'FREQUENTLY ASKED QUESTIONS' [1]

Question 1: What is the precise definition of the 'clinical validation' of 3rd phase, what exactly will be demanded, how will it be organized and what is to be covered by the allocated budget? Who is taking care of making the tests/clinical validation, the economic operator or the different partners of the consortium?

The EC-IVD will be fully in place by the end of the oncNGS project and any oncNGS solution to be used in routine diagnostics at that moment will have to fully comply with the specifications of the EC-IVD regulation.
The oncNGS consortium will request from the suppliers a clear description of how they intend to comply with this regulation when placing the oncNGS solution on the market.

Within the oncNGS PCP, the oncNGS consortium will request in the Call for Tender that the analytical and clinical performance of the developed oncNGS solution matches the requirements set within the EC-IVD. Demonstration of analytical and clinical performance is to be conducted by the suppliers.

The analytical performance of the developed oncNGS solution will need to be demonstrated fully in phase 2. With respect to 'clinical validation', the oncNGS consortium is aware that a full validation including a prospective clinical trial demonstrating clinical validation and utility is not feasible within the timeframe and budget of the PCP and would resort more on an eventual follow-up PPI.

For this, 'clinical validation' will consist of demonstrating clinical performance on specimens both at the suppliers level and at the buyers sites. More specifically, the suppliers will be asked to demonstrate clinical performance and feasibility of the oncNGS solution on a set of markers already in phase 2.
In phase 3, suppliers can complete their clinical performance and feasibility for the rest of the markers and a prospective clinical feasibility of the use of the solution will be tested at the buyers facilities using their own samples. Thus, the consortium wishes to corroborate the clinical performance of the provided oncNGS solutions only in phase 3.

Full details on which markers are expected to be tested at the respective phases will be presented in the Call for Tender. Details on the requirements for analytical and clinical performance and feasibility will be outlined in detail also in the Call for Tender.

[1] All rights reserved. This FAQ contains the questions that were currently asked and provides answers given with the information available at the given time. Questions can always be added and answers can be changed when the information that was available at the given time is no longer accurate. No legal rights may be derived from the information listed in the FAQ. This document has been drawn up with the utmost care, but no guarantees are given regarding its soundness and/or completeness. Any errors, inaccuracies or imperfections can be reported via the contact form provided on the oncNGS website (http://oncngs.eu).

Question 2: What are the partnerships options within the oncNGS PCP; is it possible to apply in a partnership or not? What does the notion 'more than 50% of R&D in EU' precisely means? How will the interaction with the oncNGS buyers at the different steps in the PCP? What about the partner matching tool?

Tenders can be submitted either individually or in consortium with other economic operators (under no circumstances it will be allowed to any natural or legal person to submit more than one bid). In agreement with the Guidance PCP procurement documents for the H2020 Programme (Version 2.1 07 January 2020), it is imperative that more than 50% of the R&D activities that are justified by the partnership are performed in EU Member States or Horizon 2020 associated countries.
Suppliers that have obtained a contract for a particular phase of the oncNGS PCP will have opportunities to interact with the oncNGS buyers (and eventually also the supporting entities) at regular intervals along the phases. These interaction moments will be clearly outlined within the Call for Tender as milestones in the process.

Questions to the oncNGS consortium can be forwarded at all time during the project through the contact facility within the oncNGS website.

A partner match page has been opened on the oncNGS website where request for partners can be announced. oncNGS secretariat will manage the online noticing of the request. If a supplier wishes to utilize this facility, please inform the oncNGS secretariat by the contact mail.

Question 3: What is the precise impact of the implementation of the EC-IVD regulation on the deployment of the oncNGS solution? How should the stipulations laid down within the EC-IVD regulation be integrated into the oncNGS PCP offers/PCP?

The EC-IVD will be fully in place by the end of the oncNGS project and any oncNGS solution to be used in routine diagnostics at that moment will have to fully comply with the specifications of the EC-IVD regulation.

The oncNGS consortium will request from the suppliers a clear description of how they intend to comply with this regulation when placing the oncNGS solution on the market.

Within the oncNGS PCP, the oncNGS consortium will request in the Call for Tender that the analytical and clinical performance of the developed oncNGS solution matches the requirements set within the EC-IVD. Or more explicit clarification of the scope of the clinical validation, we refer to Question 1 of this document.

Question 4: What are the IP rules applicable for the oncNGS solution?

The IP ownership and obligations will be set forth in detail in the Call for Tender documents and Contract Notice. In agreement with the Guidance PCP procurement documents for the H2020 Programme (Version 2.1 07 January 2020):

- the selected operators (R&D service providers) retain ownership of the intellectual property rights (IPRs) that they generate during the PCP (together with the responsibility and the costs for protecting those IPRs) and are able to use them to exploit the developed solutions beyond the procurers;
- 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 PCP 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 or use the results to the detriment of the public interest *(including security interests)*.

Question 5: Is price an issue for the oncNGS solution considering in the different partner countries, reimbursement of molecular diagnostics is subjected to different rulings; how is this issue going to be addressed within the oncNGS offers/PCP?

oncNGS consortium is fully aware that the reimbursement of the oncNGS solution through the local healthcare systems (HCS) may differ considerably in the different countries. Not only are the reimbursement fees for molecular diagnostics at this point in time different, also the treatments and care pathways can be different what may impact positioning of the use of the oncNGS solution in the various HCS.

It is NOT the purpose of the oncNGS PCP to provide a one-fit-all solution for the real-life implementation of the oncNGS solution in each HCS.
oncNGS PCP challenges 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
However, we will request the suppliers to provide the Buyers Group a clear indication on how they foresee the placing on the market of their solution what will include to some extent a price indication. It remains at the full liberty of the suppliers how they wish to market their solution but the oncNGS buyers have clearly indicated that a sustainable local utilization of the oncNGS solution in their laboratory facilities and local analyses of the sequence data is essential.

Question 6: Does the oncNGS solution have to be compatible with (all) different NGS technology platforms?

The oncNGS solution does not limit the scope of utilization to one particular NGS technology. Considering that the aim of the oncNGS PCP is to bring innovation to all patients, NGS technology should not be a limiting factor and preference will be given to compatibility with as many technologies as within the possibilities of the PCP timeframe and budget according to the supplier's estimation. A justification for the latter will be required from the supplier and detailed in the Call for Tender.

Question 7: Will the oncNGS solution only be applied in routine diagnostics or is a broader deployment could be envisaged (basic research, clinical trials, …)

The oncNGS solution is indeed primarily aimed at being used in routine diagnostics in oncology. This does not mean that the solution should be deployable in any laboratory that wishes to perform complex NGS analysis in their laboratory. It is understood that the use of the oncNGS solution will require availability of not only suitable NGS infrastructures including IT infrastructures but also skilled personnel to perform, analyse, interpret and communicate the oncNGS results.

Nevertheless, the application of the oncNGS solution in other fields or domains can be foreseen and will be considered an asset to the oncNGS solution. One can especially think of the application of the oncNGS solution in basic research, clinical trials, and as reference for material assessment.

A concise conceptual proposal for deployment of the oncNGS solution within a broader scope (e.g. for basic research, clinical trials, …) could be considered within the business case to be presented by the supplier. However, oncNGS will not demand any "Proof of Concept" of such deployment.

Question 8: Should the oncNGS solution also cover 'Minimal Residual Disease' (MRD) detection?

MRD is indeed a very interesting component in assessing the outcome of the treatment and an essential element in follow-up of cancer therapies. It is understood by the oncNGS consortium that applying MRD detection requires a substantially different approach than screening for genomic variation aiming to diagnose the cancer or to determine prognostic and/or predictive markers for therapeutic use.

The primary aim of oncNGS as presented at the OMC webinars is to develop a tool for diagnosis, prognosis, prediction, theranostic and the agnostic use in case patients have an advanced cancer. As such, the Call for Tender will address basically these three applications.

MRD detection could be an interesting secondary use of the solution and the oncNGS consortium would certainly welcome proposals from the suppliers on how to integrate MRD with the oncNGS solution for diagnosis, prognosis, theranostic or prediction. A sound conceptual approach may thus be considered as an interesting asset. We do not expect though that within the timeframe and budget currently made available any practical aspects can be already developed as to MRD detection.

Question 9: Does the oncNGS consortium envisage a single NGS panel for all applications or could distinct panels be proposed within e.g. a single context/setup?

As indicated in the OMC webinars, the oncNGS solution is to be considered as an integrated solution. An Integrated Solution is a "result from the problem solving work process that integrates across two or more functions in a business or technology that is referred to as an enterprise to maximize financial value (e.g., sales and productions planning, etc.) as well as combined with complementary technologies such as robotics (e.g., driving, robotic surgery, etc.) to provide integrated solutions" (The Project Definition – for your project success!).

To translate this definition to our oncNGS project, we seek to develop oncNGS as covering our unmet need in assessing genetic variation in liquid biopsies from patients with an advanced solid or hematologic tumour by NGS.

Question 10: How will be the selection criteria for the oncNGS PCP? Are there any pre-defined KPIs defined in the way you will assess the economical operators answers for Phase 1, 2 and 3?

In the Call for Tender, the selection and the awarding criteria that will be applied to finally assign a contract to a particular bidder will be clearly outlined. Different levels of criteria apply to each phase but in essence for all steps exclusion, selection and award criteria will be outlined. For each criteria Key Performance Indicators have been defined by the Buyers Group, which will be described in detail in the Call for tender.

Question 11: Can all type of industry apply?

Experience in the field of the object of the contract will need to be demonstrated. The tenderer has to comply to certain selection criteria that will be asked in the tender documents. In the PIN there was given an indication of the CPV-codes that are applicable on this tender.

Question 12: What can be covered by the budgets attributed to each phase? Will the budget e.g. allow also to purchase library prep equipment and sequencers?

All the buyers in charge of running a clinical performance have already their own sequencing platforms. By the way it is considered relevant to remember that oncNGS PCP is an R&D service contract. The definition of 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, from Phase 1 to Phase 3.
In case the Bidder considers that a specific equipment is needed to provide oncNGS R&D services, it will need to justify it accordingly in its technical offer and enter the relevant biding unit price in its financial offer.
In agreement with the Guidance PCP procurement documents for the H2020 Programme (Version 2.1 07 January 2020), the total value of products offered in phase 1 respectively phase 2 must be less than 50 % of the value of the phase 1 respectively phase 2 contract and the total value of products offered in phase 3 must be so that the total value of products offered in all phases (1,2 and 3) is less than 50% of the total value of the PCP framework agreement.

Question 13: How will research and development be performed at the buyers' sites? Will all run in parallel similar tests or will each of them focus on a given application area or technology based application? It is assumed that different institutes have different sequencing platforms today and may have access to different type of tumour samples.

All buyers in charge of running a clinical performance, independently of their sequencing platforms, commit to test the prospective feasibility of the at least one of the solutions using their own samples.

The number of samples as well as quantitative and qualitative criteria that will be considered in the evaluation will be included in the Call for Tender. Of note, solution provider will have to provide input on the analytical performance in Phase 2.

The suppliers will be required to install their oncNGS prototypes at the oncNGS pilot sites, provide all consumables for the wetlab analysis and operationalize the IT analytical and reporting tool at the oncNGS pilot site. Bidders financial offer will include binding unit prices for all foreseeable items for the duration of the whole PCP (from Phase 1 to Phase 3).
Samples, personnel and sequencer equipment to handle the workflow will be provided by the oncNGS pilot sites. Permissions to install the oncNGS solution locally at the buyers 'site will be taken on by the oncNGS pilot sites.

Question 14: Please precise the notice "Research as a service" within a pre-commercial procurement

In agreement with the Guidance PCP procurement documents for the H2020 Programme (Version 2.1 07 January 2020), oncNGS 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.
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 does not include quantity production or supply to establish the commercial viability or to recover R&D costs.[2] 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.

Question 15: How many targets and samples are we talking about in terms of number of markers/SNPs or targeted capture? Have the targets for predictive, prognostic & diagnostic outcomes already been defined by the partners in this consortium, or is this to be defined by this research program? Any clarity if the solution sought is for DNA or for DNA & RNA both ? Non coding RNA and Epigenetic markers? Should the participated solutions cover all of the possible types of mutation (SNV, Del/Ins, fusions and CNV)? The tender refers to primer optimization – does this mean there is a preference for an amplicon or capture-based approach to the solution?

The oncNGS consortium has listed a minimal set of targets to be covered in the oncNGS solution. The complete list will be disclosed in the Call for tender but aims at covering > 300 markers in solid cancers, while about 100 targets are envisaged for lymphoma.

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

The solution should be able to analyse DNA and/or RNA and implicate the use of NGS analysis as the key technology .

There has been no restriction set as to the type of markers to be assessed. It is important though that sufficient evidence or clear justification for inclusion of a particular marker in the oncNGS solution is available.

OncNGS does not restrict to any particular NGS technology nor approach. It is however to be kept in consideration that oncNGS aims to be deployable at large in a sustainable way. A concise description of how the suppliers envisage such deployment within the Healthcare systems in the buyers' countries will be requested.

Question 16: Will the bids have to cover the complete workflows from pre-analytics through library preparation, gene panels, sequencing, bioinformatics to patient? Do we have to set up the consortium or, for example, if we are BioIT company, can we have the view of the wetlab part and proposed our solution? Will the tender contain several lots for different parts of the workflow or will each bidder (or bidding communities) have to cover the whole workflow? Will this kind of information be disclosed during the OMC phase?

As indicated at the OMC webinars, oncNGS aims to produce a fully integrated solution to the buyers' needs. For this, the buyers are convinced that all steps from analyte till final report need to be integrated in a single workflow by a single application. Thus, the complete workflows from pre-analytics through library preparation, gene panels, sequencing, bioinformatics to report for the clinician is to be considered as a whole.

Suppliers which cover only part of the oncNGS solution e.g. only the wetlab, and wish to bid for the oncNGS tender will need to complement their expertise to cover the full workflow envisaged by the oncNGS solution. (A partner match page has been opened on the oncNGS website where request for partners can be announced. oncNGS secretariat will manage the online noticing of the request. If a supplier wishes to utilize this facility, please inform the oncNGS secretariat by the contact mail.)

All details on the requirements set for the oncNGS PCP at the different phases will be outlined in the Call for tender.

Question 17: How does OncNGS relate to the other European initiatives?

The oncNGS PCP is an independently financed Horizon 2020 project and concise information on the general call can be found on the Cordis website. NGS diagnostics in 21st century oncology: the best, for all, at all times | oncNGS Project | H2020 | CORDIS | European Commission (europa.eu)

It is clear though that the final goal of the oncNGS PCP is to deliver a tool to the hospitals that brings a highly valuable innovation to patients with advanced cancer. All along the development of the oncNGS solution, it will be possible though within any legal constraints and upon agreement by all parties, to seek synergies with other initiatives that may be launched within the many future programs by the European Commission (e.g. Europe's Beating Cancer plan, the Mission on Cancer, the 1+MillionGenomes project, the European Health Data Space initiatives, …).

Question 18: Can UK suppliers bid either alone or in a partnership?

The EU-UK withdrawal agreement from February 2020 dealt with the position of UK entities in ongoing funding programmes from the 2014-2020 MFF period (like Horizon 2020). The Brexit deal from end 2021 addressed the position of UK entities in new funding programmes from the 2021-2027 period (like Horizon Europe). The Brexit deal did not change the position of UK entities in ongoing funding programmes from the 2014-2020 MFF period (like Horizon 2020), as this was already agreed in the EU-UK withdrawal agreement.

So, yes, as long as projects are running under the Horizon 2020 programme, these projects have to keep referring to the February 2020 EU-UK withdrawal agreement. UK suppliers can bid and their R&D activities can account for the more than 50% obligatory R&D activities within the EU.

Question 19: In the oncNGS Request for tender, the following requirements are listed, amongst many others:

- SUST.03 - oncNGS solution SHALL be deployable locally and interfaced with existing local tools to avoid sample and data transfer, which could infringe on privacy issues
- SUST.04 - OncNGS SHALL provide with an upgradable technology. Being upgradable the inclusion of: Bio IT tools
- BIOINFOR.SUST.MAINT.01 - OncNGS solution bioinformatics pipeline SHALL be executed with minimal computational requirement as measured by required RAM and CPUs

It is questioned whether complying with all three requirements is possible without considering cloud services or 'heavy infrastructures in the lab'.

We are fully aware that full local deployment of the complete oncNGS solution requires major investment as to IT infrastructure and logistics. We consider though that such option should be made available by the oncNGS supplier, well understood that the investments for operationalizing the local deployment is the burden of the buyer. When locally deployed, the oncNGS supplier should optimize the required RAM/CPU to fully operationalize the oncNGS solution in as much as possible though.

In addition, as correctly pointed out, if buyers do not wish to make the investment for locally installing the full oncNGS solution, a cloud service can be foreseen and the oncNGS supplier has to prove how such analysis can be performed in a secure way matching all required levels of data protection, privacy and security.

Thus, SUST.03 does not exclude cloud services nor does BIOINFOR.SUST.MAINT.01 exclude that IT investments could be major. It is demanded however that a full local deployment is possible.

As to SUST.04, we also recognize that Bio IT tools are most easily upgradable trough a cloud service and can understand that for several buyers this option could suffice. However, the buyers wish in addition that locally developed algorithms and obtained results can be combined/integrated in the oncNGS Bio Tools in a secured way. It is one of the challenges the oncNGS consortium wishes to put forward to the suppliers. The consortium welcomes the suppliers to propose options for such secure combination and integration.

Question 20: How will the scoring of the bids for oncNGS be performed? What are the main drivers of your scoring decision, is it cost or actionability?

The Evaluation of the tenders will be done in agreement with Section 6.6, the Annex 5 Awarding Criteria and Annex 6 Scoring Model for the Price of the Call for Tender.

As can be observed in the matrix, both cost and actionability are important but while actionability/coverage is estimated more important at the early stage and then is decreasing, price follows the reverse trajectory. This reflects the pathway from research to (commercial) deployment.

Question 21: Is it acceptable in the context of this PCP to use, within one single workflow, several panels to better address the question of cost vs content; routine diagnostics testing vs Clinical Trial/Translational Research for instance? In your definition of gene content are you looking at routine actionability or exploratory (clinical trials)? In hot spots genes are you looking at a full coverage of the gene or just the hot spots?

The oncNGS PCP aims at developing an integrated solution for predictive, prognostic and diagnostic analysis in liquid biopsies of solid tumours (including appropriate haematological indications) based on NGS technology. It is thus perfectly possible to develop 'tailored' panels to specific needs applying the overall standardized workflow of the oncNGS solution (sample, NGS, bioinformatics, interpretation & reporting). However we do request that suppliers develop the panels described in the Call for Tender (Pan-cancer oncNGS LB panel (=Panel 1) & Hemato/Lymphoma oncNGS LB panel (= Panel 2)). It is up to the supplier to decide whether to include the full coding sequence or just hotspots.

As to the scope of the panels, we have listed the required biomarkers that the buyers identified as important – these markers are considered important for p and could be used predictive, prognostic and diagnostic analysis and are primarily focused to routine actionability notwithstanding the opportunity for exploratory use.(e.g. clinical trials)

The nature of the variations to be covered for each of the biomarkers, or combination of biomarkers, is open to the suppliers to decide what should be included but should be justifiable by scientific argumentation – both omitting or adding decision elements.

Question 22: Does English annotations meet the criteria or multilingual is necessary?

Annotation can be in English only for the PCP.

Question 23: Does the solution need to be for DNA and RNA, or can it be for DNA only?

The solution need to cover both, DNA and RNA.

Question 24: In the tender document, two different TAT (turnaround time) are mentioned, one being 48h and one being < 7 days. Which one applies?

TAT of 48h is the one requested at wetlab level (from Nucleic acid to NGS sequencing). We mention that we strive to a TAT of <7days for a total workflow, from available samples to reporting.

Question 25: Is it mandatory to address all Must Have Criteria in awarding criteria, or do we just get some "penalties" in the scoring if not (fully) addressed?

All Must Have criteria are required to be addressed in the tender. In principle any must have criterion failing to be addressed leads the tender not to meeting the minimal requirements and in principle to be excluded.

Question 26: What happens if the overall Technical Feasibility scores sum less than the Min Points set in the Scoring Table?

The Technical Excellence score results summing up the scores achieved in all its subcriteria (from 1 to 11). The Technical Feasibility results summing up the Technical Excellence score and the Development plan score. In case the Technical Feasibility is not meeting the Min Points, the tender will be excluded.