Instand-NGS4P OMC Questionnaires

The final questionnaires addressed to users (66 pages), patient associations (37 pages) and solution providers (58 pages) prepared by the project consortium experts and uploaded to Survey Monkey are displayed.

USER'S Questionnaire INSTAND-NGS4P

PROJECT INTRODUCTION

INSTAND-NGS4P is an EU-funded Pre-Commercial Procurement (PCP) project for improving cancer patient's benefit from Next Generation Sequencing (NGS). Driven by patient and clinical needs, two innovative NGS workflows from sample pre-analytics to medical decision-making will be developed for routine diagnostics of common and rare adult and paediatric cancers complying with the IVDR. The developed workflows will compile information from cancer gene testing, pharmacogenetics 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 PCP project provides funding for a public consortium to define unmet medical and technical needs based on an Open Market Consultation, which lays the foundation for a call for tenders addressing solution providers (companies) to develop their products to better meet user needs. At three cut-off periods, companies 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 companies for product development (in total 8.55 M€) will finally lead to two integrated standardized NGS workflows, including decision support.

The different lots of this project cover the entire workflow for integration and standardization of targeted and whole genome DNA sequencing and decision making at the bedside:

- lot 1: Pre-sequencing (specimen collection, nucleic acid isolation, library preparation)

- lot 2: Sequencing

- lot 3: Bioinformatics analysis

- lot 4: Integrated reporting

The procurement will take the form of a pre-commercial procurement (PCP) under which R&D service contracts will be awarded to a number of solution providers in parallel in a phased approach. This will make it possible to compare competing alternative solutions.

Each selected operator will be awarded a framework agreement that covers 3 R&D phases.

The 3 phases are:

- Design of lots

- Prototype of lots

- Fully integrated NGS workflow.

Each of the 3 phases will address all 4 lots.

USER'S Questionnaire INSTAND-NGS4P

PURPOSE OF THE QUESTIONNAIRE

This questionnaire is part of the Open Market Consultation (OMC) which aims at refining the clinical, patient and technical needs defined by the project consortium, as well as the emerging solutions available or under development to address these needs. For this purpose, three questionnaires were developed for three different stakeholder groups – users, solution providers and patient associations. The feedback collected from the questionnaires will support the subsequent preparation of the call for tenders. The questionnaires also allow disclosure of confidential information to the project consortium, which will be treated with high confidentiality. Aggregated data from the results of the survey will potentially be published in an anonymous way, excluding the information labelled as confidential.

The personal information collected through the questionnaires will be exclusively used for the purposes of the project, will not be shared with third parties, and will be deleted after the closure of the project.

GUIDANCE

The questionnaire is addressed to all solution providers in the field of NGS, and is divided into the following sections: General questions, Lot 1, Lot 2, Lot3, Lot4. After answering the general questions, you will be asked for each section whether you want to fill it in or not. We would highly appreciate if you would take the time to fill in the section(s) related to your expertise. However, if you do not find the question relevant, feel free to select N/A (not applicable) as an answer or skip the question and to move on to the next one.

Please submit the questionnaire by May 31st, 2021. Thank you in advance for contributing.

* 1. Organisation profile

Organisation name	
Address	
City/Town	
Country	

* 2. Contact person

First name	
Family name	
Email Address	
Phone Number	

USER'S Questionnaire INSTAND-NGS4P

General questions

* 3. How is your organization positioned in the NGS scene (more than one answer possible):

- [ ] Provider
- [ ] Manufacturer
- [ ] Includes Research & Development
- [ ] Hospital/medical centre
- [ ] Academic hospital
- [ ] Diagnostic laboratory
- [ ] Patient organization
- [ ] Other (please specify)

* 4. What is your current position in your organization?

5. Are you currently performing production/diagnostic activities for products used or diagnostics in the NGS workflow in (if yes, please specify the percentage in the textbox):

Europe	
North America	
Asia	
South America	
Australia	

* 6. Are you currently performing research and development activities for products/diagnostics used in the NGS workflow in (if yes, please specify the percentage in the textbox):

Europe	
North America	
Asia	
South America	
Australia	

* 7. Are you using NGS sequencing for research or for diagnostics?

- Yes
- No
- N/A

* 8. Do you have access to sequencing facilities?

- Yes
- No
- N/A

* 9. Do you perform sequencing in house or externally?

- In house
- Externally
- N/A

* 10. What platform do you use?

- Illumina
- Ion Torrent
- Gene-Reader
- Oxford Nanopore
- MGI
- Pac Bio
- N/A
- Other (please specify)

* 11. How many samples are you typically sequencing per week?

- Less than 1
- 1-10
- 10-50
- 50-100
- More than 100
- N/A

* 12. How interested are you in whole exome sequencing? (0-not interested in all, 5 - very interested)

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 13. How interested are you in gene panels? (0-not interested in all, 5 - very interested)

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 14. How interested are you in whole genome sequencing? (0-not interested in all, 5 - very interested)

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 15. Are you a user (current or future) of NGS in the clinical setting?

- ○ Yes
- ○ No

USER'S Questionnaire INSTAND-NGS4P

CLINICAL NEEDS

16. Do you currently employ NGS in your clinical practice?

- ◯ Yes
- ◯ No
- ◯ For clinical research purpose only

17. Do you currently base clinical decisions in daily clinical practice on NGS?

- ◯ Yes
- ◯ No
- ◯ I am not sure

18. How many times do you perform NGS during the patient's journey?

- ◯ At diagnosis
- ◯ At diagnosis and progression
- ◯ As a monitoring tools

19. Do you or your center/hospital participate in precision oncology trials?

- ◯ Yes
- ◯ No
- ◯ I am not sure
- ◯ No, but would be interested in

If yes, please specify:

20. What is the turn around time (from sample collection) in which you expect to receive an NGS report?

- ◯ <72h
- ◯ 72h-1 week
- ◯ 1-2 weeks
- ◯ 2-3 weeks
- ◯ 3-6 weeks
- ◯ >6 weeks
- ◯ Not important

21. Which type of cancers do you mainly treat?

- ◯ Adult
- ◯ Childhood
- ◯ Adult and childhood

22. If you treat adult cancers, which kind of cancers do you treat?

- ☐ Lung
- ☐ Breast
- ☐ Colo-rectal
- ☐ Bilio-pancreatic
- ☐ Gastric
- ☐ Melanoma
- ☐ Adult sarcoma
- ☐ Prostate
- ☐ Bladder
- ☐ Gynecological
- ☐ Head and neck
- ☐ Other (please specify)

23. If you treat childhood cancers, which kind of cancers do you treat?

- ☐ All
- ☐ AML
- ☐ CML
- ☐ Lymphoma
- ☐ Neuroblastoma
- ☐ Ewing Sarcoma
- ☐ Osteosarcoma
- ☐ Other (please specify)

24. Which kind of samples do you currently collect routinely?

- ◯ Tumor
- ◯ Blood
- ◯ Bone marrow

Other (please specify). If blood or bone marrow, please specify sample collection tubes:

25. How are the samples processed?

- ◯ Formalin-fixed and paraffin embedded (FFPE)
- ◯ Fresh frozen
- ◯ Fresh refrigerated
- ◯ Don't know
- ◯ Other (please specify)

26. How important is it for your NGS analysis and report to collect and process fresh or fresh frozen tumor?

- ◯ Very low
- ◯ Low
- ◯ Intermediate
- ◯ High
- ◯ Very high

27. Which information do you need covered by an NGS workflow?

- ☐ Risk stratification
- ☐ Prognostic factors
- ☐ Predisposition/Hereditary syndromes
- ☐ Therapeutic targets
- ☐ Pharmacogenetics
- ☐ Other (please specify)

28. Which types of genetic variants are relevant for cancer predisposition?

- [ ] Single nucleotide variants (SNV)/small insertions and deletions (INDEL)
- [ ] Copy number aberrations (CNV)
- [ ] Other (please specify)

29. Which types of genetic variants are relevant as actionable targets?

- [ ] Single nucleotide variants (SNV)/small insertions and deletions (INDEL)
- [ ] Copy number aberrations (CNV)
- [ ] Fusions
- [ ] Overexpression
- [ ] Other (please specify)

30. How important is it to include the level of evidence of genetic variants for suggested targeted treatments in the report (ie clinical variants actionable/clinical trials restricted/research mutations only) ?

- ○ Very low
- ○ Low
- ○ Intermediate
- ○ High
- ○ Very high

31. How important is it to include the level of evidence of single and combined targeted treatments in the report?

- ○ Very low
- ○ Low
- ○ Intermediate
- ○ High
- ○ Very high

32. How important is it to include pharmacogenetic information in the report?

- ○ Very low
- ○ Low
- ○ Intermediate
- ○ High
- ○ Very high

33. What kind of pharmacogenetic information do you think is useful (please select all that apply)?

- [ ] Avoiding toxicity
- [ ] Evaluation of drug-drug interactions
- [ ] Drug dose assessment
- [ ] Other (please specify)

34. How important is it to include response predictions to targeted therapies in a report?

- ◯ Very low
- ◯ Low
- ◯ Intermediate
- ◯ High
- ◯ Very high

35. If it is not an approved drug for the use in pediatric patients, how important is it to provide information on recommended treatment schedules and dose modifications?

- ◯ Very low
- ◯ Low
- ◯ Intermediate
- ◯ High
- ◯ Very high

36. Is it important to state clearly in the report suspect germline mutations?

- ◯ Yes
- ◯ No
- ◯ Only for restricted cancer type, specify

37. Is it important to quote in the report suspect clonal hematopoiesis?

- ◯ Yes
- ◯ No
- ◯ Don't know

38. How important is it to determine and clarify the allele frequency of single gene alteration in the report

- Very low
- Low
- Intermediate
- High
- Very high

39. How is it important to list all VUS in the final report?

- Very low
- Low
- Intermediate
- High
- Very high

40. How important is it to report “complex” biomarker like TMB/HR/DNA Repair deficiency

- Very low
- Low
- Intermediate
- High
- Very high

41. How important is it to include the possibility to match genetic findings to clinical trial active for enrollment in your country?

- Very low
- Low
- Intermediate
- High
- Very high

42. Do you currently participate in molecular tumor boards?

- Yes
- No
- No, but interested in

If yes, please specify which and if they are virtual

43. If you have any further comments in the context of clinical needs. Please let us know.

44. Is this information confidential?

- Yes
- No

USER'S Questionnaire INSTAND-NGS4P

Introduction lot 1

* 45. Would you like to answer questions related to Lot 1 (Pre-Analytics and Library preparation)?

- Yes
- No

USER'S Questionnaire INSTAND-NGS4P

Lot 1

CHALLENGE 1:

Improving the analytical performance by standardizing and or simplifying the pre-analytical processes

46. Most commonly used/produced samples for NGS analysis

Which are the types of specimens most commonly analyzed in your Lab?

- [ ] FFPE
- [ ] Frozen tissues
- [ ] Blood
- [ ] FNAs
- [ ] Plasma
- [ ] N/A
- [ ] Other (please specify)

47. Is the information above confidential?

- ◯ Yes, it is confidential
- ◯ No, it can be shared

Among the following, please indicate the specimen(s) you consider most challenging in terms of defining detailed pre-analytical processing standards. Please weight each of them on the basis of their importance from 1 (lower) to 5 (higher).

48. FFPE

	1	2	3	4	5	N/A
DNA	◯	◯	◯	◯	◯	◯
RNA	◯	◯	◯	◯	◯	◯

49. Frozen tissues

	1	2	3	4	5	N/A
DNA	◯	◯	◯	◯	◯	◯
RNA	◯	◯	◯	◯	◯	◯

50. Blood/plasma

	1	2	3	4	5	N/A
DNA						
RNA						
cfDNA						
cfRNA						

51. Fine Needle Aspirates

	1	2	3	4	5	N/A
DNA						
RNA						

52. Circulating Tumor Cells

	1	2	3	4	5	N/A
DNA						
RNA						

53. Extracellular vesicles

	1	2	3	4	5	N/A
DNA						
RNA						

54. Saliva

	1	2	3	4	5	N/A
DNA						

55. Other

	1	2	3	4	5	N/A
DNA						
RNA						

56. If you selected other, please specify

PROBLEM: Preanalytical processing procedures can cause variations in the test result

SOLUTION: Standardisation according to ISO and CEN documents

Is your organization aware of the following standards? Please select the first box if there is awareness and the second if your organization works according to or applies the standard:

57. ISO 15189 Medical Laboratories – Requirements for quality and competence

- Aware
- Applies

58. ISO 20166-1:2018 Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for formalin-fixed and paraffin-embedded (FFPE) tissue - Part 1: isolated RNA

- Aware
- Applies

59. ISO 20166-3:2018 Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for formalin-fixed and paraffin-embedded (FFPE) tissue - Part 3: isolated DNA

- Aware
- Applies

60. ISO 20184-1:2018 Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for frozen tissue - Part 1: isolated RNA

- Aware
- Applies

61. ISO 20186-1:2019 Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for venous whole blood - Part 1: isolated cellular RNA

- Aware
- Applies

62. ISO 20186-2:2019 Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for venous whole blood - Part 2: isolated genomic DNA

- Aware
- Applies

63. ISO 20186-3:2019 Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for venous whole blood - Part 3: isolated circulating cell free DNA from plasma

- Aware
- Applies

64. CEN/TS 17390-1:2020 (WI=00140123) Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for circulating tumor cells (CTCs) in venous whole blood - Part 1: Isolated RNA

- Aware
- Applies

65. CEN/TS 17390-2:2020 (WI=00140125) Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for circulating tumor cells (CTCs) in venous whole blood - Part 2: Isolated DNA

- Aware
- Applies

66. Do you adhere to other ISO standards for NGS pre-analytics or library preparation?

- Yes
- No

If yes, please specify

67. Does your organization see ISO standardization as a good and useful approach?

- Yes
- No

Comment

PROBLEM Many quality issues in pre-analytics arise even before nucleic acid extraction, during the whole process starting from sample collection, processing and storage.

SOLUTION: An entry-level quality check to confirm the sample is fit for purpose.

68. In your opinion, this would be:

- Not needed
- Helpful
- Crucial to develop

69. Which parameters beyond adherence to standards would be needed to be checked

for fixed, paraffin-embedded samples	
for fresh frozen tissue	
for white blood cells (PBMC)	
for liquid biopsies	

PROBLEM Sample transport and storage might be required which can change the nucleic acids' quality/quantity.

SOLUTION: Stabilization of DNA and RNA (this can include all different types of DNA and RNA depending on the source and target situation)

70. Is your organization interested in further development of such an approach?

- Yes
- No

Comment

71. PROBLEM Sample pre-analytical processing can influence the final result of NGS.

SOLUTION: The project participants have compiled a list of key challenges in sample and library preparation that could be improved within the next 2 – 3 years.

Please weight each of them on the basis of their importance from 1 (lower) to 5 (higher).

	0	1	2	3	4	5
Increase in sample stability	○	○	○	○	○	○
Increase in sample quantity	○	○	○	○	○	○
Increase target concentration in the sample	○	○	○	○	○	○
Direct or long range sequencing	○	○	○	○	○	○
Alternative innovative stabilization methods	○	○	○	○	○	○
Compatibility of sample stabilizers with analytical test procedure that need to be performed or have been performed on the same sample (e.g. histology/cytology)	○	○	○	○	○	○
Efficiency of the analyte isolation/extraction procedure	○	○	○	○	○	○
Quality assessment of the isolated analyte	○	○	○	○	○	○
Sample storage	○	○	○	○	○	○
Analyte storage	○	○	○	○	○	○
Automation of the isolation procedures	○	○	○	○	○	○
Standardization	○	○	○	○	○	○
Other	○	○	○	○	○	○

Other (please specify)

72. Is your organization interested in further development in one or more of these approaches?

- ○ Yes
- ○ No

73. Please give the numbers with the highest priority first, down to the lowest priority you are interested in:

,

Increase in sample stability

,

Increase in sample quantity

,

Increase target concentration in the sample

,

Direct or long range sequencing

,

Alternative innovative stabilization methods

,

Compatibility of sample stabilizers with analytical test procedure that need to be performed or have been performed on the same sample (e.g. histology/cytology)

,

Efficiency of the analyte isolation/extraction procedure

,

Quality assessment of the isolated analyte

,

Sample storage

,

Analyte storage

,

Automation of the isolation procedures

,

Standardization

74. Comment and explain your choice for the highest and second highest priority.

PROBLEM During nucleic acid isolation, it is often impossible to obtain more than one NA target especially when dealing with small size samples.

SOLUTION: Simultaneous Isolation of multiple nucleic acid types (e.g. DNA and RNA) in the same run.

75. Is your organization interested for further development in this approach?

- Yes
- No

76. Please weight the importance of the further development of this approach from 1 (lower) to 5 (higher)

					N/A
Š	Š	Š	Š	Š	

77. Please let us know if you have any comment

PROBLEM Each target situation and type of nucleic acid imply different isolation procedures resulting in multiple kits to choose from and large stocks that might expire before they can be used up.

SOLUTION: Compatibility of NA isolation methods with multiple source target situations

78. Is your organization interested in further development in this approach?

- Yes
- No

Comment

PROBLEM Panels are constantly in need of extension for addition of new diagnostic marker sequences and need to be verified and validated before use. This complicates library preparation due to optimal selection of changing panels to diagnostically cover the case to be analysed.

SOLUTION: Whole Genome Sequencing (WGS) and Whole Exome Sequencing (WES) instead of targeted NGS approach

79. Is your organization interested in such an approach?

- Yes
- No

Comment

80. In case of R&D involvement, would financial support available in the Instand-NGS4P project be

- not needed
- helpful
- crucial to develop this approach

Please comment and specify if your this answer is confidential or it can be shared

PROBLEM The ligation of adapters is a critical step in library preparation. Insufficient adapter ligation leads to low library complexity, especially for low input samples

81. Which approach(es) are you currently using:

- [ ] amplicon-based library preparation
- [ ] full length adapters
- [ ] stubby adapters
- [ ] Other (please specify)

82. What is the guaranteed ligation efficacy you can acquire:

- <70%
- 70-80%
- 80-90%
- 90-95%
- >95%

SOLUTION: Improve the adapter design and library preparation protocol.

1. use of alternatives to adapter- and amplicon-based approaches
2. improve adapter design
3. improve ligation process

83. Is your organization interested in such an approach?

- Yes
- No

If yes, please give the number of the solution your organization is interested in

84. Please weight the importance of the further development of approaches from 1 (lower) to 5 (higher):

					N/A
Š	Š	Š	Š	Š	

PROBLEM WGS and WES are difficult with FFPE tissue.

SOLUTION:

1. Use alternatives for FFPE tissue, like frozen tissue
2. Use other fixation/ stabilization methods that preserve the histologic qualities and stabilizes DNA and RNA for use in NGS

85. Is your organization interested or involved in R&D for such an approach?

- Yes
- No

If yes, please give the number of the solution your organization is interested in (highest priority first)

86. In case of R&D involvement, would financial support available in the Instand-NGS4P project be

- not needed
- helpful
- crucial to develop this approach

Let us know if you have any comments and if these are confidential

87. Please weight the importance of the further development of this approach from 1 (lower) to 5 (higher)

					N/A
Š	Š	Š	Š	Š	

88. Comment

PROBLEM WGS and WES difficult for Liquid Biopsy (cfDNA and cfRNA, exosome and CTCs)

SOLUTION:

1. Maximise the yield and quality of isolated targets
2. Increase sequence sensitivity and precision

89. Is your organization interested or involved in R&D for such an approach?

- Yes
- No

If yes, please give the number of the solution your organization is interested in (highest priority first):

90. In case of R&D involvement, would financial support available in the Instand-NGS4P project be

- not needed
- helpful
- crucial to develop this approach

Let us know if you have any comments and if these are confidential

91. Please weight the importance of the further development of this approach from 1 (lower) to 5 (higher)

N/A

92. Comment

PROBLEM Complexity and the large number of steps needed for the complete library preparation, which can also differ in various specific situations, increases the risk of error causing failure or variations in the end result.

SOLUTION: Below you can find a list of possible approaches to solve the problem.

93. Please weight each of them on the basis of their importance from 1 (lower) to 5 (higher).

	1	2	3	4	5	N/A
Universal approach for different sample types and targets	○	○	○	○	○	○
Automation of library preparation	○	○	○	○	○	○
Automation of nucleic acid isolation alone	○	○	○	○	○	○
Automation from nucleic acid isolation (different targets and DNA and RNA, low and high yield) to sequencing (closed system)	○	○	○	○	○	○
Direct or long range sequencing	○	○	○	○	○	○
Reduced number of steps needed	○	○	○	○	○	○
UMIs mandatory (for mutation detection down to 0.01-0.1% allele frequency)	○	○	○	○	○	○
Improvement of library preparation success rate	○	○	○	○	○	○
Improvement of library yield	○	○	○	○	○	○
Minimal quality and quantity requirements for the input material	○	○	○	○	○	○
Other	○	○	○	○	○	○

Other (please specify)

94. Is your organization interested in one or more of these approaches?

- ○ Yes
- ○ No

95. In case of R&D involvement, would financial support available in the Instand-NGS4P project be

- not needed
- helpful
- crucial to develop this approach

Let us know if you have any comments and if these are confidential

96. Please give the numbers with the highest priority first, down to the lowest priority:

,

Universal approach for different sample types and targets

,

Automation of library preparation

,

Automation of nucleic acid isolation alone

,

Automation from nucleic acid isolation (different targets and DNA and RNA, low and high yield) to sequencing (closed system)

,

Direct or long range sequencing

,

Reduced number of steps needed

,

Reduced need for pre-amplification

,

UMIs mandatory (for mutation detection down to 0.01-0.1% allele frequency)

,

Improvement of library preparation success rate

,

Minimal quality and quantity requirements for the input material

97. Comment

PROBLEM Waste of material due to package sizes and stability of reagents

SOLUTION:

1. Increased long term stability of reagents and simplified storage requirements

2. Reduce and recycle packaging and consumables
3. Scalability of reagents

98. Is your organization interested in further development in one or more of these approaches?

- Yes
- No

Please give the numbers of interest or involvement with the highest priority first, down to the last priority:

99. In case of R&D involvement, would financial support available in the Instand-NGS4P project be

- not needed
- helpful
- crucial to develop this approach

Let us know if you have any comments and if these are confidential

CHALLENGE 2:

Integrating pre-analytical, analytical processes and data analytics into a standardized workflow

PROBLEM WGS and WES are difficult for FFPE material because of the multitude of chemical changes present in the sample.

SOLUTION: Alternative isolation/stabilisation methods suitable for WGS and WES need to be compatible with other diagnostic methods, like histology and cytology.

100. Is your organization interested in further development of such an approach?

- Yes
- No

Comment

101. In case of R&D involvement, would financial support available in the Instand-NGS4P project be

- not needed
- helpful
- crucial to develop this approach

Let us know if you have any comments and if these are confidential

PROBLEM WGS and WES are difficult for low yield samples (e.g. plasma cfDNA, cfRNA).

SOLUTION:

1. Alternative isolation/stabilisation methods giving highest yield possible

2. Increased sequencing sensitivity

102. Is your organization interested in the further development of such an approach?

- Yes
- No

Please give the numbers of interest or involvement with the highest priority first, down to the lowest priority:

103. In case of R&D involvement, would financial support available in the Instand-NGS4P project be

- not needed
- helpful
- crucial to develop this approach

Let us know if you have any comments and if these are confidential

1. PROBLEM Isolated nucleic acid preparations can contain interfering substances. This can impair the reliability of the results and the compatibility of isolation methods with multiple sequencing methods.

SOLUTION:

1. The isolates are tested for inhibitory substances for various sequencing methods

2. Development of alternative procedures to avoid known interfering substances

104. Is your organization interested or involved in R&D for such an approach?

- Yes
- No

Comment

105. In case of R&D involvement, would financial support available in the Instand-NGS4P project be

- not needed
- helpful
- crucial to develop this approach

Let us know if you have any comments and if these are confidential

PROBLEM Long turnaround times (for pre-analytics and library preparation).

SOLUTION: Below you can find a list of possible approaches to solve the problem.

106. Please weigh each of them on the basis of their importance from 1 (lower) to 5 (higher) .

	1	2	3	4	5	N/A
Faster nucleic acid isolation methods						
Faster library preparation procedures						
Integration of multiple steps in nucleic acid isolation procedure						
Integration of multiple steps in library preparation						
Integration of multiple steps in isolation and library preparation						
Automation						
Other						

Other (please specify)

107. Comment

CHALLENGE 3:

Defining genetic variants with established medical implications for common and rare, adult and pediatric, cancers including pharmacogenetic variants relevant for therapy selection in cancer care

PROBLEM High nucleic acid yields are needed as input for NGS whereas often only small samples are available and NGS is not always able to deal with difficult genomic regions, low-yield materials and somatic mutations at low variant allele frequency.

SOLUTION:

1. Increase the efficiency of nucleic acid isolation methods

2. Increased sequencing sensitivity.

108. Is your organization interested or involved in R&D for such an approach?

- Yes
- No

Please give the numbers with the highest priority first, down to the lowest priority

109. In case of R&D involvement, would financial support available in the Instand-NGS4P project be

- not needed
- helpful
- crucial to develop this approach

Let us know if you have any comments and if these are confidential

PROBLEM The NGS diagnostic result is used for determination of the treatment for patients. This involves the administration of complex and hazardous drugs, although it is not known if the drugs are metabolized normally.

SOLUTION: Including Pharmacogenomic Analysis in panels targeted on somatic mutations

110. Is your organization interested in further development of such an approach?

- Yes
- No

Comment

111. In case of R&D involvement, would financial support available in the Instand-NGS4P project be

- not needed
- helpful
- crucial to develop this approach

Let us know if you have any comments and if these are confidential

CHALLENGE 4:

Developing reference material for quality control

PROBLEM Availability of suitable internal quality control (QC) approaches and reference materials to monitor the NGS workflow as a whole.

SOLUTION: Multiple QC steps for each phase of the workflow to act as stop/go criteria to avoid wasting time and resources.

112. Is your organization interested in further development of such an approach?

- ◯ Yes
- ◯ No

Comment

113. In case of R&D involvement, would financial support available in the Instand-NGS4P project be

- ◯ not needed
- ◯ helpful
- ◯ crucial to develop this approach

Let us know if you have any comments and if these are confidential

PROBLEM Availability of well-designed NGS performance testing (PT), External Quality Assessment (EQA) and reference material.

SOLUTION: Use of PT, EQA and reference material for NGS workflows

114. Please select the box if your organization is using or wants to use it:

	Use	Wants to use
PT	☐	☐
EQA	☐	☐
Reference material	☐	☐

Please specify what kind and what is your source

115. The reference material:

	Yes	No
is introduced into the workflow during pre-analytic processing	○	○
matches authentic sample matrix	○	○
covers diagnostically relevant variants	○	○
includes RNA	○	○
contains 'difficult' Variants Of interest	○	○

Comment

PROBLEM Patient identity of patient material is sometimes swapped with that of another patient. In doubt the material must be re-identified with ID SNP. This requires a lot of extra time.

Solution: Inclusion of patient ID SNP's in the sequence panel or result.

116. Is your organization involved in R&D for such an approach?

- ○ Yes
- ○ No

Comment

117. Is your organization interested in further development of such an approach?

- ○ Yes
- ○ No
- ○ Comment

118. In case of R&D involvement, would financial support available in the Instand-NGS4P project be

- ○ not needed
- ○ helpful
- ○ crucial to develop this approach

Comment and let us know if your comments are confidential

119. If you have any further comments in the context of pre-analytics and library preparation, please let us know and specify if these comments are confidential

USER'S Questionnaire INSTAND-NGS4P

Introduction Lot 2

* 120. Would you like to answer questions related to Lot 2 (Sequencing)?

- Yes
- No

USER'S Questionnaire INSTAND-NGS4P

Lot 2

121. How important is sequencing time for you? (0- not important at all, 5-very important)

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

122. What is your maximum acceptable time for a routine sequencing run in hours, from library to variant calls?

123. How important are over-weekend runs for you? (0- not important at all, 5-very important)

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

124. What is your preferred pricing model?

- ○ Per analysis
- ○ Per reagents
- ○ Per infrastructure

125. How important is reduced hands-on time for you? (0- not important at all, 5-very important)

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

126. How much would you prefer higher costs for reagents and automated solutions in exchange for reduced hands-on time? (0- not at all, 5-very much)

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

127. Do you use reference material (inter-/intrarun control)?

- ○ Yes
- ○ No

If yes, please specify

128. Do you use reference material (inter-/intrarun control)?

- Yes
- No

If yes, please specify

129. How important would longer reads (>600bp) be for you? (0- not important at all, 5-very important)

0	1	2	3	4	5	N/A

130. How you important is it for you to read biochemical information (ex. methylation status)? (0- not important at all, 5-very important)

0	1	2	3	4	5	N/A

131. What data should be generated for quality control of the sequencing?

132. Do you consider sequencing noise a problem? (0- not at all, 5-very much)

0	1	2	3	4	5	N/A

133. How big is the impact of systemic sequencing artefacts on your work? (0-no impact, 5-very big)

	0	1	2	3	4	5	N/A
Homopolymers							
GC rich regions							
Low complexity regions							

134. How important is paired-end sequencing for you? (0- not important at all, 5-very important)

0	1	2	3	4	5	N/A

135. How important is the size of the instrument for you? (0- not important at all, 5-very important)

0	1	2	3	4	5	N/A

136. How important is flexibility of the platform for scalable throughput for you? (0- not important at all, 5-very important)

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

137. How important is it for you to pool various libraries in one run? (0- not important at all, 5-very important)

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

138. Do you perform sequencing as a lab-developed test?

- ○ Yes
- ○ No

139. How important are IVDR-CE certified tests for you? 0- not important at all, 5-very important)

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

140. How important are IVDR-CE instruments for you? 0- not important at all, 5-very important)

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

PROBLEM High nucleic acid yields are needed as input for NGS whereas often only small samples are available and NGS is not always able to deal with difficult genomic regions, low-yield materials and somatic mutations at low variant allele frequency.

SOLUTION:

1. Increase the efficiency of nucleic acid isolation methods
2. Increased sequencing sensitivity.

141. Is your organization interested or involved in R&D for such an approach?

- ○ Yes
- ○ No

142. Please give the numbers with the highest priority first, down to the lowest priority.

143. Comment

144. If you have any further comments in the context of sequencing, please let us know.

145. Is the information above confidential?

- Yes
- No

USER'S Questionnaire INSTAND-NGS4P

Introduction Lot 3

* 146. Would you like to answer questions related to Lot 3 (Bioinformatics)?

- Yes
- No

USER'S Questionnaire INSTAND-NGS4P

Lot 3

147. How is your organization / specialized unit positioned in the field of Next Generation Sequencing (NGS) fo r Personalized Therapy? (Please select all relevant points). Are you a...?

- [ ] Sequencing facility
- [ ] Computational facility
- [ ] Bioinformatics software developer
- [ ] Software service provider
- [ ] Diagnostic facility
- [ ] Research facility
- [ ] Commercial company
- [ ] Other (please specify)

148. Are you currently using results from NGS bioinformatics analysis for

(Please choose all relevant points and estimate percentage) (0 = 0/not at all, 1 = up to 20%, 2 = 20-40%, 3 = 40-60%, 4 = 60-80%, 5 = more than 80%)

	0	1	2	3	4	5
Diagnostic	☐	☐	☐	☐	☐	☐
Research	☐	☐	☐	☐	☐	☐
Software development	☐	☐	☐	☐	☐	☐

Other (please specify)

149. From which type of samples is NGS data derived from for bioinformatics analysis?

- [ ] I have already replied to the following questions in Lot 1

150. FFPE

	1	2	3	4	5	N/A
DNA	☐	☐	☐	☐	☐	☐
RNA	☐	☐	☐	☐	☐	☐

151. Frozen tissues

	1	2	3	4	5	N/A
DNA						
RNA						

152. Blood/plasma

	1	2	3	4	5	N/A
DNA						
RNA						
cfDNA						
cfRNA						

153. Fine needle aspirates

	1	2	3	4	5	N/A
DNA						
RNA						

154. Circulating Tumor Cells

	1	2	3	4	5	N/A
DNA						
RNA						

155. Extracellular vesicles

	1	2	3	4	5	N/A
DNA						
RNA						

156. Saliva

	1	2	3	4	5	N/A
DNA						

RNA	☐	☐	☐	☐	☐

157. Other

	1	2	3	4	5	N/A
DNA	☐	☐	☐	☐	☐	☐
RNA	☐	☐	☐	☐	☐	☐

158. If other, please specify

159. What is the indication that you are looking for a solution for?

- ○ Adult cancer
- ○ Pediatric cancer
- ○ Rare diseases
- ○ Other (please specify)

160. Which type of NGS data do you process?

- ○ Targeted sequencing (Panels)
- ○ Whole Exome Sequencing (WES)
- ○ Whole Genome Sequencing (WGS)
- ○ Gene Expression (RNA-Seq)
- ○ ChIP-seq
- ○ Methylation
- ○ Other (please specify)

161. Where are the raw NGS (unprocessed) data produced for the bioinformatics analysis?

(Please choose all relevant points)

- ☐ Inhouse
- ☐ Another department
- ☐ External non-commercial organization
- ☐ Commercial provider
- ☐ Other (please specify)

162. Where is the NGS bioinformatics analysis performed?

(Please choose all relevant points)

- [ ] At the place of NGS data generation
- [ ] Inhouse
- [ ] Another department
- [ ] External non-commercial organization
- [ ] Commercial provider
- [ ] Other (please specify)

163. Who assesses the results of the NGS bioinformatics analysis for actionable items?

(Please choose all relevant points)

- [ ] Inhouse
- [ ] Another department
- [ ] External non-commercial organization
- [ ] Commercial provider
- [ ] Other (please specify)

164. How do you currently access the raw NGS data for the bioinformatics analysis?

(Please choose all relevant points)

- [ ] No access required to raw data
- [ ] Raw data not available
- [ ] Available Inhouse
- [ ] Available within organization
- [ ] Download from (internal / external) sequencing provider
- [ ] Other (please specify)

165. How do you currently access the results of the NGS bioinformatics analysis?

(Please choose all relevant points)

- [ ] By downloading from a server
- [ ] By running our solution locally
- [ ] Other (please specify)

166. Which type of software is used for the bioinformatics analysis?

(Please choose all relevant points)

- [ ] Inhouse software (not available)
- [ ] open-source software (Non-commercial)
- [ ] open-source software (Commercial)
- [ ] Commercial software (source code not available)
- [ ] Not known
- [ ] Other (please specify)

167. Do you use any workflow manager / workflow description standard? (multiple answer possible)

- [ ] No, I only use command line
- [ ] Yes, Galaxy
- [ ] Yes, Common Workflow Language (CWL)
- [ ] Yes, Taverna
- [ ] Yes, Orange
- [ ] Yes, KNIME
- [ ] Yes, Workflow Definition Language (WDL)
- [ ] Yes, Next Flow
- [ ] Yes, Snake Make
- [ ] Other (please specify)

168. Which file formats are used to exchange data?

- FASTQ
- BAM / CRAM
- VCF
- CSV
- JSON
- Other (please specify)

169. Please indicate the software license (if known)

(Please choose all relevant points)

- [ ] GNU General Public License
- [ ] MIT License
- [ ] Apache License
- [ ] BSD License
- [ ] Commercial products
- [ ] Not sure
- [ ] Other (please specify)

170. What type of annotations do you currently get?

- Variant classification
- Variant population frequency
- Variant Effect prediction
- Disease gene panel
- Disease-gene association
- Clinical actionable items
- Drug-gene interactions
- Dosage sensitivity
- Other (please specify)

171. What type of annotations do you need? (Please choose all relevant points)

- [ ] Variant classification
- [ ] Variant population frequency
- [ ] Variant Effect prediction
- [ ] Disease gene panel
- [ ] Disease-gene association
- [ ] Clinically actionable items
- [ ] Drug-gene interactions
- [ ] Dosage sensitivity
- [ ] Other (please specify)

172. Is the annotation information from

(Please choose all relevant points)

- [ ] Inhouse resources
- [ ] Findable Accessible Interoperable Reusable (FAIR) data providers
- [ ] Free available data
- [ ] Commercial data
- [ ] Other (please specify)

173. What kind of QC do you perform for your bioinformatics pipeline?

- ○ Validation using criteria for accredited labs
- ○ Regular proficiency testing (benchmarking yourself with other labs, normally required for accredited labs)
- ○ None. This is a task of our service/software provider
- ○ Other (please specify)

174. Is the NGS bioinformatics analysis certified / accredited to

- ISO27001:2013 (information security standard)
- IEC 62304 (Software Lifecycle)
- ISO 14155:2011 (Clinical investigation of medical devices for human subjects)
- ISO 14971 (Risk management)
- ISO13485:2016 (Medical devices)
- Not sure
- Other (please specify)

Future of NGS bioinformatics analysis for diagnostics

NGS bioinformatics analyses have been performed in a research setting for a few years, but their use in the diagnostic setting is not widely applied yet.

175. Which challenges are the highest immediate priority? (scoring 0-5)

	0	1	2	3	4	5
Automation / Reduced manual work						
Reproducibility						
Packaging (e.g. containers)						
Portability						
Long-term availability						
Long-term maintainability						
Standardized data exchange						
Standardized data storage formats						
Encryption / data security						

Other (please specify)

176. Which challenges are the highest long-term priority? (scoring 0-5)

	0	1	2	3	4	5
Automation / Reduced manual work	○	○	○	○	○	○
Reproducibility	○	○	○	○	○	○
Packaging (e.g. containers)	○	○	○	○	○	○
Portability	○	○	○	○	○	○
Long-term availability	○	○	○	○	○	○
Long-term maintainability	○	○	○	○	○	○
Standardized data exchange	○	○	○	○	○	○
Standardized data storage formats	○	○	○	○	○	○
Encryption / data security	○	○	○	○	○	○

Other (please specify)

177. Which challenges are the highest long-term priority? (scoring 0-5)

	0	1	2	3	4	5
Automation / Reduced manual work	○	○	○	○	○	○
Reproducibility	○	○	○	○	○	○
Packaging (e.g. containers)	○	○	○	○	○	○
Portability	○	○	○	○	○	○
Long-term availability	○	○	○	○	○	○
Long-term maintainability	○	○	○	○	○	○
Standardized data exchange	○	○	○	○	○	○
Standardized data storage formats	○	○	○	○	○	○
Encryption / data security	○	○	○	○	○	○

Other (please specify)

178. Are there specific challenges to apply NGS bioinformatics analysis in your diagnostics service?

- ◯ No
- ◯ Yes, lack of bioinformatics staff
- ◯ Yes, lack of bioinformatics training
- ◯ Yes, lack of computational processing
- ◯ Yes, lack of long-term storage
- ◯ Yes, unsure which solutions fits our needs best
- ◯ Yes, other (please specify)

179. What kind of training / capacity building activities in the field of bioinformatics do you consider most suitable? (score each 0-5)

	0	1	2	3	4	5
face-to-face	◯	◯	◯	◯	◯	◯
online training courses	◯	◯	◯	◯	◯	◯
online training materials (asynchronous tutorials, videos, presentations).	◯	◯	◯	◯	◯	◯
books and/or scientific papers about the subject	◯	◯	◯	◯	◯	◯

Software and pipelines

Automation offers the execution of different software products at different steps, which allows a standardized and reproducible analysis at different places. This can include different software solutions but ultimately allows harmonizing the detection of genomic events.

180. What do you believe are the key challenges to overcome in relation to introducing standardized pipelines and software to detect actionable items for diagnostics purposes? Score each (0-5)

	0	1	2	3	4	5
getting commercial support for open source products	○	○	○	○	○	○
long-time support for commercial products	○	○	○	○	○	○
troubleshooting problems with products	○	○	○	○	○	○
usability	○	○	○	○	○	○
reproducibility	○	○	○	○	○	○
complying with standard data formats	○	○	○	○	○	○
adjusting workflows	○	○	○	○	○	○
integration in open-source pipeline systems	○	○	○	○	○	○
testing of pipelines with standardized samples	○	○	○	○	○	○
scalability to whole genome sequencing	○	○	○	○	○	○
organisation of shared work on the data	○	○	○	○	○	○
lack of training opportunities	○	○	○	○	○	○

Other (please specify)

Which are in your opinion the relevant standards on this topic and how ready are they to be used in diagnostics? (please rate the relevant standards for readiness 0-5)

181. Software file formats and secure data exchange protocols

	0	1	2	3	4	5
BAM/SAM/FASTQ format	○	○	○	○	○	○
VCF format	○	○	○	○	○	○
gVCF format	○	○	○	○	○	○
GA4GH HTSGet	○	○	○	○	○	○
Encryption (Crypt4GH)	○	○	○	○	○	○
CRAM format	○	○	○	○	○	○

Other (please specify)

ISO standards

ISO 20397-2:2021 "Biotechnology — Massively parallel sequencing — Part 2: Quality evaluation of sequencing data"

182. Please score the relevance of software license model regarding their use in diagnostics? (score each 0-5)

	0	1	2	3	4	5
Open Source (https://docs.github.com/en/github/creating-cloning-and-archiving-repositories/licensing-a-repository#choosing-the-right-license)	○	○	○	○	○	○
Closed source	○	○	○	○	○	○
BSD 3	○	○	○	○	○	○
Apache	○	○	○	○	○	○
CC	○	○	○	○	○	○
GNU GPL (v1,v2, v3)	○	○	○	○	○	○
OSL	○	○	○	○	○	○
MIT	○	○	○	○	○	○

Other (please specify)

Annotation resources

The annotation of variants or genomic events is fundamental to identify actionable items.

183. What do you believe are the key challenges to overcome the standardized use of annotation resources fo r diagnostics purposes?

- [ ] Updating external resources
- [ ] Standardized list of approved annotation resources
- [ ] Quality of resources (CE marking, ISO standard)
- [ ] Lifetime of resource
- [ ] Size of resource
- [ ] Licensing of resources
- [ ] Other (please specify)

Data storage and sharing

The storing and sharing of data is an integral part of a bioinformatics pipeline. The types of data include raw NGS data, result files from the pipeline as well as metadata.

Finally, it needs to be decided which data should be stored, where should they be stored, for how long and who should have access to?

184. What do you believe are the key challenges to overcome in relation to storing & sharing of relevant data for diagnostics purposes? score each (0-5)

	0	1	2	3	4	5
Location of storage (GDPR)	○	○	○	○	○	○
GA4GH standards	○	○	○	○	○	○
encryption	○	○	○	○	○	○
longtime storage	○	○	○	○	○	○
Patient access	○	○	○	○	○	○
Data size	○	○	○	○	○	○

Other (please specify)

185. How long is your legal obligation to store data for patient care?

186. Do you have a solution in place to store the data to address this legal requirement of data storage?

- ○ Yes
- ○ No

187. How big is your expected data volume generated in the next 5 years?

- < 1 PB
- 1-5 PB
- 5-10 PB
- >10 PB

Security

The acquired NGS data in diagnostics are very sensitivity and can identify patients.

188. What do you believe are the key challenges to overcome in relation to the secure handling of NGS data in diagnostics? score each (0-5)

	0	1	2	3	4	5
standardization						
awareness of personnel						
training of personnel						
quality of solutions (CE marked)						
security updates						
GDPR requirements properly addressed to national implementation						

Other (please specify)

189. If you have any further comments in the context of bioinformatics analysis, please let us know.

190. Is this information confidential?

- Yes
- No

USER'S Questionnaire INSTAND-NGS4P

Introduction Lot 4

* 191. Would you like to answer questions related to Lot 4 (Integrated reporting)?

- Yes
- No

USER'S Questionnaire INSTAND-NGS4P

Lot 4

The aim of Lot 4 is to provide innovative solutions for translating NGS results into medical decision-making reports. This should be achieved by integrating NGS results with pharmacogenomics panels and existing e-medication tools containing information on 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. The relevant clinical information should be reported in a concise and clear way, reporting only data with validated evidence for clinical decisions and in a form minimizing the risk of data misinterpretation. The questionnaire should help defining the specifications of the integrated reporting tool.

192. Do you use tools for integrated reporting?

- Yes
- No

193. Are you interested in implementing tools for integrated reporting?

- Yes
- No

194. Are you a solution provider for integrated reporting tools?

- Yes
- No

195. Do you have a solution for integrated reporting of NGS results that integrates the following data and information (multiple answers may apply)

	Yes	No
Cancer–related variants	○	○
Actionable items	○	○
Pharmacogenomic variants	○	○
Level of evidence for cancer-related variants (level of evidence could be companion-diagnostics, drug-label, guidelines, databases, scientific literature)	○	○
Level of evidence for pharmacogenomic variants (level of evidence could be companion-diagnostics, drug-label, guidelines, databases, scientific literature)	○	○
Information on clinical trials	○	○

Other (please specify)

196. How important is the integration of the following data and information in reporting of NGS results in order to support medical decision making (please select score; 0=not relevant; 5=highly relevant).

	0	1	2	3	4	5	N/A
Information on informed consent	○	○	○	○	○	○	○
Information on the sample analyzed	○	○	○	○	○	○	○
Information on the analytical method	○	○	○	○	○	○	○
Information on the quality of the analysis	○	○	○	○	○	○	○
Results on cancer – related variants	○	○	○	○	○	○	○
Information on actionable items	○	○	○	○	○	○	○
Information on pharmacogenomics variants	○	○	○	○	○	○	○
Information on the level of evidence for cancer-related variants	○	○	○	○	○	○	○
Information on the level of evidence for pharmacogenomics variants	○	○	○	○	○	○	○
Information on drug-drug interaction, dosing, side effects and contra indications (e.g., e-medication)	○	○	○	○	○	○	○
Information on relevant clinical data (e.g., heart, liver, kidney function)	○	○	○	○	○	○	○
Information on running clinical trials	○	○	○	○	○	○	○
Information on possible compassionate use	○	○	○	○	○	○	○

Other (please specify)

197. Please indicate how important is the following information on clinical evidence for decision making. Evidence based on the following facts (please select score; 0=not relevant; 5=highly relevant).

	0	1	2	3	4	5	N/A
Companion-diagnostics	○	○	○	○	○	○	○
Drug-label	○	○	○	○	○	○	○
Guidelines of medical societies	○	○	○	○	○	○	○
Curated databases	○	○	○	○	○	○	○
Scientific literature	○	○	○	○	○	○	○
Information on open clinical trials – national	○	○	○	○	○	○	○
Information on open clinical trials – Europe	○	○	○	○	○	○	○
Information on open clinical trials – international	○	○	○	○	○	○	○

What is your preferred reference for assessing the clinical evidence? Please describe

198. How important are the following features of integrated reporting for decision support

(please select score; 0=not relevant; 5=highly relevant)

	0	1	2	3	4	5	N/A
Desktop solution	○	○	○	○	○	○	○
Mobile device (e.g., tablet 12')	○	○	○	○	○	○	○
Touch screen	○	○	○	○	○	○	○
WLAN	○	○	○	○	○	○	○
Off-line mode	○	○	○	○	○	○	○

Other (please specify)

199. How important is graphical presentation (data visualization) of results for decision support? (please select score; 0=not relevant; 5=highly relevant)

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

200. Do you have a preferred solution for graphical presentation of results?

- Yes
- No

If yes, please describe the solution

201. How important is it that the results of integrated reporting are also integrated in electronic health records (EHR) and the hospital information systems (HIS)? (please select score; 0=not relevant; 5=highly relevant)

	0	1	2	3	4	5	N/A
Relevance of integration in EHR							
Relevance of integration in HIS							

202. What hospital information system are you using?

Please describe:

203. Have you tested different products for integrated reporting and decision support?

- Yes
- No
- If yes please describe which products

204. How are you satisfied with current products on the market for integrated reporting and decision support? (please select score; 0=not relevant; 5=highly relevant)

0	1	2	3	4	5	N/A

205. How important is it that the integrated reporting and decision support system generates a special report for patients? (please select score; 0=not relevant; 5=highly relevant)

0	1	2	3	4	5	N/A

206. How important is it that the data analysis for integrated reporting is performed locally or via a webservice? (please select score; 0=not relevant; 5=highly relevant)

	0	1	2	3	4	5	N/A
Local data analysis	○	○	○	○	○	○	○
Data analysis via webservice	○	○	○	○	○	○	○

207. If you have any further comments in the context of integrated reporting and e-medication, please let us know.

208. Is this information confidential?

- ○ Yes
- ○ No

USER'S Questionnaire INSTAND-NGS4P

Last question

209. Would you like to share with us any additional information related to any section of the questionnaire? If yes please use the free field to do so.

210. Is the provided information confidential?

- Yes
- No

PATIENTS' NEEDS QUESTIONNAIRE Instand-NGS4P

Welcome to My Survey

The questionnaire arises from an EU funded project called INSTAND-NGS4P. The aim of the questionnaire is to investigate the current standard of knowledge on Next Generation Sequencing (NGS), which is one piece of the puzzle to enable the development of individual treatments for every patient, often known as personalized medicine or precision medicine.

Personalized medicine aims to tailor therapies for every patient to allow optimized therapies to ensure better patient care. One step in this direction is the application of NGS, which allows the detailed analysis and interpretation of the human genome.

But what does NGS mean for a patient? NGS is a new technology to sequence the genome of any individual. Therefore, the DNA (deoxyribonucleic acid) of a person is extracted from cells, like blood cells or tissue samples. The DNA is made of so-called nucleotides, which are A's (adenosine), T's (thymine), C's (cytosine) and G's (guanine). Thereby, it encodes all our hereditary information and around 22,000 genes, which make us to the person we are. Sequencing is applied to determine all these single nucleotides of a person. This information is then used to be compared to DNA of other individuals (also named reference DNA). This allows the identification of so-called mutations, which are positions where a human subject does not have the same nucleotide as the reference DNA. Such mutations can be meaningless, but they can also provide highly valuable information for physicians and geneticists. Mutations can cause diseases, but they can also give a hint as to how well a person might respond to a therapy or how well a certain drug works. Therefore, these sequencing data also help to gain such knowledge. Imagine having plenty of such DNA sequencing information of patients with certain cancers, but also healthy individuals. Comparing and interpreting their genomes can lead to new discoveries on mutations they share. This can be further used to understand diseases. But patients might also share mutations that help to learn whether a medication will work or fail in a patient, which is the research area of pharmacogenetics – the interplay of genetics and pharmacology. When clinicians use pharmacogenetic data for therapy decision making it means that for some mutations there is information about how well cancer cells with the specific mutation respond to different therapies, and they use it when deciding for a treatment option. If positive or negative response is predicted based on the mutations in the patient at diagnosis, the therapy of choice can offer the patient better chances for response to therapy and spare the patient from side effects of therapies which would not kill the cancer cells.

The personal information collected through the questionnaire will be exclusively used for the purposes of the project, will not be shared with third parties, and will be deleted after the closure of the project.

The following questions aim to address the current level of knowledge on what NGS means, what advantages it has, but also which concerns might arise among patients.

The questionnaires also allow disclosure of confidential information to the project consortium, which will be treated with high confidentiality. Aggregated data from the results of the survey will potentially be published in an anonymous way, excluding the information labelled as confidential.

Filling in the questionnaire will take less than 20 minutes of your time. Please submit the questionnaire by May 31st, 2021. Thank you in advance for contributing.

PATIENTS' NEEDS QUESTIONNAIRE Instand-NGS4P

Organisation profile

* 1. Organisation profile

Organization name	
Address	
City	
Country	

* 2. Contact person

First name	
Family name	
Current position in the organisation	
E-mail	
Telephone	

* 3. Does your organization represent adult or childhood cancer patients?

- ◯ Childhood
- ◯ Adults
- ◯ Adult and childhood

PATIENTS' NEEDS QUESTIONNAIRE Instand-NGS4P

CHILDHOOD PATIENTS QUESTIONNAIRE

I. General questions about NGS – addressed to your organization

Please answer the following questions, to the best of your knowledge, on behalf of your organization.

* 4. Do you know what Next Generation Sequencing (NGS) means?

- ◯ Yes
- ◯ No
- ◯ Not sure

* 5. Does your association have knowledge about NGS?

Please answer on a scale from 0 to 5 (0 - not at all; 5 - a lot; N/A - not sure).

0	1	2	3	4	5	N/A
◯	◯	◯	◯	◯	◯	◯

* 6. How well does your organization know that NGS can be used in cancer diagnostics?

Please answer on a scale from 0 to 5 (0 - not at all; 5 - a lot; N/A - not sure).

0	1	2	3	4	5	N/A
◯	◯	◯	◯	◯	◯	◯

* 7. How much experience does your organization have with NGS?

Please answer on a scale from 0 to 5 (0 - not at all; 5 - a lot; N/A - not sure).

0	1	2	3	4	5	N/A
◯	◯	◯	◯	◯	◯	◯

* 8. Is your organization prepared to advice and help patients and/or their parents to answer questions regarding NGS?

Please answer on a scale from 0 to 5 (0 - not at all; 5 - a lot; N/A - not sure).

0	1	2	3	4	5	N/A
◯	◯	◯	◯	◯	◯	◯

* 9. Do you already have any initiatives and/or material, like brochures, to explain NGS to patients and/or their parents?

- Yes
- No
- Not sure

* 10. Has any patient and/or parent asked for information about NGS, pharmacogenetics, or personalized medicine?

- Yes
- No, never
- Not sure

11. Please share with us any other thoughts on NGS in the context of your organization:

II. General questions about NGS – addressed to patients and parents

Please answer the following questions, to the best of your knowledge, on behalf of patients and/or parents.

* 12. Do patients and/or parents know what NGS means?

- Yes
- No
- Not sure

* 13. How likely is it that patients and/or parents have heard about NGS in the context of childhood cancer therapy and treatment already?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very likely; N/A – not sure)

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 14. How well do patients and/or parents know that NGS can be used in cancer diagnostics?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very well; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 15. How well do patients and/or parents understand the benefit of using NGS in cancer diagnostics?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very well; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 16. How well do you think patients and/or parents know why NGS is an important diagnostic method?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very well; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 17. Do patients and/or parents know that the genetic constitution of the patient can enhance cancer therapy decision making?

- ○ Yes
- ○ No, it needs further clarification
- ○ Not sure

* 18. Do patients and/or parents understand the benefit of selecting a therapy based on the genetic constitution of the patient?

- ○ Yes
- ○ No, it needs further clarification
- ○ Not sure

* 19. Do patients and/or parents know that the individual genetic constitution may affect the efficacy and possible side (and late) effects of certain drugs (also known as pharmacogenetics)?

- ○ Yes
- ○ No, it needs further clarification
- ○ Not sure

* 20. How likely is it that patients and/or parents understand the consequences regarding the information they get about their genome and how to handle this?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very well; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 21. How likely is it that patients and/or parents understand the consequences regarding the generated data and data security?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very well; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 22. Do you think patients and/or parents will have any ethical concerns regarding the data produced by NGS?

- ○ Yes
- ○ No. Patients understand that it will strictly be used for diagnostic purposes.
- ○ Not sure

23. If your answer is “yes”, please share: which ethical concerns are you thinking of?

- ○ This information is used against the patient’s interest (eg. by employers or insurances)
- ○ Possible relevance for family members
- ○ Other (please specify)

* 24. What level of evidence would patients and/or parents like to have in order to agree on a treatment based on NGS results?
Select all that apply (multiple answers possible) and provide a ranking of importance from 0-5 (0 – not at all; 5- very important; N/A – not sure).

	0	1	2	3	4	5
NGS is approved for therapeutic decision-making by regulatory authorities	○	○	○	○	○	○
Recommended by the medical society	○	○	○	○	○	○
Evidence is published in a scientific journal	○	○	○	○	○	○
Experience from other patients or patient advocacy groups	○	○	○	○	○	

III. Evaluating the educational requirements on NGS for patients and/or parents
Please answer the following questions from a patient’s perspective to the best of your knowledge.

* 25. How important is thorough information about the diagnostic procedure, before sequencing, for patients and/or parents?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very important; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 26. How important is it for patients and/or parents to receive a document before sequencing, with detailed explanations about the procedure?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very important; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

27. If you think it is important, what is the preferred option

- ○ As part of the informed consent
- ○ In a document separate from the informed consent, in a printed format
- ○ In a document separate from the informed consent, in a digital format

* 28. How important is it for patients and/or parents to receive a document that explains for which analyses/projects the NGS data will be used for?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very important; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

29. If you think it is important, what is the preferred option

- ○ As part of the informed consent
- ○ In a document separate from the informed consent, in a printed format
- ○ In a document separate from the informed consent, in a digital format

* 30. How important is it for patients and/or parents to receive detailed information, like a brochure, that explains the advantages, but also the impact NGS might have on their and their families' lives, as well as the risks, especially concerning the NGS data produced?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very important; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

31. If you think it is important, what is the preferred option

- As part of the informed consent
- In a document separate from the informed consent, in a printed format
- In a document separate from the informed consent, in a digital format

* 32. How important is it for patients and/or parents to receive a document on how data security is guaranteed, and how they can withdraw that data any time based on the General Data Protection Regulation?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very important; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

IV. Evaluating the rights of the patients and parents to receive the results in an appropriate format

Please answer the following questions from a patient's perspective to the best of your knowledge.

* 33. How important is it for patients and/or parents to receive a report, after the NGS analysis, containing the results?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very important; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 34. Should patients and/or parents have the choice to receive the results?

- Yes
- No
- Not sure

* 35. Should patients and/or parents have the possibility to choose between different options on the how comprehensive the returned results should be? The comprehensiveness could reach from no results, to results only regarding the current treatment, to all the detailed results of the NGS analysis.

- Yes
- No
- Not sure

* 36. How important is it for the patients and/or parents that the final report contains information about those implications of the NGS analysis that affect family members?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very important; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 37. How important is it for patients and/or parents to have genetic consultation assistance during and after the discussion of the results?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very important; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 38. Should the patients and/or parents have the pharmacogenetic results available on a mobile device or in a printed form?

- ○ Only in a digital form on a mobile device
- ○ Only in a printed form
- ○ On a mobile device and in a printed form

* 39. If provided in a digital form on a mobile device, does a security level similar to that used for e-banking provide good level of data security confidence to the patient and/or parents?

- ○ Yes
- ○ No
- ○ Not sure

V. Evaluating the rights of a former childhood cancer patient to be informed about an earlier NGS analysis, a second meeting with a well-informed physician, and their right to reconsider

* 40. Should former childhood cancer patients be automatically informed that NGS was applied, as soon as they turn 18?

- ○ Yes
- ○ No
- ○ Not sure

41. If yes, how should they be informed?

- Per email
- Per post
- Face to face
- Phone call
- Other (please specify)

* 42. Should this notification include the offer for an appointment with a well-informed physician, geneticist, and psychologist?

- Yes
- No
- Not sure

* 43. Should former childhood cancer patients also receive detailed information to have the option of withdrawing their data based on the General Data Protection Regulation, in case they wish to do so?

- Yes
- No
- Not sure

* 44. Should the patient have the pharmacogenetic results available on a mobile device or in a printed form?

- Only in a digital form on a mobile device
- Only in a printed form
- On a mobile device and in a printed form

* 45. If provided in a digital form on a mobile device, does a security level similar to that used for e-banking provide a good level of data security confidence to the patient?

- Yes
- No
- Not sure

PATIENTS' NEEDS QUESTIONNAIRE Instand-NGS4P

ADULT PATIENTS QUESTIONNAIRE

VI. General questions about NGS – addressed to your organization

Please answer the following questions, to the best of your knowledge, on behalf of your organization.

* 46. Does your association have knowledge about NGS?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – a lot; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 47. How well does your organization know that NGS can be used in cancer diagnostics?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – a lot; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 48. How much experience does your organization have with NGS?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – a lot; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 49. Does your organization have the knowledge to advice and help patients to answer questions regarding NGS?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – a lot; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 50. Do you already have any initiatives and/or material, like brochures, to explain NGS to patients?

- ○ Yes
- ○ No
- ○ Not sure

* 51. Is your association familiar with biological therapies?

Please answer on a scale from 0 to 5 (0 – not familiar at all; 5-very well informed and we educate our members).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 52. Is your association familiar with immunotherapies?

Please answer on a scale from 0 to 5 (0 – not familiar at all; 5-very well informed and we educate our members).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 53. Does your association have knowledge about molecular testing or genetic testing in clinical practice?

Please answer on a scale from 0 to 5 (0 – not at all; 5-very well informed and we educate our members).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 54. Is your association familiar with biomarkers?

Please answer on a scale from 0 to 5 (0 – not at all; 5-very well informed and we educate our members).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 55. Has any patient asked for information about the above mentioned therapies?

- ○ Yes
- ○ No, never

56. Please share with us any other thoughts on NGS in the context of your organization:

VII. General questions about NGS – addressed to patients

Please answer the following questions, to the best of your knowledge, on behalf of patients.

* 57. How likely is it that patients have heard about NGS in the context of cancer therapy and treatment already?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very likely; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 58. How well do patients know that NGS can be used in cancer diagnostics?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very likely; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 59. How well do patients understand the benefit of using NGS in cancer diagnostics?

Please answer on a scale from 0 to 5 (0 – not at all; 5-they understand very well).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 60. How well do you think patients know why Next Generation Sequencing is an important diagnostic method?

Please answer on a scale from 0 to 5 (0 – not at all; 5-they know very well).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 61. Do patients know that the genetic constitution of the patient can be used in cancer therapy decision making?

- ○ Yes
- ○ No, it needs further clarification

* 62. Do patients understand the benefit of selecting therapy based on the genetic constitution of the patient?

- ○ Yes
- ○ No, it needs further clarification

* 63. Do patients know that the individual genetic constitution may affect the efficacy and possible side effects of certain drugs (the term we use for this is pharmacogenetics)?

Please answer on a scale from 0 to 5 (0 – not at all; 5 - they know very well).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 64. How likely is it that patients understand the indications regarding the generated data and data security?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very likely; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 65. Do you think patients will have any ethical concerns regarding the data produced by NGS?

- ○ Yes
- ○ No. Patients understand that it will strictly be used for diagnostic purposes
- ○ Not sure

66. If your answer is “yes”, please share: which ethical concerns are you thinking of?

- ○ This information is used against the patient’s interest (eg. by employers or insurances)
- ○ Possible relevance for family members
- ○ Other (please specify)

VIII. Evaluating the educational requirements on NGS for patients

Please answer the following questions from a patient’s perspective to the best of your knowledge.

* 67. How important is thorough information about the diagnostic procedure, before sequencing, for patients?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very important; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 68. How important is it for patients to receive a document before sequencing, with detailed explanations about the procedure?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very important; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

69. If you think it is important, what is the preferred option

- ○ As part of the informed consent
- ○ In a document separate from the informed consent, in a printed format
- ○ In a document separate from the informed consent, in a digital format

* 70. How important is it for patients to receive a document that explains for which analyses/projects the NGS data will be used for?

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

71. If you think it is important, what is the preferred option

- ○ As part of the informed consent
- ○ In a document separate from the informed consent, in a printed format
- ○ In a document separate from the informed consent, in a digital format

* 72. How important is it for patients to receive detailed information, like a brochure, that explains the advantages, but also the impact NGS might have on their and their families' lives, as well as the risks, especially concerning the NGS data produced?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very important; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

73. If you think it is important, what is the preferred option

- ○ As part of the informed consent
- ○ In a document separate from the informed consent, in a printed format
- ○ In a document separate from the informed consent, in a digital format

* 74. How important is it for patients to receive a document on how data security is guaranteed, and how they can withdraw that data any time based on the General Data Protection Regulation?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very important; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

IX. Evaluating the rights of the patients to receive the results in an appropriate format

* 75. How important is it for patients to receive a report, after the NGS analysis, containing the results?

Please answer on a scale from 0 to 5 (0 – not at all; 5-very important).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 76. Should patients have the choice to receive the results?

- ○ Yes
- ○ No
- ○ Not sure

* 77. Should patients have the possibility to choose between different options on the how comprehensive the returned results should be? The comprehensiveness could reach from no results, to results only regarding the current treatment, to all the detailed results of the NGS analysis.

- ○ Yes
- ○ No
- ○ Not sure

* 78. How important is it for the patients that the final report contains information about those implications of the NGS analysis that affect family members?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very important; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 79. How important is it for patients to have genetic consultation assistance during and after the discussion of the results?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very important; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 80. From a patient's perspective, should the genetic results and pharmacogenetic results be part of one report or separated in two reports?

- All results should be part of one report, in a printed format
- All results should be part of one report, in a digital format
- They should be separated in two reports, in a printed format
- They should be separated in two reports, in a digital format

* 81. Should the patient have the pharmacogenetic results available on a mobile device or in a printed form?

- Only in a digital form on a mobile device
- Only in a printed form
- On a mobile device and in a printed form

82. If provided in a digital form on a mobile device, does a security level similar to that used for e-banking provide a good level of data security confidence to the patient?

- Yes
- No
- Not sure

* 83. How important is it for the patient who has access to the results of the genetic testing (including mutated genes and diagnosis)?

Please answer on a scale from 0 to 5 (0 – not at all; 5-very important).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 84. From a patient's perspective, how limited should the access to the results from the genetic testing be?

- Very limited (ex. only the patient and the clinician in cancer care should have access)
- Mildly limited (ex. the patient, the clinician in cancer care and other clinicians the patient goes to should have access)
- Limited (ex. the patient, the clinician in cancer care and other clinicians the patient goes to, as well as the pharmacists should have access)
- Not limited (anyone can have access)

* 85. How important is it for the patient who has access to pharmacogenetic results?

Please answer on a scale from 0 to 5 (0 – not at all; 5-very important).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 86. From a patient's perspective, how limited should the access to the pharmacogenetic results be?

- ○ Very limited (ex. only the patient and the clinician in cancer care should have access)
- ○ Mildly limited (ex. the patient, the clinician in cancer care and other clinicians the patient goes to should have access)
- ○ Limited (ex. the patient, the clinician in cancer care and other clinicians the patient goes to, as well as the pharmacists should have access)
- ○ Not limited (anyone can have access)

* 87. What level of evidence would a patient like to have in order to be treated based on NGS results?

Select all that apply (multiple answers possible) and provide ranking of importance from 0-5 (0 – not at all; 5-very important).

	0	1	2	3	4	5
The NGS test is approved for therapy decision by regulatory authorities	○	○	○	○	○	○
Recommended by the medical society	○	○	○	○	○	○
Evidence is published in a scientific journal	○	○	○	○	○	○
Experience from other patients or patient advocacy groups	○	○	○	○	○	

* 88. How important is it that the patients receive information about existing clinical trials the patient can participate in (in the patient's country or neighboring countries), and that the information is generated through the diagnostic procedure?

Please answer on a scale from 0 to 5 (1 – not at all; 5-very important).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 89. How important is it for the patient to be informed of incidental findings relevant to the disease object of the research or any further incidental finding relevant to her/his health as well as her/his genetical relatives?

Please answer on a scale from 0 to 5 (1 – not at all; 5-very important).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 90. How important is it for the patient to have a psychological assistance during/after the communication of the results of the test?

Please answer on a scale from 0 to 5 (1 – not at all; 5-very important).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

PATIENTS' NEEDS QUESTIONNAIRE Instand-NGS4P

CHILDHOOD PATIENTS QUESTIONNAIRE

I. General questions about NGS – addressed to your organization

Please answer the following questions, to the best of your knowledge, on behalf of your organization, in the context of childhood patients.

* 91. Do you know what Next Generation Sequencing (NGS) means?

- Yes
- No
- Not sure

* 92. Does your association have knowledge about NGS?

Please answer on a scale from 0 to 5 (0 - not at all; 5 - a lot; N/A - not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 93. How well does your organization know that NGS can be used in cancer diagnostics?

Please answer on a scale from 0 to 5 (0 - not at all; 5 - a lot; N/A - not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 94. How much experience does your organization have with NGS?

Please answer on a scale from 0 to 5 (0 - not at all; 5 - a lot; N/A - not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 95. Is your organization prepared to advice and help patients and/or their parents to answer questions regarding NGS?

Please answer on a scale from 0 to 5 (0 - not at all; 5 - a lot; N/A - not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 96. Do you already have any initiatives and/or material, like brochures, to explain NGS to patients and/or their parents?

- Yes
- No
- Not sure

* 97. Has any patient and/or parent asked for information about NGS, pharmacogenetics, or personalized medicine?

- Yes
- No, never
- Not sure

98. Please share with us any other thoughts on NGS in the context of your organization:

II. General questions about NGS – addressed to patients and parents

Please answer the following questions, to the best of your knowledge, on behalf of patients and/or parents, in the context of childhood patients.

* 99. Do patients and/or parents know what NGS means?

- Yes
- No
- Not sure

* 100. How likely is it that patients and/or parents have heard about NGS in the context of childhood cancer therapy and treatment already?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very likely; N/A – not sure)

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 101. How well do patients and/or parents know that NGS can be used in cancer diagnostics?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very well; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 102. How well do patients and/or parents understand the benefit of using NGS in cancer diagnostics?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very well; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 103. How well do you think patients and/or parents know why NGS is an important diagnostic method?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very well; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 104. Do patients and/or parents know that the genetic constitution of the patient can enhance cancer therapy decision making?

- ○ Yes
- ○ No, it needs further clarification
- ○ Not sure

* 105. Do patients and/or parents understand the benefit of selecting a therapy based on the genetic constitution of the patient?

- ○ Yes
- ○ No, it needs further clarification
- ○ Not sure

* 106. Do patients and/or parents know that the individual genetic constitution may affect the efficacy and possible side (and late) effects of certain drugs (also known as pharmacogenetics)?

- ○ Yes
- ○ No, it needs further clarification
- ○ Not sure

* 107. How likely is it that patients and/or parents understand the consequences regarding the information they get about their genome and how to handle this?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very well; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 108. How likely is it that patients and/or parents understand the consequences regarding the generated data and data security?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very well; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 109. Do you think patients and/or parents will have any ethical concerns regarding the data produced by NGS?

- ○ Yes
- ○ No. Patients understand that it will strictly be used for diagnostic purposes.
- ○ Not sure

110. If your answer is “yes”, please share: which ethical concerns are you thinking of?

- ○ This information is used against the patient’s interest (eg. by employers or insurances)
- ○ Possible relevance for family members
- ○ Other (please specify)

* 111. What level of evidence would patients and/or parents like to have in order to agree on a treatment based on NGS results?
Select all that apply (multiple answers possible) and provide a ranking of importance from 0-5 (0 – not at all; 5- very important; N/A – not sure).

	0	1	2	3	4	5
NGS is approved for therapeutic decision-making by regulatory authorities	○	○	○	○	○	○
Recommended by the medical society	○	○	○	○	○	○
Evidence is published in a scientific journal	○	○	○	○	○	○
Experience from other patients or patient advocacy groups	○	○	○	○	○	

III. Evaluating the educational requirements on NGS for patients and/or parents

Please answer the following questions from a patient’s perspective to the best of your knowledge, in the context of childhood patients.

* 112. How important is thorough information about the diagnostic procedure, before sequencing, for patients and/or parents?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very important; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 113. How important is it for patients and/or parents to receive a document before sequencing, with detailed explanations about the procedure?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very important; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

114. If you think it is important, what is the preferred option

- ○ As part of the informed consent
- ○ In a document separate from the informed consent, in a printed format
- ○ In a document separate from the informed consent, in a digital format

* 115. How important is it for patients and/or parents to receive a document that explains for which analyses/projects the NGS data will be used for?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very important; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

116. If you think it is important, what is the preferred option

- ○ As part of the informed consent
- ○ In a document separate from the informed consent, in a printed format
- ○ In a document separate from the informed consent, in a digital format

* 117. How important is it for patients and/or parents to receive detailed information, like a brochure, that explains the advantages, but also the impact NGS might have on their and their families' lives, as well as the risks, especially concerning the NGS data produced?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very important; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

118. If you think it is important, what is the preferred option

- As part of the informed consent
- In a document separate from the informed consent, in a printed format
- In a document separate from the informed consent, in a digital format

* 119. How important is it for patients and/or parents to receive a document on how data security is guaranteed, and how they can withdraw that data any time based on the General Data Protection Regulation?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very important; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

IV. Evaluating the rights of the patients and parents to receive the results in an appropriate format

Please answer the following questions from a patient's perspective to the best of your knowledge, in the context of childhood patients.

* 120. How important is it for patients and/or parents to receive a report, after the NGS analysis, containing the results?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very important; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 121. Should patients and/or parents have the choice to receive the results?

- Yes
- No
- Not sure

* 122. Should patients and/or parents have the possibility to choose between different options on the how comprehensive the returned results should be? The comprehensiveness could reach from no results, to results only regarding the current treatment, to all the detailed results of the NGS analysis.

- Yes
- No
- Not sure

* 123. How important is it for the patients and/or parents that the final report contains information about those implications of the NGS analysis that affect family members?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very important; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 124. How important is it for patients and/or parents to have genetic consultation assistance during and after the discussion of the results?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very important; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 125. Should the patients and/or parents have the pharmacogenetic results available on a mobile device or in a printed form?

- ○ Only in a digital form on a mobile device
- ○ Only in a printed form
- ○ On a mobile device and in a printed form

* 126. If provided in a digital form on a mobile device, does a security level similar to that used for e-banking provide good level of data security confidence to the patient and/or parents?

- ○ Yes
- ○ No
- ○ Not sure

V. Evaluating the rights of a former childhood cancer patient to be informed about an earlier NGS analysis, a second meeting with a well-informed physician, and their right to reconsider

* 127. Should former childhood cancer patients be automatically informed that NGS was applied, as soon as they turn 18?

- ○ Yes
- ○ No
- ○ Not sure

128. If yes, how should they be informed?

- Per email
- Per post
- Face to face
- Phone call
- Other (please specify)

* 129. Should this notification include the offer for an appointment with a well-informed physician, geneticist, and psychologist?

- Yes
- No
- Not sure

* 130. Should former childhood cancer patients also receive detailed information to have the option of withdrawing their data based on the General Data Protection Regulation, in case they wish to do so?

- Yes
- No
- Not sure

* 131. Should the patient have the pharmacogenetic results available on a mobile device or in a printed form?

- Only in a digital form on a mobile device
- Only in a printed form
- On a mobile device and in a printed form

* 132. If provided in a digital form on a mobile device, does a security level similar to that used for e-banking provide a good level of data security confidence to the patient?

- Yes
- No
- Not sure

PATIENTS' NEEDS QUESTIONNAIRE Instand-NGS4P

ADULT PATIENTS QUESTIONNAIRE

General questions about NGS – addressed to your organization.

Please answer the following questions, to the best of your knowledge, on behalf of your organization in the context of adult patients.

VI. General questions about NGS – addressed to your organization

Please answer the following questions, to the best of your knowledge, on behalf of your organization, in the context of adult patients.

* 133. Does your association have knowledge about NGS?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – a lot; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 134. How well does your organization know that NGS can be used in cancer diagnostics?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – a lot; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 135. How much experience does your organization have with NGS?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – a lot; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 136. Does your organization have the knowledge to advice and help patients to answer questions regarding NGS?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – a lot; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 137. Do you already have any initiatives and/or material, like brochures, to explain NGS to patients?

- Yes
- No
- Not sure

* 138. Is your association familiar with biological therapies?

Please answer on a scale from 0 to 5 (0 – not familiar at all; 5-very well informed and we educate our members).

0	1	2	3	4	5	N/A

* 139. Is your association familiar with immunotherapies?

Please answer on a scale from 0 to 5 (0 – not familiar at all; 5-very well informed and we educate our members).

0	1	2	3	4	5	N/A

* 140. Does your association have knowledge about molecular testing or genetic testing in clinical practice?

Please answer on a scale from 0 to 5 (0 – not at all; 5-very well informed and we educate our members).

0	1	2	3	4	5	N/A

* 141. Is your association familiar with biomarkers?

Please answer on a scale from 0 to 5 (0 – not at all; 5-very well informed and we educate our members).

0	1	2	3	4	5	N/A

* 142. Has any patient asked for information about the above mentioned therapies?

- Yes
- No, never

143. Please share with us any other thoughts on NGS in the context of your organization:

VII. General questions about NGS – addressed to patients

Please answer the following questions, to the best of your knowledge, on behalf of your organisation in the context of adult patients.

* 144. How likely is it that patients have heard about NGS in the context of cancer therapy and treatment already?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very likely; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 145. How well do patients know that NGS can be used in cancer diagnostics?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very likely; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 146. How well do patients understand the benefit of using NGS in cancer diagnostics?

Please answer on a scale from 0 to 5 (0 – not at all; 5-they understand very well).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 147. How well do you think patients know why Next Generation Sequencing is an important diagnostic method?

Please answer on a scale from 0 to 5 (0 – not at all; 5-they know very well).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 148. Do patients know that the genetic constitution of the patient can be used in cancer therapy decision making?

- ○ Yes
- ○ No, it needs further clarification

* 149. Do patients understand the benefit of selecting therapy based on the genetic constitution of the patient?

- ○ Yes
- ○ No, it needs further clarification

* 150. Do patients know that the individual genetic constitution may affect the efficacy and possible side effects of certain drugs (the term we use for this is pharmacogenetics)?

Please answer on a scale from 0 to 5 (0 – not at all; 5 - they know very well).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 151. How likely is it that patients understand the indications regarding the generated data and data security?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very likely; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 152. Do you think patients will have any ethical concerns regarding the data produced by NGS?

- ○ Yes
- ○ No. Patients understand that it will strictly be used for diagnostic purposes
- ○ Not sure

153. If your answer is “yes”, please share: which ethical concerns are you thinking of?

- ○ This information is used against the patient’s interest (eg. by employers or insurances)
- ○ Possible relevance for family members
- ○ Other (please specify)

VIII. Evaluating the educational requirements on NGS for patients

Please answer the following questions from a patient’s perspective to the best of your knowledge in the context of adult patients.

* 154. How important is thorough information about the diagnostic procedure, before sequencing, for patients?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very important; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 155. How important is it for patients to receive a document before sequencing, with detailed explanations about the procedure?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very important; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

156. If you think it is important, what is the preferred option

- ○ As part of the informed consent
- ○ In a document separate from the informed consent, in a printed format
- ○ In a document separate from the informed consent, in a digital format

* 157. How important is it for patients to receive a document that explains for which analyses/projects the NGS data will be used for?

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

158. If you think it is important, what is the preferred option

- ○ As part of the informed consent
- ○ In a document separate from the informed consent, in a printed format
- ○ In a document separate from the informed consent, in a digital format

* 159. How important is it for patients to receive detailed information, like a brochure, that explains the advantages, but also the impact NGS might have on their and their families' lives, as well as the risks, especially concerning the NGS data produced?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very important; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 160. How important is it for patients to receive a document on how data security is guaranteed, and how they can withdraw that data any time based on the General Data Protection Regulation?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very important; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

IX. Evaluating the rights of the patients to receive the results in an appropriate format

* 161. How important is it for patients to receive a report, after the NGS analysis, containing the results?

Please answer on a scale from 0 to 5 (0 – not at all; 5-very important).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 162. Should patients have the choice to receive the results?

- ○ Yes
- ○ No
- ○ Not sure

* 163. Should patients have the possibility to choose between different options on the how comprehensive the returned results should be? The comprehensiveness could reach from no results, to results only regarding the current treatment, to all the detailed results of the NGS analysis.

- ○ Yes
- ○ No
- ○ Not sure

* 164. How important is it for the patients that the final report contains information about those implications of the NGS analysis that affect family members?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very important; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 165. How important is it for patients to have genetic consultation assistance during and after the discussion of the results?

Please answer on a scale from 0 to 5 (0 – not at all; 5 – very important; N/A – not sure).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 166. From a patient’s perspective, should the genetic results and pharmacogenetic results be part of one report or separated in two reports?

- ○ All results should be part of one report, in a printed format
- ○ All results should be part of one report, in a digital format
- ○ They should be separated in two reports, in a printed format
- ○ They should be separated in two reports, in a digital format

* 167. Should the patient have the pharmacogenetic results available on a mobile device or in a printed form?

- Only in a digital form on a mobile device
- Only in a printed form
- On a mobile device and in a printed form

168. If provided in a digital form on a mobile device, does a security level similar to that used for e-banking provide a good level of data security confidence to the patient?

- Yes
- No
- Not sure

* 169. How important is it for the patient who has access to the results of the genetic testing (including mutated genes and diagnosis)?

Please answer on a scale from 0 to 5 (0 – not at all; 5-very important).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 170. From a patient's perspective, how limited should the access to the results from the genetic testing be?

- Very limited (ex. only the patient and the clinician in cancer care should have access)
- Mildly limited (ex. the patient, the clinician in cancer care and other clinicians the patient goes to should have access)
- Limited (ex. the patient, the clinician in cancer care and other clinicians the patient goes to, as well as the pharmacists should have access)
- Not limited (anyone can have access)

* 171. How important is it for the patient who has access to the pharmacogenetic results?

Please answer on a scale from 0 to 5 (0 – not at all; 5-very important).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 172. From a patient's perspective, how limited should the access to the pharmacogenetic results?

- Very limited (ex. only the patient and the clinician in cancer care should have access)
- Mildly limited (ex. the patient, the clinician in cancer care and other clinicians the patient goes to should have access)
- Limited (ex. the patient, the clinician in cancer care and other clinicians the patient goes to, as well as the pharmacists should have access)
- Not limited (anyone can have access)

* 173. What level of evidence would a patient like to have in order to be treated based on NGS results?

Select all that apply (multiple answers possible) and provide ranking of importance from 0-5 (0 – not at all; 5-very important).

	0	1	2	3	4	5
The NGS test is approved for therapy decision by regulatory authorities	○	○	○	○	○	○
Recommended by the medical society	○	○	○	○	○	○
Evidence is published in a scientific journal	○	○	○	○	○	○
Experience from other patients or patient advocacy groups	○	○	○	○	○	

* 174. How important is it that the patients receive information about existing clinical trials the patient can participate in (in the patient's country or neighboring countries), and that the information is generated through the diagnostic procedure?

Please answer on a scale from 0 to 5 (1 – not at all; 5-very important).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 175. How important is it for the patient to be informed of incidental findings relevant to the disease object of the research or any further incidental finding relevant to her/his health as well as her/his genetical relatives?

Please answer on a scale from 0 to 5 (1 – not at all; 5-very important).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 176. How important is it for the patient to have a psychological assistance during/after the communication of the results of the test?

Please answer on a scale from 0 to 5 (1 – not at all; 5-very important).

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

PATIENTS' NEEDS QUESTIONNAIRE Instand-NGS4P

Last question

177. Would you like to share with us any additional information related to any section of the questionnaire? If yes please use the free field to do so.

178. Is the provided information confidential?

- Yes
- No

SOLUTION PROVIDERS Questionnaire

PROJECT INTRODUCTION

INSTAND-NGS4P is an EU-funded Pre-Commercial Procurement (PCP) project for improving cancer patient's benefit from Next Generation Sequencing (NGS). Driven by patient and clinical needs, two innovative NGS workflows from sample pre-analytics to medical decision-making will be developed for routine diagnostics of common and rare adult and paediatric cancers complying with the IVDR. The developed workflows will compile information from cancer gene testing, pharmacogenetics 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 PCP project provides funding for a public consortium to define unmet medical and technical needs based on an Open Market Consultation, which lays the foundation for a call for tenders addressing solution providers (companies) to develop their products to better meet user needs. At three cut-off periods, companies 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 companies for product development (in total 8.55 M€) will finally lead to two integrated standardized NGS workflows, including decision support.

The different lots of this project cover the entire workflow for integration and standardization of targeted and whole genome DNA sequencing and decision making at the bedside:

lot 1: Pre-sequencing (specimen collection, nucleic acid isolation, library preparation)

lot 2: Sequencing

lot 3: Bioinformatics analysis

lot 4: Integrated reporting

The procurement will take the form of a pre-commercial procurement (PCP) under which R&D service contracts will be awarded to a number of solution providers in parallel in a phased approach. This will make it possible to compare competing alternative solutions.

Each selected operator will be awarded a framework agreement that covers 3 R&D phases.

The 3 phases are:

Design of lots

Prototype of lots

Fully integrated NGS workflow.

Each of the 3 phases will address all 4 lots.

SOLUTION PROVIDERS Questionnaire

PURPOSE OF THE QUESTIONNAIRE

This questionnaire is part of the Open Market Consultation (OMC) which aims at refining the clinical, patient and technical needs defined by the project consortium, as well as the emerging solutions available or under development to address these needs. For this purpose, three questionnaires were developed for three different stakeholder groups – users, solution providers and patient associations. The feedback collected from the questionnaires will support the subsequent preparation of the call for tenders. The questionnaires also allow disclosure of confidential information to the project consortium, which will be treated with high confidentiality. Aggregated data from the results of the survey will potentially be published in an anonymous way, excluding the information labelled as confidential.

The personal information collected through the questionnaires will be exclusively used for the purposes of the project, will not be shared with third parties, and will be deleted after the closure of the project.

GUIDANCE

The questionnaire is addressed to all solution providers in the field of NGS, and is divided into the following sections: General questions, Lot 1, Lot 2, Lot 3, Lot 4. After answering the general questions, you will be asked for each section whether you want to fill it in or not. We would highly appreciate if you would take the time to fill in the section(s) related to your expertise. However, if you do not find the question relevant, feel free to select N/A (not applicable) as an answer or skip the question and to move on to the next one..

Please submit the questionnaire by May 31st, 2021. Thank you in advance for contributing.

* 1. Organisation profile

Organisation name	
Address	
City/Town	
Country	

* 2. Contact person

First name	
Family name	
Email Address	
Phone Number	

SOLUTION PROVIDERS Questionnaire

General questions

* 3. How is your organization positioned in the NGS scene (more than one answer possible):

- [ ] Provider
- [ ] Manufacturer
- [ ] Includes Research & Development
- [ ] Hospital/medical centre
- [ ] Academic hospital
- [ ] Diagnostic laboratory
- [ ] Patient organization
- [ ] Other (please specify)

* 4. What is your current position in your organization?

* 5. Are you currently performing production/diagnostic activities for products used or diagnostics in the NGS workflow in (please specify the percentage in the textbox):

Europe	
North America	
Asia	
South America	
Australia	
N/A	

* 6. Are you currently performing research and development activities for products/diagnostics used in the NGS workflow in (please specify the percentage in the textbox):

Europe	
North America	
Asia	
South America	
Australia	
N/A	

* 7. Are you using NGS sequencing for research or for diagnostics?

- Yes
- No
- N/A

* 8. Do you have access to sequencing facilities?

- Yes
- No
- N/A

* 9. Do you perform sequencing in house or externally?

- In house
- Externally
- N/A

* 10. What platform do you use?

- Illumina
- Ion Torrent
- Gene-Reader
- Oxford Nanopore
- MGI
- Pac Bio
- N/A
- Other (please specify)

* 11. How many samples are you typically sequencing per week?

- Less than 1
- 1-10
- 10-50
- 50-100
- More than 100
- N/A

* 12. How interested are you in whole exome sequencing? (0-not interested in all, 5 - very interested)

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 13. How interested are you in gene panels? (0-not interested in all, 5 - very interested)

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

* 14. How interested are you in whole genome sequencing? (0-not interested in all, 5 - very interested)

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

SOLUTION PROVIDERS Questionnaire

Introduction lot 1

* 15. Would you like to answer questions related to Lot 1 (Pre-Analytics and Library preparation)?

- Yes
- No

SOLUTION PROVIDERS Questionnaire

Lot 1, page 1/2

CHALLENGE 1:

Improving the analytical performance by standardizing and or simplifying the pre-analytical processes

16. Most commonly used/produced samples for NGS analysis

Which are the types of specimens most included in the test procedure kit produced or is produced as a kit by your organization?

- [ ] FFPE
- [ ] Frozen tissues
- [ ] Blood
- [ ] FNAs
- [ ] Plasma
- [ ] Other
- [ ] Other (please specify)

17. Is the information above confidential?

- ◯ Yes, it is confidential
- ◯ No, it can be shared

Among the following, please indicate the specimen(s) you consider most challenging in terms of defining detailed pre-analytical processing standards. Please weight each of them on the basis of their importance from 1 (lower) to 5 (higher).

18. FFPE

	1	2	3	4	5	N/A
DNA	◯	◯	◯	◯	◯	◯
RNA	◯	◯	◯	◯	◯	◯

19. Frozen tissues

	1	2	3	4	5	N/A
DNA	◯	◯	◯	◯	◯	◯
RNA	◯	◯	◯	◯	◯	◯

20. Blood/plasma

	1	2	3	4	5	N/A
DNA						
RNA						
cfDNA						
cfRNA						

21. Fine Needle Aspirates

	1	2	3	4	5	N/A
DNA						
RNA						

22. Circulating Tumor Cells

	1	2	3	4	5	N/A
DNA						
RNA						

23. Extracellular vesicles

	1	2	3	4	5	N/A
DNA						
RNA						

24. Saliva

	1	2	3	4	5	N/A
DNA						

25. Other

	1	2	3	4	5	N/A
DNA						
RNA						

26. If you selected other, please specify

27. Is the information above confidential?

- Yes, it is confidential
- No, it can be shared

PROBLEM: Preanalytical processing procedures can cause variations in the test result.

SOLUTION: Standardisation according to ISO and CEN documents

Is your organization aware of the following standards? Please select the first box if there is awareness and the second if your organization works according to or applies the standard:

28. ISO 15189 Medical Laboratories – Requirements for quality and competence

- Aware
- Applies

29. ISO 20166-1:2018 Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for formalin-fixed and paraffin-embedded (FFPE) tissue - Part 1: isolated RNA

- Aware
- Applies

30. ISO 20166-3:2018 Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for formalin-fixed and paraffin-embedded (FFPE) tissue - Part 3: isolated DNA

- Aware
- Applies

31. ISO 20184-1:2018 Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for frozen tissue - Part 1: isolated RNA

- Aware
- Applies

32. ISO 20186-1:2019 Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for venous whole blood - Part 1: isolated cellular RNA

- Aware
- Applies

33. ISO 20186-2:2019 Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for venous whole blood - Part 2: isolated genomic DNA

- Aware
- Applies

34. ISO 20186-3:2019 Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for venous whole blood - Part 3: isolated circulating cell free DNA from plasma

- Aware
- Applies

35. CEN/TS 17390-1:2020 (WI=00140123) Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for circulating tumor cells (CTCs) in venous whole blood - Part 1: Isolated RNA

- Aware
- Applies

36. CEN/TS 17390-2:2020 (WI=00140125) Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for circulating tumor cells (CTCs) in venous whole blood - Part 2: Isolated DNA

- Aware
- Applies

37. Do you adhere to other ISO standards for NGS pre-analytics or library preparation? If yes, please specify

38. Is the information above confidential?

- Yes, it is confidential
- No, it can be shared

39. Does your organization see ISO standardization as a good and useful approach?

- Yes
- No

Comment

40. Is the information above confidential?

- Yes, it is confidential
- No, it can be shared

PROBLEM Many quality issues in pre-analytics arise even before nucleic acid extraction, during the whole process starting from sample collection, processing and storage.

SOLUTION: An entry-level quality check to confirm the sample is fit for purpose.

41. In your opinion, this would be:

- Not needed
- Helpful
- Crucial to develop

42. Which parameters beyond adherence to standards would be needed to be checked

for fixed, paraffin-embedded samples	
for fresh frozen tissue	
for white blood cells (PBMC)	
for liquid biopsies	

43. Is the information above confidential?

- Yes, it is confidential
- No, it can be shared

PROBLEM Sample transport and storage might be required which can change the nucleic acids' quality/quantity.

SOLUTION: Stabilization of DNA and RNA (this can include all different types of DNA and RNA depending on the source and target situation)

44. Is your organization involved in R&D for such an approach?

- Yes
- No

45. In case of R&D involvement, would financial support be:

- Not needed
- Helpful
- Crucial to develop this approach

Comment

46. Is the information above confidential?

- Yes, it is confidential
- No, it can be shared

47. PROBLEM Sample pre-analytical processing can influence the final result of NGS.

SOLUTION: The project participants have compiled a list of key challenges in sample and library preparation that could be improved within the next 2 – 3 years.

Please weight each of them on the basis of their importance from 1 (lower) to 5 (higher).

						N/A
Increase in sample stability	○	○	○	○	○	○
Increase in sample quantity	○	○	○	○	○	○
Increase target concentration in the sample	○	○	○	○	○	○
Direct or long range sequencing	○	○	○	○	○	○
Alternative innovative stabilization methods	○	○	○	○	○	○
Compatibility of sample stabilizers with analytical test procedure that need to be performed or have been performed on the same sample (e.g. histology/cytology)	○	○	○	○	○	
Efficiency of the analyte isolation/extraction procedure	○	○	○	○	○	○
Quality assessment of the isolated analyte	○	○	○	○	○	○
Sample storage	○	○	○	○	○	○
Analyte storage	○	○	○	○	○	○
Automation of the isolation procedures	○	○	○	○	○	○
Standardization	○	○	○	○	○	○
Other	○	○	○	○	○	○

Other (please describe and specify if this information is confidential)

48. Is your organization involved in R&D in one or more of these approaches?

- ○ Yes
- ○ No

49. Please give the numbers with the highest priority first, down to the lowest priority you are involved in:

50. Is the information above confidential?

- ◯ Yes, it is confidential
- ◯ No, it can be shared

51. In case of R&D involvement, would financial support be

- ☐ Not needed
- ☐ helpful for
- ☐ crucial to develop this approach
- ☐ Comment

52. Is the information above confidential?

- ◯ Yes, it is confidential
- ◯ No, it can be shared

53. For the highest priority please explain why?

54. Is the information above confidential?

- ◯ Yes, it is confidential
- ◯ No, it can be shared

55. For the second highest priority please explain why?

56. Is the information above confidential?

- ◯ Yes, it is confidential
- ◯ No, it can be shared

PROBLEM During nucleic acid isolation, it is often impossible to obtain more than one NA target especially when dealing with small size samples.

SOLUTION: Simultaneous Isolation of multiple nucleic acid types (e.g. DNA and RNA) in the same run.

57. Is your organization interested for further development in this approach?

- Yes
- No

58. Please weight the importance of the further development of this approach from 1 (lower) to 5 (higher)

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59. In case of R&D involvement, would financial support be

Not needed	
helpful for	
crucial to develop this approach	

60. Is the information above confidential?

- Yes, it is confidential
- No, it can be shared

PROBLEM Each target situation and type of nucleic acid imply different isolation procedures resulting in multiple kits to choose from and large stocks that might expire before they can be used up.

SOLUTION: Compatibility of nucleic acid isolation methods with multiple targets and applications.

61. Is your organization interested in further development in this approach?

- Yes
- No

62. In case of R&D involvement, would financial support be

Not needed	
helpful for	
crucial to develop this approach	

63. Is the information above confidential?

- Yes, it is confidential
- No, it can be shared

PROBLEM Panels are constantly in need of extension for addition of new diagnostic marker sequences and need to be verified and validated before use. This complicates library preparation due to optimal selection of changing panels to diagnostically cover the case to be analysed.

SOLUTION: Whole Genome Sequencing (WGS) and Whole Exome Sequencing (WES) instead of targeted NGS approach

64. Is your organization interested in further development in this approach?

- Yes
- No

65. In case of R&D involvement, would financial support available in the Instand-NGS4P project be

Not needed	
helpful for	
crucial to develop this approach	

66. Is the information above confidential?

- Yes, it is confidential
- No, it can be shared

PROBLEM The ligation of adapters is a critical step in library preparation. Insufficient adapter ligation leads to low library complexity, especially for low input samples

67. Which approach(es) are you currently using:

- amplicon-based library preparation
- full length adapters
- stubby adapters
- Other (please specify)

68. Is the information above confidential?

- Yes, it is confidential
- No, it can be shared

69. What is the guaranteed ligation efficacy you can acquire:

- <70%
- 70-80%
- 80-90%
- 90-95%
- >95%

SOLUTION: Improve the adapter design and library preparation protocol.

1. use of alternatives to adapter- and amplicon-based approaches
2. improve adapter design
3. improve ligation process

70. Is your organization involved in R&D for novel approaches?

- Yes
- No
- If yes, give the number of the solution your organisation is involved in

71. Is the information above confidential?

- Yes, it is confidential
- No, it can be shared

72. Please weight the importance of the further development of approaches from 1 (lower) to 5 (higher):

73. In case of R&D involvement, would financial support be

Not needed	
helpful for	
crucial to develop this approach	

PROBLEM WGS and WES are difficult with FFPE tissue.

SOLUTION:

1. Use alternatives for FFPE tissue, like frozen tissue

2. Use other fixation/ stabilization methods that preserve the histologic qualities and stabilizes DNA and RNA for use in NGS

74. Is your organization interested or involved in R&D for such an approach?

- Yes
- No
- If yes, please give the number of the solution your organization is interested in (highest priority first)

75. Is the information above confidential?

- Yes, it is confidential
- No, it can be shared

76. Please weight the importance of the further development of this approach from 1 (lower) to 5 (higher)

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77. In case of R&D involvement, would financial support available in the Instand-NGS4P project be

Not needed	
helpful for	
crucial to develop this approach	

PROBLEM WGS and WES difficult for Liquid Biopsy (cfDNA and cfRNA, exosome and CTCs)

SOLUTION:

1. Maximise the yield and quality of isolated targets

2. Increase sequence sensitivity and precision

78. Is your organization interested or involved in R&D for such an approach?

- Yes
- No

If yes, please give the number of the solution your organization is interested in (highest priority first):

79. Is the information above confidential?

- Yes, it is confidential
- No, it can be shared

80. Please weight the importance of the further development of this approach from 1 (lower) to 5 (higher)

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81. In case of R&D involvement, would financial support available in the Instand-NGS4P project be

Not needed	
helpful for	
crucial to develop this approach	

82. Is the information above confidential?

- Yes, it is confidential
- No, it can be shared

PROBLEM Complexity and the large number of steps needed for the complete library preparation, which can also differ in various specific situations, increases the risk of error causing failure or variations in the end result.

SOLUTION: Below you can find a list of possible approaches to solve the problem.

83. Please weight each of them on the basis of their importance from 1 (lower) to 5 (higher).

	1	2	3	4	5	N/A
Universal approach for different sample types and targets	○	○	○	○	○	○
Automation of library preparation	○	○	○	○	○	○
Automation of nucleic acid isolation alone	○	○	○	○	○	○
Automation from nucleic acid isolation (different targets and DNA and RNA, low and high yield) to sequencing (closed system)	○	○	○	○	○	○
Direct or long range sequencing	○	○	○	○	○	○
Reduced number of steps needed	○	○	○	○	○	○
UMIs mandatory (for mutation detection down to 0.01-0.1% allele frequency)	○	○	○	○	○	○
Improvement of library preparation success rate	○	○	○	○	○	○
Improvement of library yield	○	○	○	○	○	○
Minimal quality and quantity requirements for ○	○	○	○	○	○ the input material	
Other	○	○	○	○	○	○

Other (please specify)

84. Is the information above confidential?

- ○ Yes, it is confidential
- ○ No, it can be shared

85. Is your organization interested in further development in one or more of these approaches?

- Yes
- No
- Please give the numbers of interest or involvement with the highest priority first, down to the last priority:

86. Is the information above confidential?

- Yes, it is confidential
- No, it can be shared

87. In case of R&D involvement, would financial support be

Not needed	
helpful for	
crucial to develop this approach	

88. Comment

89. Is the information above confidential?

- Yes, it is confidential
- No, it can be shared

90. Is the information above confidential?

- Yes, it is confidential
- No, it can be shared

PROBLEM Waste of material due to package sizes and stability of reagents

SOLUTION:

1. Increased long term stability of reagents and simplified storage requirements
2. Reduce and recycle packaging and consumables
3. Scalability of reagents

91. Is your organization interested in further development in one or more of these approaches?

- Yes
- No
- Please give the numbers of interest or involvement with the highest priority first, down to the last priority:

92. Is the information above confidential?

- Yes, it is confidential
- No, it can be shared

93. In case of R&D involvement, would financial support available in the Instand-NGS4P project be

Not needed	
helpful for	
crucial to develop this approach	

94. Comment

CHALLENGE 2:

Integrating pre-analytical, analytical processes and data analytics into a standardized workflow

PROBLEM WGS and WES are difficult for FFPE material because of the multitude of chemical changes present in the sample.

SOLUTION: Alternative isolation/stabilisation methods suitable for WGS and WES need to be compatible with other diagnostic methods, like histology and cytology.

95. Is your organization interested in further development of such an approach?

- ◯ Yes
- ◯ No

96. In case of R&D involvement, would financial support be

Not needed	
helpful for	
crucial to develop this approach	

97. Comment

98. Is the information above confidential?

- ◯ Yes, it is confidential
- ◯ No, it can be shared

PROBLEM WGS and WES are difficult for low yield samples (e.g. plasma cfDNA, cfRNA).

SOLUTION:

1. Alternative isolation/stabilisation methods giving highest yield possible

2. Increased sequencing sensitivity

99. Is your organization interested in the further development of such an approach?

- Yes
- No
- Please give the numbers of interest or involvement with the highest priority first, down to the lowest priority:

100. Is the information above confidential?

- Yes, it is confidential
- No, it can be shared

101. In case of R&D involvement, would financial support be

Not needed	
helpful for	
crucial to develop this approach	

102. Comment

103. Is the information above confidential?

- Yes, it is confidential
- No, it can be shared

PROBLEM Isolated nucleic acid preparations can contain interfering substances. This can impair the reliability of the results and the compatibility of isolation methods with multiple sequencing methods.

SOLUTION:

1. The isolates are tested for inhibitory substances for various sequencing methods
2. Development of alternative procedures to avoid known interfering substances

104. Is your organization interested or involved in R&D for such an approach?

- Yes
- No

105. In case of R&D involvement, would financial support be

- [ ] Not needed
- [ ] helpful for
- [ ] crucial to develop this approach

106. Comment

107. Is the information above confidential?

- ◯ Yes, it is confidential
- ◯ No, it can be shared

PROBLEM Long turnaround times (for pre-analytics and library preparation).

SOLUTION: Below you can find a list of possible approaches to solve the problem.

108. Please weigh each of them on the basis of their importance from 1 (lower) to 5 (higher) .

	1	2	3	4	5	N/A
Faster nucleic acid isolation methods	◯	◯	◯	◯	◯	◯
Faster library preparation procedures	◯	◯	◯	◯	◯	◯
Integration of multiple steps in nucleic acid isolation procedure	◯	◯	◯	◯	◯	◯
Integration of multiple steps in library preparation	◯	◯	◯	◯	◯	
Integration of multiple steps in isolation and library preparation	◯	◯	◯	◯	◯	◯
Automation	◯	◯	◯	◯	◯	◯
Other	◯	◯	◯	◯	◯	◯

Other (please describe and specify if this information is confidential)

109. Is your organization involved in R&D in one or more of these approaches?

- ◯ Yes
- ◯ No

110. In case of R&D involvement, would financial support be

- [ ] not needed
- [ ] helpful
- [ ] crucial to develop this approach

Comment

111. Is the information above confidential

- ( ) Yes
- ( ) No

CHALLENGE 3:

Defining genetic variants with established medical implications for common and rare, adult and pediatric, cancers including pharmacogenetic variants relevant for therapy selection in cancer care

PROBLEM High nucleic acid yields are needed as input for NGS whereas often only small samples are available and NGS is not always able to deal with difficult genomic regions, low-yield materials and somatic mutations at low variant allele frequency.

SOLUTION:

1. Increase the efficiency of nucleic acid isolation methods
2. Increased sequencing sensitivity

112. Is your organization interested or involved in R&D for such an approach?

- ( ) Yes
- ( ) No

Please give the numbers with the highest priority first, down to the lowest priority

113. Is the information above confidential?

- ( ) Yes, it is confidential
- ( ) No, it can be shared

114. In case of R&D involvement, would financial support be

Not needed	
helpful for	
crucial to develop this approach	

115. Comment

116. Is the information above confidential?

- Yes, it is confidential
- No, it can be shared

PROBLEM The NGS diagnostic result is used for determination of the treatment for patients. This involves the administration of complex and hazardous drugs, although it is not known if the drugs are metabolized normally.

SOLUTION: Including Pharmacogenomic Analysis in panels targeted on somatic mutations

117. Is your organization interested in further development of such an approach?

- Yes
- No

118. In case of R&D involvement, would financial support available in the Instand-NGS4P project be

Not needed	
helpful for	
crucial to develop this approach	

119. Comment

120. Is the information above confidential?

- Yes, it is confidential
- No, it can be shared

CHALLENGE 4:

Developing reference material for quality control

PROBLEM Lack of availability of suitable internal quality control (QC) approaches and reference materials to monitor the NGS workflow as a whole.

SOLUTION: Multiple QC steps for each phase of the workflow to act as stop/go criteria to avoid wasting time and resources.

121. Is your organization interested in further development of such an approach?

- Yes
- No

122. In case of R&D involvement, would financial support be

Not needed	
helpful for	
crucial to develop this approach	

123. Comment

124. Is the information above confidential?

- Yes, it is confidential
- No, it can be shared

PROBLEM Availability of well-designed NGS performance testing (PT), External Quality Assessment (EQA) and reference material.

SOLUTION: Use of PT, EQA and reference material for NGS workflows

125. Please select the box if your organization is using or wants to use it:

	Develops	Produces
PT		
EQA		
Reference material		

Please specify what kind and what is your source

126. Is the information above confidential?

- Yes, it is confidential
- No, it can be shared

127. The reference material:

	Yes	No
is introduced into the workflow during pre-analytic processing	○	○
matches authentic sample matrix	○	○
covers diagnostically relevant variants	○	○
includes RNA	○	○
contains 'difficult' Variants Of interest	○	○

Comment

128. Is the information above confidential?

- ○ Yes, it is confidential
- ○ No, it can be shared

PROBLEM Patient identity of patient material is sometimes swapped with that of another patient. In doubt the material must be re-identified with ID SNP. This requires a lot of extra time.

Solution: Inclusion of patient ID SNP's in the sequence panel or result.

129. Is your organization involved in R&D for such an approach?

- ○ Yes
- ○ No

130. In case of R&D involvement, would financial support be

- ☐ Not needed
- ☐ helpful for
- ☐ crucial to develop this approach

131. Comment

132. Is the information above confidential?

- Yes, it is confidential
- No, it can be shared

133. If you have any further comments in the context of pre-analytics and library preparation, please let us know.

134. Is the information above confidential?

- Yes, it is confidential
- No, it can be shared

SOLUTION PROVIDERS Questionnaire

Introduction Lot 2

* 135. Would you like to answer questions related to Lot 2 (Sequencing)?

- Yes
- No

SOLUTION PROVIDERS Questionnaire

Lot 2

136. How important is sequencing time for you? (0- not important at all, 5-very important)

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

137. What is your maximum acceptable time for a routine sequencing run in hours, from library to variant calls?

138. How important are over-weekend runs for you? (0- not important at all, 5-very important)

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

139. What is your preferred pricing model?

- ○ Per analysis
- ○ Per reagents
- ○ Per infrastructure

140. How important is reduced hands-on time for you? (0- not important at all, 5-very important)

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

141. How much would you prefer higher costs for reagents and automated solutions in exchange for reduced hands-on time? (0- not at all, 5-very much)

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

142. Do you use reference material (inter-/intrarun control)?

- ○ Yes
- ○ No

If yes, please specify

143. Are you interested in using reference material in the future (inter-/intrarun control)?

- Yes
- No

If yes, please specify

144. How important would longer reads (>600bp) be for you? (0- not important at all, 5-very important)

0	1	2	3	4	5	N/A

145. How important is it for you to read biochemical information (ex. methylation status)? (0- not important at all, 5-very important)

0	1	2	3	4	5	N/A

146. What data should be generated for quality control of the sequencing?

147. Do you consider sequencing noise a problem? (0- not at all, 5-very much)

0	1	2	3	4	5	N/A

148. How big is the impact of systemic sequencing artefacts on your work? (0-no impact, 5-very big)

	0	1	2	3	4	5	N/A
Homopolymers							
GC rich regions							
Low complexity regions							

149. How important is paired-end sequencing for you? (0- not important at all, 5-very important)

0	1	2	3	4	5	N/A

150. How important is the size of the instrument for you? (0- not important at all, 5-very important)

0	1	2	3	4	5	N/A

151. How important is flexibility of the platform for scalable throughput for you? (0- not important at all, 5-very important)

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

152. How important is it for you to pool various libraries in one run? (0- not important at all, 5-very important)

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

153. Do you perform sequencing as a lab-developed test?

- ○ Yes
- ○ No

154. How important are IVDR-CE certified tests for you? 0- not important at all, 5-very important)

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

155. How important are IVDR-CE instruments for you? 0- not important at all, 5-very important)

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

PROBLEM High nucleic acid yields are needed as input for NGS whereas often only small samples are available and NGS is not always able to deal with difficult genomic regions, low-yield materials and somatic mutations at low variant allele frequency.

SOLUTION:

1. Increase the efficiency of nucleic acid isolation methods
2. Increased sequencing sensitivity.

156. Is your organization interested or involved in R&D for such an approach?

- ○ Yes
- ○ No

157. Please give the numbers with the highest priority first, down to the lowest priority.

158. Is the above provided data confidential?

- Yes, it is confidential
- No, it can be shared

159. Comment

160. Are the comments confidential?

- Yes, they are confidential
- No, they can be shared

161. If you have any further comments in the context of sequencing, please let us know.

162. Is the information above confidential?

- Yes
- No

SOLUTION PROVIDERS Questionnaire

Introduction Lot 3

* 163. Would you like to answer questions related to Lot 3 (Bioinformatics)?

- Yes
- No

SOLUTION PROVIDERS Questionnaire

Lot 3

164. How is your organization / specialized unit positioned in the Next Generation Sequencing (NGS) for Personalized Therapy field? (Please select all relevant points). Are you a...?

- [ ] Sequencing facility
- [ ] Computational facility
- [ ] Bioinformatics software developer
- [ ] Software service provider
- [ ] Diagnostic facility
- [ ] Research facility
- [ ] Commercial company
- [ ] Other (please specify)

165. Does your analysis solution support bioinformatics data from (please check all that applies).

- [ ] I have already replied to this question in the context of Lot 1.

166. FFPE

	1	2	3	4	5	N/A
DNA	☐	☐	☐	☐	☐	☐
RNA	☐	☐	☐	☐	☐	☐

167. Frozen tissues

	1	2	3	4	5	N/A
DNA	☐	☐	☐	☐	☐	☐
RNA	☐	☐	☐	☐	☐	☐

168. Blood/plasma

	1	2	3	4	5	N/A
DNA						
RNA						
cfDNA						
cfRNA						

169. Fine needle aspirates

	1	2	3	4	5	N/A
DNA						
RNA						

170. Circulating Tumor Cells

	1	2	3	4	5	N/A
DNA						
RNA						

171. Extracellular vesicles

	1	2	3	4	5	N/A
DNA						
RNA						

172. Saliva

	1	2	3	4	5	N/A
DNA						

173. Other

	1	2	3	4	5	N/A
DNA						
RNA						

174. If other, please specify and let us know if this data is confidenti al.

175. What is the indication that you are looking for a solution for?

- ◯ Adult cancer
- ◯ Pediatric cancer
- ◯ Rare diseases
- ◯ Other (please specify)

176. Which type of NGS data do you process?

- ◯ Targeted sequencing (Panels)
- ◯ Whole Exome Sequencing (WES)
- ◯ Whole Genome Sequencing (WGS)
- ◯ Gene Expression (RNA-Seq)
- ◯ ChIP-seq
- ◯ Methylation
- ◯ Other (please specify)

177. Where are the raw NGS (unprocessed) data produced for the bioinformatics analysis?

(Please choose all relevant points)

- ☐ Inhouse
- ☐ Another department
- ☐ External non-commercial organization
- ☐ Commercial provider
- ☐ Other (please specify)

178. Where is the NGS bioinformatics analysis performed?

(Please choose all relevant points)

- [ ] At the place of NGS data generation
- [ ] Inhouse
- [ ] Another department
- [ ] External non-commercial organization
- [ ] Commercial provider
- [ ] Other (please specify)

179. Who assesses the results of the NGS bioinformatics analysis for actionable items?

(Please choose all relevant points)

- [ ] The user
- [ ] We provide a service for the user
- [ ] Other (please specify)

180. How do users provide the raw NGS data for the bioinformatics analysis?

- [ ] By uploading to a server
- [ ] By running our solution locally
- [ ] Other (please specify)

181. How do you currently access the results of the NGS bioinformatics analysis?

(Please choose all relevant points)

- [ ] By downloading from a server
- [ ] By running our solution locally
- [ ] Other (please specify)

182. Which type of software is used for the bioinformatics analysis?

(Please choose all relevant points)

- [ ] open-source software (Non-commercial)
- [ ] open-source software (Commercial)
- [ ] Commercial software (source code not available)
- [ ] Other (please specify)

183. Do you use any workflow manager / workflow description standard? (multiple answer possible)

- [ ] No, I only use command line
- [ ] No, I only support my stand-alone solution
- [ ] Yes, Galaxy
- [ ] Yes, Common Workflow Language (CWL)
- [ ] Yes, Taverna
- [ ] Yes, Orange
- [ ] Yes, KNIME
- [ ] Yes, Workflow Definition Language (WDL)
- [ ] Yes, Next Flow
- [ ] Yes, Snake Make
- [ ] Yes, other (please specify)

184. Which file formats are used to exchange data?

- ◯ FASTQ
- ◯ BAM / CRAM
- ◯ VCF
- ◯ CSV
- ◯ JSON
- ◯ Other (please specify)

185. Please indicate the software license (if known)

(Please choose all relevant points)

- [ ] GNU General Public License
- [ ] MIT License
- [ ] Apache License
- [ ] BSD License
- [ ] Commercial products
- [ ] Not sure
- [ ] Other (please specify)

186. What type of annotations do you currently get?

- ( ) Variant classification
- ( ) Variant population frequency
- ( ) Variant Effect prediction
- ( ) Disease gene panel
- ( ) Disease-gene association
- ( ) Clinical actionable items
- ( ) Drug-gene interactions
- ( ) Dosage sensitivity
- ( ) Other (please specify)

187. Is the annotation information from

(Please choose all relevant points)

- [ ] Findable Accessible Interoperable Reusable (FAIR) data providers
- [ ] Free available data
- [ ] Commercial data
- [ ] Other (please specify)

188. What kind of QC do you perform for your bioinformatics pipeline?

- Validation using criteria for accredited labs, shared with users
- CE certification by notified bodies
- Other (please specify)

189. Is the NGS bioinformatics analysis certified / accredited to

- ISO27001:2013 (information security standard)
- IEC 62304 (Software Lifecycle)
- ISO 14155:2011 (Clinical investigation of medical devices for human subjects)
- ISO 14971 (Risk management)
- ISO13485:2016 (Medical devices)
- Not sure
- Other (please specify)

Future of NGS bioinformatics analysis for diagnostics

NGS bioinformatics analyses have been performed in a research setting for a few years, but their use in the diagnostic setting is not widely applied yet.

190. Which challenges are the highest immediate priority? (scoring 0-5)

	0	1	2	3	4	5
Automation / Reduced manual work						
Reproducibility						
Packaging (e.g. containers)						
Portability						
Long-term availability						
Long-term maintainability						
Standardized data exchange						
Standardized data storage formats						
Encryption / data security						

Other (please specify)

191. Which challenges are the highest long-term priority? (scoring 0-5)

	0	1	2	3	4	5
Automation / Reduced manual work						
Reproducibility						
Packaging (e.g. containers)						
Portability						
Long-term availability						
Long-term maintainability						
Standardized data exchange						
Standardized data storage formats						
Encryption / data security						

Other (please specify)

Software and pipelines

Automation offers the execution of different software products at different steps, which allows a standardized and reproducible analysis at different places. This can include different software solutions but ultimately allows harmonizing the detection of genomic events.

192. What do you believe are the key challenges to overcome in relation to introducing standardized pipelines and software to detect actionable items for diagnostics purposes? Score each (0-5)

	0	1	2	3	4	5
managing software versions	○	○	○	○	○	○
compatibility between tools or databases	○	○	○	○	○	○
reproducibility	○	○	○	○	○	○
complying with standard data formats	○	○	○	○	○	○
adjusting workflow for different customers	○	○	○	○	○	○
integration in open-source pipeline systems	○	○	○	○	○	○
testing of pipelines with standardized samples	○	○	○	○	○	○
scalability to whole genome sequencing	○	○	○	○	○	○

Other (please specify)

Which are in your opinion the relevant standards on this topic and how ready are they to be used in diagnostics? (please rate the relevant standards for readiness 0-5)

193. Software file formats and secure data exchange protocols

	0	1	2	3	4	5
BAM/SAM/FASTQ format	○	○	○	○	○	○
VCF format	○	○	○	○	○	○
gVCF format	○	○	○	○	○	○
GA4GH HTSGet	○	○	○	○	○	○
Encryption (Crypt4GH)	○	○	○	○	○	○
CRAM format	○	○	○	○	○	

○ Other (please specify)

ISO standards

ISO 20397-2:2021 "Biotechnology — Massively parallel sequencing — Part 2: Quality evaluation of sequencing data"

194. Please score the relevance of software license models regarding their use in diagnostics? (score each 0-5)

	0	1	2	3	4	5
Open Source (https://docs.github.com/en/github/creating-cloning-and-archiving-repositories/licensing-a-repository#choosing-the-right-license)	○	○	○	○	○	○
Closed source	○	○	○	○	○	○
BSD 3	○	○	○	○	○	○
Apache	○	○	○	○	○	○
CC	○	○	○	○	○	○
GNU GPL (v1,v2, v3)	○	○	○	○	○	○
OSL	○	○	○	○	○	○
MIT	○	○	○	○	○	○

Other (please specify)

Annotation resources

The annotation of variants or genomic events is fundamental to identify actionable items.

195. What do you believe are the key challenges to overcome the standardized use of annotation resources for diagnostics purposes?

- [ ] Updating external resources
- [ ] Standardized list of approved annotation resources
- [ ] Quality of resources (CE marking, ISO standard)
- [ ] Lifetime of resource
- [ ] Size of resource
- [ ] Licensing of resources
- [ ] Other (please specify)

Data storage and sharing

The storing and sharing of data is an integral part of a bioinformatics pipeline. The types of data include raw NGS data, result files from the pipeline as well as metadata.

Finally, it needs to be decided which data should be stored, where should they be stored, for how long and who should have access to?

196. What do you believe are the key challenges to overcome in relation to storing & sharing of relevant data for diagnostics purposes? score each (0-5)

	0	1	2	3	4	5
Location of storage (GDPR)	○	○	○	○	○	○
GA4GH standards	○	○	○	○	○	○
encryption	○	○	○	○	○	○
longtime storage	○	○	○	○	○	○
Patient access	○	○	○	○	○	○
Data size	○	○	○	○	○	

○ Other (please specify)

Security

The acquired NGS data in diagnostics are very sensitive and can identify patients.

197. What do you believe are the key challenges to overcome in relation to the secure handling of NGS data in diagnostics? score each (0-5)

	0	1	2	3	4	5
standardization	○	○	○	○	○	○
awareness of personnel	○	○	○	○	○	○
training of personnel	○	○	○	○	○	○
quality of solutions (CE marked)	○	○	○	○	○	○
security updates	○	○	○	○	○	○
GDPR requirements properly addressed to	○	○	○	○	○ national implementation	

Other (please specify)

198. If you have any further comments in the context of bioinformatics analysis, please let us know.

199. Is this information confidential?

- Yes
- No

SOLUTION PROVIDERS Questionnaire

Introduction Lot 4

* 200. Would you like to answer questions related to Lot 4 (Integrated reporting)?

- Yes
- No

SOLUTION PROVIDERS Questionnaire

Lot 4

The aim of Lot 4 is to provide innovative solutions for translating NGS results into medical decision-making reports. This should be achieved by integrating NGS results with pharmacogenomics panels and existing e-medication tools containing information on 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. The relevant clinical information should be reported in a concise and clear way, reporting only data with validated evidence for clinical decisions and in a form minimizing the risk of data misinterpretation. The questionnaire should help to define the specifications of the integrated reporting tool.

201. Do you use tools for integrated reporting?

- Yes
- No

202. Are you interested in implementing tools for integrated reporting?

- Yes
- No

203. 32. Are you a solution provider for integrated reporting tools?

- Yes
- No

204. Do you have a solution for integrated reporting of NGS results that integrates the following data and information (multiple answers may apply)

	Yes	No
Cancer–related variants	○	○
Actionable items	○	○
Pharmacogenomic variants	○	○
Level of evidence for cancer-related variants (level of evidence could be companion-diagnostics, drug-label, guidelines, databases, scientific literature)	○	○
Level of evidence for pharmacogenetic variants (level of evidence could be for example companion-diagnostics, drug-label, guidelines, databases, scientific literature)	○	○
Information on clinical trials	○	○

Other (please specify)

205. How important is the integration of the following data and information in reporting of NGS results in order to support medical decision making (please select score; 0=not relevant; 5=highly relevant).

	0	1	2	3	4	5	N/A
Information on informed consent	○	○	○	○	○	○	○
Information on the sample analyzed	○	○	○	○	○	○	○
Information on the analytical method	○	○	○	○	○	○	○
Information on the quality of the analysis	○	○	○	○	○	○	○
Results on cancer – related variants	○	○	○	○	○	○	○
Information on actionable items	○	○	○	○	○	○	○
Information on pharmacogenomics variants	○	○	○	○	○	○	○
Information on the level of evidence for cancer-related variants	○	○	○	○	○	○	○
Information on the level of evidence for pharmacogenomics variants	○	○	○	○	○	○	○
Information on drug-drug interaction, dosing, side effects and contra indications (e.g., e-medication)	○	○	○	○	○	○	○
Information on relevant clinical data (e.g., heart, liver, kidney function)	○	○	○	○	○	○	○
Information on running clinical trials	○	○	○	○	○	○	○
Information on possible compassionate use	○	○	○	○	○	○	○

Other (please specify)

206. Please indicate how important is the following information on clinical evidence for decision making. Evidence based on the following facts (please select score; 0=not relevant; 5=highly relevant).

	0	1	2	3	4	5	N/A
Companion-diagnostics	○	○	○	○	○	○	○
Drug-label	○	○	○	○	○	○	○
Guidelines of medical societies	○	○	○	○	○	○	○
Curated databases	○	○	○	○	○	○	○
Scientific literature	○	○	○	○	○	○	○
Information on open clinical trials – national	○	○	○	○	○	○	○
Information on open clinical trials – Europe	○	○	○	○	○	○	○
Information on open clinical trials – international	○	○	○	○	○	○	○

What is your preferred reference for assessing the clinical evidence? Please describe

207. How important are the following features of integrated reporting for decision support

(please select score; 0=not relevant; 5=highly relevant)

	0	1	2	3	4	5	N/A
Desktop solution	○	○	○	○	○	○	○
Mobile device (e.g., tablet 12')	○	○	○	○	○	○	○
Touch screen	○	○	○	○	○	○	○
WLAN	○	○	○	○	○	○	○
Off-line mode	○	○	○	○	○	○	○

Other (please specify)

208. How important is graphical presentation (data visualization) of results for decision support? (please select score; 0=not relevant; 5=highly relevant)

0	1	2	3	4	5	N/A
○	○	○	○	○	○	○

209. Do you have a preferred solution for graphical presentation of results?

- Yes
- No

If yes please describe the solution

210. How important is it that the results of integrated reporting are also integrated in electronic health records (EHR) and the hospital information systems (HIS)? (please select score; 0=not relevant; 5=highly relevant)

	0	1	2	3	4	5	N/A
Relevance of integration in EHR							
Relevance of integration in HIS							

211. What hospital information system are you using?

Please describe:

212. Have you tested different products for integrated reporting and decision support?

- Yes
- No

If yes, describe which products

213. How satisfied are you with current products on the market for integrated reporting and decision support? (please select score; 0=not relevant; 5=highly relevant)

0	1	2	3	4	5	N/A

214. How important is it that the integrated reporting and decision support system generates a special report for patients? (please select score; 0=not relevant; 5=highly relevant)

0	1	2	3	4	5	N/A

215. How important is it that the data analysis for integrated reporting is performed locally or via a webservice? (please select score; 0=not relevant; 5=highly relevant)

	0	1	2	3	4	5	N/A
Local data analysis	○	○	○	○	○	○	○
Data analysis via webservice	○	○	○	○	○	○	○

216. If you have any further comments in the context of integrated reporting and e-medication, please let us know.

217. Is this information confidential?

- ○ Yes
- ○ No

SOLUTION PROVIDERS Questionnaire

Last question

218. Would you like to share with us any additional information related to any section of the questionnaire? If yes please use the free field to do so.

219. Is the provided information confidential?

- Yes
- No