their research and development. Giving each Contractor the ownership of the IPRs attached to the results it generates during the PCP means that they can widely exploit the newly developed solutions commercially. In return, the tendered price must contain a financial compensation for keeping the IPR ownership compared to the case where the IPRs would be transferred to the procurers (the tendered price must be the 'non-exclusive development price'). Moreover, the Procurers must receive rights to use the R&D results for internal use and licensing rights subject to certain conditions.

For more information, *see PCP on the Europa website*.

1.5 Exemption from EU public procurement directives, the WTO Government Procurement Agreement (GPA) and EU state aid rules

PCP procurements are exempted from the **EU public procurement directives** because the procurers do not retain all the benefits of the R&D (the IPR ownership stays with the Contractors).[2]

They are also exempted from the **WTO Government Procurement Agreement (GPA)** because this Agreement does not cover R&D Services[3] (the PCP being limited to such services — and any subsequent PPI procurements relating to commercial-scale supply of such solutions not being part of the PCP procurement).

PCP procurements do not constitute state aid under the **EU state aid rules**[4] if they are implemented as defined in the PCP communication[5], namely by following an open, transparent, competitive procedure with risk- and benefit-sharing at market price. The division of all rights and obligations *(including IPRs)* and the selection and award criteria for all phases must be published at the outset; the PCP must be limited to R&D Services and clearly separated from any potential follow-up PPI procurements; PCP Contractors may not be given any preferential treatment in a subsequent procurement for provision of the final products or services on a commercial scale.

2 See Article 16(f) of Directive 2004/18/EC (Article 14 of Directive 2014/24/EU), Article 24(e) of Directive 2004/17/EC (Article 32 of Directive 2014/25/EU) and Article 13(f)(j) of Directive 2009/81/EC.

3 See the EU's Annex IV of Appendix I to the WTO GPA.

4 See Point 33 of the Commission Communication on a framework for state aid for research and development and innovation (C(2014) 3282).

5 Commission Communication: Pre-Commercial Procurement: driving innovation to ensure sustainable, high quality public services (COM(2007) 799) and PCP staff working document (SEC(2007)1668).

1.6 Open market consultation

The start of this PCP procurement was preceded by an open market consultation (OMC, see section 2.1.2). The summary, outcomes and Q&A of the OMC are presented on the website www.instandngs4p.eu.

1.7 EU funding

This PCP procurement is part of a project that receives funding by the European Union's Horizon 2020 Research and Innovation Programme, under grant agreement No. 874719 — Instand-NGS4P (see www.instandngs4p.eu).

The contracts will therefore be subject to additional rules that come from the EU grant(s).

For more information, *see 'innovation procurement' and 'links to regional policy' in the Funding & Tenders Portal Online Manual*.

⚠ **Attention:** The EU is not participating as a contracting authority in this procurement.

2. Tender profile: Services to be procured, tender closing time, procurers, contracting approach, budget, timetable and IPR

2.1 Description of services to be procured

PCP challenge

This procurement is for R&D Services to develop solutions to tackle the following **main challenge**:

Development of two fully integrated, standardized NGS workflows, from sample-pre-analytics to medical decision making, for routine diagnostics of common and rare cancers from adults and children within the Instand-NGS4P project.

Instand-NGS4P is an EU-co-funded Pre-Commercial Procurement (PCP) project for improving cancer patient's benefit from Next Generation Sequencing (NGS) by developing an integrated and standardized NGS workflow. For this, it will compile information from cancer gene testing, pharmacogenomics testing and e-medication in proper presentation to medical doctors for supporting therapy decision making at bedside widely applicable in health systems. The EU co-funded Instand-NGS4P project represents a consortium to define unmet medical and technical needs based on an Open Market Consultation, which lays the foundation for a request for tenders addressing companies

or institutions to develop their products to better meet user needs. Tenderers responding to this call will be evaluated regarding their ability to answer these users' needs from design perspective until the product phase. The total funding allocated to tenderers for product development (in total 8.55 M€) will finally lead to two integrated standardized NGS workflows, including decision support and reporting.

Subsequent medical decisions are often affected by the heterogeneity of pre-analytic conditions during sample preparation and nucleic acid (NA) extraction, as well as by the compatibility of pre-analytical processes with analytical platforms and bioinformatics data analysis. Furthermore, there is a major gap between the technological progress of NGS, pharmacogenomics and e-medication, and the actual implementation of this complex information in routine healthcare. Bringing NGS closer to the bedside and increasing the benefit for patients is the objective of Instand-NGS4P PCP. To achieve this goal, major emphasis is placed on actively involving patients through patient advocacy groups, as well as clinicians from the very beginning. By providing integrated information from NGS-based cancer gene testing, pharmacogenomics and e-medication to medical doctors in an appropriate format, decision making on targeted therapies and additional medications will be supported at the bedside.

Driven by patient and clinical needs (see https://www.instandngs4p.eu/), two innovative NGS workflows with integrated steps from sample pre-analytics to medical decision-making must be developed for routine diagnostics of common and rare adult and paediatric cancers considering IVDR requirements:

- well-defined genetic markers for diagnosis,
- validated prognostic genetic markers,
- the availability of validated actionable genetic markers.

This is a common challenge shared by all Procurers in the Buyers group.

The main clinical needs identified by the consortium and underlined by the responses to the OMC are:

- **Medical needs**:
    - better survival using targeted vs. conventional therapy
    - need for an early and accurate diagnostic (short turn-around time)
    - NGS solution should cover risk stratification, prognostic factors, predisposition/hereditary syndromes and therapeutic targets
    - incorporate pharmacogenomics information, as a major driver of precision medicine
    - integration of current medical knowledge for off-label use of drugs and open clinical trials
- **Sampling**:

- provide solutions for FFPE, fresh, fresh frozen and liquid biopsies
- importance of sample stabilization
- need for simplification/automation of isolation steps and to develop methods to isolate DNA/RNA with the same procedure
- consider the need for a combinatorial profile (germline and somatic)
- consider the compatibility with other diagnostic methods (e.g. histology and cytology)
- in particular for paediatric cancer diagnostic, develop solutions that adapt to a low sample volume

- **Technology**:
  - the choice sequencing approaches should take into account the precise clinical needs
  - achieve compliance with IVDR, especially for lab-developed tests and genome-wide approaches
  - improve sequencing accuracy and UMI panels
  - reduce hands-on time and costs
  - provide reference material for various workflows
- **Data analysis**:
  - provide evidence for moving variants into the clinical space
  - consider infrastructure and data management requirements
  - consider how to validate bioinformatics pipelines
  - achieve uniformity in interpretation of results
  - focus on training of pipeline users
  - comply with regulations
- **Medical Reporting**:
  - consider the need for standardization of medical reporting and for its integration in diverse existing systems
  - include response predictions to targeted therapies, pharmacogenomics data, drug interaction and dosing, and clinical evidence
  - provide decision support for physicians, including matching with active clinical trials (including basket trials)
  - reports should be prepared for physicians and patients
  - should be rapid and easy to interpret by patients, and shareable
  - consider the issues of data and privacy protection

The main <u>patient needs</u> identified by the consortium and highlighted by the responses to the OMC are:

- NGS has the potential to modify the oncological therapeutic scenario; may lead to fewer side effects to the patients
- informed consents must be explained to the patients; privacy and pseudonymization of data should be considered
- patients need to receive information on the NGS process, advantages and risks of NGS, impact on their lives and the lives of their families, possible outcome and treatment options after a multi-disciplinary team has assessed the results
- information should be given in an easy-to-understand format and language, and support by a genetic counseling expert should be provided
- patients should hold rights to share their diagnostic report and to have all the information to decide the follow-up; in particular for children, there is a need to assess needs and rights after turning 18 years old and to receive information about the rights to withdraw data based on GDPR

Global objectives of the Instand-NGS4P PCP:

- Improving the analytical performance by standardizing pre-analytical processes
- Integrating pre-analytical, analytical processes and data analytics into a standardized workflow
- Defining genetic variants with established medical implications for common and rare cancer of adult and paediatric cancers including pharmacogenomic variants relevant for drugs used in cancer care
- Developing reference material for quality control and metrological traceability as well as designing quality assessment procedures for each step of the workflow
- Considering requirements of the European *in vitro*-diagnostics regulation
- Improving benefits for patients and health systems from NGS-based molecular diagnostics.

As the achievement of the common main challenge depends on solving a number of technical challenges related to the different parts of the NGS workflows, the workflow is divided into 4 Lots, each corresponding to one **sub-challenge**. Each of the 3 phases will address the **4 Lots**, which at the end of Phase 3 have to be modularly integrated into two workflows, for the diagnosis and treatment decision-making (including pharmacogenomics) in common and rare cancers. Lots are defined as:

Lot 1: Pre-Sequencing

Lot 2: Sequencing

Lot 3: Bioinformatics Analysis

Lot 4: Integrated Reporting

All sub-challenges are shared by all Procurers in the Buyers group and were refined by feedback obtained from wide group of end-users and potential solution providers during the Instand-NGS4P OMC. A summary of the main conclusions and lessons learned from the OMC can be found on the Instand-NGS4P website. This summary includes the relevant clinical and patients' needs, as well as the technical needs defined by potential NGS workflow users and solution providers, and provides a valuable list of challenges and their relative priority to the potential users.

The modular design of the workflow (Lots) will enable in particular SMEs to contribute, and provides flexibility to adopt emerging user needs and technologies e.g., by updating one Lot. Specifications and upcoming development phases will also support the selected Contractors in addressing regulatory requirements for IVDs –to be applied in May 2022. Another aspect concerns the joint contributions to international standards, requiring development of reference materials and implementation of external quality assessment schemes, covering the whole workflow.

Each Lot contains a defined number of technical challenges (listed below) that were identified by the Buyers and refined by the feedback received during the OMC virtual meeting, webinars and questionnaires. These technical challenges thus reflect the needs of a large user community of the NGS workflow and establish a list of demands/requirements that the Contractors should try to solve. It is not mandatory that a Contractor covers every issue mentioned under the technical challenges for each Lot. The evaluation of the Tender will take into account the number of challenges addressed per Lot and how well the solutions cover them based on the fulfilment of criteria (see Chapter 3.4 for minimum requirements and award criteria), including the innovation level in addressing them. The submission of Tenders with highly innovative solutions to be used in routine healthcare are encouraged.

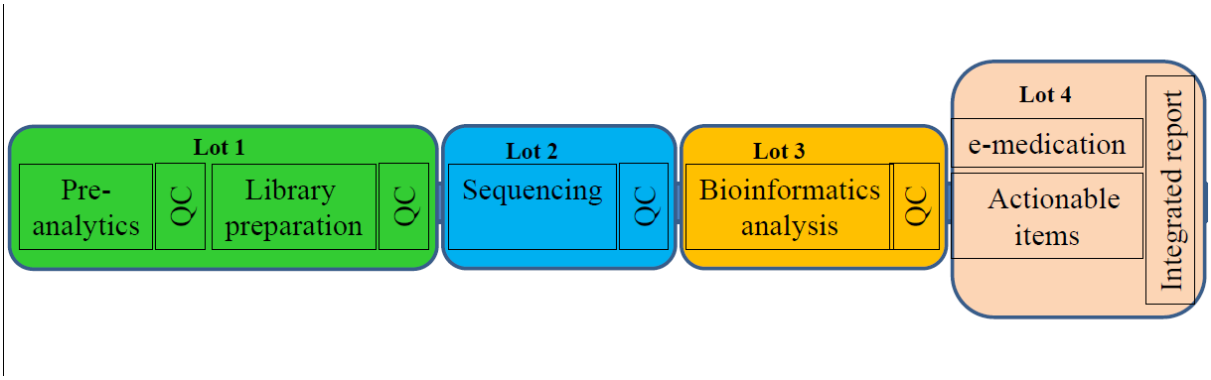


Figure 2: Overview on the different Lots of a complete integrated and standardized NGS workflow. QC: quality control for metrological traceability and integration of solutions of the different Lots into the workflow.

Lot 1: Pre-Sequencing

a) Specimen collection, NA isolation:

State of the art: The initial part of the workflow includes collection of the specimen, storage and transport which is key for success in integrating the entire NGS workflow into personalized medicine. If the pre-analytical part is not standardized, controlled and documented, it can lead to changes in the native NA profiles as they were in the patient's body and analyte quality changes, e.g., biased NA isolation and NA purity. The net and potentially harmful consequence may be the generation of false NGS results, which are not representative of the actual condition present in the patient.

Unfortunately, this pre-analytical part still is broadly ignored and is therefore one of the main reasons for issues with NGS, including bias and lack of data quality. Standardization of pre-analytics is key for implementation of NGS in routine diagnostic use, and will need to adhere to the EU IVDR new ISO/IS and CEN/TS standards (e.g. for RNA/DNA from FFPE tissue and cellular RNA, genomic DNA, circulating cell-free DNA from blood: ISO 20166-1, ISO 20166-3, ISO 20186-1, ISO 20186-2, ISO/FDIS 20186-3, CEN/TS 16835-3) which describe requirements for pre-analytical handling and preservation of analyte quality. Commercial providers have started to address this issue with (IVD and RUO) products for stabilization of NA in biological specimens, in particular for genomic DNA and RNA from solid tissues, cell-free DNA, genomic DNA and cellular RNA in venous blood. Building these frontend-systems into future NGS workflows is a major prerequisite for improving NGS test results. For an optimal link between these pre-analytical workflow steps and the next step of the NGS workflow, which is library preparation, the relevant requirements and technical specifications have to be met as well as possible and proven by formal verification. These include the NA quality including but not limited to the required integrity and unbiased NA profile, required eluate conditions (e.g. pH, salt concentrations), required NA quantity and concentration. QC of the extracted DNA and RNA will therefore be implemented including assessment of these parameters. These QC steps will secure the technical requirements and specifications for the NGS test including sensitivity, repeatability, reproducibility etc. for the NGS detection of targets. For example, this is especially important for liquid biopsy samples where i) low total circulating cell-free DNA yield and ii) low abundance of tumour/cancer target DNA in a wild-type background (in many cancer types <5%, for sub-clonal variants often <1%) can cause bias and issues in NGS, in particular with target enrichment and library preparation procedures. The required quantity of DNA strongly depends on the selected library preparation method including the number of pre-amplification cycles during target enrichment. Typically 10-40 ng of input DNA is used for the first part of the NGS workflow. Other specimen types such as circulating tumour cells (single cells) from blood or cell free DNA from urine are emerging targets of interest for use of NGS in personalized health care.

b) Library preparation

State of the Art: This step is highly challenging for the reliability and reproducibility of sequencing data by NGS. As this workflow part usually consists of multiple individual steps including DNA fragmentation, amplification, clean-up and normalization, it is vital that NA profiles that are representative of the *in vivo* situation do not get biased during library preparation.

A list of current shortcomings related to this crucial step that have to be considered by solution providers is reported below. It has to be taken into account that each of the following issues can differently affect the output of the procedure and thus the NGS results, depending on the type of sample, sample quality/integrity, the amount of sample available, and the availability of automation systems. Consequently, the weighting of each of the shortcomings listed below needs to be approached in the context of concrete diagnostic applications.

The **principal shortcomings** affecting the library preparation are:

-The lack of specific instructions about the procedure and compatible reagents to be used for the preparation and conservation of NAs relative to the specific NGS approach to be used.

-The lack of specific information regarding the evaluation of the input material for the definition of adequacy/inadequacy of the NA samples to be tested and the potential derived artefacts or failures.

-The lack of common reagents and protocols for pooled analysis of different patient specimens needed to reach a complete molecular profile.

-The lack of automation in several library-preparation procedures.

-The lack of internal controls for monitoring intermediate library preparation steps and conservation

- The limited availability of systems able to check confidently and simultaneously the quantity and the quality of a library.

- The lack of strategies to prevent bias among different indexing barcodes.

-The lack of solutions to prevent and/or monitor cross-contamination among NA samples.

- The need for solutions to minimise the number of reads shorter than end-to-end length, especially for amplicon-based systems.

- The need for solutions to solve complex regions with high probability of error or failure (homopolymer or repetitive regions) reducing the risk of false positive and negative results.

- The need for solutions to limit the interferences due to homologous sequences.

- The lack of suitable solutions to fulfil the analysis of regions involving small sequence variations as well as copy-number alterations and structural rearrangements by the construction of a unique library.

- The need for solutions to improve the amplification of GC-rich regions to facilitate the epigenetic analysis of promoters.

- The need for specific solutions to preserve the original balancing among different transcript isoforms for RNA samples.
- The need for specific solutions for the selective analysis of different RNA types starting from the same sample.
- Desirable specific library design to allow the detection of sequence variations in RNA samples.
- Desirable library design preferentially based on multiple overlapping regions to improve accuracy.

Technical challenges to be addressed for Lot 1:

- Preservation of the native NA profiles as they were in the patient's body, in a standardized, controlled and documented way, to ensure reliable downstream NGS results, representative of the actual condition present in the patient. This is reflected by the worries expressed by users and providers (in the OMC) in extracting NA with standardized protocols, with the most challenging being DNA and RNA from FFPE and extracellular vesicles, RNA from frozen tissue, and cfDNA and cfRNA from blood/plasma.
- Improve the isolation procedures from liquid biopsies to use in WES and WGS.
- Standardization of pre-analytics will need to adhere to the EU IVDR, new ISO/IS and CEN/TS standards which describe requirements for pre-analytical handling and preservation of analyte quality. Indeed, the answers from users and solution providers to the Instand-NGS4P questionnaires show that most organizations are aware of the different available ISO and CEN documents but not all work according to them. Thus, there is a need for implementing such standards in routine praxis in the near future. Interestingly, this is ranked as the top priority challenge by the solution providers. Examples of standards to be considered include (see also the List of NGS-Relevant Standardization Documents available on the project website):

  EN ISO 20166, Molecular in vitro diagnostic examinations — Specifications for pre-examination processes for formalin-fixed and paraffin-embedded (FFPE) tissue — Part 1: Isolated RNA and Part 3: Isolated DNA

  EN ISO 20184, Molecular in vitro diagnostic examinations — Specifications for pre-examination processes for frozen tissue — Part 1: Isolated RNA and Part 3: Isolated DNA

  EN ISO 20186, Molecular in vitro diagnostic examinations — Specifications for pre-examination processes for venous whole blood — Part 1: Isolated cellular RNA, Part 2: Isolated genomic DNA and Part 3: Isolated circulating cell free DNA from plasma

  ISO 4307:2021, Molecular in vitro diagnostic examinations — Specifications for pre-examination processes for saliva – Isolated human DNA

  ISO/TS 20658:2017, ISO/AWI 20658:2020, Medical laboratories — Requirements for collection, transport, receipt, and handling of samples

  CEN/TS 17390-1:2020, Molecular in vitro diagnostic examinations — for pre-examination processes for circulating tumor cells (CTCs) in venous whole blood — Part 1: Isolated RNA and Part 2: Isolated DNA

ISO/TS 20658:2017 Medical laboratories — Requirements for collection, transport, receipt, and handling of samples

EN ISO 20387:2020, Biotechnology — Biobanking — General requirements for biobanking

- QC of the extracted NA must be implemented throughout the process to confirm the sample is fit for purpose and to avoid downstream issues in pre-analytics. This should include, e.g. the assessment of the integrity and unbiased NA profile, and the monitoring of the efficiency of the extraction procedures. Of note, although this is a challenge of high importance for the users, solution providers do not rank it as high, which denotes a gap to be filled. There is thus a need for using performance testing, external quality assessment and reference material, which is recognized and desired by the users.
- Compatibility of sample stabilizers and NA isolation procedures suitable for WGS and WES with other analytical test procedures to be performed (e. g. histology/cytology) - ranked as the top priority challenge by the users, in particular when using FFPE samples
- Increase efficiency and possibly achieve automation of the analyte isolation/extraction procedure (ranked as high priority by users, as well as of the library preparation (ranked as high priority by both users and solution providers). Increasing the efficiency of NA isolation methods (and also of the sequencing sensitivity) may contribute to easier detection of genetic variants from low-amount samples and is considered as a need by the Buyers group.
- Usage of Unique Molecular Identifier (UMI, also known as random molecular barcodes) technology, which is the top ranked challenge by solution providers to reduce the complexity of library preparation and is also highly ranked by users.
- Development of a universal approach for different sample types and targets during library preparation, which is the top ranked challenge by users but not by solution providers and could thus be an important focus point for innovative developments.
- Improvement of library preparation success rate, a challenge highly ranked by both users and solution providers, which goes in line with the previously defined need by the Buyers group to improve library conversion rates and reliability. This is particularly important in childhood cancers, where the amount of samples is often limited and impacts the ability to detect somatic mutations at low variant allele frequency and mutations in difficult genomic regions.
- Better definition of the minimal quality and quantity requirements for the input material, highly ranked by both users and solution providers.

Lot 2: Sequencing

State of the Art: The actual sequencing part of an integrated NGS workflow very much depends on the properties and specific requirements from the technology and instrument provider. One of the main technical pitfalls is the accurate connection of the biological process of nucleotide binding/depletion to generation of a chemical or physical signal for transfer into sequence information, which can be controlled by, e.g. using sensitive imaging and real-time base calling. Another part which is essential for verification/validation is reproducibility and precision – an important requirement of the EU IVDR. This project aims to ensure that the NGS technology platform used will achieve the required sensitivity and precision, and avoid sequencing bias by reporting analyte profiles as they were *in vivo.*

For gene panels, there are significant cost and efficiency differences between different methods (e.g., hybridisation based vs PCR based, blocking oligos between different manufacturers, unique molecular barcodes, and evenness of coverage) and often long turn-around times of up to half a year for delivery of customized gene panels. Gene panels for rare cancers and pharmacokinetic/dynamic testing are either not available and/or have variable gene coverage.

Pharmacogenomic genes, which can broadly be divided into genes that impact drug pharmacokinetics or pharmacodynamics, vary in their complexity, and the main issues will relate to i) which genes are covered in gene panels; ii) which variants are covered within the genes (based on current evidence of utility); iii) how dynamic the testing will be to either include or remove genes/variants from panels as the evidence base improves; and iv) whether the NGS platform will be able to identify all variants.

Technical challenges to be addressed for Lot 2:

- the accurate connection of the biological process of nucleotide binding/depletion to generation of a chemical or physical signal for transfer into sequence information.
- reproducibility and precision (an important requirement of the EU IVDR), essential for verification/validation. The used NGS technology should achieve the required sensitivity and precision, avoiding sequencing bias for reporting analyte profiles as they are *in vivo*.
- decreased turn-around times for diagnostic procedures (highlighted by the solution providers and on the clinical needs OMC questionnaires), which can be achieved by reducing the hands-on timing, pooling various libraries in one run and reducing the sequencing time. Accordingly, the flexibility of the platform for scalable throughput should be considered.
- for WGS analysis, ensure uniform genome coverage, e.g. for high-resolution characterization of copy number alterations. Increasing the efficiency of long-read sequencing should also be considered.

- reduction of costs (particularly important for rare cancers including childhood cancers where multiplexing is hard) by reduced chemistry expenses and introduction of reusable materials and flow cells, for example.
- consider the compliance with IVDR, which is more challenging for genome-wide approaches and laboratory-developed tests than for defined target panels. This was considered important by the Buyers group and it was also reflected in the solution providers' answers to the questionnaire.

Sequencing output formats:

Independent of the sequencing platform, the standard formats for sequence data are the **FASTQ-format** or the **unaligned BAM-format**. These file formats encompass the name of each sequence read, the nucleotides in each sequence read, and the (phred-scaled) quality value for each nucleotide in each sequencing read. The ID of the input sample/NGS library is coded into the file name. The amount of sequences per NGS library must correspond to the amount of NGS library that is put into the sequencing cartridge.

Lot 3: Bioinformatics Analysis

State of the Art: Despite the huge improvements achieved in the field of NGS technology, the complexity of the bioinformatics required to efficiently analyze the sequencing output is severely hampering the introduction of NGS technologies into clinical practice. Bioinformatics analysis may introduce variations in NGS results and there is a lack of high quality, user-friendly, bioinformatics tools dedicated to the annotation and graphical reporting of somatic/genetic mutations. In particular:

- Current open source tools are mostly usable via a command line interface only and are not intuitive for the medical users, but rather tailored for bioinformaticians. Specifically, tolls are mainly unavailable as web-based or graphical user interfaces. Analysis pipelines consist of a multitude of different programs that must be set up, tested and validated.
- Different tools need to be implemented into specific pipelines for different types of data (for example, gene panel vs WES or WGS)
- Available commercial products for analysis on the other hand are intuitive, but not flexible enough to address the specific needs of certain diagnostic issues and do not keep up with current progress in sequence alignment, quality control and annotation.

Specifically, NGS data analysis is currently suffering from a series of major issues:

1) Lack of standardized bioinformatics protocols: currently a myriad of different bioinformatics tools is available to perform NGS tasks such as sequence alignment, variant calling and reporting. Often, a significant fraction of these tools lacks solid validation. These tools are subject to versioning, and often to dependencies on other software packages or operating system versions. Hence R&D Services are required to develop a unified, long-term-stable, user-friendly platform for NGS analysis, which should be also complemented by a thorough analysis of platform sensitivity and specificity in function of the global coverage for an extensive list of major variants under rigorous experimental settings.

2) The majority of the NGS pipelines are composed of a complex concatenation of command line commands, often executing a significant number of different tools. This complex framework is one of the major hurdles in broad NGS implementation in health care, as the use of these instruments is typically reserved for specialized bioinformaticians. In addition, a large number of NGS analytical reports lack the implementation of a complete versioning system, which prevents the ability to track back and reproduce previous analyses in order to fulfil documentation requirements.

3) Annotation: to facilitate a proper interpretation of the NGS variants, the development of a detailed annotation tool is strongly recommended. This tool should generate a clear and easily interpretable report, covering an extensive set of different datasets (10.1038/gim.2015.30, 10.1016/j.jmoldx.2016.10.002), such as: dbSNP annotation, OncoScore, ClinVar, SIFT score, SIFT prediction, Polyphen2 HDIV score, Polyphen2 HDIV prediction, Polyphen2 HVAR score, Polyphen2 HVAR prediction, LRT score, LRT prediction, MutationTaster score, MutationTaster prediction, MutationAssessor score, MutationAssessor prediction, FATHMM score, FATHMM prediction, PROVEAN score, PROVEAN prediction, VEST3 score, CADD raw, CADD phred, DANN score, fathmm-MKL coding score, fathmm-MKL coding prediction, MetaSVM score, MetaSVM prediction, MetaLR score, MetaLR prediction, integrated fitCons score, integrated confidence value, GERP++ RS, phyloP7way vertebrate, phyloP20way mammalian, phastCons7way vertebrate, phastCons20way mammalian, SiPhy 29way logOdds, Exac annotation (SNV) andCosmic_Somatic_Annotation.

Also, this tool should be easily updated either by the end user or by the system itself in order to keep the knowledge base up to date. In summary: the lack of standardized bioinformatics protocols, coupled with a significant complexity in the current pipelines requires the development of fully validated, user-friendly operating-system-independent tools dedicated to the analysis of targeted panels, supporting complete versioning and annotation lots.

<u>Technical challenges to be addressed for Lot 3:</u>

- Verification of all components of data management, transfer and analysis throughout the entire workflow process (bioinformatics, in-silico data modelling, e-reporting) to reduce

complexity for clinicians as well as users, and to fulfil regulatory requirements (EU IVDR, FDA etc.), but at the same time avoid analysis bias and false information.

- Ensure that sequencing data is processed, filtered, analysed and displayed in the best possible way so that the final NGS information reflects the real molecular status of the patient.
- Specification of clinically relevant cut-offs for the intended NGS tests and their verification, as well as the specification and development of robust calling algorithms.
- For each disease, the business processes and metadata schemas should be defined following the entire clinical pathway from the medical specialist's request for genomic analysis inside a patient's electronic health record (EHR), the laboratory workflow (standard operating procedure - SOP), bioinformatics pipeline and returning results back to the patient's EHR where they will be visualized in textual and graphical form. The necessary SOPs and bioinformatics pipelines should be updated when needed, according to clinical requirements and state-of-the-art bioinformatics knowledge.
- Processing of patient data has to ensure secure handling of NGS data (including in diagnostic security updates), according to the ranking of high-priority challenges by the solution providers in the OMC questionnaire. In this regard, compliance with data protection regulation (GDPR) and training and awareness of personnel should be enforced.
- Dedicated infrastructures will have to be available for storage of large amounts of NGS data and backup of data should be automated to prevent data loss.
- The lack of standardized bioinformatics protocols, coupled with a significant complexity in the current pipelines, requires the development of fully validated, user-friendly tools dedicated to the analysis of targeted panels, WES or WGS or other data, supporting complete versioning and annotation lots. (See also the List of NGS-Relevant Standardization Documents available on the project website).
- Related to the standardization of pipelines and software that detect actionable items for diagnostics, solution providers highlighted that efforts still need to be focused on annotation and analysis reproducibility, compatibility between tools and databases, complying with standard data formats and testing of pipelines with standardized samples. In accordance, automation/reduced manual work is listed as a top priority challenge to overcome.

Data input and output formats to be used for Lot 3

Input formats:

Independent of the sequencing platform, the standard formats for sequence data exchange are the **FASTQ-format** or the **unaligned BAM-format**. These file formats encompass the name of each sequence read, the nucleotides in each sequence read, and the (phred-scaled) quality value for each nucleotide in each sequencing read. However, some existing data analysis tools require platform-dependent files to identify different molecules for purposes of error-correction or PCR-duplicates-counting (unique molecular identifier sequence), for example the Avenio (Roche) or the Dragen (Illumina) software. Therefore, the **platform-dependent sequencing output** can alternatively be considered for **sample and/or molecule identifiers**. Examples of platforms that are currently popular in the EU are listed, in alphabetic order: For Illumina platforms, the sequencing output in **BCL-format** can be considered. For Oxford Nanopore platforms, the sequencing output in the **fast5-format** may be considered. For PacBio platforms, the sequencing output in the unaligned analysis-ready "**subreads.BAM**" format can be considered. For ThermoFisher Torrent platforms, the sequencing output in **WELL format** can be considered.

The Buyers require that sequence data with sample indexes and with unique molecular identifiers to be used as input data for the bioinformatics analysis. The Buyers clearly prefer the FASTQ-format or the unaligned BAM-format rather than platform-dependent formats.

To enable verification of the bioinformatics solution, the Buyers additionally require that validated results data can be used as input into the solution to enable bioinformatics comparison with self-computed results. Typically, the verification of the solution in the lab will be performed by the diagnostic lab user, using reference data that has been generated by the Contractor for previously agreed test samples or reference data. This means that output formats must also be used as input formats for the verification analyses.

Output formats:

Genomic VCF (gVCF) version 4.3- this format carries the information for all types of variants (SNVs, indels, CNVs and other more complex structural variants) and the sequencing coverage information.

BAM - this format carries the alignment details that is nowadays still required for interactive manual validation of the bioinformatics variant-calls.

Lot 4: Integrated Reporting

One of the main issues in NGS-based diagnostics is how to report the clinically relevant information in a concise and clear manner. Data generated by NGS are often overwhelming in terms of raw quantity and complexity. Hence significant efforts must be dedicated to convey to physicians only the relevant clinical information and to avoid reporting of variants of unknown significance (VUS) or lacking

validated clinical utility. Incorrect interpretation of NGS data generated in a clinical setting may lead to erroneous clinical decisions.

Translating NGS results into reports supporting medical decision-making should be achieved in this Lot. For this goal NGS results should be integrated with pharmacogenomics results and existing e-medication tools containing information on drug dosing and drug interactions. Since this information has to be made available to healthcare professionals and patients at the bedside for rapid interpretation, it will be important to determine the optimal method to clearly present NGS results and their medical relevance. Moreover, most clinicians will not have a deep knowledge of variants and their consequences. Therefore a report format which provides them with the relevant background information supporting appropriate interpretation (based on the evidence) of NGS results and enabling clinicians to take the responsibility for decision based on NGS analyses is crucial. Furthermore, information should also be made available to patients in an easily understandable manner, and proper protection of privacy is essential. These needs are underlined by the answers to the Instand-NGS4P questionnaire, which revealed the lack of satisfaction from the users on the current products available on the market for integrated reporting and medical decision support.

<u>Technical challenges to be addressed for Lot 4:</u>

- The solution should be usable on-line and off-line as well as on mobile devices.
- Results should be clearly presented by employing advanced information visualization technology.
- The solution should support different European languages.
- Reports for therapy decision-making at bedside should be generated for clinicians comprising the following information, according to the Buyers' needs and the responses from users to the OMC questionnaires: NGS results on cancer-related variants (and their level of clinical evidence and the type of evidence; e.g., companion diagnostics, guidelines of medical societies, curated databases, current clinically validated and computationally predicted knowledge on the deleteriousness of the mutations, and literature), quality of the analysis and actionable items (top ranked by users); furthermore, information on the sample analyzed, the analytical method, open clinical trials and possible compassionate use are also highly ranked by users and should also be included.
- The inclusion of results from pharmacogenomics analysis is a defined need by the Buyers; the users prioritize other information in the OMC questionnaire, but their responses confirm that most do not have a solution to incorporate pharmacogenomics data in the medical report

and thus this is rarely incorporated in current reports. The questionnaires show that inclusion of information on avoidance of toxicity, drug-drug interactions and drug dose assessment is of high importance.

- Separate reports should be generated for patients in an easily understandable language (examples will be provided by patient advocacy groups participating in Instand-NGS4P), as identified during the discussions held by the Buyers group and confirmed by the OMC questionnaires .
- Pharmacogenomics results should also be made accessible via secure mobile Apps for patients.
- Interoperability with bioinformatics pipelines and electronic health records/hospital information systems should be achieved, as it was highly ranked by the potential users. This can be achieved by using standardized data formats such as HL7 and FHIR.
- Proper documentation of versions (software versions and changes in ontologies and classifications as well as emerging clinical evidence) should be ensured.
- High level of cyber security and privacy protection should be achieved.
- The solution should consider requirements of relevant ISO and CEN standards.
- Detailed technical documentation of the solution for integrated reporting should be provided.
- A draft user manual should be made available.

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2.1.1 In-kind contributions from the Buyers

Solutions offered by the tenderers must be tested by using clinical samples, isolated NAs or data; test materials will be provided by the Buyers as an in-kind contribution.

Samples for testing the developed prototypes and complete workflow:

The involved Buyers can provide test samples, according to availability, as an in-kind contribution. Samples can be requested to test the developed products in Lots 1 and 2 in Phases 2 and 3. The samples that can be provided are from common cancers (e.g. lung, colon, ovarian cancer and soft tissue sarcoma) as well as adult rare and paediatric cancers (e.g. hematologic neoplasias). They can be provided in different diagnostic sample types. Most commonly FFPE tissue sections, but also tissues preserved in PAX gene tissue (PFPE), cryopreserved or liquid biopsies like plasma from whole blood collection tubes with or without stabilizers for ccfDNA (2.5 - 4 ml aliquots) can be made available. These samples can be provided with pre-analytical parameters such as transport time, formalin fixation time according to requirements of applicable ISO standards for the pre-examination process, and main disease diagnosis. Such samples can for instance be used to demonstrate pre-analytical robustness of diagnostic workflows and can generate key quality parameters of libraries as output in Lot 1, which must be compatible as input for Lot 2 solutions. The FFPE tissue sections contain a variation of tissue

sizes, usually about 0.5 cm^2, but they can be smaller (e.g. biopsies) or larger. Samples that have been used for NGS diagnosis with known and reported variants can be supplied upon request, if available. In case these materials cannot be produced newly for the project, similar material will be made available by biobanks. Of note, the availability of samples cannot be guaranteed for all variants for all disease entities, especially in the case of rare cancers (including paediatric cancers), and it will depend on patients' informed consents and/or biobank availability. All variant types will however be covered by the test material to be provided by the Buyers as in-kind contribution. The Buyers can also provide isolated NAs or library preps as input for the sequencing solutions in Lot 2. In addition, pharmacogenomics samples in the form of extracted genomic DNA with known and reported variants, characterized on purity and concentration can be made available for Lots 1 and 2 in Phases 2 and 3.

For evaluation and actions of the PGx data in Lot 4, the involved Contractors should refer to curated databases (e.g., PharmGKB), which interpret and summarise PGx information that are approved by recognized international organizations such as FDA, EMA, Swissmedic, PMDA and HCSC. Note: Contractors are responsible for ensuring appropriate licensing for database access.

Sequencing files can be provided in different formats upon request with additional medical information for testing of the bioinformatics pipelines in Lot 3, which can be used as input for generating a report in Lot 4.

Advice for standardization and IVDR requirements can also be provided by the Buyers as in-kind contribution. Furthermore, Contractors are encouraged to join via their national standardization organization the CEN Technical Committee 140 that is currently developing a standard for the whole diagnostic NGS workflow.

A detailed list of samples to be provided is included in Tables 1 and 2 (Chapter 3.4.2).

2.1.2 Preparation for the PCP

The starting point was the unmet need for NGS-based diagnostics of cancer of the Buyers group, also referring to experience from the large networks of more than 200 leading medical centers cooperating with the Buyers.

Moreover, as part of the preparation phase of the project, an OMC was organized, as an open dialogue with potential tenderers and end-users, with the objective of refining the unmet medical and technical needs previously defined by the Buyers. The results of the OMC have been taken into account for defining and fine-tuning the final specifications of the Instand-NGS4P request for tender and the award criteria for each Lot and phase included in this document (section 3.4).

As announced in the Prior Information Notice (PIN) published on December 28th 2020 in the Official Journal of the EU (OJEU), the OMC of the Instand-NGS4P project consisted of three parts:

1. Virtual OMC Event
2. Explanatory webinars
3. Questionnaires

Due to the COVID-19 pandemic, the virtual OMC event took place as an online event on March 22nd and March 23rd 2021 via Cisco Webex, instead of in person in Vienna as initially planned. There were a total of 176 attendees on the first day and 160 attendees on the second day, with similar attendance throughout the different sessions including Biotech and Pharmaceutical industry, academic research institutions, representatives from the health care system, as well as governmental organizations/regulatory bodies and patient associations. The presentations from the virtual meeting are publically available on the project website through the following link: https://www.instandngs4p.eu/pcp/open-market-consultation/

The Instand-NGS4P project consortium has organized two webinars as part of the OMC, with the aim of providing additional information to stakeholders on the PCP process and to support the partnering of solution providers in the preparation for the tendering process: the informative webinar "Tendering process", on April 28th 2021, with a presentation by the project coordinator on the objectives of the project, its different phases and timelines, benefits for the R&D providers, basic concepts of the evaluation process and evaluation criteria, tendering procedure, documentation and contracts to be implemented, and the partnering webinar, May 18th 2021, in order to support the Solution Providers in their search for suitable partners for providing an optimal solution for the Lot (s) of interest in response to the Request for Tenders. A partnering platform was also created (https://www.instandngs4p.eu/pcp/open-market-consultation/partnering-platform/) to help potential solution providers finding matching collaborators. Of note, the project consortium only acts as a supporter of this process and does not get involved in any partnering agreements.

As the third part of the OMC, questionnaires were used to obtain broader and quantitative insights from different stakeholders. The purpose of the questionnaires was to further assess the clinical, patient and technical needs, as well as the readiness of the solution providers to address the users' needs. The questionnaires were designed for different stakeholder groups and made publically available on the project website. In total, we have received 18 responses from users, 48 from solution providers and 40 from patient associations.

2.1.3 Expected outcomes (per phase)

The objectives and their expected associated output, results and tasks to be carried out (milestones and end of phase deliverables) for each of the three phases are described below:

Expected outcomes					
Phase 1: Solution design					
	Objective:	Perform research to: 1. elaborate the solution design and determine the approach to be taken to develop the new solutions and 2. demonstrate the technical, financial and commercial feasibility of the proposed concepts and approach to meet the procurement need			
	Output and results:	A clear and feasible technological, organizational, regulatory, safety, budgetary and commercial plan has been generated.			
	Milestones and deliverables		**By when?**	**How?**	**Output and results**
	Milestones:	M1.1) Solution providers have submitted all deliverables on time, meeting at least all minimum requirements.	End of the Phase 1	Document sent by email to Lead Procurer	Finalisation of the solution development offer
	Deliverables:	D1.1 Project abstract and list of pre-existing IP (for EU)	Start of Phase 1	Document sent by email to Lead Procurer	Project abstract

		D1.2 End of Phase Report & non-confidential summary	End of Phase 1	Document sent by email to Lead Procurer	End of phase report
		D1.3 Phase 2 Offer	End of Phase 1	Document sent by email to Lead Procurer	Phase 2 Proposal
Phase 2: Prototyping					
	Objective:	Develop, demonstrate and test performance of prototypes by Contractors			
	Output and results:	Contractors have produced working prototypes which allow the Buyers Group to understand how the solutions can be implemented			
	Milestones and deliverables		**By when?**	**How?**	**Output and results**
	Milestones:	M2.1) Mid-term follow-up	M7 of the Phase 2	On-line meeting presentation	Project progress update
		M2.2) End of Phase 2 Review	End of Phase 2	On Line meeting Presentation	Evaluation of the Contractors solution prototype
	Deliverables:	D2.1) Project abstract and list of pre-existing IP (for EU)	Start of Phase 2	Document	Project Abstract
		D2.2) First performance	M 7 of Phase 2	Document sent by email to Lead Procurer	Prototype progress assessment

		evaluation of the prototypes			
		D2.3 End of Phase 2 Report & non-confidential summary	End of Phase 2	Document sent by email to Lead Procurer	Demonstration of the developed prototypes
		D2.4 Phase 3 Offer	End of Phase 2	Document sent by email to Lead Procurer	Phase 3 Proposal
Phase 3: Development & testing					
	Objective:	Original development performance verification and testing in a real-world medical environment of a limited set of first products (the test series)			
	Output and results:	Working prototype tested by Buyers for performance and usability and integration into diagnostic workflows			
	Milestones and deliverables		**By when?**	**How?**	**Output and results**
	Milestones:	M3.1) Having a limited set prototype solution installed and ready for testing at the Buyers site	Within 12 weeks from start of Phase 3	Prototype installed	Installation checked and testing starts
		M3.2) Mid-term follow-up	M 5 of the Phase 3	Documents and meeting	Solution testing update

		M3.3) End of Phase Review	End of Phase 3	Documents and meeting	Evaluation of the Contractor's solutions performance usability and possibility to be integrated into diagnostic NGS workflows
	Deliverables:	D3.1 Project abstract and list of pre-existing IP (for EU)	Start of Phase 3	Document sent by email to Lead Procurer	Project abstract
		D3.2 Installation and operational test-series at the Buyers' site	Within 12 weeks from start of Phase 3	Document sent by email to Lead Procurer	Installation of the prototype
		D3.3 Mid-term Performance results	M 6 of Phase 3	Document sent by email to Lead Procurer	Solution testing progress update
		D3.4 End of phase report & non-confidential Summary	End of Phase 3	Document	Demonstration of the final solutions developed

Description of Milestones and Deliverables

Phase 1:

M1.1) Solution providers have submitted all deliverables on time, meeting all minimum requirements.

M1.2) End of the Phase 1 review by Instand-NGS4P Buyers.

D1.1) Project abstract and list of pre-existing IP in the format required by the EU for publication.

D1.2) End of Phase 1 report containing a description of the main results and conclusions achieved with a detailed description of how the proposed solution will meet the challenges. The report should also include a commercialization plan, an assessment of the R&D efforts for the prototype and lab testing, measures taken to protect results (IPR), a list of names and location of personnel that carried out the R&D activities, cost reporting.

A non-confidential summary to be published on the Instand-NGS4P website (and other communication channel) containing the description of the main results is also requested together with the end of phase report.

D1.1 and 1.2 shall be in the format required by the EU for publication. The format will be available on the Instand-NGS4P website.

D1.3 Phase 2 Offer.

Phase 2:

M2.1) Mid-Term follow-up. Having a developed prototype of the Instand-NGS4P solution ready for performance testing by the Contractor using test material provide as in-kind contribution by the Buyers.

M2.2) End of the Phase 2 review by Instand-NGS4P Buyers

D2.1) Project abstract and list of pre-existing IP (for EU) (in the format required by the EU for publication)

D2.2) First evaluation of the prototypes. Documentation of results obtained from performance testing by the Contractor using test material provide as in-kind contribution by the Buyers.

D2.3) End of Phase 2 Report in compliance with the guidance notes issued by the Procurers as amended from time to time or as otherwise required by the Procurers, and shall include the description of the deliverables and milestones including detailed description of the relevant solution, methods, data generated, results, final conclusions together with management information and any other information relating to the PCP Project including explanations for any deviations from the Technical Offer up to the Completion Date. Verification of prototypes must be documented (including reference

material data) using test materials and/or other data supplied by the Procurers The market analysis and commercial plan for the technologies developed within the Instand-NGS4P PCP provided at the end of Phase I must be updated.

A non-confidential summary to be published on the Instand-NGS4P website (and other communication channel) containing the description of the main results is also requested together with the End of Phase Report.

D2.1, 2.2 and 2.3 shall be in the format required by the EU for publication. The format will be available on the Instand-NGS4P website.

D2.4) Phase 3 Offer.

Phase 3:

M3.1) Having a limited set of first products of the Instand-NGS4P solution installed and ready for testing at the Buyers site.

M3.2) Mid-term follow-up. Preliminary results of prototypes, assembled and integrated into a diagnostic NGS workflow, tested at the Buyers' site.

M3.3) End of Phase 3 Review.

D3.1) Project abstract and list of pre-existing IP.

D3.2) Installation and operational test-series at the Buyers' site, including provision of draft user manual, training of Buyers for testing the prototype.

D3.3) Mid-term Performance results. Report of the results of the performance verification, usability testing and integration of the prototypes into diagnostic NGS workflows at the Buyers' sites.

D3.4) End of Phase 3 report, in compliance with the guidance notes issued by the Procurers as amended from time to time or as otherwise required by the Procurers, and shall include the description of the deliverables and milestones including detailed description of the relevant solution, methods, data generated, results, final conclusions together with management information and any other information relating to the PCP Project including explanations for any deviations from the Technical Offer up to the Completion Date. Report must include the performance verification results, the usability and the integration into diagnostic NGS workflow (i.e., interoperability with solutions from the other Lots). Report must contain results obtained from reference materials and test materials and data provided by the Buyers to demonstrate that they meet the users' needs and standardization as indicated in the Instand-NGS4P challenges. Report should highlight the progress beyond state-of-the-art due to the research and development work within this project and readiness of the technology for use in future developments. Report should also include the details on the process of migration of

prototypes to the real-world medical environment of the Buyers and the adaptability/usability of the prototypes in the integrated workflow. An update of the market analysis and business plan provided at the end of Phase 2 for the technologies developed within the PCP should also be included as well as the IPR measures taken by the Contractor to protect these results.
A non-confidential summary to be published on the Instand-NGS4P website (and other communication channel) containing the description of the main results is also requested together with the End of Phase Report
D3.1, 3.2 and 3.3 shall be in the format required by the EU for publication. The format will be available on the Instand-NGS4P website.

For Phase 2, prototype verification is expected to be done at the premises of the Contractors using test material provided by the Buyers (see "In-kind contribution", chapter 2.1.1) in standard data format.

For Phase 3, the Buyers (one or more) will carry out the testing and independent verification of the solutions at their premises and optionally at another medical center in Romania. The Contractors need to set aside resources for this testing of the usability of the developed solutions as well as the interoperability of solutions from different Lots (to ensure that solutions developed in different Lots ultimately work together in an integrated and standardized workflow as expected).

2.2 Tender closing time

Tender closing time will be: **December 15th, 2021, 17.00h CET**

2.3 Procurer(s) and other parties involved in the PCP

This procurement relates to a joint PCP that will be carried out by the following **Lead Procurer**:

Medizinische Universität Graz, Austria

The Medical University of Graz (MUG) is associated with the University Clinics of Graz, with 1600 beds and 78000 patients/ year. Cancer care is provided by a certified Comprehensive Cancer Center. The Diagnostic and Research Institute of Human Genetics is ISO 15189 accredited. MUG teaches 4300 students and offers 6 PhD Programs and 7 Doctoral Schools. The Diagnostics and research Institutes of Pathology and Human Genetics operate 2 Illumina MiSeq and 2 Illumina NextSeq (1 Illumina NovaSeq is planned), 2x Ion Torrent S5XL + Ion Chef + 3x Torrent Server as Cluster + Ion Reporter, and Qiagen

sequencing platforms (for research only), and perform 4.596 NGS diagnostic tests per year mainly in oncology including common and rare cancers in adults and children.

Expertise: Medical care, molecular diagnostics, research, education and training, biobanking, biomarker development, CEN and ISO standards, quality management and regulatory affairs

The Lead Procurer is appointed to coordinate and lead the joint PCP, and to sign and award the framework agreement and the specific contracts for all phases of the PCP, in the name and on behalf of the following **Buyers group**:

- **Università Degli Studi di Firenze, Italy**

The University of Florence is an important and influential centre for research and higher training in Italy, which offers a wide range of study programmes at various levels and in all areas of knowledge. It is one of the largest and most productive public research systems in Italy. Due to an intensive participation in research programmes of national and international relevance and to the significant scientific results achieved. This combination of factors qualifies the Florentine institution as a modern research university and accounts for its excellent position in national and world rankings. Researchers at the University of Florence operate within 21 different departments and have at their disposal approximately 40 research structures comprising inter-departmental and inter-university centres as well as specialised research, knowledge transfer and advanced training centres. The UNIFI unit involved in this project is the Department of Experimental and Clinical Biomedical Sciences, which conducts both research activities (in the field of pathology, clinical biochemistry and molecular biology) and clinical activities in collaboration with the largest Teaching Hospital in the Tuscany Region: the AOU CAREGGI.

- **Erasmus Universitair Medisch Centrum Rotterdam, Netherlands**

The Department of Pathology of the Erasmus MC, includes a large team of pathologists, molecular diagnostics, biomedical scientists, research technicians and managerial personnel who join forces to implement and improve high standards of diagnostic pathology and experimental research breast, brain, colon and urogenital cancers. The major part of the research is dedicated to cancer research embedded within the Erasmus MC, which is the largest academic medical center in the Netherlands with over 13,000 personnel. The Molecular diagnostic unit of the department of Pathology performs over 3000 diagnostic NGS cases per year, with over 600 NGS determinations on ccfDNA. This work is performed on an Ion Torrent platform under ISO15189 standards. Due to the ever growing amount of genes in some of the cases to evaluate, collaboration with the Hematology department was sought

where an Illumina platform can be used for WES or WGS for tissue diagnostics. The unit has a strong regional function in molecular diagnostics for peripheral hospitals and even national and abroad. A large array of complex molecular techniques is performed where for NGS 17 different panels are used where custom made panels and TMB's are included. Research is performed to increase the diagnostic performance and tests Molecular Diagnostics can provide. Current main focuses: molecular diagnostics of adult and childhood brain tumours, application of cfDNA analysis for lung cancer treatment and follow-up, and tumour tissue-based BRCA diagnostics.

Expertise: Molecular diagnostics, NGS, pre-analytics, research, education, training, clinical care, biobanking, CEN and ISO in vitro diagnostic standards, biomarker development, bioinformatics, management, Ethical-Legal-Societal-Issues. Erasmus MC belongs to the Instand-NGS4P Buyers group and, therefore, has a particular interest to contribute with their expertise to the complete procurement process. In particular the tendering, monitoring and evaluation over the different phases of the PCP project.

- **St. Anna Kinderkrebsforschung GmbH– Children Cancer Research Institute (CCRI GmbH), Austria**

The CCRI GmbH was founded in 1988 with the overall aim to improve the treatment options for children suffering from cancer through basic and translational research. The CCRI GmbH is closely affiliated with the St. Anna Children's Hospital (the largest clinical haemato-oncological centre for the treatment of childhood cancer in Austria) and with Labdia Labordiagnostik GmbH (spin-off SME). Currently, the CCRI GmbH has 16 research groups focusing on a number of immune-therapeutic approaches and on a selected spectrum of paediatric oncological diseases such as Leukaemia, Neuroblastoma, Ewing Sarcoma, Osteosarcoma, Wilms' tumour, Lymphoma, Langerhans cell histiocytosis and secondary diseases relevant in immunocompromised patients such as mycosis and viral infections. The Clinical Trial Unit for Studies & Statistics for Integrated Research & Projects (S^2IRP) is an important link between the CCRI GmbH laboratory research activities and the clinical application of trials at the St. Anna Children's Hospital. Essentially, S2IRP fosters clinical research in paediatric oncology by coordinating and facilitating international clinical trials.

The CCRI GmbH/St. Anna Children's Hospital is the coordinator of the European Reference Network on Paediatric Cancer (ERN-PAEDCAN), one of the 24 European Reference Networks (ERNs) that are virtual networks involving healthcare providers across Europe. They aim to facilitate discussion on complex or rare diseases and conditions that require highly specialised treatment, and concentrate knowledge and resources. In particular, (ERN-PAEDCAN) aims at reducing inequalities in childhood cancer survival by providing high quality, accessible and cost-effective cross-border healthcare to

children and adolescents with cancer, regardless of where they live. This network gathers some of the most influential stakeholders from 18 European Countries in the field of paediatric oncology.

The CCRI GmbH is also a member of the European Joint Programme on Rare Diseases (EJP-RD). This is a 5-year programme co-funded by the European Commission that brings over 130 institutions from 35 countries to improve the integration, the efficacy, the production and the social impact of research on RD. EJP-RD fosters the development, demonstration and promotion of Europe/world-wide sharing of research and clinical data, resources and know-how.

Currently, the CCRI GmbH is engaged in 20 projects funded nationally and 19 projects funded internationally, most of which are financed by the European Union.

The CCRI GmbH has developed into the largest centre for research related to childhood cancer in Austria. Our comprehensive approach bundles all fields of childhood cancer research within a permanent cycle: basic, translational and clinical research, the improvement of diagnostic and prognostic methods, and immunological therapies. The CCRI GmbH is the international trial coordinating centre in 3 main areas: ALL stem cell transplantation (ALLSCT FORUM trial), Langerhans cell histiocytosis (LCH IV trial) and high-risk neuroblastoma (HR-NBL1/SIOPEN trial, LTI Trial).

- **Universita' Degli Studi di Milano-Bicocca, Italy**

The University of Milano-Bicocca is a public, state-funded, multidisciplinary academic institution. Research Centres cooperate with public and private third parties, and are managed according to guidelines that guarantee high scientific standards. UNIMIB has a Medical School that offer training in medicine, surgery, public health, and operate in collaboration with the University hospital San Gerardo, both located in Monza. With 900 beds, 20 operating theatres, intensive care units, 50 departments and specialized units, a complete range of diagnostic services and more than 3,000 health care professionals, the hospital is the fourth largest in Lombardy Region. It will cooperate with the high level institutions involved in the project to diffuse technology and experience also among the other health institutions of the area.

UNIMIB intensely promote the translation of research results supporting the technology transfer. The operating structure involved in this project is Department of Medicine and Surgery that will provide the resources and expertise to carry out the project activities. The department has developed extensive expertise in clinical and translational research, with the aim of supporting medical and biotechnological development and technology transfer. Main expertise includes the study of different physio-pathological processes for the development of new diagnostic and therapeutic tools and accelerate the transfer from basic science to clinics in the fields of oncology, immunology,

transplantation, rare diseases. Diagnostic and therapeutic projects benefit from interdisciplinary collaborations.

Expertise: Research, education and training, clinical care, biobanking, biomarker development, bioinformatics, management, Ethical-Legal-Societal-Issues.

- **University Clinic of Schleswig-Holstein, Germany**

The Institute of Clinical Molecular Biology (IKMB) is part of the University Hospital of Schleswig-Holstein (UKSH), which drives interdisciplinary studies on innovative diagnostic and therapeutic principles with clinicians. Therefore, empowering physicians to direct therapies is a key commitment of the Institute. Research in biomedicine should enable new perspectives on disease processes and measurable advances for patients. Translation of the knowledge on genetic causations and markers to clinical decision-making algorithms is at the starting point for clinical use.

The institute employs scientists from different disciplines. An excellent infrastructure has been developed that allows them to choose their tools from a broad range of established cutting-edge technologies. Focusing on inflammatory diseases our approaches range from large-scale genome-wide association studies and whole genome sequencing to mechanistic studies and *in vivo* models.

The IKMB is the coordinating institute for several larger German projects: BMBF Systems Medicine application sysINFLAME (e:Med program, DFG Excellence Cluster Inflammation at Interfaces, DFG PhD Research Training Group "Genes, Environment and Inflammation". The IKMB operates the Centre for Molecular Life Sciences at the CAU that hosts one of Germany's largest academic sequencing (Sanger and NGS) and genotyping platforms. The associated Biobank PopGen covers the Northern part of Germany and is responsible for 20,000 individuals of the German National cohort.

The University Hospital of Schleswig-Holstein (UKSH) operates the second largest German university hospital center, including a comprehensive cancer center consisting of cancer centers that are accredited by OnkoZert together with a Molecular Tumor Board installed in 2018, which builds on extended molecular diagnostics as well as Whole Exome and Transcriptome sequencing. Next-Generation Sequencing based pre-clinical studies have been ongoing for many years between IKMB and most of the UKSH cancer centers. Routine diagnostic next-generation sequencing based testing for breast cancer and ovarian cancer is ongoing since 2016.

- **Centre Leon Berard, France**

The Centre Léon Bérard (CLB) is part of the twenty French Comprehensive Cancer Centers, providing a global management of cancer patients on a unique area, from diagnosis to treatment and beyond.

The Centre is a regional, national and international recognized reference cancer Centre assigned with three essential missions: Care, Research and Education and is willing to continuously improve the quality and accessibility of care for cancer patients. More than 30,000 patients are received each year, on consultations or exams and 6,000 new cancer cases are diagnosed.

The CLB has technical and treatment facilities (operating rooms, radiation therapy center, medical imaging departments, pathology and nuclear medicine departments). The bench-to-bedside process is one of the strength of the Centre Léon Bérard along with the pathology and NGS service. The Centre Léon Bérard develops an excellence and multidisciplinary research, in association with the cares carried out on site and institutional and private partners. The foundations of this development lay in the medical and scientific project. The CLB aims to reinforce the bench-to-bedside process by facilitating translational research to help innovation and speed-up its access to patients for diagnoses and therapies. Biological resource Center has been certified NF-96 900, clinical research has been certified ISO 9001 since 2013 and is thus one of the strength of the Centre. As a result, more than 20% of patients were included in clinical trials in 2016. At the Centre Léon Bérard 1,700 persons work in cares, research, education and supportive care (200 physicians, 500 researchers, 600 caregivers) a work highlighted by the COFRAC certification (number 8-3503). CLB is nationally recognized for its expertise as leader of the AURAGEN initiative (France médecine génomique 2025) specialized in genomics and for its role of reference center within the European Reference Network (ERN) EURACAN Horizon H2020 project (European sarcoma guidelines). Moreover, its participation in the ICGC (International Cancer Genome Consortium) which allowed detailed characterization of about 50 types and subtypes of tumours.

Expertise: Medical care, basic research, translational research, early stage clinical and clinical research, biobanking, therapeutic innovation, bioinformatics, sequencing NGS.

The lead procurer is part of the Buyers group.

2.4 Contracting approach

The PCP will be implemented by means of a **Framework Agreement** and of **Specific Contracts** for each of the 3 R&D phases (altogether 'contracts'). The law governing the contracts is the Austrian law, because the Lead Procurer is based there.

Following the tendering stage, a framework agreement and a specific contract for Phase 1 will be awarded to a minimum of 4 contractors per Lot.

For Phase 2, a minimum of 3 contracts per Lot will be awarded. Only offers from contractors that successfully completed Phase 1 will be eligible for Phase 2 (see details of evaluation in section 3.4).

The offer for Phase 2 is requested at the end of Phase 1 as a deliverable (according to section 2.1.3). The contractors will test in the Phase 2 the performance of their prototypes themselves, i.e., in their labs. A minimum of 2 contracts per Lot will be awarded for Phase 3. Only offers from Contractors that successfully completed Phase 2 will be eligible for Phase 3 (see details of evaluation in section 3.5). The offer of Phase 3 is requested at the end of Phase 2 as a deliverable (according to section 2.1.3). Phase 3 testing in a real-world diagnostic medical environment is expected to take place at a minimum of 2 of the medical sites where the Procurers of the Buyer group are based and optionally at another medical centre in Romania.

Successful completion of the previous phase will be assessed before the evaluation of the offers for the next phase to determine which offers are eligible to proceed to the next phase.

The Framework Agreement will set all the framework conditions for the entire duration of the PCP (covering all the phases). There will be no renegotiation. The Framework Agreement will remain binding for the duration of all phases for which Contractors remain in the PCP. Tenders that are awarded a Framework Agreement will also be awarded a Specific Contract for the Phase 1. Tenderers should not only submit their detailed offer for Phase 1, but also state their goals, and outline their plans *(including price conditions)* for Phases 2 and 3 - thus giving specific details of the steps that would lead to commercial exploitation of the R&D results.

Brief overview of the overall timing of the PCP (including the expected start and finish dates) and of the individual phases:

Phase 0 Publication of tender / submit proposals / signing agreements: 15.10.2021-15.04.2022

Phase 1 Developing solution design by tenderers: 16.04.2022-15.08.2022

Phase 1 Evaluation of Phase 1 and signing Phase 2 contracts: 16.08.2022-15.11.2022

Phase 2 Developing prototypes by tenderers: 16.11.2022-15.01.2024

Phase 2 Evaluation of Phase 2 and signing Phase 3 contracts: 16.01.2024 – 15.04.2024

Phase 3 Developing test products by tenderers: 16.04.2024-15.04.2025

Phase 3 Evaluation of Phase 3 and closing of the PCP: 16.04.2025-31.05.2025

2.5 Total budget and budget distribution (per phase)

A total budget of € 8.554.099,75 excluding VAT is available to fund PCP contracts. All prices and payments will be in Euro. This sum includes a 10% own contribution from the Buyers e.g. for provision

of test material, and for testing solutions for performance, usability and integration into the workflow at the Buyers' sites in Phase 3.

For Phase 1 a maximum budget of ca. 770.000 EUR is available (excluding the 10% Buyers' contribution)

For Phase 2 a maximum budget of ca. 4.620.000 EUR is available (excluding the 10% Buyers' contribution)

For Phase 3 a maximum budget of ca. 2.300.000 EUR is available (excluding the 10% Buyers' contribution).

For Lot 1 and Lot 2, respectively, a maximum budget corresponding to 20% of the total budget per Phase will be available.

For Lot 3 and Lot 4, respectively, a maximum budget corresponding to 30% of the total budget per Phase, will be available.

Maximum budget per Tender per Lot and Phase (excluding the 10% Buyers' contribution)

	Phase 1	Phase 2	Phase 3
Lot 1	€ 38.500.-	€ 308.000.-	€ 230.000.-
Lot 2	€ 38.500.-	€ 308.000.-	€ 230.000.-
Lot 3	€ 57.750.-	€ 462.000.-	€ 345.000.-
Lot 4	€ 57.750.-	€ 462.000.-	€ 345.000.-

Depending on the price offered and the number of tenders passing the evaluation for each Lot, a leftover budget allocated for a specific Lot will be transferred to another Lot(s). In case a tender does not address all technical challenges of a Lot, then it should address scalability of the solution and interoperability with other solutions that are needed to fully address the technical specifications of a Lot.

For Phases 1 and 2, contracts will be financed until the remaining budget is insufficient to fund the next best tender per Lot. The exact number of contracts finally awarded will thus depend on the prices offered and the number of tenders passing the evaluation. As leftover budget from the previous phase of a Lot will be transferred to the next phase, the total budget available for Phases 2 and 3 may eventually be higher than stated here (but the maximum budget per Contractor for Phases 2 and 3 will remain the same). The lower the average price of tenders, the more contracts can be awarded. However, the total value of the contracts awarded per Lot can also be lower than initially expected if

there are fewer tenders than expected that meet the evaluation criteria. In this case the unused budget can be transferred to another Lot or Phase, respectively.

Tenderers may address up to 3 different Lots of the NGS workflow and must submit separate Submission forms (Annexes A-F) for each Lot which will be evaluated and awarded independently.

2.6 Time schedule

All the dates are indicative and they will be confirmed in each Phase. The rights to change are reserved.

Planned time schedule	
Date	**Activity**
	First tender procedure (framework agreement and Phase 1 contracts)
15.10.2021	Publication of contract notice in TED
15.10.2021	Opening of the Request for tenders
6.12.2021	Deadline for submitting questions about tender documents
10.12.2021	Deadline for lead procurer to publish replies to questions (Q&A document)
15.12.2021	Deadline for submission of tenders for the framework agreement and Phase 1
16.02.2022	Tenderers notified of decision on awarding contracts
15.04.2022	Signing of Framework Agreements and Phase 1 specific contracts
15.04.2022	Publication of contract award notice in TED
	Implementation of Phase 1
16.04.2022	Start of Phase 1
16.04.2022	Names of winning Phase 1 Contractors and their project abstracts to be sent to EU (template) and published on the Instand-NGS4P website
15.08.2022	Deadline for Phase 1 final milestone(s)/final report/deliverable(s) (including offer for Phase 2)

15.10.2022	Summary of the results and conclusions achieved by each contractor during the phase sent to EU (template)
16.10.2022	Phase 1 Contractors notified as to whether they have completed this phase satisfactorily and successfully
	Contractors whose performance is considered satisfactory and successful are to submit the final invoice for Phase 1
	Payment of balance for Phase 1 to Contractors that completed this phase satisfactorily
16.10.2022	End of Phase 1
	Second tender procedure
16.10.2022	Contractors notified of decision on awarding Phase 2 contracts
15.11.2022	Signing of Phase 2 specific contracts
	Implementation Phase 2
16.11.2022	Start of Phase 2
16.11.2022	Names of winning Phase 2 Contractors and their project abstracts to be sent to EU (template) and published on Instand-NGS4P website
15.06.2023	Deadline for Phase 2 interim milestone(s)/deliverable(s)
	Interim payments (if applicable)
15.01.2024	Deadline for submission of Phase 2 final milestone(s)/final report /deliverable(s) (including offer for Phase 3)
15.03.2024	Assessment of Phase 2 final milestone(s)/final report/deliverable(s)
16.03.2024	Phase 2 Contractors notified as to whether they have completed this phase satisfactorily and successfully
16.03.2024	Summary of the results and conclusions achieved by each contractor during the phase sent to EU (template)

	Payment of balance for Phase 2 to Contractors that completed this phase satisfactorily
16.03.2024	End of Phase 2
	Third tender procedure
16.03.2024	Contractors notified of decision to award Phase 3 contracts
15.04.2024	Signing of Phase 3 specific contracts
	Implementation Phase 3
16.04.2024	Start of Phase 3
16.04.2024	Names of winning Phase 3 Contractors and their project abstracts to be sent to EU (template) and published on Instand-NGS4P website
15.10.2024	Deadline for Phase 3 interim milestone(s)/deliverable(s)
	Interim payments (if applicable)
15.04.2025	Deadline for submission of Phase 3 final milestone(s)/final report/ deliverable(s)
15.04.2025	Final demonstration of products/services developed during Phase 3 *(including to EU representatives)*
15.05.2025	Assessment of Phase 3 final milestone(s)/final report/deliverable(s)
16.05.2025	Phase 3 contractors notified as to whether they have completed this phase satisfactorily and successfully
16.05.2025	Summary of the results and conclusions achieved by each contractor during the PCP sent to EU for publication purposes (template).
	Payment of balance for Phase 3 to Contractors that completed this phase satisfactorily
31.05.2025	End of Phase 3

2.7 IPR issues

2.7.1 Ownership of results (foreground)

Each Contractor will keep ownership of the IPRs attached to the results they generate during the PCP implementation. The tendered price is expected to take this into account.

The ownership of the IPRs will be subject to the following:

- the Buyers group has the right to:
  - access Results, on a royalty-free basis, for their own use
  - grant (or to require the Contractors to grant) non-exclusive licences to third parties to exploit the results under fair and reasonable conditions (without the right to sub-license)
- the Buyers group has the right to require the Contractors to transfer ownership of the IPRs if the Contractors fail to comply with their obligation to commercially exploit the results *(see below)* or use the Results to the detriment of the public interest *(including security interests)*.

2.7.2 Commercial exploitation of results

The Contractor shall, within five (5) years after the end of the Framework Agreement, take measures to ensure that the Results are exploited commercially (directly or indirectly, in particular through licensing). The Contractor will report on request of the Lead Procurer about the progress on the commercial exploitation of the Results during the 5-year period aforementioned (max. twice per year). The Contractor may grant non-exclusive licenses to third parties to exploit the Results to the extent that such licenses do not affect the Procurers' access rights related to such Results.

If the Contractor fails to commercially exploit the Results within this period, or uses the Results to the detriment of the public interest, the Contractor shall at Lead Procurer's request, transfer the ownership of the Results to the Procurers free of costs or sub-licenses IPRs to third parties indicated by the Lead Procurer.

'Failure to commercially exploit Results' means not marketing a commercial application of the Results (directly or indirectly, through a subcontractor or licensee).

The Contractors have to make a reliable plan to secure access for the Buyers Group to the solutions resulting from the R&D Services provided within the Instand-NGS4P PCP. It should be guarantee that the Buyers Group can continue to benefit from the solutions after the project has ended. Contractors are expected to protect their Intellectual Property and commercially exploit the results of the R&D Services undertaken in the PCP within a period of five years after the end of the Framework Agreement.

The Buyers Group invites Suppliers to explore several innovative approaches and propose them with a future proof business model and commercialization plan.

The business and commercialization plan should explain the proposed approach to commercially exploit the Results of the PCP and to bring viable products or services to market.

Contractors have to consider dedicated activities beyond product development to commercially exploit the Results, e.g. certification (CE marking according to IVDR) of solutions or contribution to standardization.

The feasibility of the business plan to commercially exploit the Results will be assessed as part of the award criteria. Furthermore, the commercialization plan will be part of the End-of-Phase reports of all three phases, as well as of the offers for Phases 2 and 3.

In addition to the activities for the commercialization implemented by the Contractors, the Instand-NGS4P Buyers Group will promote the Results through a dissemination activity via associated organizations (e.g., OECI, ERN PAEDCAN, ERN EURACAN) and will provide connections to leading European hospitals and other related organisations. A list of partnering centres is available on Instand-NGS4P website.

The Buyers Group will help to develop a working market for the developed solutions in order to ensure their usability and sustainability at a more global scale.

The Buyers Group will also organize a final event where the developed solutions will be presented.

2.7.3 Declaration of pre-existing rights (background)

The ownership of pre-existing rights will remain unchanged.

In order to be able to distinguish clearly between Results and pre-existing rights (and to establish which pre-existing rights are held by whom):

- Tenderers are requested to list the pre-existing rights for their proposed solution in their offers
- and they will be requested to establish a list of pre-existing rights to be used before the start of the contract.

The Buyers (see 2.3) providing in-kind contributions to the PCP do not hold any pre-existing rights relevant to the PCP contracts. The description of in-kind contributions provided by the Buyers is reported in 2.1.1 and in Tables 1 and 2.

3. Evaluation of tenders

3.1 Eligible tenderers, joint tenders and subcontracting

Participation in the tendering procedure is **open** on equal terms to **all types of operators from any country,** regardless of their geographic location, size or governance structure.

Tenders may be submitted by a **single entity** or in collaboration with others. The latter can involve either submitting a **joint tender** or subcontracting, or a combination of the 2 approaches.

Joint tenders:

Joint tenders, consisting of a combination of companies or public institutions (Consortium), can participate as one Tender. This combination can also include Third Parties (Subcontractors). Consortia can participate in this PCP tender procedure, providing that their participation is in accordance with the principles of EU and applicable national competition law. The following requirements apply for joint tenders:

● The members of a Consortium must jointly appoint a lead contractor and a party authorized to act in the name and on their behalf;

● All members of the Consortium are individually tested against the Exclusion Criteria.

● The members of the Consortium must jointly meet the Selection Criteria.

● All members of the Consortium must accept joint and several liability by completing and adding General Form Annex A - Statement of Consortium;

●Each member of the Consortium must be listed in the professional register or trade register or a foreign equivalent in accordance with the legislation in force in the country where it is established.

Subcontracting:

A Subcontractor is a third party which entered into an agreement on business conditions with one or more beneficiaries, in order to carry out part of the work of the project without the direct supervision of the beneficiary and without a relationship of subordination.

In the General Tender Form it shall be stated by the tenderer which part of the Instand-NGS4P PCP sub-challenge, if any, is intended to be subcontracted to other entities. The assignment of tasks to Subcontractors has to be declared in advance to the Procurers and needs the approval of the Procurers. The execution of tasks assigned to a Subcontractor may not be the subject of further subcontracting.

A tenderer that wishes to rely on the resources of any Subcontractor for the fulfilment of the requirements for participation in the PCP (and, where, applicable, an awarded contract), should demonstrate that these resources will be available to him. One way of demonstrating this is to submit a written commitment, a template to be signed by the subcontracting- party, showing that the resources required of the Subcontractor will be at the tenderers disposal for the full duration of the Contract.

If the tenderer needs to change Subcontractor, these new partners will have to prove that they have at least the same competences as the Subcontractor or consortium partners they will replace and that

they comply with all the applicable contractual conditions that are in the Framework Agreement and specific contracts: e.g. complying with the place of performance conditions, respecting the same IPR conditions. The Contractor has the responsibility to ensure that all contractual conditions that are in the Framework Agreement and specific contracts are fulfilled by the Sub –contractor.

The Contractor will allow the European Commission, the European Court of Auditors (ECA) and the European Anti-fraud Office (OLAF) to exercise their rights under Articles 22 and 23 Grant Agreement (mutatis mutandis) and will comply with Articles 17.1, 18, 34, 35, 37, 36, 38, 39 and 46 Grant Agreement (mutatis mutandis) (see the website for further information on the Grant Agreement clauses)

The Contractor will ensure that in all subcontracts the conditions from the Grant Agreement set out in the above clauses are imposed upon the Subcontractor.

A third party may replace a Contractor or a member of the Contractor in case of a consortium as a result of universal succession in the position of the Contractor following corporate restructuring, including takeover, merger, acquisition or in an Insolvency Event, provided that said third party meets all exclusion, selection, compliance and minimal technical criteria and the succession does not entail a substantial modification.

⚠ **Attention:**

There will, however, be a requirement relating to the place of performance of the R&D services *(see below)*.

For Phases 2 and 3, participation is limited to Contractors that successfully have completed the preceding phase.

EVALUATION CRITERIA- Overview

The process to award the Framework Agreements and the Specific Contracts is based on the following criteria:

- The exclusion criteria: evaluate the individual situation of a Tenderer;
- The selection criteria: determine whether a Tenderer has the financial, technical and professional capacity necessary to carry out and perform the work;
- The compliance criteria: evaluate if the submitted Tender is compliant with the principles of PCP, public financing, place of performance, research integrity and security;
- The award criteria: award contracts to the best-ranked Tenders that have addressed at least the Minimum Requirements.

3.2 Exclusion criteria

The exclusion criteria are as follows:

Exclusion criteria	Evidence
A) Conflict of Interest	A) a declaration of honour for 'absence of conflict of interest'- Annex D
B) Bankruptcy	B) a declaration of absence of bankruptcy - Annex D
c) Criminal offences	c) a declaration of absence of criminal offences - Annex D

Tenderers that do not comply with these criteria will be excluded.

A) Conflict of interest

Tenderers that are subject to a conflict of interest may be excluded. If there is a potential conflict of interest, Tenderers must immediately notify the lead Procurer in writing.

A conflict of interest covers both personal and professional conflicts.

Personal conflicts are any situation where the impartial and objective evaluation of Tenders and/or implementation of the Contract is compromised for reasons relating to economic interests, political or national affinity, family, personal life *(e.g. family of emotional ties)* or any other shared interest.

Professional conflicts are any situation in which the Contractor's (previous or ongoing) professional activities affect the impartial and objective evaluation of tenders and/or implementation of the contract.

⚠ **Attention:** If an actual or potential conflict of interest arises at a later stage *(i.e. during the implementation of the contract)*, the Contractor must contact the Lead Procurer, who is required to notify the EU and to take steps to rectify the situation. The EU may verify the measures taken and require additional information to be provided and/or further measures to be taken.

B) Bankruptcy

A tenderer or contractor can be excluded from further participation in the PCP if it or any Sub-Tenderer on whose resources it relies upon in this procurement:

● Is bankrupt or is being wound up, is under compulsory administration or is the subject of a composition or has indefinitely stopped its payments or is subject to a prohibition on conducting business.

● Is the subject of proceedings for a declaration of bankruptcy, for an order for compulsory winding up or administration by the court or composition or any other similar proceedings.

● Has been convicted by a judgment which has the force of res judicata for an offence relating to professional practice. Has been guilty of grave professional misconduct and the procuring agencies can prove this.

● Has not fulfilled its obligations relating to social insurance charges or tax in its own country.

● In some material respect has failed to provide information requested or provided incorrect information required pursuant to this Request for Tenders document.

Tenderers must confirm by signing the Declaration in Annex 4, the Tender Form, that they are not subject to one of the above mentioned situations.

Attention: Should there be any doubt as to any of these criteria, tenderers may be requested to provide additional information such as an extract of the local chamber of commerce.

C) Criminal offences

If the Procurers becomes aware that a tenderer, or a representative of the tenderer, or Sub-Tenderer, under a judgment that has entered into final legal force has been sentenced for a criminal offence listed below, such tenderer can be excluded from the PCP. Tenderers must confirm by signing the Declaration in Annex 4, Tender Form that they are not subject to any of the criminal offences indicated below:

Participation in a criminal organization; this includes the following conduct:

Conduct by any person who, with intent and with knowledge of either the aim and general criminal activity of the organization or the intention of the organization to commit the offences in question, actively takes part in:

• Activities of a criminal organization, which shall be taken to mean a structured association, established over a period of time, of more than two persons, acting in concert with a view to committing offences which are punishable by deprivation of liberty or a detention order of a maximum of at least four years or by a more serious penalty, whether such offences are an end in themselves or a means of obtaining material benefits and, where appropriate, of improperly influencing the operation of public authorities, even where that person does not take part in the actual execution of the offences concerned and, subject to the general principles of the criminal law of the Member State concerned, even where the offences concerned are not actually committed;

• The organization's other activities in the further knowledge that its participation will contribute to the achievement of the above-mentioned criminal activities of the organization;

• Conduct by any person consisting in an agreement with one or more persons that an activity should be pursued which, if carried out, would amount to the commission of an offence as mentioned above, even if that person does not take part in the actual execution of the activity;

• Corruption; corruption shall be taken to mean deliberately promising or giving, directly or through an intermediary, an advantage of any kind whatsoever to an official, for himself or for a third party for him to act or refrain from acting in accordance with his duty or in the exercise of his functions in breach of his official duties; or in the private sector, directly or through an intermediary, deliberately promising, offering or giving an undue advantage of any kind whatsoever, for himself or for a third party, in the course of business activities of that person in order that the person should perform or refrain from performing an act, in breach of his duties;

• Fraud; fraud meaning both expenditure fraud and revenue fraud. This means any act or deliberate omission involving the use or presentation of false, incorrect or incomplete statements or documents which has as its effect the misappropriation or wrongful retention of funds from, or the illegal diminution of the resources of the general budget of the European Communities or budgets managed by, or on behalf of, the European Communities, non-disclosure of information in violation of a specific obligation, with the same effect, the misapplication if such funds for the purpose other than those for which they were originally granted or the misapplication of a legally obtained benefit with the same effect;

• Money laundering, which shall be taken to mean:

o The conversion or transfer of property, knowing that such property is derived from criminal activity or from an act of participation in such activity, for the purpose of concealing or disguising the illicit origin of the property or of assisting any person who is involved in the commission of such activity to evade the legal consequences of his actions;

o The concealment or disguise of the true nature, source, location, disposition, movement, rights with respect to, or ownership of property, knowing that such property is derived from criminal activity or from an act of participation in such activity;

o The acquisition, possession or use of property, knowing, at the time of receipt, that such property was derived from criminal activity or from an act of participation in such activity;

o Participation in, association to commit, attempts to commit and aiding, abetting, facilitating and counselling the commission of any of the actions mentioned in the foregoing three paragraphs;

The exclusion criteria will remain unchanged for the entire duration of the PCP, thus applying also for for the Phases 2 and 3.

3.3 Selection criteria

Selection criteria are used to determine if a Tenderer has the financial, economic, technical and professional capacity necessary to carry out and perform the R&D Services.

These selection criteria will be evaluated on a pass/fail basis: "fail" means that the evidence given does not provide sufficient indication of the Tenderer's expertise, ability and/or equipment to meet the project's objectives. The selection criteria will remain unchanged for the entire duration of the PCP, thus applying also for the Phases 2 and 3.

Tenderers that do not comply with these criteria will be excluded.

The selection criteria are as follows:

Selection criteria	**Evidence**
A) Ability to perform R&D Services up to original development of the first products or services and to commercially exploit the Results of the PCP, *including intangible results in particular IPRs*	Description of the capacity, materials and equipment that are available to the tenderer for research, prototyping and limited production and supply of the first set of products or services. Description of the financial and organisational structures that are available to the tenderer for management, exploitation of IPRs and for generating revenue by marketing commercial applications of the results- Annex E

A) Ability to perform R&D Services up to original development of the first products or services and to commercially exploit the Results of the PCP, including intangible results in particular IPRs

Tenderers must have:

- the capacity, tools, material and equipment to:
  - carry out research and produce prototypes
  - produce and supply a limited set of first products or services and demonstrate that these products or services are suitable for production or supply in quantity and to quality standards defined by the Procurers
- the financial and organisational structures to
  - manage, exploit and transfer or sell the Results of the PCP *(including tangible and intangible results, such as new product designs and IPRs)*

- generate revenue by marketing commercial applications of the Results *(directly or through subcontractors or licensees)*.

Attention: Should there be any doubt as to any of these criteria, tenderers may be requested to provide additional information.

3.4 Award criteria

The award criteria are comprised of

- On/off (compliance) award criteria
- Minimum requirements
- Weighted award criteria

3.4.1 On/off (compliance) award criteria

The compliance criteria are used to determine whether the Tender is compliant with the principles of PCP, public financing, place of performance, research integrity and security. These compliance criteria will be evaluated on a pass/fail basis.

Tenderers must comply with all of the following on/off award or compliance criteria (also applied to Phases 2 and 3). Suppliers that do not comply with these criteria will be excluded.

On/off award criteria	**Evidence**
A) Compliance with the definition of R&D services	Declaration of compliance with the definition of R&D services-Annex F
B) Compatibility with other public financing	Declaration (absence of other incompatible public financing) as part of annex-Annex F
C) Compliance with the requirements regarding the place of performance of the contract	Declaration (compliant with performing at least 50% of the R&D activities in EU member states or H2020 associated countries-Annex F
D) Compliance with ethics requirements	If the tender involves activities that raise ethical issues, the tenderer must submit an ethics self-assessment-Annex F
E) Compliance with security requirements	If the output of activities or results proposed in the tender raise security issues or uses EU-classified information, the tenderer must show that these issues are being handled correctly. Annex F

A) Compliance with the definition of R&D services

This contract is an R&D services contract, which entails that the value of the R&D services should be more than 50%.

Tenders that go beyond the provision of R&D services will be excluded.

R&D Services covers fundamental research, industrial research and experimental development, as per the definition given in the EU R&D&I state aid framework[6]. It may include exploration and design of solutions and prototyping up to the original development of a limited volume of first products or services in the form of a test series. Original development of a first product or service may include limited production or supply in order to incorporate the results of field-testing and to demonstrate that the product or service is suitable for production or supply in quantity to acceptable quality standards.[7] R&D Services does not include quantity production or supply to establish commercial viability or to recover R&D costs. It also excludes commercial development activities such as incremental adaptations or routine or periodic changes to existing products, services, production lines, processes or other operations in progress, even if such changes may constitute improvements. The purchase of commercial volumes of products or services is not permitted.

The definition of R&D Services means that the value of the total amount of products covered by the contract must be less than 50 % of the total value of the PCP Framework Agreement.

The following evidence is required:

6 See Point 15 of the Commission Communication on a framework for state aid for research and development and innovation (C(2014) 3282).

7 See Article XV(1)(e) WTO GPA 1994 and the Article XIII(1)(f) of the revised WTO GPA 2014.

- the financial part of the offer for the framework agreement must provide binding unit prices for all foreseeable items for the duration of the whole framework agreement
- the financial part of the offer for each phase must give a breakdown of the price for that phase in terms of units and unit prices for every type of item in the contract, distinguishing clearly the units and unit prices for items that concern products
- the offers for all 3 phases may include only items needed to address the challenge in question and to deliver the R&D services described in the request for tenders
- the offers for all 3 phases must offer services For more than 50% of the contract value matching the R&D definition above
- the total value of products offered in Phase 1 matches the allocated budget for each Phase and Lot.

B) Compatibility with other public financing

Tenders that receive public funding from other sources will be excluded if this leads to double public financing or an accumulation of different types of public financing that is not permitted by EU legislation, *including EU state aid rules*. Tenderers shall - for each of the PCP phases - sign a declaration of honour stating the 'absence of other incompatible public financing'.

C) Compliance with requirements relating to the place of performance of the contract

Tenders will be excluded if they do not meet the following requirements relating to the place of performance of the contract:

- at least 50% of the total value of activities covered by each specific contract for PCP Phase 1 and 2 must be performed in the EU Member States or in H2020 associated countries. The key R&D staff working on each specific contract must be located in the EU Member States or H2020 associated countries.
- at least 50% of the total value of activities covered by the framework agreement *(i.e. the total value of the activities covered by Phase 1 + the total value of the activities covered by Phase 2 + the total value of the activities covered by Phase 3)* must be performed in the EU Member States or H2020 associated countries. The key R&D staff working on the PCP must be located in the EU Member States or H2020 associated countries.

The percentage is calculated as the part of the total monetary value of the contract that is allocated to activities performed in the EU Member States or in other countries associated to Horizon 2020. All activities covered by the contract are included in the calculation *(i.e. all R&D and operational activities that are needed to perform the R&D Services, e.g. research, development, testing and certifying*

solutions). This includes all activities performed under the Contract by Contractors and, if applicable, their Subcontractors.

The key R&D staff are the main researchers, developers and testers responsible for leading the R&D Service covered by the contract.

The countries associated to Horizon 2020 are those listed as associated countries in the Funding & Tenders Portal Online Manual[8].

The following evidence is required:

- the financial part of the offer must provide binding unit prices for all foreseeable items for the duration of the whole Framework Agreement and give a breakdown of the price for the current phase in terms of units and unit prices *(hours and unit price per hour)*, for every type of item in the contract *(e.g. junior and senior researchers);*
- a list of staff working on the Specific Contract *(including for subcontractors)*, indicating clearly their role in performing the Contract *(i.e. whether they are principal R&D staff or not)* and the location *(country)* where they will carry out their tasks under the Contract;
- a confirmation or declaration of honour that, where certain activities forming part of the contract are subcontracted, Subcontractors will be required to comply with the place of performance obligation to ensure that the minimum percentage of the total amount of activities that has to be performed in the EU Member States or in countries participating in Horizon 2020 is respected.
-

D) Ethics and research integrity

Tenders will be excluded if they:

- do not comply with the following rules:
  - ethical principles *(including the highest standards of research integrity, notably as set out in the European Code of Conduct for Research Integrity[9], and, in particular, avoiding fabrication, falsification, plagiarism and other research misconduct)*
  - applicable international, EU and national law
- include activities that do not focus exclusively on civil applications
- do not comply with the following ethics requirements:
  - Attempting re-identification: the re-identification of patient's samples based on genetic sequencing results or data sequencing generated by the analysis of test samples provided by the procurers is not allowed.

8 List of H2020 associated countries.

9 The European Code of Conduct for Research Integrity of ALLEA (All European Academies).

- The distribution of test samples to third parties to third parties not specified in the tender documents.

If the Tender involves activities that raise ethical issues, the tenderer must submit an ethics self-assessment that:

- describes how the Tender meets the legal and ethical requirements of the country or countries where the tasks raising ethical issues are to be carried out;
- explains in detail how the Tenderer intends to address the ethical issues identified, in particular as regards:
  - objectives *(e.g. dealing with vulnerable populations and dual-use goods[10])*
  - methodology *(e.g. involvement of children and related consent procedure and protection of data collected)*
  - the potential impact *(e.g. issues relating to the dual use of goods, environmental damage, stigmatisation of particular social groups, political or financial retaliation, benefit-sharing and malevolent use of results)*.

 For information on ethics issues, *see the guidance for EU grant beneficiaries How to complete your ethics self-assessment*.

⚠ **Attention:**

Before starting the particular task that raises ethical issues, contractors must provide a copy of:

- any ethics committee opinion required under national law; and
- any notification or authorisation for activities raising ethical issues required under national law.

The Framework Agreement contains a provision on ethics.

E) Security

Instand-NGS4P project will not involve activities or results raising security issues, nor will it involve 'EU classified information' as background or results.

Tenders will be excluded if they do not:

- comply with:
  - EU, national and international law on dual-use goods or dangerous materials and substances;
  - comply with data protection requirements as provided under the GDPR.

Tenders themselves must not contain any classified information.

10 See Article 2(1) EU Export Control Regulation No 428/2009.

If the output of R&D Services or Results proposed in the Tender raise security issues or uses EU-classified information, the Tenderer must show that these issues are being handled correctly. In such a case, Tenderers are required to ensure and to provide evidence of the adequate clearance of all relevant facilities. They must examine any issues (*such as those relating to access to classified information or export or transfer control*) with the national authorities before submitting their offer. Tenders must include a draft security classification guide (SCG), indicating the expected levels of security classification.

⚠ **Attention:**

If necessary for the tender procedure or for performing the Contract itself, Contractors will be requested to ensure appropriate security clearance for third parties *(e.g. for personnel)*.

Offers for Phases 2 and 3 may request that this security information be updated in the offers submitted for that phase.

Before starting the particular task that raises security issues, Contractors must provide a copy of any export or transfer licences required under EU, national or international law.

The Framework Agreement contains provisions on security.

For information on security, *see the guidance for EU grant beneficiaries: Guidelines for the handling of classified information in EU research projects*.

⚠ **Attention:** Should there be any doubt as to any of these criteria, Tenderers may be requested to provide additional information.

3.4.2. Minimum Requirements

The aim of the INSTAND-NGS4P PCP Project is to improve cancer patients' benefit from Next Generation Sequencing (NGS) by developing an integrated and standardized NGS workflow and integrating information from cancer gene testing, pharmacogenomics testing and e-medication in proper presentation to medical doctors for supporting therapy decision-making at bedside.

Considering the fast development of the field, the Buyers' group will take into consideration only proposals that can address at least, but are not limited to, the analysis of the following two groups of molecular alterations:

a) **Actionable variant genes and variant types of tumour entities listed in Table 1**
b) **Gene variants relevant for pharmacogenomics (Table 2)**

The proposals for each Lot should be planned in such a way that the integrated and standardized NGS workflow can reach these goals. Solutions shall be designed to demonstrate the capability of meeting these requirements in Phase 1, and the performance shall be shown in Phase 2 and verified by the Buyers in Phase 3.

a) Minimum requirements for the analysis of tumour specimens of common and rare cancers and provision of samples for performance testing.

NGS pre-sequencing (Lot 1), sequencing (Lot 2), bioinformatics analysis (Lot 3) and integrated reporting (Lot 4) should cover all **actionable variant types and genes in the tumour entities listed in Table 1** below, for at least one of the sample types (i.e., cryoconserved tissue, FFPE tissue, PAXGene tissue, stabilized blood for ccfDNA).

The analytical performance of the solutions on the variant and sample types shall be shown in Phase 2. For performance testing in Phase 2, the Buyers group will provide test samples of the tumour entities and sample types listed below. These samples will be generated according to the relevant international standards. Details regarding test sample provision by the Buyers will be defined with the Contractors upon entering Phase 2 and will depend on specific needs according to the R&D Service. The test samples from the different tumour types will cover all types of genetic variants (SNVs, CNVs, fusion genes, small indels, aberrant expression, etc) but it cannot be guaranteed that every sample contains all listed variants (Table 1).

For independent performance testing of Lot 2 libraries may be provided for major sequencing platforms. For independent performance testing of Lot 3, genomic sequences may be provided. For performance testing of Lot 4 test data from bioinformatics pipelines in gVCF file format as well as test clinical data may be provided.

In order to ensure standardized quality, relevant standards have to be considered and quality control for metrological traceability has to be established for Lots 1, 2 and 3). Standard data formats have to be used in order to allow integration of solutions developed within the R&D Services into the workflow. Integration will be tested by the Buyers in Phase 3.

Table 1. Tumour entities, sample types, actionable variant genes and variant types. Molecular alterations shown are approved as "required" or "actionable" by recognized International organizations.

Tumour Entity	Sample types	Typical Variant Types	Genes
Adult cancers			

lung cancer	cryoconserved	SNV, fusion,	BRAF, EGFR, ALK, ROS1, MET, RET, ERBB2, KRAS, NRAS, PIK3CA
	FFPE		
	PFPE		
	Plasma from EDTA, PAXgene ccfDNA or Streck BCT ccfDNA blood collection tubes	SNV	BRAF, EGFR, KRAS, NRAS
ovarian cancer	cryoconserved	microsatellite instability, aberrant expression, SNV	PIK3CA, KRAS. BRAF, BRCA1/2
	FFPE		
	PFPE		
	PAXGene ccfDNA plasma		
soft tissue sarcoma	cryoconserved	fusion	ALK, NTRK1, ROS1
	FFPE		
	PFPE		
	PAXGene ccfDNA plasma		
lymphomas (ALL, lymphoplasmocytic lymphoma, hairy cell leukemia, follicular lymphoma)	White blood cells / DNA (cryoconserved)	SNVs, BCR/ABL minor brkpt. IGH/BCL2 rearrangement	BCR, ABL1, BRAF
	FFPE (few sections/case)		
Paediatric Cancers			
AML	cryoconserved	Fusion	CBFB-MYH11, RUNX1-RUNX1T1
		SNV/small indel	GATA1
		ITD (quantitative detection), SNV/small indel	FLT3
B-ALL	cryoconserved	Fusion	KMT2A-AFF1, KMT2A (other fusions), TCF3-PBX1, ETV6-RUNX1, IGH-DUX4
		CNV	CDKN2A, CDKN2B, PAX5, IKZF1, ERG
		Fusion, CNV	PAR1/P2RY8-CRLF2
T-ALL/T-LBL	cryoconserved	SNV/small indel	NOTCH1
APL	cryoconserved	Fusion	PML-RARA
Neuroblastoma	frozen, extracted DNA	SNV/small indel, CNV	ALK
		CNV	MYCN
		CNV	genome-wide copy number (1 MB resolution) for segmental and numerical chromosomal aberrations

Note: It is not mandatory to show the analytical performance for all individual variants per sample type/gene. However, at least the analytical performance for all types of genetic variants shall be shown.

b) Minimum requirements for pharmacogenomics and provision of samples for performance testing.

NGS pre-sequencing (Lot 1), sequencing (Lot 2), bioinformatics analysis (Lot 3) and integrated reporting (Lot 4) should cover relevant **pharmacogenomics variants of the genes listed in Table 2** below. NGS analysis for pharmacogenomics (PGx) testing should focus on the genes and variants that are labelled as 'Actionable' "Testing required" or "Testing recommended" as listed in PharmGKB.

In case a Tenderer cannot provide solutions for pharmacogenomics within the period of this PCP a clear concept has to be provided how the solution is scalable to address pharmacogenomics in the future since this is a major user need.

Table 2. Minimal requirements for PGx: relevant genes, evidence (as listed in PharmGKB) and corresponding drugs

Gene	Evidence	Drug
NUDT15	Testing recommended	mercaptopurine
UGT1A1	Actionable PGx	irinotecan, erlotinib, belinostat, nilotinib,
CYP2D6	Testing required	tamoxifen, gefitinib
CYP2C9	Actionable PGx	erdafitinib
TPMT	Testing recommended	thioguanin, mercaptopurine
DPYD	Testing required	fluorouracil, capecitabine (actionable PGx)
HLA-B (HLAB*57.01)	Actionable PGx	pazopanib
G6PD	Testing required	rasburicase

For performance testing of PGx, the Buyers group will provide samples of whole blood or isolated genomic DNA. Details regarding sample provision by the Buyers will be defined with the Contractors upon entering Phase 2 and will depend on specific needs according to the R&D Services. The samples will cover all types of variants but it cannot be guaranteed that every sample contains all variants.

3.4.3 Weighted Award Criteria

Tables 3 to 6 list the following criteria per Phase for Lots 1, 2, 3 and 4 respectively:

A) Technical quality criteria

B) Feasibility

C) Price

Each table is followed by a description of the elements for the evaluation related to each criterion.

TABLE 3: WEIGHTED AWARD CRITERIA FOR LOT 1: PRE-SEQUENCING

Admission to Phase 1-SOLUTION DESIGN; assessment based on the solutions proposal			
A) Technical quality criteria Evaluation based on how ***users' needs are addressed, level of innovation***			
	Maximum points	**Thresholds**	**Weighting %**
A1) Sample stabilization	0-5		100
A2) Nucleic acids extraction	0-5		100
A3) Quality control for NA extraction	0-5		100
A4) Library preparation	0-5		100
A5) Quality control for library preparation	0-5		100
B) Feasibility			
B1) How realistic the technical development of the solution is (clear plan for the	0-5		100

development/implementation of the solution and for finishing Phase 3 on time)			
B2) Commercial feasibility of the solution (commercialization plan/route to market)	0-5		100
B3) Crucial risks (technical, commercial, others…) are identified and countermeasures have been identified	0-5		100
B4) Composition of the project team	0-5		100
C1) Prices	0-5		200
TOTAL POINTS	0-55		
Admission to Phase 2-PROTOTYPING; assessment based on the evaluation of the solution design developed in Phase 1 and on the offer for Phase 2			
A) Technical quality criteria Evaluation based on expected ***Analytical Performance including Metrological Traceability.***			
	Maximum points	**Thresholds**	**Weighting %**
A6) Solution design developed in Phase 1	0-5	3	200
A7) Sample stabilization	0-5		100
A8) Nucleic acids extraction	0-5		100
A9) Quality control for NA extraction	0-5		100
A10) Library preparation	0-5		100
A11) inclusion of Quality control for library preparation	0-5		100
B) Feasibility			
B5) How realistic the technical development of the solution is (clear plan for the development/implementation of the solution and for finishing Phase 3 on time)	0-5		100
B6) Commercial feasibility of the solution	0-5		100

(commercialization plan/route to market)			
B7) Crucial risks (technical, commercial, others…) are identified and countermeasures have been identified	0-5		100
B8) Composition of the project team	0-5		100
C2) Price	0-5		200
TOTAL POINTS	0-65		
Admission to Phase 3-DEVELOPMENT AND TESTING; assessment based on evaluation of the prototype developed in Phase 2 and on the offer for Phase 3			
A) Technical quality criteria Evaluation based on ***Analytical Performance verified by Buyers, Usability, Standardization, Integration into complete workflow***			
	Maximum points	**Thresholds**	**Weighting %**
A12) Report on results from Phase 2	0-5	3	200
A13) Sample stabilization	0-5		100
A14) Nucleic acids	0-5		100
A15) Quality control for NA extraction	0-5		100
A16) Quality control for library preparation	0-5		100
A17) Quality of the report on results from Phase 2 on quality control of library preparation	0-5		100
B) Feasibility			
B9) How realistic the technical development of the solution is (clear plan for the development/implementation of the solution and for finishing Phase 3 in time)	0-5		100
B10) Commercial feasibility of the solution (commercialization plan/route to market)	0-5		100
B11) Crucial risks (technical, commercial,	0-5		100

others…) are identified and countermeasures have been identified			
B12) Composition of the project team	0-5		100
C3) Price	0-5		200
TOTAL POINTS	0-65		

Specific elements for the evaluation related to each criterion are listed below.

A1) SAMPLE STABILIZATION Principle of the stabilization procedure/reagents (e.g., including fixative or not), sample stability (e.g., duration, simultaneous stability of multiple analytes, analyte quality e.g., DNA/RNA integrity); avoidance of chemical modifications, sample transport conditions; stability of the stabilizer/preservative; minimal toxicity and/or carcinogenic profile, addressing regulatory requirements for IVDs and refer to international standards (e.g., ISO/CEN standards).

How the proposal addresses users' needs, the progress beyond the state of the art (level of innovation), the feasibility and the value for money.

A2) NUCLEIC ACIDS EXTRACTION

Principle of the isolation/extraction procedure/reagents; expected target yield and concentration; expected quality of the isolated analyte (e.g., high molecular weight DNA for gDNA, low molecular weight DNA for cfDNA); approach to automation (fully, partially or manual); number of steps/run time; compatibility of the isolation/extraction method with multiple targets and applications, sample quantity needed; presence of interfering substance with the analytical test procedure; stability of the reagents; scalability; quality assessment of the isolated analyte; addressing regulatory requirements for IVDs and refer to international standards.

A3) QUALITY CONTROL for NUCLEIC ACID EXTRACTION

Description of the materials/procedures to be developed for the internal controls (e.g., extraction controls); design of reference material for QC (metrological traceability) related to sample stabilization and extraction; addressing regulatory requirements for IVDs and compliance with international standards.

A4) LIBRARY PREPARATION

Expected efficiency of the library preparation (success rate in relation to the type of sample, including low abundant samples); type of the proposed approach: WGS/WES vs target panel; adapter ligation efficacy; automation; number of steps/run time, direct or long range; library yield; target quantity needed, including UMI; compatibility of the library isolation method with multiple target and applications, compatibility with analytical test procedure; stability of the reagents, scalability; quality

assessment of the library; addressing regulatory requirements for IVDs and compliance with international standards.

A5) QUALITY CONTROL for LIBRARY PREPARATION

Availability of internal controls, development of reference material for QC related to library preparation; addressing regulatory requirements for IVDs and refer to international standards.

B1) HOW REALISTIC THE TECHNICAL DEVELOPMENT OF THE SOLUTION IS (CLEAR PLAN FOR THE DEVELOPMENT/IMPLEMENTATION OF THE SOLUTION AND FOR FINISH PHASE 3 ON TIME)

Feasibility of the Project plan and schedule, including methodology.

B2) COMMERCIAL FEASIBILITY OF THE SOLUTION (COMMERCIALIZATION PLAN/ROUTE TO MARKET)

Completeness, sense of reality and feasibility of the commercialisation plan including the market analysis and risk management. Sense of reality and feasibility of the principles for licensing, pricing, distribution.

B3) CRUCIAL RISKS (TECHNICAL, COMMERCIAL, OTHERS…) ARE IDENTIFIED AND COUNTERMEASURES HAVE BEEN IDENTIFIED

The extent to which crucial risks (technical, commercial and others) to project success are identified, and how effectively these will be managed during this phase. Preferably to be summarized in a risk management table, including risk mitigation solutions.

B4) COMPOSITION OF THE PROJECT TEAM

The extent to which the Tenderer and/or Subcontractor shows readiness, or demonstrates to be able to dedicate the resources (e.g., expertise, human capital, basic equipment, etc.) necessary to perform the R&D Services.

C1) PRICE

The cost of the R&D Services in relation to the maximum budget as defined per Tender per Lot and Phase. The weight given for Price score in relation to the other scores ensures a favourable value for money ratio.

A6) SOLUTION DESIGN DEVELOPED IN PHASE 1

The solution design developed based on the Tender provided for Phase 1 will be evaluated considering how the patients' and users' needs were addressed, the progress beyond the state of the art (level of innovation), the feasibility and the value for money.

A7) SAMPLE STABILIZATION

Evaluation of the solution design to produce sample stabilization prototype and to test its performance. Special emphasis will be placed on pre-analytical requirements as specified in the applicable ISO Standards and requirements according to IVDR.

A8) NUCLEIC ACID EXTRACTION

Evaluation of the solution design for nucleic acid extraction in terms of expected precision, reproducibility, linearity/assay, reportable range, traceability, reagents stability, analytical sensitivity; Extraction Equivalency Study; interfering substances testing. Special emphasis will be placed on requirements of the nucleic acid extraction as specified in the applicable ISO Standards and requirements according to IVDR.

A9) QUALITY CONTROL for NUCLEIC ACID EXTRACTION

Evaluation of the solution design for the quality control for nucleic acid extraction and reference material to be included in the prototype: Expected performance of quality controls on stability, analytical sensitivity and traceability and how QC reference samples can meet the requirements as specified in the applicable ISO Standards and requirements according to IVDR.

A10) LIBRARY PREPARATION

Evaluation of the solution design for library preparation. Expected performance of the library preparation prototype in terms of precision, reproducibility, linearity/assay reportable range, traceability, reagents stability, analytical sensitivity, interfering substances, amount of starting material (NA input), minimum amount of NA needed. Special emphasis will be placed on library preparation requirements as specified in the applicable ISO Standards and requirements according to IVDR.

A11) QUALITY CONTROL of LIBRARY PREPARATION

Evaluation of the solution design for quality control for library preparation and reference material to be included in the prototype: Expected performance of quality controls on stability, analytical sensitivity and traceability and how QC reference samples can meet the requirements as specified in the applicable ISO Standards and requirements according to IVDR.

B5-B8: see B1-B4

C2): see C1)

A12) REPORT ON RESULTS FROM PHASE 2

The report on Phase 2 will be evaluated considering the level of implementation of the solution and with special emphasis on the basis of the performance data, including results generated by the Contractor using test samples and reference materials provided by the Buyers.

A13) SAMPLE STABILIZATION

Evaluation of the performance data generated by the Contractor in Phase 2 including the solution for metrological traceability and considerations for applicable ISO standards and requirements of the IVDR. Special emphasis will be placed on how the Contractor will make the solution available to the Buyers for verifying the performance and to evaluate the usability of the prototype. In addition, it will be evaluated how the solution will be integrated into the NGS workflow.

A14) ON NUCLEIC ACID EXTRACTION Quality of the performance data (as indicated in A7) generated by the Contractor in Phase 2 including the solution for metrological traceability and considerations for applicable ISO standards and requirements of the IVDR. Quality of the R&D proposal of the Phase 3; special emphasis will be placed on how the Contractor will make the solution available to the Buyers to verify the performance data and evaluate the usability of the prototype. In addition, it will be evaluated how the solution will be integrated into the NGS workflow.

A15) QUALITY CONTROL OF NUCLEIC ACID EXTRACTION

Quality of the performance data (as indicated in A8) generated by the Contractor in Phase 2 including the solution for metrological traceability and considerations for applicable ISO standards and requirements of the IVDR. Special emphasis will be placed on how the Contractor will make the solution available to the Buyers to verify the performance data and evaluate the usability of the prototype. In addition it will be evaluated how the solution will be integrated into the NGS workflow.

A16) LIBRARY PREPARATION

Quality of the performance data for library preparation (as indicated in A9) generated by the Contractor in Phase 2 including the solution for metrological traceability and considerations for applicable ISO standards and requirements of the IVDR; special emphasis will be placed on how the Contractor will make the solution available to the Buyers to verify the performance data and evaluate the usability of the prototype. In addition it will be evaluated how the solution will be integrated into the NGS workflow.

A17) QUALITY CONTROL OF LIBRARY PREPARATION

Quality of the performance data (as indicated in A10) on QC samples generated by the Contractor in Phase 2 including the metrological traceability and considerations for applicable ISO standards and requirements of the IVDR. Special emphasis will be placed on how the Contractor will make the solution available to the Buyers to verify the performance data and evaluate the usability of the prototype. In addition, it will be evaluated how the solution will be integrated into the NGS workflow.

B9-B12: see B1-B4

C3): see C1)

TABLE 4 WEIGHTED AWARD CRITERIA FOR LOT 2: SEQUENCING

Admission to Phase 1-SOLUTION DESIGN; assessment based on the solutions proposal			
A) Technical quality criteria Evaluation based on how ***users' needs are addressed, level of innovation***			
	Maximum points	**Thresholds**	**Weighting %**
A1) Concept for Scalability	0-5		100
A2) Concept for Integration	0-5		100
A3) Concept for Flexibility	0-5		100
A4) Concept for reducing hands-on time	0-5		100
A5) Concept for reducing Sequencing run time (library to FastQ)	0-5		100
A6) Concept in consideration of relevant standards (CEN or ISO)	0-5		100
A7) Concept for improving the quality of the sequencing result	0-5		100
B) Feasibility			
B1) How realistic the technical development of the solution is (clear plan for the development/implementation of the solution and for finishing Phase 3 on time)	0-5		100

B2) Commercial feasibility of the solution (commercialization plan/route to market)	0-5		100
B3) Crucial risks (technical, commercial, others…) are identified and countermeasures have been identified	0-5		100
B4) Composition of the project team	0-5		100
C1) Price	0-5		200
TOTAL POINTS	0-65		

Admission to Phase 2-PROTOTYPING; assessment based on the evaluation of the solution design developed in Phase 1 and on the offer for Phase 2

A) Technical quality criteria Evaluation based on expected ***Analytical Performance including Metrological Traceability.***

	Maximum points	**Thresholds**	**Weighting %**
A8) Solution design developed in Phase 1	0-5	3	200
A9) R&D plan for Scalability	0-5		100
A10) R&D plan for Integration	0-5		100
A11) R&D plan for Flexibility	0-5		100
A12) R&D plan for reducing hands-on time	0-5		100

A13) R&D plan for reducing sequencing run time (library to FastQ)	0-5		100
A14) R&D plan with respect to consideration of relevant standards (CEN or ISO)	0-5		100
A15) R&D plan for improving the quality of the sequencing result	0-5		100
B) Feasibility			
B5) How realistic the technical development of the solution is (clear plan for the development/implementation of the solution and for finishing Phase 3 on time)	0-5		100
B6) Commercial feasibility of the solution (commercialization plan/route to market)	0-5		100
B7) Crucial risks (technical, commercial, others…) are identified and countermeasures have been identified	0-5		100
B8) Composition of the project team	0-5		100
C2) Price	0-5		300
TOTAL POINTS	0-80		

Admission to Phase 3-DEVELOPMENT AND TESTING; assessment based on evaluation of the prototype developed in Phase 2 and on the offer for Phase 3

A) Technical quality criteria

Evaluation based on ***Analytical Performance Data shown by Contractor to be verified by Buyers, incl. Usability, Standardization, Integration into complete workflow***

	Maximum Points	**Thresholds**	**Weighting %**
A16) Report on results from Phase 2	0-5	3	200
A17) R&D plan on scalability for Phase 3	0-5		100
A18) R&D plan on integration, for Phase 3	0-5		100
A19) R&D plan on flexibility for Phase 3	0-5		100
A20) R&D plan on reducing hands-on time for Phase 3	0-5		100
A21) R&D plan on reducing sequencing run time for Phase 3	0-5		100
A22) R&D plan for Phase 3 on consideration of relevant standards (CEN or ISO),	0-5		100
A23) R&D plan for Phase 3 on improving the quality of the sequencing result	0-5		100

B) Feasibility

B9) How realistic the technical development of the solution is (clear plan for the development/implementation of the solution and for finishing Phase 3 on time)	0-5		100
B10) Commercial feasibility of the solution (commercialization plan/route to market)	0-5		100
B11) Crucial risks (technical, commercial, others…) are identified and countermeasures have been identified	0-5		100
B12) Composition of the project team	0-5		100
C3) Price	0-5		300
TOTAL POINTS	0-80		

Specific elements for the evaluation related to each criterion are listed below.

A1) CONCEPT FOR SCALABILITY

Principle of the scalability i.e., cost versus batch size, number of samples and sequencing depth. Which solutions are proposed to enable small labs as well as large labs to cost effectively sequence small lots of samples with short turn-around-times vs large lots of samples. Which innovative solutions are proposed to improve the balancing of sequencing output per library, especially when different library types (e.g., cfDNA vs tissue DNA libraries vs whole blood DNA libraries) are sequenced in the same run. Which solutions are proposed to solve the environmental problems caused by reagent production, logistics, packaging and other waste, that will come when sequencing will be performed on a large scale in Europe.

A2) CONCEPT FOR INTEGRATION

Description of the integration that should be developed as an innovative solution. For example, existing sequencing solutions may integrate clonal amplification, sequencing and primary bioinformatics. Innovative solutions may for example integrate solutions or solution proposals from LOTs 1, 2 and 4.

A3) CONCEPT FOR FLEXIBILITY

Description of how the proposed innovative solution may deliver sequences in different modes (paired-end vs single-end, different read lengths) or different performance (e.g., output, turn-around time). How can various library types (including library types from different vendors) be sequenced.

A4) CONCEPT FOR REDUCING HANDS-ON-TIME

Description of how hands-on-time should be reduced, with expected hands-on-times for the proposed solution, for each of the different operating modes, performance modes and library types.

A5) CONCEPT FOR REDUCING SEQUENCING RUN TIME

Description of sequencing run time should be reduced. Expected total run times for the proposed solution, for each of the different operating or performance modes and library types. How long are the core sequencing times from library to FASTQ.

A6) CONCEPT IN CONSIDERATION OF RELEVANT STANDARDS

Description of how the proposed innovative solution will consider the relevant (CEN/ISO) standards.

A7) CONCEPT FOR IMPROVING THE QUALITY OF SEQUENCING RESULT

Description of how the proposed innovative solution will improve the quality of the sequencing result. Expected quality values for the proposed innovative solution, and how they compare to current quality metrics. Quality metrics should include accuracy, system-specific errors and library-dependent errors. They should allow comparison between the proposed solution and the current status. More stringent quality threshold metrics than e.g., Q30 may additionally be used to describe improvements in sequencing-error critical sequencing applications such as liquid biopsy. Reference materials proposed for the verification according to IVDR at the user site.

B1) HOW REALISTIC THE TECHNICAL DEVELOPMENT OF THE SOLUTION IS (CLEAR PLAN FOR THE DEVELOPMENT/IMPLEMENTATION OF THE SOLUTION AND FOR FINISH PHASE 3 IN TIME)

Feasibility of the proposed R&D Services and schedule, including methodology.

B2) COMMERCIAL FEASIBILITY OF THE SOLUTION (COMMERCIALIZATION PLAN/ROUTE TO MARKET)

Completeness, sense of reality and feasibility of the commercialisation plan including the market analysis and risk management. Sense of reality and feasibility of the principles for licensing, pricing, distribution.

B3) CRUCIAL RISKS (TECHNICAL, COMMERCIAL, OTHERS…) ARE IDENTIFIED AND COUNTERMEASURES HAVE BEEN IDENTIFIED

The extent to which crucial risks (technical, commercial and other) to project success are identified, and how effectively these will be managed during this phase. Preferably to be summarized in a risk management table, including risk mitigation solutions.

B4) COMPOSITION OF THE PROJECT TEAM

The extent to which the Tenderer and/or Subcontractor shows readiness, or demonstrates to be able to have dedicated the resources (e.g., expertise, human capital, basic equipment, etc.) necessary to perform the scope of the tender.

C1) Price

The cost of the R&D Services in relation to the maximum budget as defined per Tender per Lot and Phase. The weight given for Price score in relation to the other scores ensures a favourable value for money ratio.

A8) SOLUTION DESIGN DEVELOPED IN PHASE 1 The solution design developed based on the concept provided for Phase 1 will be evaluated considering how the patients' and users' needs were addressed, the progress beyond the state of the art (level of innovation), the feasibility and the value for money.

A9) R&D PLAN FOR SCALABILITY

R&D plan regarding the scalability proposed in Phase 1, and R&D proposal to produce the prototype and test its performance regarding scalability. In this Phase 2, testing will be done by the Contractor. Expected reduction of environmental waste (including but not limited to plastics, CO_2, toxic waste and decommissioned instrument tonnage) for the proposed new design and associated recycling/re-use, compared to current designs.

A10) R&D PLAN FOR INTEGRATION

R&D plan for the integration proposed in Phase 1, and R&D proposal to test the prototype regarding integration. In this Phase 2, testing will be done at the premise of the Contractor.

A11) R&D PLAN FOR FLEXIBILITY

R&D plan for the flexibility proposed in Phase 1, and R&D proposal to test the prototype regarding flexibility (paired-end vs single-end, different read length, different outputs, turn-around times, various libraries). In this Phase 2, testing will be done by the Contractor.

A12) R&D PLAN FOR REDUCING HANDS-ON-TIME

R&D plan for the reduction of hands-on-time described in Phase 1. R&D proposal to test the prototype's performance regarding hands-on-time. In this Phase 2, testing will be done by the Contractor.

A13) R&D PLAN FOR REDUCING SEQUENCING RUN TIME

R&D plan for the reduction of sequencing run time described in Phase 1. R&D proposal to test the prototype's performance regarding run time. In this Phase 2, testing will be done by the Contractor.

A14) R&D PLAN WITH RESPECT TO CONSIDERATION OF RELEVANT STANDARDS

R&D plan with respect to consideration of relevant standards and reference materials in the prototype. Emphasis will be placed on the R&D proposal how the Contractor will test performance considering the applicable standards and according to IVDR.

A15) R&D PLAN FOR IMPROVING THE QUALITY OF THE SEQUENCING RESULT

R&D plan for improving the quality of the sequencing result. R&D proposal to test the prototype's performance with respect to sequencing quality metrics. Expected quality values for the accuracy, system-specific errors and library-dependent errors of the prototype.

B5-B8: see B1-B4

C2: see C1

A16) REPORT ON THE RESULTS FROM PHASE 2

The report on Phase 2 will be evaluated considering the level of implementation of the solution and with special emphasis on the basis of the performance data, including results generated by the Contractor using test samples provided by the Buyers.

A17) R&D PLAN ON SCALABILITY FOR PHASE 3

Evaluation of the proposal for Phase 3. Special emphasis will be placed on how the Contractor will make the solution available to the Buyers to verify the performance data and evaluate the usability. In addition, it will be evaluated how the solution will be integrated into the NGS workflow

A18) R&D PLAN ON INTEGRATION FOR PHASE 3

Evaluation of the proposal for Phase 3. Special emphasis will be placed on how the Contractor will make the solution available to the Buyers to verify the performance data and evaluate the usability. In addition, it will be evaluated how the solution will be integrated into the NGS workflow.

A19) R&D PLAN FOR PHASE 3 ON FLEXIBILITY

Evaluation of the proposal for Phase 3. Special emphasis will be placed on how the Contractor will make the solution available to the Buyers to verify the performance data and evaluate the usability. In addition, it will be evaluated how the solution will be integrated into the NGS workflow.

A20) R&D PLAN FOR PHASE 3 ON REDUCING HANDS-ON-TIME

Evaluation of the proposal for Phase 3. Special emphasis will be placed on how the Contractor will make the solution available to the Buyers to verify the performance data and evaluate the usability. In addition, it will be evaluated how the solution will be integrated into the NGS workflow.

A21) R&D PLAN FOR PHASE 3 ON REDUCING SEQUENCING RUN TIME

Evaluation of the proposal for Phase 3. Special emphasis will be placed on the Contractor will make the solution available to the Buyers to verify the performance data and evaluate the usability. In addition, it will be evaluated how the solution will be integrated into the NGS workflow.

A22) R&D PLAN FOR PHASE 3 ON CONSIDERATION OF RELEVANT STANDARDS

Evaluation of the proposal for Phase 3. Special emphasis will be placed on how the Contractor will make the solution available to the Buyers to verify the performance data and evaluate the usability under consideration of the relevant standards, reference materials and requirements of IVDR.

A23) R&D PLAN FOR PHASE 3 ON IMPROVING THE QUALITY OF SEQUENCING RESULT

Evaluation of the proposal for Phase 3. Special emphasis will be placed on how the Contractor will make the solution available to the Buyers to verify the performance data and evaluate the usability. In addition, it will be evaluated how the solution will be integrated into the NGS workflow.

B9-B12) see B3-B4

C3) see C1

TABLE 5: WEIGHTED AWARD CRITERIA FOR LOT 3: BIOINFORMATICS ANALYSIS

Admission to Phase 1-SOLUTION DESIGN; assessment based on the solutions proposal			
A) Technical quality criteria Evaluation based on how ***users' needs are addressed, level of innovation***			
	Maximum points	**Thresholds**	**Weighting %**
A1) Concept for long-term maintainability and availability	0-5		100
A2) Concept for automation	0-5		100
A3) Concept for data handling (compliance with regulations, management, privacy, exchange, filtering)	0-5		100
A4) Concept for Linking with external resources	0-5		100
A5) Concept for verification/QC of	0-5		100

Bioinformatics			
B) Feasibility			
B1) How realistic the technical development of the solution is (clear plan for the development/implementation of the solution and for finishing Phase 3 on time)	0-5		100
B2) Commercial feasibility of the solution (commercialization plan/route to market)	0-5		100
B3) Crucial risks (technical, commercial, others…) are identified and countermeasures have been identified	0-5		100
B4) Composition of the project team	0-5		100
C1) Price	0-5		200
TOTAL POINTS	0-55		
Admission to Phase 2-PROTOTYPING; assessment based on the evaluation of the solution design developed in Phase 1 and on **the offer for Phase 2**			
A) Technical quality criteria Evaluation based on expected ***Performance, Metrological Traceability***			
	Maximum Points	**Threshold**	**Weighting %**
A6) Solution design developed in Phase 1	0-5	3	200
A7) R&D plan for Long-term maintainability and availability	0-5		100
A8) R&D plan for automation	0-5		100
A9) R&D plan for data handling (management, exchange, filtering)	0-5		100
A10) R&D plan for linking with external resources	0-5		100
A11) R&D plan for verification/QC of	0-5		100

Bioinformatics			
B) Feasibility			
B5) How realistic the technical development of the solution is (clear plan for the development/implementation of the solution and for finishing Phase 3 on time)	0-5		100
B6) Commercial feasibility of the solution (commercialization plan/route to market)	0-5		100
B7) Crucial risks (technical, commercial, others…) are identified and countermeasures have been identified	0-5		100
B8) Composition of the project team	0-5		100
C2) Price	0-5		200
TOTAL POINTS	0-65		
Admission to Phase 3-DEVELOPMENT AND TESTING; assessment based on evaluation of the prototype developed in Phase 2 and on the offer for Phase 3			
A) Technical quality criteria Evaluation based on ***Analytical Performance verified by Buyers, Usability, Standardization, Integration into complete workflow***			
	Maximum Points	**Threshold**	**Weighting %**
A12) Report on results from Phase 2	0-5	3	200
A13) R&D plan for Phase 3 on long-term maintainability and availability	0-5		100
A14) R&D plan for Phase 3 on automation	0-5		100
A15) R&D plan for Phase 3 on data handling (management, exchange, filtering)	0-5		100
A16) R&D plan for Phase 3 on linking with external resources	0-5		100

A17) R&D plan for Phase 3 on Verification/QC of Bioinformatics	0-5		100
B) Feasibility			
B9) How realistic the technical development of the solution is (clear plan for the development/implementation of the solution and for finishing Phase 3 on time)	0-5		100
B10) Commercial feasibility of the solution (commercialization plan/route to market)	0-5		100
B11) Crucial risks (technical, commercial, others…) are identified and countermeasures have been identified	0-5		100
B12) Composition of the project team	0-5		100
C3) Price	0-5		200
TOTAL POINTS	0-65		

Specific elements for the evaluation related to each criterion are listed below.

A1) CONCEPT FOR LONG-TERM MAINTAINABILITY AND AVAILABILITY

This includes containerization, availability of operating systems, ability to react to issues, use of versioning system and testing of the expected detection level.

A2) CONCEPT FOR AUTOMATION

This includes how interactive work is streamlined or how automated the whole workflow is performed minimizing the level of human interaction.

A3) CONCEPT FOR DATA HANDLING (MANAGEMENT, EXCHANGE, FILTERING)

This includes data privacy (GDPR and national) regulations, IDVR requirements (encryption), data exchange in standardized formats, filtering of data (automatically or interactively for virtual panels), tracking of data changes, tracking of data access, storage/performance optimizations for large data sets (genomes, deep panels).

A4) CONCEPT FOR LINKING WITH EXTERNAL RESOURCES

This includes disease relevant databases/resources, learning tools and other external tools. The ability to continuously provide versioned and up-to-date releases and integrate or connect between such resources. Example types of resources include population data, computational and predictive data, segregation data, functional data and potential other resources.

A5) CONCEPT FOR VERIFICATION / QC OF BIOINFORMATICS

Features that allow users to compare the results of the solution's analysis with "truth" results, e.g., comparison of data from VCF, BAM or other file types against provided references. Ability to detect quality issues from different types of errors. Please see D7.4 which includes the 20397-2:2021 ISO specification.

B1) HOW REALISTIC THE TECHNICAL DEVELOPMENT OF THE SOLUTION IS (CLEAR PLAN FOR THE DEVELOPMENT/IMPLEMENTATION OF THE SOLUTION AND FOR FINISH PHASE 3 IN TIME)

Feasibility of the Project plan and schedule, including methodology.

B2) COMMERCIAL FEASIBILITY OF THE SOLUTION (COMMERCIALIZATION PLAN/ROUTE TO MARKET)

Completeness, sense of reality and feasibility of the commercialisation plan including the market analysis and risk management. Sense of reality and feasibility of the principles for licensing, pricing, distribution.

B3) CRUCIAL RISKS (TECHNICAL, COMMERCIAL, OTHERS…) ARE IDENTIFIED AND COUNTERMEASURES HAVE BEEN IDENTIFIED

The extent to which crucial risks (technical, commercial and other) to project success are identified, and how effectively these will be managed during this phase. Preferably to be summarized in a risk management table, including risk mitigation solutions.

B4) COMPOSITION OF THE PROJECT TEAM

The extent to which the tenderer and/or subcontractor shows readiness, or demonstrates to be able to have dedicated the resources (e.g., expertise, human capital, basic equipment, etc.) necessary to perform the R&D Services.

C1) PRICE

The cost of the R&D Services in relation to the maximum budget as defined per Tender per Lot and Phase. The weight given for Price score in relation to the other scores ensures a favourable value for money ratio.

A6) SOLUTION DESIGN DEVELOPED IN PHASE 1

The solution design developed based on the concept provided for Phase 1 will be evaluated considering how the patients' and users' needs were addressed, the progress beyond the state of the art (level of innovation), the feasibility and the value for money.

A7) R&D PLAN FOR LONG-TERM MAINTAINABILITY AND AVAILABILITY

Evaluation of the R&D proposal for long-term maintainability of the service and availability. How this can be implemented with the ability to be transferred to future IT hardware/software.

A8) R&D PLAN FOR AUTOMATION

Evaluation of the R&D proposal for automation. How the interactive work can be minimized and streamlined, on the basis of the users test data. Ability to automate the secure intake and outwards transfer of data. Special consideration should be given on aligning with the GA4GH standards (https://www.ga4gh.org/)

A9) R&D PLAN FOR DATA HANDLING (MANAGEMENT, EXCHANGE, FILTERING)

Evaluation of the R&D proposal for data handling (management, exchange, filtering). How are data privacy regulations(GDPR and national), IDVR requirements, data exchange in standardized formats, filtering of data (automatically or interactively), tracking of data changes and access, ability to handle large data sets in an efficient way (from whole genomes, deep panels, etc), implemented on the basis of test data provide by the Buyers.

A10) R&D PLAN FOR LINKING WITH EXTERNAL RESOURCES

Evaluation of the R&D proposal for linking with external resources. Which databases, learning tools and other external tools is the solution linked with, versioned, ability to update and how was the linking implemented.

A11) R&D PLAN FOR VERIFICATION / QC OF BIOINFORMATICS

Evaluation of the R&D proposal for verification/QC of Bioinformatics. How is the verification feature implemented that allows users to compare the results of the solution's analysis with provided reference datasets e.g., comparison of data from VCF files. Results generated with the provided test data.

B5-B8) see B1-B4

C2) see C1)

A12) REPORT ON THE RESULTS FROM PHASE 2

The report on Phase 2 will be evaluated considering the level of implementation of the solution and with special emphasis on the basis of the performance data, including results generated by the Contractor using FASTQ files or unaligned BAM files provided by the Buyers.

A13) R&D PLAN FOR PHASE 3 ON LONG-TERM MAINTAINABILITY AND AVAILABILITY

Evaluation of the R&D proposal of the Phase 3: special emphasis will be placed on how the Contractors will make the solution available to the Buyers to verify the performance data and evaluate the usability. In addition, it will be evaluated how the solution will be integrated into the NGS workflow.

A14) R&D PLAN FOR PHASE 3 ON AUTOMATION

Evaluation of the R&D proposal of the Phase 3 and how users can test and compare the automation benefit to their previous workflows (time saving, stability), on the basis of the users test data.

Special emphasis will be placed on how the Contractors will make the solution available to the Buyers to verify the performance data and evaluate the usability. In addition, it will be evaluated how the solution will be integrated into the NGS workflow.

A15) R&D PLAN FOR PHASE 3

DATA HANDLING (MANAGEMENT, EXCHANGE, FILTERING) Performance include users test data exchange in standardized formats, filtering of data (automatically or interactively), tracking of data changes, storage/performance optimizations for large data sets (genomes, deep panels), implemented, on the basis of the test data provide by the Buyers. R&D proposal of the Phase 3 and how Buyers can test and compare the data handling benefits to their previous workflows (time saving), on the basis of the test data. Special emphasis will be placed on how the Contractors will make the solution available to the Buyers to verify the performance data and evaluate the usability. In addition, it will be evaluated how the solution will be integrated into the NGS workflow.

A16) R&D PLAN FOR PHASE 3 ON LINKING WITH EXTERNAL RESOURCES

Performance include users test which databases, learning tools and other external tools, the solution is linked with, and how the linking was implemented. R&D proposal of the Phase 3 how Buyers can test and compare the benefits to their previous workflows (time saving), on the basis of the users test data. Special emphasis will be placed on how the Contractor will make the solution available to the Buyers to verify the performance data and evaluate the usability (alignment with ISO and GA4GH standards). In addition, it will be evaluated how the solution will be integrated into the NGS workflow.

A17) R&D PLAN FOR PHASE 3 ON VERIFICATION / QC OF BIOINFORMATICS Performance include the verification feature that compares the results of the solution's analysis with provided reference datasets e.g., comparison of data from VCF files, using the provided test data.

B9-B12) see B1-B4

C3) see C1)

TABLE 6: WEIGHTED AWARD CRITERIA FOR LOT 4: INTEGRATED REPORTING

Admission to Phase 1-SOLUTION DESIGN; assessment based on the solutions proposal			
A) Technical quality criteria Evaluation is based on: ***How users' needs are addressed, level of Innovation***			
	Maximum points	**Thresholds**	**Weighting %**
A1) Concept for integration of the following information: NGS results from cancer gene testing and pharmacogenomics analysis, e-medication data, clinical evidence for therapy decision making at bedside	0-5		100
A2) Concept for optimal usability for bedside use: Application on mobile device, off-line use, clear data visualization	0-5		100
A3) Concept for interoperability with bioinformatics pipelines and hospital information systems	0-5		100
A4) Concept for generation of reports for clinician and patients; separate report on pharmacogenomics results for patients made accessible via secure mobile Apps	0-5		100
A5) Concept for advanced protection of data and privacy	0-5		100
A6) Concept for documentation of versions	0-5		100
B) Feasibility			
B1) How realistic the technical development of the solution is (clear plan for the development/implementation of the solution and for finishing Phase 3 on time)	0-5		100

B2) Commercial feasibility of the solution (commercialization plan/route to market)	0-5		100
B3) Crucial risks (technical, commercial, others…) are identified and countermeasures have been identified	0-5		100
B4) Composition of the project team	0-5		100
C1) Price	0-5		200
TOTAL POINTS	0-60		
Admission to Phase 2-PROTOTYPING; assessment based on the evaluation of the solution design developed in Phase 1 and on **the offer for Phase 2**			
A) Technical quality criteria Evaluation based on expected ***(analytical) performance***			
	Maximum points	**Thresholds**	**Weighting %**
A7) Solution design developed in Phase 1	0-5	3	200
A8) R&D plan for performance testing of integration of different data sources	0-5		100
A9) R&D plan for performance testing in on-line and off-line mode	0-5		100
A10) R&D plan for implementation and testing of data security and privacy protection	0-5		100
A11) R&D plan to demonstrate support of different European languages	0-5		100
A12) Concept for flexibility for updates	0-5		100
B) Feasibility			
B5) How realistic the technical development of the solution is (clear plan for the development/implementation of the solution and for finishing Phase 3 in	0-5		100

time)			
B6) Commercial feasibility of the solution (commercialization plan/route to market)	0-5		100
B7) Crucial risks (technical, commercial, others…) are identified and countermeasures have been identified	0-5		100
B8) Composition of the project team	0-5		100
C2) Price	0-5		200
TOTAL POINTS	0-65		
Admission to Phase 3-DEVELOPMENT AND TESTING; assessment based on evaluation of the prototype developed in Phase 2 and on the offer for Phase 3			
A) Technical quality criteria Evaluation based on ***(analytical) performance verified by Buyers, usability, standardization, integration into complete workflow***			
	Maximum points	**Threshold**	**Weighting %**
A13) Report on results from Phase 2	0-5	3	200
A14) Concept to enable usability testing by Buyers	0-5		100
A15) Reports generated by the solution for integrated reporting	0-5		100
A16) Concept for integration of the solution for integrated reporting with bioinformatics pipelines (Lot 3) and hospital information systems	0-5		100
A17) Compliance with relevant ISO and CEN standards	0-5		100
A18) Documentation the solution for integrated reporting	0-5		100
B) Feasibility			
B9) How realistic the technical development of the solution is (clear plan for the	0-5		100

development/implementation of the solution and for finishing Phase 3 on time)			
B10) Commercial feasibility of the solution (commercialization plan/route to market)	0-5		100
B11) Crucial risks (technical, commercial, others…) are identified and countermeasures have been identified	0-5		100
B12) Composition of the project team	0-5		100
C3) Price	0-5		200
TOTAL POINTS	0-65		

Specific elements for the evaluation related to each criterion are listed below.

A1) CONCEPT FOR INTEGRATION OF THE FOLLOWING INFORMATION: NGS RESULTS FROM CANCER GENE TESTING AND PHARMACOGENOMICS ANALYSIS, E-MEDICATION DATA, CLINICAL EVIDENCE FOR THERAPY DECISION MAKING AT BEDSIDE.

Description of data sources, data formats and technologies that will be used to generate integrated reports. The Buyers will provide different NGS test data sets generated from bioinformatics pipelines (gVCF files) and anonymized clinical data as in-kind contribution.

A2) CONCEPT FOR OPTIMAL USABILITY FOR BEDSIDE USE: APPLICATION ON MOBILE DEVICE, OFF-LINE USE, CLEAR DATA VISUALISATION.

Not all hospitals have stable WLAN connections at the bedside. Therefore, solutions should also work in off-line modus. For use at the bedside mobile devices, preferably with touchscreens are needed. The use of the device should be easy with a clear structure of (pull-down) menus and easy understandable data visualization.

A3) CONCEPT FOR INTEROPERABILITY WITH BIOINFORMATICS PIPELINES AND HOSPITAL INFORMATION SYSTEMS.

Specifications of bioinformatics pipelines as described for Lot 3 should be considered to design the interface for gVCF files. Test data sets from different bioinformatics pipelines that are in use at the Buyer's hospitals will be provided. Interoperability with different hospital information systems that are most commonly used in Europe is desired. This should be achieved by supporting standardized data formats such as HL7 and FHIR.

A4) CONCEPT FOR GENERATION OF REPORTS FOR CLINICIAN AND PATIENTS; SEPARATE REPORTS SHOULD BE GENERATED FROM PHARMACOGENOMICS RESULTS FOR PATIENTS MADE ACCESSIBLE VIA SECURE MOBILE APPS.

Different types of reports have to be generated for clinicians and patients. Reports should cover a broad spectrum of information including information on informed consent, the sample analyzed, the analytical method, the quality of the analysis, results on cancer–related variants, actionable items, pharmacogenomics variants, level of evidence for cancer-related variants, level of evidence for pharmacogenomics variants, drug-drug interaction, dosing, side effects and contraindications (e.g., information from e-medication solutions), medication relevant clinical data (e.g., heart, liver, kidney function), running clinical trials, possible compassionate use. Results from pharmacogenomics testing should also be made available to patients in an easily understandable manner by secure mobile apps. In case that not all information can be addressed by the solution designed, a concept is needed how the solution can be further developed to completely address the users' needs or how the solution can be integrated with other solutions that complement each other.

A5) CONCEPT FOR ADVANCED PROTECTION OF DATA AND PRIVACY.

Cybersecurity and protection of privacy is an essential patient and user requirement. Solutions developed have to take into account requirements of GDPR, particularly rights of data subjects (patients). Innovative solutions for secure health apps to report pharmacogenomics results to patients are encouraged.

A6) CONCEPT FOR DOCUMENTATION OF VERSIONS.

This is not limited to software but has to include the versions of medical information, such as nomenclature, disease classifications and the clinical evidence used for decision making. The sources used as evidence for decision making (e.g., guidelines, curated databases) have to be specified and information should be provided on how these sources are updated regularly.

B1) HOW REALISTIC THE TECHNICAL DEVELOPMENT OF THE SOLUTION IS (CLEAR PLAN FOR THE DEVELOPMENT/IMPLEMENTATION OF THE SOLUTION AND FOR FINISH PHASE 3 oN TIME)

Feasibility of the Project plan and schedule, including methodology.

B2) COMMERCIAL FEASIBILITY OF THE SOLUTION (COMMERCIALIZATION PLAN/ROUTE TO MARKET)

Completeness, sense of reality and feasibility of the commercialisation plan including the market analysis and risk management. Sense of reality and feasibility of the principles for licensing, pricing, distribution.

B3) CRUCIAL RISKS (TECHNICAL, COMMERCIAL, OTHERS…) ARE IDENTIFIED AND COUNTERMEASURES HAVE BEEN IDENTIFIED

The extent to which crucial risks (technical, commercial and other) to project success are identified, and how effectively these will be managed during this phase. Preferably to be summarized in a risk management table, including risk mitigation solutions.

B4) COMPOSITION OF THE PROJECT TEAM

The extent to which the Tenderer and/or Subcontractor shows readiness, or demonstrates to be able to have dedicated the resources (e.g., expertise, human capital, basic equipment, etc.) necessary to perform the R&D Services.

C1) PRICE

The cost of the R&D Services in relation to the maximum budget as defined per Tender per Lot and Phase. The weight given for Price score in relation to the other scores ensures a favourable value for money ratio.

A7) SOLUTION DESIGN DEVELOPED IN PHASE 1.

The solution design developed based on the concept provided for Phase 1 will be evaluated considering how the patients' and users' needs were addressed, the progress beyond the state of the art (level of innovation), the feasibility and the value for money.

A8) R&D PLAN FOR PERFORMANCE TESTING OF INTEGRATION OF DIFFERENT DATA SOURCES.

A concrete R&D plan should be provided on how the Contractor will test the performance of the integrated reporting solution. Test data comprising NGS results in data formats as generated by bioinformatics pipelines (e.g., gVCF files derived from sequencing of tumour types and PGx variants as listed in Tables 1 and 2) and anonymized clinical data will be provided by the Buyers.

A9) R&D PLAN FOR PERFORMANCE TESTING IN ON-LINE AND OFF-LINE MODE.

Performance testing as described in A8) should be performed in on-line and off-line mode.

A10) R&D PLAN FOR IMPLEMENTATION AND TESTING OF DATA SECURITY AND PRIVACY PROTECTION.

Performance of data security and privacy protection solutions should be tested in Phase 2 in various implementation modes (on-line, off-line, mobile apps). Solutions might also consider specific security requirements for cloud services. Test data will be provided by the Buyers (see A8).

A11) R&D PLAN TO DEMONSTRATE SUPPORT OF DIFFERENT EUROPEAN LANGUAGES.

Since reporting has to be in national language, the solution for integrated reporting should be applicable to European languages. This has to be demonstrated for at least three languages (including English, German, Italian, French or Dutch).

A12) CONCEPT FOR FLEXIBILITY FOR UPDATES.

Since medical needs, technology and knowledge is rapidly evolving the solution should support regular updates in an easy manner.

B5-B9) see B1-B4

C2) see C1)

A13) REPORT ON RESULTS FROM PHASE 2.

The report on Phase 2 based the will be evaluated considering the level of implementation of the solution and on the basis of the performance data including screenshots generated by the Contractor by using test data provided by the Buyers (see A8).

A14) CONCEPT TO ENABLE USABILITY TESTING BY BUYERS.

The concept has to provide a concrete plan on how the solution for integrated reporting will be made available to the Buyers for verifying performance testing and to test usability in a real world hospital environment in Phase 3.

A15) REPORTS GENERATED BY THE SOLUTION FOR INTEGRATED REPORTING.

The reports generated in context of performance testing by the Contractors should provide the information as defined by patients' and users' needs in a well structured and easy to read manner.

A16) CONCEPT FOR INTEGRATION OF THE SOLUTION FOR INTEGRATED REPORTING WITH BIOINFORMATICS PIPELINES (LOT 3) AND HOSPITAL INFORMATION SYSTEMS. The concept should enable integration of different bioinformatics pipelines as well as hospital information systems that are most widely used with European hospitals. Therefore standardized data formats such as HL7 and FHIR should be used. Concerning integration with bioinformatics pipelines this should be demonstrated by using the test data provided by the Buyers (see A8). The concept should also address how the integration of the solution can be tested by the Buyers.

A17) COMPLIANCE WITH RELEVANT ISO AND CEN STANDARDS.

The concept should demonstrate how requirements of applicable CEN and ISO standards are addressed. Special emphasis should be placed on standards developed by ISO TC 215. (see also report on the NGS-relevant standard landscape and ongoing standardization activities on the Instand-NGS4P website).

A18) DOCUMENTATION THE SOLUTION FOR INTEGRATED REPORTING.

A detailed product description, documentation of the solution for integrated reporting should be provided. Furthermore, a draft version of a user manual should be provided which will be needed by the Buyers for testing the solution. The documentation may also include documentation for open source solutions, if applicable.

B9-B12) see B1-B4

C3) see C1)

SCORING OF THE AWARD CRITERIA

For each and every **Tender** there will be an assessment of criteria **- separately, in each phase**:

a. On a scale 0 to 5 the Expert ranks each technical criterion (A) separately for any of the Lots addressed by the tender (0 = technical challenge not addressed and/or the proposal is not innovative (no progress beyond the state of the art), 1 = technical challenge is addressed to minor extent and/or minor innovative, 3 = technical challenge is moderately addressed and/or moderately innovative, 4 = technical challenge is addressed to a major extent and/or major innovative, 5 = technical challenge is fully addressed and the proposal is highly innovative (great progress beyond the state of the art). The ranking will consider in the scoring both the level to which the technical challenge is addressed and the level of innovation. For instance, in case a technical challenge is moderately addressed (score 3) but the proposed R&D Service is highly innovative (score 5) this will result in a total score of 4.

b. On a scale 0 to 5 the Expert ranks each feasibility criterion (B) separately for any of the Lots addressed by the tender (0 = the feasibility of the proposal or the value for money is very low (the proposal is unrealistic and does not show advantageous combination of cost and quality; 5 = the feasibility of the proposal or the value for money is high (the proposal is realistic and shows an advantageous combination of cost and quality).

c. On a scale 0 to 5 the Expert ranks each Price criterion (C) separately for any of the Lots addressed by the tender. The maximum budget is defined per Tender per Lot and Phase in section 2.5. The scoring considers the price of the R&D Service in relation to the maximum budget (0 = price is higher than the maximum budget as defined for each Lot and phase, 1 = price is 100%>90% of maximum budget; 2= price is 89%>80 of maximum budget; 3 = price is 79%>70% of maximum budget; 4 = price is 69%>60% of maximum budget; 5 = price is less than 59% of maximum budget.

The scores assigned to each criterion with a weight of 100% will be summed up with the exception of those with a weight of 200% that will be multiplied by 2 and those with a weight of 300% will be multiplied by 3 and then summed up to give the Total Points value, which is used for the ranking of the Tenders. The weight given for Price score in relation to the other scores ensures a favourable value for money ratio.

3.5 Evaluation procedure: opening of tenders & evaluation

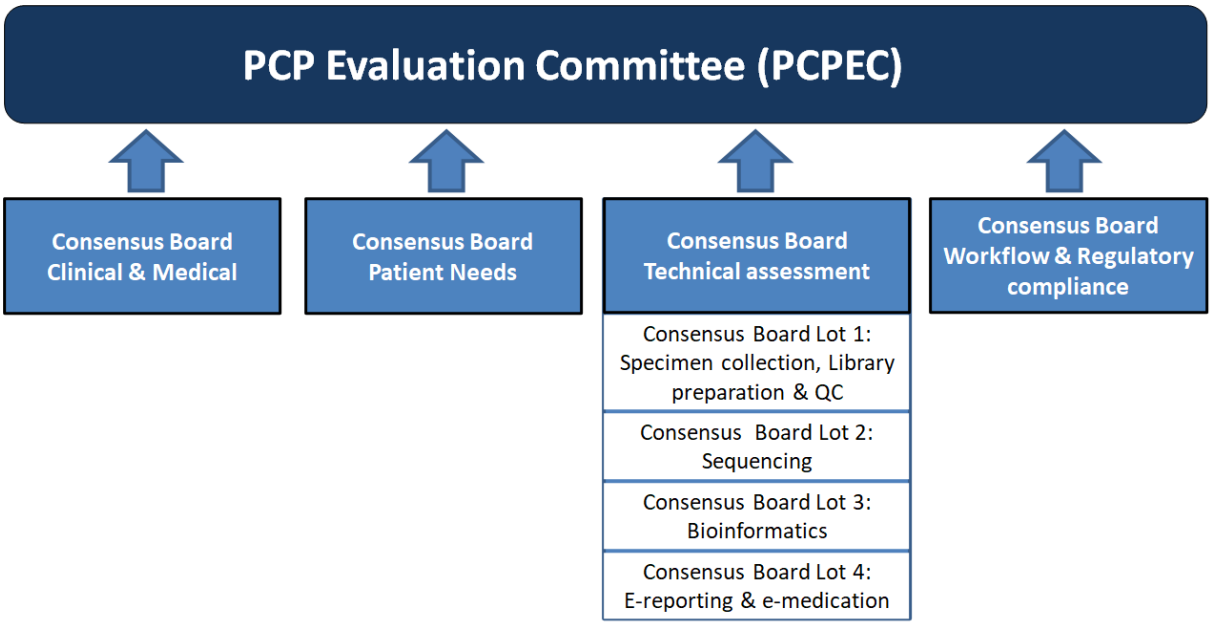

Figure 3: Overview on Evaluation Committees (Consensus Boards and PCP Evaluation Committee)

PCP Evaluation Committee:

The PCP Evaluation Committee (PCPEC) consists in principle of one representative (usually the Principle Investigator of the Buyers group in the Instand-NGS4P project) of each member of the Buyers' group and will be the same for evaluation of the tender and of the different phases. The role of the committee is to provide a final ranking of the tenders, which should be reached by consensus for those ranks that are eligible for contracts. If unanimity cannot be reached, the reasons must be documented and only then a final vote is cast, which must be equal for a majority of at least 60% of the number of members of the PCP Evaluation Committee to reach a decision. Where one representative is present from a member of the Buyers group, this representative has the right to vote with 1 vote. Where more than one representative is present in the evaluation committee from a member of the Buyers group, each member of the Buyers group shall appoint only one representative that gets 1 vote to be used in every voting round, before the voting starts.

Rules for evaluation: Each PCPEC member must take into account the evaluation reports as advice from the consensus boards (see Figure 3). Those boards consist of expert panel members that advise the PCP Evaluation Committee with a summary report with their ranking/evaluation, which forms the

basis for the final ranking of the Tenders by the PCP Evaluation Committee. A member of the PCP Evaluation Committee may serve as a member of an Expert Panel.

Interest (CoI): Rules for Conflict of members of the PCP Evaluation Committee must self-report and document any CoI or potential bias for a specific tenderer. A CoI for a specific tenderer means that this member must abstain from ranking the respective tenderer.

The expert/PCPEC member must perform his/her work impartially and take all measures to prevent any situation where the impartial and objective implementation of the work is compromised for reasons involving economic interest, political or national affinity, family or emotional ties or any other shared interest ('conflict of interests').

The following situations will automatically be considered as conflict of interest:

(a) if the expert/PCPEC member was involved in the preparation of one of the Tenders;

(b) would benefit or be disadvantaged, if one of the Tenders is accepted or rejected;

(c) has close family ties (spouse, domestic or non-domestic partner, child, sibling, parent etc.) or other close personal relationship with a person (including linked third parties or other third parties) involved in the preparation of one of the Tenders, or with a person which would benefit if one of the Tenders is accepted or rejected;

(d) is a director, trustee or partner or is in any way involved in the management of a Tenderer (or subcontractor or other third party involved in the action);

(e) is employed or contracted by one of the Tenderers (subcontractors or other third parties);

The following situations may be considered as a conflict of interest:

a) employment of the expert/PCPEC member by one of the Tenderers (or subcontractor or third parties) in the last three years;

(b) involvement of the expert/PCPEC member in a contract, grant, prize or membership of management structures (e.g. member of management or advisory board etc.) or research collaboration with a Tenderer (or subcontractor or third parties) in the last three years;

(c) any other situation that could cast doubt on his/her ability to participate in the evaluation impartially, or that could reasonably appear to do so in the eyes of an outside third party.

However, in exceptional and duly justified cases, the PCPEC may decide to nevertheless invite the expert to follow the evaluation session with no right to cast a vote, if:

- the expert works in a different department/laboratory/institute from the one where the action is to be carried out and

- the departments/laboratories/institutes within the organisation concerned operate with a high degree of autonomy and
- the participation is justified by the requirement to appoint the best available experts and by the limited size of the pool of qualified experts.

In this case, the group of evaluators will be informed about the situation of the expert.

Expert Panel:

There are four different **consensus boards** giving their advice to the PCPEC on the ranking. Each consensus board consists of an expert panel, or in case of the technical consensus board expert panels, with their specific expertise focussed on the subject to evaluate.

- The **technical assessment** consensus board is selected after opening of the Tender, from a previously defined list of experts for each Lot. These are either selected from partners of the project or are external experts. The individual proposals are assigned to experts that match their expertise. The workload needs to be divided: 3-5 proposals per expert and each proposal shall be evaluated by at least two experts.
- The **patient needs** consensus board expert panel consists of at least 3 experts for evaluation of the proposals including experts on childhood patient needs.
- The **workflow and regulatory compliance** consensus board expert panel consists of at least 3 experts for evaluation of the proposals.
- The **clinical and medical** consensus board expert panel consists of at least 3 experts for evaluation of the proposals.

One expert may act on one or more consensus boards as well as the PCPEC.

Rules for CoI: members of the Expert Panel must self-report and document any CoI or potential bias for a specific tenderer. A CoI for a specific tenderer means that this member must abstain from ranking the respective tenderer.

Evaluation procedure after Opening of Tenders

Before evaluation, all Tenders are checked for **formal correctness** by the PCP Evaluation Committee. Tenders that do not meet formal inclusion criteria are excluded at this stage with documented justification. For Tenderers passing the formal correctness assessment, an assessment is performed as to whether the Tenderer has the capacities necessary to perform the contract, on the basis of the **selection criteria**. Every Tender is evaluated on this point by at least 2 PCPEC members and in the end

there is a plenary discussion where the exclusions of every excluded Tender are shortly presented and documented.

The remaining eligible Tenders are then assigned to the Expert Panels as a whole for evaluating the Tender based on the **on/off award criteria** followed by the evaluation of the Tender based on the **weighted award criteria**. Tenderers who are addressing several Lots (maximum 3 different Lots of the NGS workflow can be addressed by one Tenderer) have to provide separate applications for each Lot which are separately evaluated per Lot.

Consensus board expert reporting form and evaluation procedure

Structured evaluation with ranking on defined scales is mandatory to reduce bias and to assure consistency, to allow informed weighting of the ranks and to fulfil our obligation towards the EU and the Tenderers. The consensus boards use predesigned forms (scoring lists / checklist / questionnaires with defined scales) to perform the evaluation. The PCPEC will receive the completed forms from the consensus boards after the consensus board has discussed the end-result to correct ranking or evaluation amongst them. The scoring of the technical experts consensus board gives a preliminary ranking based on evaluation criteria and is presented to the other expert consensus boards and the PCPEC. The PCPEC will consider the comments of all consensus boards for the final ranking as the basis for decision-making of the PCPEC. After receipt of the forms, the PCPEC is allowed to ask questions to the involved experts;then the Tenders will receive the final evaluation report from the evaluation committee without names.

PCP Evaluation Committee Evaluation procedure

After the experts' evaluation, the PCP Evaluation Committee will review their reports and each member will assign a rank to each tender, separately for each Lot based on the scoring of the experts. The members of the PCP Evaluation Committee will justify in writing any deviations from the ranking given by the Experts, to document the decision process. Detailed instructions upfront for the review process are needed at this point. Based on the reviewed Tender evaluations, a first ranking of the Tenders will be computed per Lot. In an Evaluation meeting, the PCP Evaluation Committee will discuss the ranking and, if necessary, modify it. Minutes will document these modifications including the reasons for the modifications. Finally an unanimous decision on the ranking should be sought – abstentions are allowed as long as there is a quorum of a 60% majority of the members of the PCP Evaluation Committee.

After ranking the number of the selected proposals is known for each Lot. Therefore, the PCP Evaluation Committee can then determine the division of the resources available over the different Lots for the next phase after ranking all proposals. This will be done immediately after the ranking is determined. Resources for the different phases in total are set in the Tender and will not be changed, except when the budget is not fully used in a phase, it will be transferred to the next phase. The PCPEC shall take a decision on the basis of the ranking result how many Tenders can be awarded per Lot and allocate the funding accordingly. It could happen that the number of eligible proposals received for a Lot is lower than expected or that the cut off level of proposals that can be financed could cause a remaining budget. Any remaining budget within a Lot can be transferred to other Lots in that phase. These financial decisions will be taken jointly by the PCPEC members aiming at achieving consensus. If consensus is not reached it is finally decided by voting. The final decision then requires a qualified majority.

Evaluation at the end of each phase

The contract implementation of each phase is monitored (see 5.5 Monitoring), which results in a report. In addition, at the end of each phase the solution provider submits an End of Phase Report. These reports are used together with the original proposal of that phase to determine within the PCPEC if the proposal was finished successfully (score 3-5), satisfactory (score 1-2) or not satisfactory (score 0), which is the basis for the PCPEC payment decision. In addition, a new proposal for the next phase is submitted at the end of Phase 1 and 2. The new proposal together with the original tender are evaluated at the end of Phase 1 and 2 for entering the next phase, but only if the phase before was finished successfully. The evaluation is performed the same way as the tender was evaluated by the CBs and the PCPEC. At the end of Phase 3 the CBs and the PCPEC evaluate only the reports on the performance in a NGS workflow.

Report Conclusion to tenderers

Results and conclusions are sent to Tenderers personalized on the Tender together with available resources for that Tender if the Tender is selected for the next phase. As an annex the documentation of the evaluation committee process is provided without names of evaluators or experts and IP residing under confidentiality.

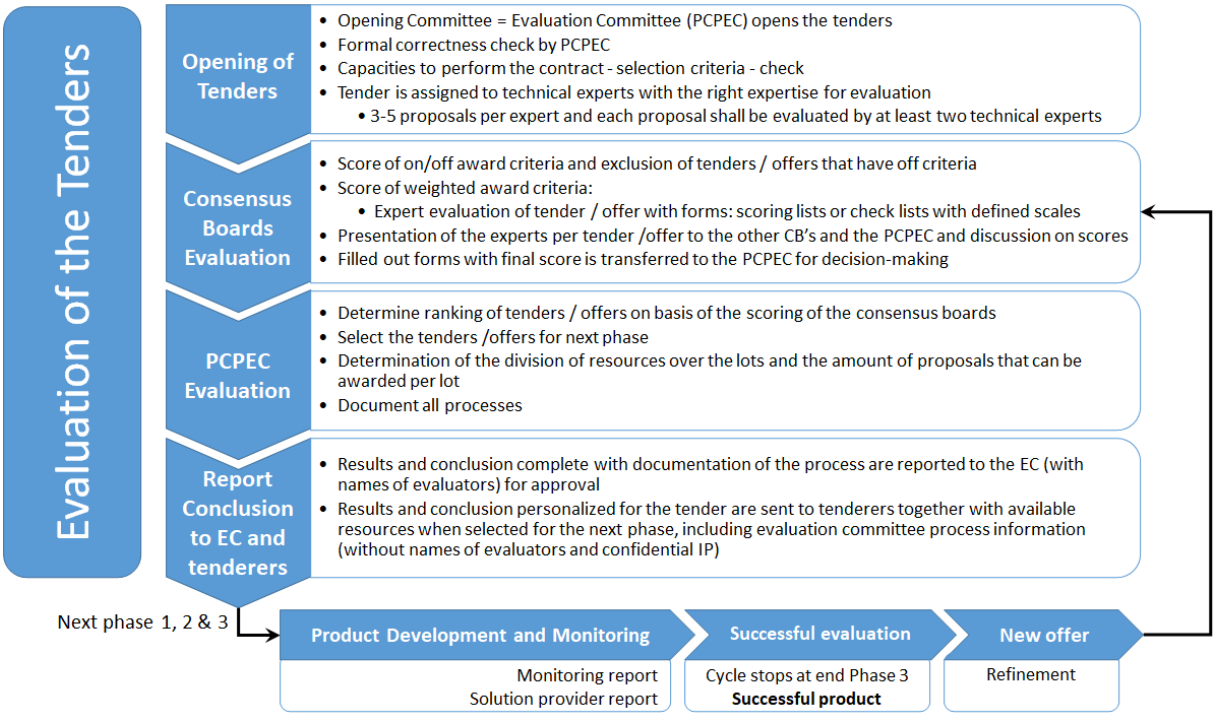

Figure 4: Schematic drawing of the tender evaluation process

4. Content & format for tenders

4.1 Submission and format of tenders, tender closing time

The following requirements will apply regarding the submission and format of Tenders. Tenders that do not comply with the formal requirements will be excluded from further participation in the PCP:

● Where a signature is requested, the relevant document must be validly signed by a duly authorized person(s). The signature must be from a staff member or staff members who according to the extract from the professional register or trade register is authorized to represent the Tenderer. If a document is signed by a person not listed in the professional register or trade register, an adequate proxy must be attached. Such a proxy must be signed by a person or persons who according to the extract from the trade register or the professional register or according to the articles of association are authorized to represent and bind the company or institution. The proxy must clearly state that the proxy holder is authorized to represent the company or institution in connection with this Tender.

● **The Tender must be completed and submitted by sending the Tender Form (annex A, B, C, D, E and F) and the applicable appendices to the following dedicated email address:** instand-tender@medunigraz.at

● The Tender has the character of an irrevocable offer with a validity period of ninety (90) calendar days, counting from the closing date for submission of Tenders.

● Amounts must be stated in euros, excluding VAT, unless otherwise stated.

● All Tenders must contain an administrative, technical and financial section (see tender form, annex A, B and C).

● The contact person for this tender of the Instand-NGS4P consortium is: Medical University of Graz (MUG, Lead Procurer) - Prof. Kurt Zatloukal and can be contacted via the following email address: instand-tender@medunigraz.at.

● **The last date and hour for submission of a complete Tender is 15/12/2021, 17:00 CEST**

● The Tenderer is responsible for timely digital submission of its Tender via email.

● **Tenders must be submitted by digital submission in pdf format**

More detailed information about the submission and layout requirements for the Phase 2 and 3 offers (which are due at the end of Phase 1 and 2 respectively) will be provided on the Instand-NGS4P website, at the latest 45 calendar days before the respective submission deadlines.

4.2 Administrative section

To ensure appropriate transparency in communication during the tender period for each Phase any communication will take place by the communication channel of the official Instand-NGS4P website www.instandngs4p.eu or tender email address instand-tender@medunigraz.at. Except where otherwise directed in these Instructions, Tenderers must not contact any person in relation to this competition other than those named in this Request for Tenderers document (or other supporting document), or if nominated, their designated deputy. The name of any designated deputy will be confirmed in writing.

All Tenders must be prepared using the Instand-NGS4P Tender Forms (see annex A, B, C, D, E and F) which is part of the tender document pack - along with all of the other competition documentation - and which can be downloaded by following the instructions on the Instand-NGS4P web page. All Tenders must be submitted in accordance with the following rules:

1. Tenders and supporting documents must be written in English or a full English translation, provided at no cost to the Procurers.

2. Tenders must not be qualified or accompanied by statements or a covering letter that might be construed as rendering the tender equivocal. Unauthorized alterations or additions must not be made to any component of the tender documents

	Overview Tender Documents:	Action to be taken by tenderer:
1	Contract Notice	For your information. The document is published on the EU's tenders electronic daily website (TED)
2	Instand-NGS4P PCP Request for Tenders (this document)	For your information. This document describes the Instand-NGS4P PCP process for the coming 3 Phases: how the selection process looks like, what Instand-NGS4P expects from Tenderers, etc. By submission of a Tender all regulations mentioned in this document will be accepted by the Tenderer. Please note that Tenderers who are awarded for the Phases 1, 2 and 3 shall sign the formal assignment for that particular phase.
3	Instand-NGS4P Framework Agreement	For your information (signature of contract needed only after awarding to Phase 1).
4	Instand-NGS4P Specific Contract for Phases 1/2/3	For your information (signature of contract needed only after awarding to Phase 1, 2 and 3, respectively).
5	Annex A: General Submission Form	Complete this form for providing general information about the tenderer
6	Annex B Tender Form Submission Form	Complete this form to describe the tenderer's technical offer, including project management and project team, impact on challenge, technical quality of the solution, and commercial feasibility and to specify the plans for and objectives for offers for the subsequent Phase 2 and 3
7	Annex C Financial Submission Form	Complete this form to provide the offer requested for Phase 1 and an estimated total price for Phases 2 and 3
8	Annex D Form for Exclusion Criteria	Complete this form which is to ensure there are no criteria which would exclude participation
9	Annex E Form for Selection Criteria	Complete this form to demonstrate the ability (financial and organisational) to complete the project
10	Annex F Form for On/Off Criteria	Complete this form which is to ensure that all the compliance criteria have been met

Tenders received after the closing date for the PCP (15.12.2021) will not be included in the evaluation process.

Tenderers must advise the Procurers if:

− their ownership or the ownership of any member of their tendering consortium (or their parent company) changes, or

− any organization involved in the preparation of this contract is acquired by them or by any member of their consortium (or an associated company).

Tenders must not exceed the page limits set out in the Tender Form. The Tender will be considered up to the number of pages per section as designed and stated in the Tender Form; the excess pages will not be considered (for more information see: Tender Forms Annex A, B, C, D, E, F).

Tenders shall be received no later than the closing date for the PCP, 15.12.2021 (see section 2.6 .for an indicative time schedule for the PCP).

The Lead Procurer may request clarification or additional evidence where there is any doubt.

4.3 Technical Section

Tenders must include a **technical offer (Annex B**)(as well as supporting annexes D, E, and F) containing:

- a technical plan that outlines: 1. the tenderer's idea for addressing all the requirements given in the PCP challenge description, relating both to functionality and performance; and 2. technical details of how this would be implemented (see Annex B)
- a draft business plan that explains the proposed approach to commercially exploit the results of the PCP and to bring a viable product or service onto the market
- a list of the pre-existing rights *(background)* relevant to the tenderer's proposed solution, in order to allow IPR dependencies to be assessed
- a risk assessment and risk mitigation strategy
- a reply to the question "Does this tender involve **ethical issues**? (YES/NO)" and if YES, an ethics self-assessment, with explanations how the ethical issues will be addressed
- a reply to the question "Does this tender involve: activities or results that may raise **security issues** and/or **EU-classified information**[1] as background or results? (YES/NO)" and if YES information on how these issues will be addressed

[1] See Decision 2015/444/EC, Euratom on the provisions on security of EU-classified information.

Attention:

Tenders failing to meet these requirements will be excluded.

The technical part must provide a detailed technical offer for Phase 1 (including an explanation of the methodology, a work plan and details of deliverables and milestones) and must specify the plans for and objectives for offers the subsequent Phase 2 and 3 and beyond including a plan for commercial exploitation of the results.

The information provided in the technical section of the Tender will be used to evaluate the Tenders, on the basis of the technical award criteria, the minimum requirements and the on/off award criteria A, D and E.

The detailed technical offers for the Phase 2 and 3 (in particular on the technical implementation plan, updated business plan and list of IPRs) will be provided at the end of Phase 1 and 2, respectively as deliverables.

4.4 Financial Section

The Tender must include a detailed **financial offer (Annex C)**. Please use the tender form to specify:

(a) binding **unit prices** for all items needed for carrying out Phase 1 and for items that are expected to be needed for Phases 2 and 3 (given in euros, excluding VAT but including any other taxes and duties)

(b) a fixed **total price** for Phase 1 and an estimated total price for Phases 2 and 3, broken down to show unit prices and the number of each unit needed to carry out Phase 1 (given in euros, excluding VAT but including any other taxes and duties).

In addition, the financial section must include:

(c) a **price breakdown** that shows the price for R&D Services and the price for supplies of products (to demonstrate compliance with the definition of R&D in compliance criterion A)

(d) a **price breakdown** that shows the location or country in which the different categories of activities are to be carried out *(e.g. x hours of senior researchers in country L at y euro/hour; a hours of junior developers in country M at b euro/hour)* (to demonstrate compliance with the requirement relating to place of performance in compliance criterion C)

e) the **financial compensation** valuing the allocation of ownership of the IPRs generated during the PCP to the Tenderer in order to ensure compliance with the EU R&D&I state aid framework: by giving as absolute value for the price reduction between the price offered in the Tender compared to the exclusive development price (i.e., the price that would have been quoted were IPR ownership to be transferred to the Procurers).

Attention: The unit prices quoted for each category of items (e.g., hourly rates for junior and senior researchers) remain binding for all phases for the duration of the framework agreement. However, they can be indexed for Phase 2 and 3 by max 5%. If a Tenderer wants to use this indexation, an explanation is required.

All the information provided in the financial section of the Tender will be used to evaluate the tenderers on the basis of the price-award criteria and the compliance criteria B and C.

The financial offers for the Phases 2 and 3 will be provided at the end of Phase 1 and 2, respectively as deliverables. The price for Phase 2 and 3 offers must be based on the binding unit prices in the Tender and the price conditions set out in the framework agreement. Where new units/unit prices (e.g. for new task equipment) are subsequently added to Phase 2 and 3 offers, they will become binding for the remaining phases. Similar prices breakdowns will be requested for the offers for Phases 2 and 3.
The VAT regime of Austria will be applied.

5. Miscellaneous

5.1 Language

All communication (relating to either the tender procedure or the implementation of the contract) must be carried out in English.
Tender's document as well as offers for Phase 1, 2 and 3 must be submitted in English.
Deliverables must be submitted in English.

5.2 Tender constitutes binding offer

A signed Tender will be considered to constitute a firm, irrevocable, unchangeable and binding offer from the Tenderer.
The signature of an authorised representative will be considered as the signature of the Tender (and will be binding on the tenderer or, for joint tenders, the group of tenderers).

5.3 Communication — Questions

For questions, you may contact the contact person of the Lead Procurer via email: instand-tender@medunigraz.at in English until 6.12.2021.
Every Tenderer is obliged to examine the Tender Documents and report all ambiguities, errors or contradictions that the Tender Documents suffer from in its opinion to the Lead Procurer at the latest by the end of the period for questions stating the reasons, otherwise the Tenderer has no further legal claims arising out of the tender procedure in connection thereof.

The summary of all questions and answers will be presented in an anonymised Q&A document that will be published on www.instandngs4p.eu in English (final version planned for 10.12.2021).
The Q&A from the open market consultation can be found on www.instandngs4p.eu

For Phase 2 and 3 a dedicated Q&A session will be opened after being announced on the Instand-NGS4P website and the answers will not be published but distributed to all Contractors that successfully completed the previous phase.

A **webinar** dedicated to all the administrative, technical and financial aspects of this Tender will be held by the Lead procurer on **November 3rd 2021** and instruction for the registration will be published on Instand-NGS4P website.

Attention: All other contacts (or attempted contacts) will be considered unauthorised and may lead to the exclusion of your tender.

5.4 Confidentiality

Tenderers must keep confidential any information obtained in the context of the tender procedure *(including EU-classified information[11])*.

5.5 Contract implementation

Successful Tenderers will be requested to sign both a Framework Agreement and Specific Contracts for Phases 1, 2 and 3 *(see the model documents provided in the Tender Documents package on the website)*.

In case of discrepancy between the Framework Agreement, on the one hand, and the PCP Request for Tender Document, on the other hand, the documents shall prevail in the following order:

(a) Framework Agreement;
(b) PCP Request for Tender Document
(c) Tender Documents (general, technical and financial forms)
(d) Other documents (exclusion, selection and on/off criteria forms)
(e) Specific Contract for Phase

Monitoring

The contract implementation will be monitored and reviewed against the expected outcomes *(milestones, deliverables and output or results)* for the phase. Phase 1 shall have at least one virtual meeting shortly before the closure. Phase 2 and 3 are periodically reviewed, at least once every two months. Frequency can be altered during monitoring meetings to be more in line with the needs. Additional meetings can be requested by the Contractor at the monitoring team or the Instand-NGS Lead Procurer or can be requested by the monitoring team to the Contractor.

[11] Commission Decision 2015/444/EC, Euratom of 13 March 2015 on the security rules for protecting EU-classified information.

Each Contractor will be assigned a main contact person (their supervisor) from the monitoring team appointed by the Procurers represented in the PCPEC. In addition, the PCPEC assigns a monitoring team for every Lot.

There will be one or more virtual monitoring meetings between the Contractor and the monitoring team. The Contractors could be asked to discuss the results achieved in the preceding period and present their updated work plan; the monitoring team could visit the Contractor's premises to periodically monitor progress. The Contractors could also visit the Procurer's premises (in particular at the start of a phase to get to know better the operational environment that solutions need to be designed for) covering its own costs and thus foresee personnel and travel budgets in its offer. Meetings that involve Contractors from the different Lots to sort out dependencies between Lots and to ensure that building blocks under development in different Lots will ultimately work together could also be planned. Feedback on the meetings is given through minutes of the meeting.

Monitoring can include an inspection to check if the information in the Tender is compliant with the contract and framework agreement and if specified technical, regulatory compliance, standardisation, financial, patient, clinical and medical needs are met within the given timeframe and the available capacity of the R&D Services.

CoI will be dealt with as described in the evaluation procedure.

Payments based on satisfactory completion of milestones and deliverables of the phase

Payments corresponding to each PCP phase will be subject to the *satisfactory* completion of the deliverables and milestones for that phase.

On the Completion Date of Phase I, the Tenderer shall submit to the Procurers an "End of Phase Report" regarding such Phase together with the deliverables belonging to Phase I, which shall thereupon be reviewed and assessed by the PCP Evaluation Committee in order to determine whether the Tenderer has complied with the Instand-NGS4P challenges and criteria. Such assessment shall be performed at any time between the Completion Date of Phase I and the starting date of the next Phase, but in any case prior to the latter.

The PCP Evaluation Committee shall issue its decision regarding the not satisfactory, satisfactory or successful completion of every Phase, not earlier than two (2) weeks and not later than six (6) weeks after the Completion Date of the Phase. In case the volume of Tenders leads to a longer evaluation process the Tenderers will be informed.

Satisfactory completion will be assessed according to the following requirements:

- if the work corresponding to that milestone / deliverable has been carried out

- if a reasonable minimum quality has been delivered
- if the reports have been submitted on time
- if the budgets have been allocated to the planned objectives
- if the budgets have been allocated and the work has been carried out according to the on/off award criteria (place of performance, public funding and R&D definition criteria)

and

- if the work has been carried out in compliance with the provisions of the contract *(including in particular verification if the contractor has duly protected and managed IPRs generated in the respective phase)*.

'Reasonable minimum quality' of a report means that:

- the report can be read by somebody who is familiar with the topic, but not an expert
- the report gives insight in the tasks performed in and the results
- the report is made using the End of Phase Report form or (if applicable) the milestone report form and the requirements of this form have been met
- the report includes a lay summary that can be read by patient's organisation

'Reasonable minimum quality' of a demonstration (for Phase 2 or 3) means:

- the demonstration can be understood by somebody who is familiar with the topic, but not an expert (for instance, somebody with operational but not technical knowledge)
- the demonstration shows how the innovation works, how it can be used and (if applicable) how it is operated and maintained
- the demonstration is accessible to parties appointed by the procurers, unless these are direct competitors of the contractor

Satisfactory completion in each of the phases does not mean successful completion (a PCP could, for instance, be satisfactorily completed even if it concludes that the innovation is not feasible).

The assessment will consider the efforts made by Contractors to take into account the feedback from the monitoring team.

Where the evaluation committee judges the completion of deliverables or milestones to be not satisfactory, the Lead Procurer may decide to reduce or withdraw payments for that deliverable and/or may terminate the Contract.

Invoices must be submitted to the Lead Procurer.

The details regarding the payments by the Lead Procurer are set out in the Framework Agreement and the Specific Contract.

Contractors' invoices must provide:

- a **price breakdown** showing the price for R&D services and the price for supplies of products (in order to demonstrate compliance with the definition of R&D in on/off award criterion A)
- a **price breakdown** showing the location or country in which the different categories of activities were performed *(e.g. x hours of senior researchers in country L at y euro/hour, a hours of junior developers in country M at b euro/hour)* (in order to demonstrate compliance with the requirement relating to the place of performance in on/off award criterion C).

Payments schedule

Services for each phase will be made according to the following provisions:

(i) Payment schedule for **Phase 1** will be:

50% at the beginning of Phase 1,

50% after satisfactory completion of Phase 1 (positive evaluation of submitted Deliverables)

ii) Payment schedule for **Phase 2** will be:

35% at the assignment to Phase 2,

35% after positive evaluation of submitted Deliverables (midterm Deliverables)

30% after satisfactory completion of the Phase 2 (positive evaluation of final Deliverables)

iii) Payment schedule for **Phase 3** will be:

35% at the assignment to Phase 3,

35% after positive evaluation of submitted Deliverables (midterm Deliverables)

30% after satisfactory completion of Phase 3 (positive evaluation of final Deliverables and successful testing of the solutions by the Procurers)

Eligibility for the next phase is based on successful completion of the previous phase

Eligibility for participation in the next phase will be subject to *successful* completion of the previous phase.

Successful completion of a phase will be assessed by the PCP Evaluation Committee against the following requirements:

- if all milestones have been successfully completed

- if the R&D results meet the minimum functionality/performance requirements of the challenge description *(i.e. the minimum quality/efficiency improvements which the procurers set forward for the innovative solutions to achieve)*
- if the results of the R&D are considered to be promising

'Promising' means:

- for Phase 1, that the feasibility is convincing.

  Note: R&D plan for the next Phase will be also evaluated; detailed R&D plan for next phase is one of the Deliverables of Phase 1.
- for Phase 2, that the feasibility, the applicability in an operational setting and the potential impact of the product is convincing and that the operation in a workflow is feasible.

Please note that there is a difference between satisfactory completion and successful completion: a **satisfactory completion** is a requirement to receive the payment for that phase. Satisfactory completion includes completion of all the deliverables & milestones in the specific phase, and meeting minimum requirements set for that phase.

A **successful completion** is a prerequisite for passing from one phase to the next and includes the same aspects as satisfactory completion, but will also depend on the assessment of how promising the R&D Services are.

Finalisation of Phase 3: Possible follow-up PPI procurements

Follow-up PPI procurements for a *limited* set of prototypes and/or test products developed during this PCP procurement *('limited follow-up PPIs')* may be awarded by negotiated procedure *(with invitation to at least 3 potential providers, including those that successfully completed this PCP)*.

Follow-up PPI procurements for a *commercial volume* of the innovative solutions developed in this PCP procurement will be subject to a new request for tenders.

5.6 Cancellation of the tender procedure

The Procurers may, at any time, cease to proceed with the tender procedure and cancel it.

The Procurers reserve the right not to award any contracts at the end of the tender procedure.

The Procurers are not liable for any expense or loss the tenderers may have incurred in preparing their offer, except for mandatory limits under national law.

5.7 Procedures for appeal

Decisions taken for the selection of Tenders, awarding them with Phases 1, 2 or 3 or excluding them from the Instand-NGS4P PCP Procedure can be challenged by means of an administrative remedy within a period of 8 days upon the formal notification of the decision.

A decision dismissing the appeal could be challenged before the Federal Administrative Court in Graz. Any dispute or claim arising out of or in connection with the execution of the Framework Agreement or of the Specific Contracts entered into between the Buyers Group and the Supplier shall be heard by the competent Court in Graz.

Interested companies or institutions are requested to submit any complaints regarding the tender procedure in the first instance through the Instand-NGS4P mailbox: instand-tender@medunigraz.at (and await the response), before they apply to the complaints reporting desk.

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ANNEX A - GENERAL SUBMISSION FORM

TENDER IDENTIFIER: write here a short name/acronym to be used as your tender identifier throughout the Tender application forms.

- Please complete a **separate form for each Lot**
- In the case of tender submitted by a Single Tenderer please fill in section 1.
- In the case of a tender submitted by a Consortium please fill in section 2.
- Delete the unused section!

1. SINGLE TENDERER

Note: List the subcontractors who will be engaged to perform part of the services, and indicate the % of their activities with regards to the total budget. You can copy the tables when needed or delete unused tables.

Indicate for which Lot you are applying:	

Single tenderer	
Name of legal entity	
VAT number	
Contact person	
E-mail	
Nationality	

Subcontractor 1	
Name of legal entity	
Project activities subcontracted (%)	

VAT number	
Contact person	
E-mail	
Nationality	

Subcontractor 2	
Name of legal entity	
Project activities subcontracted (%)	
VAT number	
Contact person	
E-mail	
Nationality	

2. CONSORTIUM

List the Members of the Consortium and possible Subcontractors. Indicate the Members and Subcontractors (if applicable) who will be engaged to perform part of the services, and indicate the % of their activities. You can multiply the tables as needed and/or delete unused ones.

Consortium member 1 and Lead Tenderer	
Name of legal entity	
Project activities performed (%)	
VAT number	
Contact person	

E-mail	
Nationality	

Consortium member 2	
Name of legal entity	
Project activities performed (%)	
VAT number	
Contact person	
E-mail	
Nationality	

2.1 SUBCONTRACTORS

Delete tables unused

Subcontractor 1	
Consortium member responsible for the subcontract	
Name of legal entity	
Project activities subcontracted (%)	
VAT number	
Contact person	

E-mail	
Nationality	

Subcontractor 2	
Consortium member responsible for the subcontract	
Name of legal entity	
Project activities subcontracted (%)	
VAT number	
Contact person	
E-mail	
Nationality	

3. STATEMENT

Statement A for single tenderer

Statement B for a consortium

Statement A

I, the undersigned, being the authorised signatory of the Single Tenderer hereby declare that I have examined and I accept without reserve or restriction the entire contents of the PCP Tender Documents for the tender procedure in the framework of the Instand-NGS4P project and of the tender submitted in its entirety.

I guarantee that the subcontractor(s) identified to perform parts of the services meet the relevant criteria as established in the Tender Documents.

I am fully aware that the subcontractor(s) cannot be replaced, nor can subcontractors be added, without the prior written authorisation of the Lead Procurer of Instand-NGS4P PCP.

I am fully aware that any dispute arising out of, or in connection with, the tender procedure shall be brought before the Federal Administrative Court in Graz as set out in the Request for Tender Chapter 5.7.

Lead tenderer – Org. Name	
Name Authorised Signatory	
Position	
Signature and Stamp if available	
Place, Date	

Statement B

I, the undersigned, being the authorised signatory of the Lead Tenderer, hereby declare that I have examined and I accept without reserve or restriction the entire contents of the PCP Tender Documents for the tender procedure in the framework of the Instand-NGS4P Tender Documents and of the tender submitted in its entirety.

I guarantee that all Consortium members and the subcontractor(s) identified to perform parts of the services meet the relevant criteria as established in the Tender Documents.

I am fully aware that the composition of the Consortium cannot be altered and that the subcontractor(s) cannot be replaced, nor can subcontractors be added, without the prior written authorisation of the Lead Procurer.

I am fully aware that the Consortium members are jointly and severally liable to the Lead Procurer for the execution of the Contracts.

I am fully aware that any dispute arising out of, or in connection with, the tender procedure shall be brought before the Federal Administrative Court in Graz as set out in the Request for Tender..

Name of Lead tenderer	
Name Authorised Signatory	
Position	
Signature and Stamp if available	

Place, Date	

5. SUBCONTRACTOR DECLARATION

NOTE:

- Declaration to be submitted by each of the Subcontractors engaged in this Tender. Only to be completed in case of the existence of Subcontractors
- If not applicable, delete this section. Otherwise MULTIPLY THIS PAGE BY THE NUMBER OF SUBCONTRACTORS.

I, the undersigned (*insert name of the signatory of this form), (position)* of (*full name of the entity to be subcontracted/person to be subcontracted),* with a registered office at (*full address)* and VAT number *(official VAT number)* declare that:

- I am fully aware of the Tender Documents for the tender procedure in the framework of the Instand-NGS4P project and of the tender submitted by *full name of the Lead Tenderer*, in its entirety.
- I possess the necessary resources (human, financial, technical) with no time restrictions to fulfil its obligations arising from my responsibilities within the awarded contracts.

Consortium member responsible for the subcontract	Partner No.) and Name
Subcontractor	**Insert subcontractor No.) and Name of the entity**
Name Authorised Signatory	
Position	
Signature and Stamp, if available	
Place, Date	

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ANNEX B - TECHNICAL SUBMISSION FORM

TECHNICAL OFFER PHASE 1

TENDER IDENTIFIER: **write here a short name/acronym to be used as your tender identifier throughout the Tender application forms.**

IMPORTANT NOTICE

- **Please complete a separate form for each Lot**
- Be sure to complete all sections of this form. You can extend the boxes and use pictures and/or other visual elements if they make your Tender more understandable. The technical offer will be assessed based on the weighted award criteria mentioned in section 3.4 of the Request for Tender.
- Please use a minimum font size of 10. Use a minimal line spacing of 1. Page limit: **12 pages**. References, tables, figures and CV do not count for this maximum.

1. GENERAL INFORMATION

SELECTION OF THE LOT or part of the LOT
Indicate here to which Lot you are applying

2. Feasibility of the R&D plan: PROJECT PLAN and PROJECT MANAGEMENT

FEASIBILITY OF THE PROJECT PLAN AND THE SCHEDULE

Detail and demonstrate the consistency of the schedule for the execution of the contract, split into Phases 1-2-3. Include time schedule, deliverables and milestones as detailed in the Request for Tenders.

Describe the work organization and supply chain.

Elaborate on your approach to selecting and managing your subcontractors.

Describe the methodology and methods used for project management, development, testing, and implementation. Include the measures to be taken with respect to risk management and quality assurance (e.g. risk assessment and risk mitigation strategy).

COMPOSITION of the PROJECT TEAM

Specify the configuration (e.g. consortium) and role of each partner and/or subcontractors, if applicable.

Demonstrate the Tenderers relevant expertise and working experience required to undertake an innovative R&D project such as Instand-NGS4P by presenting a table of staff working on the specific contract (including for sub-contractors), indicating their years of experience and their role in performing the contract. (Short CVs of key persons (max. 2 pages each) and description of references and previous projects).

3. TECHNICAL CRITERIA

Please describe your approach to ensure that the solution will meet the technical criteria for the chosen Lot specified in the Request for Tender documents

Describe how your approach meet each technical criteria

4. INNOVATIVENESS

The Instand-NGS4P Pre-Commercial Procurement is aimed specifically at pushing innovation in the field of personalized medicine using NGS workflows for cancer diagnostics. The proposed solution can build on existing technologies or applications, but has to go *beyond* the current State of the Art.

Describe how the solution encompasses novel technologies or applications and/or apply to novel user cases, considering the specific criteria of the Lot(s) of interest, which are described in section 3.4 of the Request for Tender document"

Describe how the solution encompasses novel technologies or applications and/or apply to novel user cases

5. USER'S NEED

The Instand-NGS4Ps Pre-Commercial Procurement is specifically aimed to develop solutions that meet the user's need (clinical and patient's) as described in the OMC outcome (see https://www.instandngs4p.eu/pcp/open-market-consultation/.

Describe how the solution meet the user's needs

6. SPECIFY THE PLANS FOR AND OBJECTIVES FOR OFFERS THE SUBSEQUENT PHASE 2 AND 3

Objectives and R&D Services planned for Phase 2 and Phase 3

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ANNEX C - FINANCIAL SUBMISSION FORM

FINANCIAL OFFER

Tender Identifier: **write here a short name/acronym to be used as your tender identifier throughout the Tender application forms.**

- **Please complete a separate form for each Lot**

Indicate for which Lot you are applying:	

I, THE UNDERSIGNED (NAME AND SURNAME), AUTHORISED SIGNATORY OF THE TENDERER/LEAD TENDERER			
As the [position]			
Of the following legal entity (hereafter the "Tenderer") [Legal Entity Full Name]			
WITH REGISTERED OFFICE IN			
Street + number	Postal code	City	Country
E-mail:	Telephone no.:		
VAT registration number:			
IF APPLICABLE:			
Acting in the context of a Consortium together with the following entities: - xxx In addition to the following subcontractors (if not applicable please delete) -			
PHASE 1 OFFER - BINDING			
Total Price in EURO ("Actual price") for Phase 1 (excluding VAT).	XX XXX,XX € (amount in writing/letters)		

I, the undersigned, being the authorised signatory of the Tenderer/Lead Tenderer, therefore acting on behalf of any Consortium members and subcontractors, hereby declare to take responsibility for the R&D services described in Phase 1 of the Request for Tenders (Solution Design) and detailed in for the amount stated in this financial proposal.
In addition, I recognize that the version of this Form is the official one and the only valid version under the Instand-NGS4P PCP.
Signature of the declarant, Stamp if available
Place, Date

Price breakdown (see 4.4. Financial section):

Estimated total price for Phases 2 and 3:

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ANNEX D - FORM FOR EXCLUSION CRITERIA

Tender Identifier: **write here a short name/acronym to be used as your tender identifier throughout the Tender application forms.**

Consortium member/Subcontractor name: **insert name of entity**

- Please complete a **separate form for each Lot**

Responses to these questions will be assessed as "pass" or "fail". Only those bids achieving a "pass" will be considered for further evaluation.

Indicate for which Lot you are applying:	

EXCLUSION CRITERIA
A) Conflict of interest

Tenderers submitting a Tender in respect to this PCP confirm:

- **That they do not have any conflict of interest in connection to the contract. A conflict of interest may arise in particular as a result of economic interests, political or national affinities, family or emotional ties, or any other relevant connection or shared interest;**
- **That they will inform the Lead Procurer, without delay, of any situation constituting a conflict of interest or which could give rise to a conflict of interest;**
- **That they have not made, and will not make, any offer of any type whatsoever from which an advantage can be derived under the contract;**
- **That they have not granted, sought, attempted to obtain or accepted and will not grant, seek, attempt to obtain, or accept any advantage, financial or in kind, to or from any party whatsoever, constituting an illegal or corrupt practice, either directly or indirectly, as an incentive or reward relating to the award of the contract;**

That they understand that the Lead Procurer reserves the right to verify this information and that they are aware of the consequences which may derive from any false declaration in respect of the information required by the awarding body as a condition of participation in the contract procedure.

YES/NO

B) Bankruptcy

Does any of the points listed in Chapter 3.2 of the RFT document (B. Bankruptcy) apply to your organisation, or to (any of) the director(s) and proprietor(s)?

YES/NO

C) Criminal Offences

Has your organisation or any of its directors or any other person with power of representation, decision or control of the organisation been convicted of any of the offences described in the RFT document, Chapter 3.2 Criminal Offences.

YES/NO?

I, the undersigned, being the Authorised Signatory of the Name of entity part of the insert tenderer identifier, hereby declare not to meet any of the Exclusion Criteria for this Tender.

Company Role and Name	**Partner or Subcontractor No. XX) Name**
Name of Authorised Signatory	

Position	
Signature and Stamp, if available	
Place, Date	

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ANNEX E - FORM FOR SELECTION CRITERIA

Tender Identifier: **write here a short name/acronym to be used as your tender identifier throughout the Tender application forms.**

Attention

1. Please complete a **separate form for each Lot**
2. This form should be submitted by the Tenderer or the Lead Tenderer in the case of a consortium.
3. In the case of this Tender being submitted by a consortium, these compliance criteria will be applied to the consortium as a whole.
4. Responses to these questions will be assessed as pass/fail. Only those bids achieving a "pass" will be considered for further evaluation.
5. Note that the **page limit for this Form is 10 pages** (excluding the cover page) using a minimum font size of 10 and a minimal line spacing of 1.

Indicate for which Lot you are applying:	

Demonstrate the ability to perform R&D Services up to original development of the first products or services and to commercially exploit the results of the Instand-NGS4P PCP, including intangible results in particular IPRs.
Description of the capacity, materials and equipment that are available to the tenderer for research, prototyping and limited production and supply of the first set of products or services.

Provide a description of relevant reference and/or previous projects which reflect the competences and capacity of the Tenderer in the different phases and domains of the Instand-NGS4P project. **Provide a list of current/previous services performed/developed which are similar in scope and complexity to this Tender. These references can be provided based on previous projects of the Tenderer or one or several of the consortium partners and/or Subcontractors who will be working on the project. The references should be recent and should have been finalized during the last five years. Each reference must be clearly linked to the concerned partner(s) or subcontractor(s).** **If you cannot provide at least one reference, please explain briefly why.**

Description of the financial and organisational structures that are available to the Tenderer for management, exploitation of IPRs and for generating revenue by marketing commercial applications of the results

Does your organisation have a Business Continuity / Disaster Recovery / Risk Management plan that ensures the described services are delivered in the event of a disruption affecting your business and ensures continuity of supply / service from your critical suppliers?
Yes / No
Insurance

Provide details of your current insurance cover: ● **Employer's Liability** ● **Public Liability** ● **Professional Indemnity (if applicable)** ● **Product Liability (if applicable)** ● **Other**

Please confirm whether you will take the appropriate level of insurance cover (as applicable) if you are successful in winning the contract?	**Yes / No**

I, the undersigned, being the authorised signatory of the Tenderer/Lead Tenderer hereby declare that all the information provided is accurate and applies to the Consortium as a whole (if applicable).	
Lead tenderer – Org. Name	
Name authorised signatory	
Position	
Signature	
Date, Place	
Stamp, if available	

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ANNEX F - FORM FOR ON/OFF CRITERIA

Tender Identifier: **write here a short name/acronym to be used as your tender identifier throughout the Tender application forms.**

Attention

1. Please complete a **separate form for each Lot**
2. This form should be submitted by the Tenderer or the Lead Tenderer in the case of a consortium.
3. In the case of this Tender being submitted by a consortium, these compliance criteria will be applied to the consortium as a whole.
4. Responses to these questions will be assessed as pass/fail. Only those bids achieving a "pass" will be considered for further evaluation.

A Tenderer will be excluded from participation in the contracts if a review or evaluation reveals that the information provided does not conform to the compliance criteria.

Indicate for which Lot you are applying:	

A – Compliance with the R&D definition
Name of the Tenderer or Lead Tenderer in the case of a Consortium:

A1	**The Tenderer declares that the submitted offer contains a minimum of 50% R&D Services and that the total value of products offered in each Phase will be less than 50 % of the total value of the Framework Agreement.** **The offers for all three Phases must propose services matching the R&D definition;** **See Point 15 of the Commission Communication on a framework for state aid for research and development and innovation (C(2014) 3282).** **See Article XV(1)(e) WTO GPA 1994 and the Article XIII(1)(f) of the revised WTO GPA 2014.**
	Yes / No
A2	**The Tenderer declares that the provided unit prices for each category of R&D-resources (e.g. junior, senior researchers, developers, …) in the submitted offer for Phase 1 are binding for Phases 2 and 3.**
	Yes / No
A3	- **The Tenderer declares that the financial part of the offer for the Framework Agreement must provide binding unit prices for all foreseeable items for the whole duration of the Framework Agreement.** - **The financial part of the offer for each phase must provide a breakdown of the price for that Phase in terms of units and unit prices for every type of items in the contract, distinguishing clearly the units and unit prices for product related items.** - **The offers for all three Phases will include only items (products) needed to address the challenge in question and to deliver the R&D services described in the Request for Tenders.**
	Yes / No

B – Compatibility with other public financing	
The tenderer declares that he does not receive public funding from other sources that may lead to double public funding or an accumulation of different types of public financing not permitted by EU legislation, including EU state aid rules.	**Yes / No**

C – Place of performance of the contract	
The Tenderer declares that: - **At least 50 % of the total value of activities covered by the framework agreement will be performed in the EU Member States or H2020 associated countries. The principal R&D staff working on the PCP will be located in the EU Member States or H2020 associated countries;** - **At least 50% of the total value of activities covered by each specific contract for each PCP phase must be performed in the EU Member States or in H2020 associated countries. The principal R&D staff working on each specific contract will be located in the EU Member States or H2020 associated countries.**	**Yes / No**
D – Compliance with ethics and research integrity requirements	
The submitted offer comply with ethics and research integrity requirements as specified in the Request for Tender, Chapter 3.4.	**Yes / No**
E – Compliance with security requirements	
The submitted bids comply with the EU, national and international law on dual-use goods or dangerous materials and substances.	**Yes / No**

I, the undersigned, being the authorised signatory of the Tenderer/Lead Tenderer hereby declare that all the information provided is accurate and applies to the Consortium as a whole (if applicable).	
Lead tenderer – Org. Name	
Name authorised signatory	
Position	

Signature	
Date, Place	
Stamp, if available	