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Blueprint: Recommendations for the Implementation of a Sustainable Network of Expertise on Omics in Europe (JANE WP9)

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LIST OF ABBREVIATIONS

Abbreviation	Definition
1+MG	European 1+ Million Genomes Initiative
ACCE	Analytical validity, Clinical validity, Clinical utility and ELSI
BBMRI-ERIC	European Biobanking Research Infrastructure
CAP	College of American Pathologists
CAYA	Children, Adolescents and Young Adults
CCC	Comprehensive Cancer Centre
CCCN	Comprehensive Cancer Care Networks
CCI	Comprehensive Cancer Infrastructure
CCI4EU	Comprehensive Cancer Infrastructure for the European Union
CGP	Comprehensive Genomic Profiling
CPE	Cancer Patients Europe
CraNE	Joint Action on network of Comprehensive Cancer Centres
CSA	Coordination and Support Action
CUP	Cancer of Unknown Primary
DKFZ	German Cancer Research Center
DPO	Data Protection Officer
DRUP	Drug Rediscovery Protocol
EACR	European Association for Cancer Research
EAPM	European Alliance for Personalised Medicine
EATRIS	European Infrastructure for Translational Medicine
ECHoS	European Network of National Cancer Mission Hubs
ECRIN	European Clinical Research Infrastructure Network
EHA	European Haematology Association
EHDS	European Health Data Space
EHR	Electronic Health Records
EIT	European Institute of Innovation and Technology
ELIXIR	European Life Sciences Infrastructure
ELSI	Ethical, Legal, and Societal Issues
EMA	European Medicines Agency
EMQN	European Molecular Genetics Quality Network
EORTC	European Organisation for Research and Treatment of Cancer
EPF	European Patients Forum
EQA	External Quality Assessment
ERN	European Reference Network
ESFRI	European Strategy Forum on Research Infrastructures
ESHG	European Society of Human Genetics
ESMO	European Society for Medical Oncology
ESH	European School of Haematology
ESO	European School of Oncology
EU	European Union
EUCAIM	European Cancer Imaging Initiative
EUnetHTA	European Network for Health Technology Assessment
GDI	Genomic Data Infrastructure
GDPR	General Data Protection Regulation

GenQA	Genomics Quality Assessments
IVDR	In Vitro Diagnostic Regulation
JA	Joint Action
MS	Member State
MDTB	Multidisciplinary Tumour Board
MTB	Molecular Tumour Board
NASA	National Aeronautics and Space Administration
NCT	National Center for Tumor Diseases
NGS	Next Generation Sequencing
NoE	Network of Expertise
OECI	Organisation of European Cancer Institutes
PRIME-ROSE	Precision Cancer Medicine Repurposing System Using Pragmatic Clinical Trials
SIOPE	European Society for Paediatric Oncology
SOC	Standard of Care
TRL	Technology Readiness Level
TTF	Transversal Task Force
USA	United States of America
WES	Whole Exome Sequencing
WGS	Whole Genome Sequencing
WP	Work Package

RECIPIENTS OF THIS DOCUMENT

This document is addressed to the whole JANE consortium. It is an official deliverable for the project and shall be delivered to the European Commission and appointed experts.

Table of Contents

1. Executive Summary

The continuously evolving field of omics provides a multitude of promising technologies for managing patients with cancer at the different steps from prevention, to diagnosis, treatment and follow-up. A Network of Expertise (NoE) on omics can support the complex implementation of such technologies in different domains. This report is the final deliverable of Work Package 9 (WP9), dedicated to the future European NoE on Omics as part of the JANE European Joint Action. It outlines the working methods and main advances achieved during the 2 years of the project, regarding the scope, objectives, and services provided by the future NoE on omics, endorsement criteria for expert members, organisational structure and governance, collaborative stakeholder identification and integration within the complex EU cancer landscape. The content of this blueprint will be used for the implementation of the European NoE on Omics during the next joint action JANE2.

2. Introduction

Omics[1] relates to the acceleration of large-scale sequencing and high-throughput computational analyses allowing the comprehension of the biological processes in human health and diseases. This novel domain in human science started with the sequencing of the first genome in early 2000[2]. Since then, it has been extended to a large variety of biological molecules, to the study of their structure, function, dynamics, and interactions, in body fluids, tissues, a single cell and/or in situ (spatial omics), with the need to integrate several layers. In rare diseases and oncology, omics revealed the incredible complexity of unsuspected molecular diversity within the same pathology as well as spatial and temporal heterogeneity of diseases. The integration of omics in routine oncology clinics resulted in the development of so-called 'precision (haemato-)oncology medicine'[3].

Omic sciences and technologies have undergone a technological explosion in recent years, with implications for advancing research in cancer treatment, in addition to cancer prevention. In particular, cancer medical treatment is already to date able to exploit some of the omics applications both in standard practice and in clinical research[4,5]. In 2018, 55% of all oncology clinical trials involved the use of biomarkers compared with around 15% in 2000[6]. Recently, The ESMO Precision Medicine Working Group updated recommendations for the use of next-generation sequencing (NGS) for patients in many advanced cancers[7]. Genomics is the most advanced omics area today, but transcriptomics, methylomics, proteomics, and metabolomics have also become readily included, while a wide range of other omics are maturing fast, such as epigenomics, lipidomics, and interactomics, as well as the integration of multiple omics using AI tools (multi-omics)[1]. Possible sample sources range from solid tumour biopsies to circulating tumour DNA in liquid biopsies. Omic

technologies are gradually becoming an increasingly important support for clinical decisions, especially with regard to biotherapies and advanced therapies, while of course they strongly support clinical and translational research, including the most cutting-edge. More than 25% of patients with cancer may receive a treatment based on biomarker testing[8]. However, uptake of the clinical implementation of efficient biomarker testing with novel technologies is insufficient and very unequally distributed in Europe (less than 10% of specimens requiring molecular testing are currently analysed, with many countries reporting less than 2% of cancers tested[6]). Uptake of multi-biomarker panels is highly variable across Europe, ranging from 0% to more than 50% in countries with public national reimbursement processes in place[6]. In addition to the inequal availability of infrastructures and resources, the inefficient coordination between scientific societies, regulatory bodies, and national policy decision-makers impairs the timing of the adoption of new omic tests[9]. To illustrate, it takes more than 1 year for a single molecular biomarker to be implemented in clinical practice in 15/28 European countries and this can reach 20 years for more complex tests, such as the transcriptional profiling scheme for breast cancers[6]. The challenge is to make these technologies accessible to the largest number of cancer patients across Europe through equitable and cost-effective solutions, while stimulating the advancement of these technologies in all member states (MSs), and converting possible competition into cooperation. Regulatory constraints represent a major barrier to the use of omic-based biomarkers in the access to drugs and all kinds of cancer treatments. Thus, there is a need to continuously update standards of care on the basis of research achievements and to harmonize regulatory and reimbursement patterns across MSs. Indeed, huge variations in the way omic technologies are made available throughout the EU are observed right now and these disparities may even increase in the near future. Thus, in an attempt to level healthcare in the EU avoiding current inequalities in access to care, a networking effort on omics is an urgently needed effort.

3. Methodology used (i.e. to design the NoE)

The content of this Work Package was developed applying multiple types of methods.

Literature review

A general scan of literature on the application of omics, with a specific focus on technology assessment of omics, was performed at the start of the project, allowing to build the general framework of discussion during the development of the design of the future NoE 'Omics'.

Use cases

Six use cases, wherein omics plays a pivotal role, were identified based on current interventions, activities or studies in the institution of the WP9 representatives. Their consultation aimed to facilitate the crystallization

of ideas of the NoE design and allowing corroborating the final design on its possible relevance and usage. They were a support to define the scope, the activities and their priority, the partners and collaborative stakeholders, as well as the organisation of the NoE on Omics.

Summary description of the 'Omics" use cases

Clinical trials for common cancers (ex. AURORA[10] - Philippe Aftimos – IJB – BE)

AURORA aims to study the processes of relapse in metastatic breast cancer (MBC) by performing multi-omics profiling on paired primary tumours and early-course metastases. Patients were recruited in 51 centres in Europe for targeted DNA- and RNA-sequencing. Analysis results were reported to the treating oncologist after annotation by a molecular advisory board. Patients with 'actionable' mutations are matched to targeted phase II clinical trials. The patients have a longitudinal follow-up for a maximum of 10 years with the collection of clinical data and serial plasma sampling.

Clinical trials for rare cancers (ex. EURACAN[11] - Jean-Yves Blay – Unicancer – FR)

EURACAN is one of the four European Reference Networks (ERNs) dedicated to cancer, with a focus on rare adult solid tumours. The aim of EURACAN is to provide a pan-Europe infrastructure, integrated with national healthcare systems, to improve the quality of care for patients with rare cancers. Their efforts include providing information and guidelines, training and education, improving diagnostic accuracy, expert multidisciplinary tumour boards (MDTBs), and facilitating access to innovative clinical trials for all EU patients.

Cancer genetic predisposition (ex. GENTURIS - Kathleen Claes – UZG – BE)

GENTURIS is an ERN dedicated to rare genetic tumour risk syndromes. Patients with such disorders are strongly predisposed to cancer due to inherited DNA mutations, with a lifetime risk running up to 100% and a wide variety of organ systems that can be affected. The primary challenges for such individuals are delayed diagnosis, lack of prevention for patients and healthy relatives and therapeutic mismanagement. GENTURIS aims to improve the identification and clinical outcomes of these syndromes through education, guidelines and best practices, registries and biobanks, access to multidisciplinary care, clinical research and patient empowerment. Proactive management of these conditions can lead to early detection and provide access to preventive, rather than curative, treatment.

Advanced Omics platform (ex. MASTER - Stefan Fröhling – NCT/DKFZ – DE)

MASTER is a multicentre registry trial investigating the clinical impact of comprehensive genomic, transcriptomic, and epigenomic analysis in patients with advanced rare cancers. Evidence-based clinical management recommendations derived from multi-layered molecular tumour profiles generated by WGS, RNA-seq, and DNA methylation analysis are provided to treating physicians by a cross-institutional molecular tumour board (MTB). Recommendations include assigning patients to molecularly stratified clinical trials and,

if no trial options are available, drug repurposing outside approved indications. To expand the spectrum of clinically actionable molecular profiles as starting points for NCT trials, MASTER also includes an exploratory, trial-enabling research component, which currently comprises mass spectrometry-based (phospho)proteomics, ex vivo drug testing, and spatially resolved proteomic analyses with particular focus on immune cell composition.

Non-curative indications (ex. Pharmacogenomics for pain control – Jesús González Barboteo – ICO – ES)

Despite the best analgesic treatment, 20% of patients have poor pain control or intolerable side effects from analgesic drugs. One reason is genetic factors. Over 400 genetic variants and painful phenotypes have been identified in the Human Pain Genes database. There are associations between genes and analgesic drugs, as well as their relationship with metabolizing enzymes. Systematic reviews tell us that clinical information is scarce. The limitations of the use of pharmacogenomics in this area are due to: 1) Pharmacogenomics study techniques are not available to everyone; 2) Currently, these tests do not usually cover into public health systems; 3) High economic cost; 4) Equity and ethical issues in healthcare. Some international groups are working on this issue. They have developed guidelines on the use of opioids and genetic variations (for instance, the Clinical Pharmacogenetics Implementation Consortium). In summary, there is a need to prioritize the use, research, and development of clinical guidelines on pharmacogenomics for non-curative indications such as symptoms control.

Network of Expertise on poor prognosis or Complex Cancers (ex. NatCUPMTB - Christophe Le Tourneau – Unicancer – FR)

With the increasing complexity of current diagnostic investigations, the integration of clinical, pathological and genomic characteristics is crucial for the management of patients with cancers of unknown primary (CUP). A national multidisciplinary molecular tumour board (NatCUPMTB) was created in July 2020 in France to discuss the diagnostic and therapeutic management of CUP patients. A multicentre retrospective study demonstrated that NatCUPMTB provides a significant diagnosis of the likely primary origin for 69% of patients and a therapeutic strategy recommendation for 71% of patients. In most patients, the diagnosis was based on the combination of clinical, pathological and genomic analyses (WGS, WES and transcriptome analysis performed in the two PFMG2025 (French Genomic Medicine Plan 2025) national sequencing laboratories). Personalised therapeutic strategies were recommended based on either the tissue of origin diagnosis or on actionable molecular alterations.

Expert and stakeholder meetings

In addition to JANE partners, the representatives of interested relevant stakeholders were invited to each meeting of the consortium: ELIXIR[12], the European biobanking research infrastructure (BBMRI-ERIC)[13], the European Clinical Research Infrastructure Network (ECRIN)[14], the European Strategy Forum on Research Infrastructures (ESFRI)[15] and the European Society for Medical Oncology (ESMO)[16]. ELIXIR is a life sciences infrastructure comprised of 250+ institutes in 24 European countries, which offers valuable resources, guidelines and partnership opportunities to improve the value and impact of life science research. Being identified as a priority collaborative stakeholder for the NoE, in particular for Omics infrastructures, ELIXIR was met on several occasions.

Exploration of collaborations with other JANE WPs

WP9 and **WP10 (NoE on High Tech Medical Resources)** have worked very closely together since the beginning of JANE. This close interaction relies on the fact that the aim of both WPs share similar characteristics and face common challenges, even if they have different scopes, partners and collaborators. Indeed, omics technologies and high tech medical resources cover very promising and innovative resources, which will profoundly modify and strengthen tomorrow's management of cancer. However, these resources are very expensive, not necessarily available in each cancer centre nor equally accessible or available in each EU Member State.

In practise, the scope, the objectives, the activities, the mission and vision of the NoE on innovative resources as well as the endorsement criteria for partnership and the synergies within the European cancer ecosystem were discussed and elaborated together during two joint face-to-face meetings.

WP5 (NoE on Poor Prognosis and Complex Cancer) has been proposed to be a use case for WP9, knowing the need for better characterisation and identification of therapeutic targets to improve their outcome.

TTF5 developed a toolkit about how to **engage and empower patients and citizens** (*Figure 1*). Specific topics with high relevance for WP9 were identified, such as building a trust framework for the use and secondary use of genomic data, cascade screening and family communication, risk based stratified prevention with societal support, etc. Depending on the topic, the targeted population (patients, citizens, family members, CAYA, ...) and the context (online or offline, structural or timely, large or small scale, ...) the toolkit is designed to help create a successful engagement between patients, experts and stakeholders within the NoE.

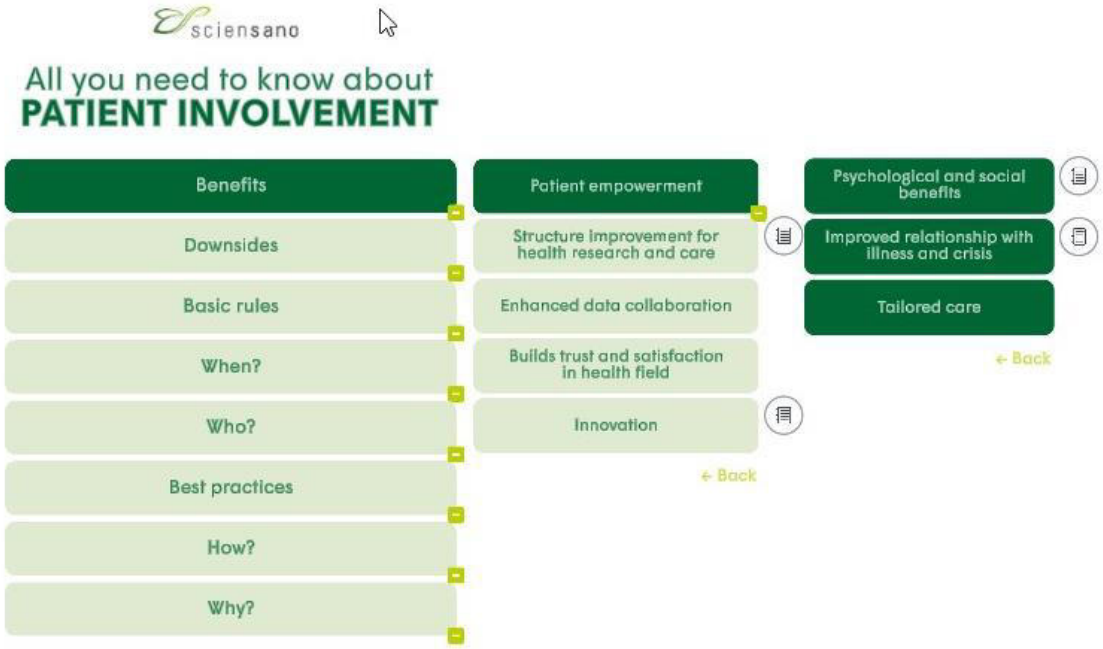

Figure 1: Toolkit developed during TTF5. Example after clicking on "Benefits" and then "Patient empowerment".

Survey

The **technology readiness level (TRL)** of the different omics by field of applications has been assessed through a survey among the JANE partners in order to prioritize them in their different fields of application. Originally developed by NASA in the '70s for space exploration technologies, TRLs assess the maturity level of a technology throughout its research, development and deployment phase progression[17]. TRLs are based on a scale from 1 to 9, with 9 being the most mature technology according to the EU definition[18] *(Table 1)*.

Table 1: Technology Readiness Level (TRL) scale (from https://www.twi-global.com/technical-knowledge/faqs/technology-readiness-levels)

4. Scope

Common objectives between WP9 and WP10 (High Tech Medical Resources):

Omics, as well as high tech medical resources are **promising and innovative resources** which have to address common issues. On the one hand, the future action of the corresponding NoEs should facilitate reaching **better access** to these resources in the EU by reducing disparities, and on the other hand, they must strive for **excellence and high quality services** for the users. Moreover, the **rapid integration** of these innovative techniques into care is essential so that cancer patients are to benefit from them as quickly as possible. Those principles will require some level of **flexibility** in line with particular contextual features in the Member States, e.g. reimbursement, ethical concerns, professional expertise, technical capacity.

These innovative resources, infrastructures as well as expert human resources, should be available in a **minimal number of Comprehensive Cancer Centres (CCCs)** / Comprehensive Cancer Infrastructures (CCI) / Comprehensive Cancer Care Networks (CCCN), whose European network is being defined and implemented within 'twin' Joint actions (CraNE and European Network of CCC), to cover the whole European population.

Field of applications

The NoE on Omics should be dedicated to the **needs of the healthcare providers** who use these resources within CCIs/CCCs/CCCNs, such as pathologists, clinical biologists, molecular geneticists, molecular biologists, bioinformaticians, as well as medical oncologists, haematologists, paediatricians, clinical geneticists and other physicians. All of them are the 'end users' of the services which will be provided by the NoE.

In addition to the **standard of care**, the field of application should include the different types of research, mostly **clinical and translational research**, including omics in patient-derived models, but also basic research to a lesser extent, in order to accelerate the integration of innovations into the precision cancer medicine during the whole journey from genetic susceptibility, diagnosis, treatment to follow-up and palliative care. This precision approach also integrates **public health** omics for fine-tuning prevention and screening programs in the general population.

The NoE on Omics could also explore the **interaction with technology providers** and set up novel pathways to **facilitate developing evidence** for a smooth transition from 'bench to bed' and reverse processes. Close collaboration with **funding organisations (national/international)** could be an important task for the NoE coordination, aligning with ongoing initiatives such as the ECHoS Cancer mission hubs, the 1+MG National initiatives, the Rare Diseases Mirror Groups, etc.

Objectives for the NoE on Omics

The following objectives have been identified as priority for the NoE on Omics. They will shape the services provided by the NoE;

1. **Identification of unmet needs**
    - Analysis of different use cases
    - Consultation of expert working groups
    - Prioritise how the needs will be addressed by the NoE
2. **Simplified organisation and procedures**
    - Build NoE on existing infrastructures that will be mapped with stakeholders
    - Explore new regulatory approaches, such as the Regulatory Sandbox, etc.
3. **Interoperability of omics platforms**
    - Harmonize data interpretation
    - Work with outputs of the 1 Million Genome project and ongoing initiatives such as GDI
4. **Data sharing**
    - Foster open database
    - Support data registration and secure data storage
    - Ensure compliance with GDPR rules, including familial inherited omics data
    - Use the outputs of the European Health Data Space (EHDS) initiative
5. **Equitable access for cancer patients within the EU**
    - Mitigate the inequalities between European member states
    - Identify gaps in resources, reimbursement and accessibility
    - Establish recommendations regarding urgent needs across Europe
6. **Guidelines and recommendations**
    - Support the integration of existing guidelines (elaborated by (inter)national scientific societies) and/or contribute to the elaboration of missing guidelines
    - Disseminate and maintain up-to-date standard operating procedures in this continuously evolving field
    - Establish recommendations to integrate omics in the health care system
    - Make recommendations to value research and innovation in collaboration with CCIs
7. **Education and capacity building**
    - Training and continuous education for health care professionals
    - Support capacity building at the national level
    - Support the development of twinning programmes

8. **Patient and citizen engagement**
    - Support patient involvement at the different steps
    - Provide public information
    - Enhance public literacy
9. **Synergies and collaborations**
    - Develop a large network of various partners, including commercial partners
    - Integration into the EU cancer landscape
    - Align with other networks currently being established (JA CraNE & EU network of CCC, CSA CCI4EU, CSA ECHoS, 1+MG, EUCAIM)
10. **Health policy and funding**
    - Expert advice on the reimbursement of evidence-based omics testing and the corresponding drugs if relevant (link with European Haematology Association (EMA) and EUnetHTA)
    - Interaction with funding organisations (national/international) to ensure sustainability

5. Technology Readiness Level Assessment of the main Omics

Literature review on assessment of Omics technologies

Omics technologies are increasingly of interest to Health Technology Assessment (HTA) agencies due to their rapid development and promising early examples of their implementation in healthcare practices[19]. HTA was defined by an international joint task group as "a multidisciplinary process that uses explicit methods to determine the value of a health technology at different points in its lifecycle, aiming to inform decision-making in order to promote an equitable, efficient, and high-quality health system"[20]. Such assessments are mainly aimed at evaluating technologies on their value for the SOC. A 2020 review on HTAs of omics showed that most HTA agencies have only assessed genomics and transcriptomics technologies, and the most prominent domains are analytical and clinical validity, clinical utility and economical aspects[19]. There is a need for standardization, although most HTA reports utilise some variation of the ACCE framework[21]. Within Europe, EUnetHTA was established with the goal of providing a sustainable European network on HTA[22]. They conduct joint clinical assessments and scientific consultations, operating under the EU HTA regulation and as such, are considered a valuable stakeholder for the NoE on omics.

Few European HTA agencies have reported assessments on omics technologies, even fewer considering cancer specifically. For example, the Belgian Health Care Knowledge Centre (KCE) reported on the challenges and organisational considerations for the use of WGS in clinical practice. Later, the Superior Health Council of Belgium published a broader report evaluating the general clinical application of omics technologies,

making recommendations for medical, ethical and societal challenges[5]. In the realm of oncology, several national HTA agencies have evaluated the use of transcriptome profiling to inform decision-making on adjuvant chemotherapy treatment[23–25]. In other examples, the Superior Health Council of France has clearly defined guidelines for the assessment of companion diagnostic tests associated with targeted therapy[26], and the Swedish Agency for Health Technology Assessment and Assessment of Social Services (SBU) has evaluated molecular urine tests (gene expression and methylation) for the diagnosis of men with a high probability for prostate cancer[27].

A more broad assessment can be made through determining the technology readiness level (TRL) of a technology depending on its intended operational environment[17], which may range from fundamental research to SOC (Table 2). Additionally, Bruno *et al.* have made excellent recommendations to consider the implementation of organisational (ORL), social (SRL), and legal (LRL) readiness scales to include the socioeconomic context vital to technology implementation[28]. These considerations should also be made by the NoE on omics, and highlight the importance of a subtask on ethical, societal and legal issues.

Despite rapid technological advances in the omics fields, a 2021 report[29] endorsed by the ECPC, Lung Cancer Europe and EU40, stated a sub-optimal uptake of biomarker testing throughout the EU. The main barriers identified were a low recognition of the benefits of biomarker testing, inadequate infrastructures compounded by workforce shortages, and a lack of EU guidance and value frameworks on biomarker testing. A policy statement from the European Alliance for Personalised Medicine (EAPM) points out a lack of synergies in the translational research process, which significantly lengthens the timeline for patient access. Public health assessment is typically conducted only after clinical trials are concluded and a medical product or technology is introduced to the market. An earlier and continuous systematic dialogue between, for example, HTA agencies and industry during the technology transfer phase, could substantially speed up and streamline the process[30]. Recently, a Lancet Oncology Commission was announced which will unite EAPM and other stakeholders in a focussed effort to accelerate the progress of development, research and clinical implementation of omics in precision oncology[31]. Such findings and concerns further stress the need for organisational and legal readiness aside from technology readiness, and validates the objectives identified for the NoE on omics.

Annex 3 provides an overview of recent scientific technology reviews of omics in cancer, for those interested in further reading on the topic.

Survey among the WP9 partners

We performed a survey among the WP9 partners to assess the level of technology readiness (TRL) of the different types of Omics (genomics, transcriptomics, methylomics, other epigenomics, proteomics,

microbiomics, lipidomics, metabolomics, multi-omics and single-cell omics) in the different fields of application (standard of care, clinical trials, basic research and public health). The results are summarized in *Table 2*. It is important to mention that this list, although exhaustive, does not cover the entirety of omics technologies as this is a rapidly evolving field.

Although all the different omics are used in basic and translational research, this survey confirmed that only genomics and to a lesser extend transcriptomics and methylomics are currently deployed and incorporated into the clinical practice as well as in clinical trials as tools providing accurate information for clinical decision-making during the molecular tumour boards.

Other epigenomics than methylomics are emerging in the clinical practice, followed by proteomics and radiomics with TRL corresponding to a development stage. They will need to be reconsidered in the upcoming months. Microbiomics is mostly developed in other contexts than cancer.

An emerging aspect will be the integration of different omics tools (Multi-omics) which will be challenging for the coming years, as well as omics in single cells and spatial omics. These very promising omics require additional computational capacities as well as the use of machine-learning and/or AI tools which still remain at the research level for the moment.

TECHNOLOGY READINESS & MATURITY LEVEL ASSESSMENT				
TECHNOLOGY	FUNDAMENTAL RESEARCH	EPIDEMIOLOGICAL STUDIES	CLINICAL TRIALS	STANDARD OF CARE
GENOMICS		Genotyping Polygenic risk scores	CGP Limited use of WGS; advanced drug repurposing trials mostly Ongoing: IMPRESS, SAPHIR, PROFILER	Wide use of small/focused panels Frequently reimbursed
TRANSCRIPTOMICS		RNA-seq	Targeted for detection of fusion genes	Targeted for detection of fusion genes Specific gene expression panels
EPIGENOMICS		Mostly DNA methylation	Mostly DNA methylation Mostly targeted (=TRL 8-9) Genome-wide; limited use (=TRL 6)	Mostly DNA methylation Mostly targeted (=TRL 8-9) Genome-wide; limited use (=TRL 6)
PROTEOMICS		Olink-type screening approaches; starting up now		
MICROBIOMICS		Mostly non-cancer application (microbiota)		
LIPIDOMICS				
METABOLOMICS				
MULTI-OMICS				
SINGLE-CELL OMICS				

Table 2: Technology readiness level assessment by fields of application of the different type of Omics. The colours correspond to the TRLs defined in Table 1. Orange = Research (TRL 1-3); Light blue = Development (TRL 4-6); Dark blue = Deployment (TRL 7-9); Dashed light/dark blue = Varying from TRL 6 to 8

After discussion, it has been decided that the large-scale measurement of non-biological phenomena is not included in this NoE on omics, however integration of radiomics (which is considered as high tech medical resources within WP10) aspects will be considered in collaboration with this WP.

6. Expert members' endorsement criteria

The expert members in the NoE on omics should work on an omics platform within CCIs/CCCs/CCNs at the national, regional or local level. For the NoE to be operational, each Member State will be represented by 1 (or even 2) experts. However, the European NoE should rely on national (or regional) networks (or organisations) which, unlike the European network (where participation is limited to 1 or 2 members per country), must be inclusive and consist of various experts from the MSs' main omics platforms.

WP9 and WP10 jointly discussed and developed criteria to characterize omics platforms, to which experts belong, driven by the following principles:

- **Prerequisite of quality and of inclusivity**
- Definition of **3 different categories** as displayed in *Figure 2*.

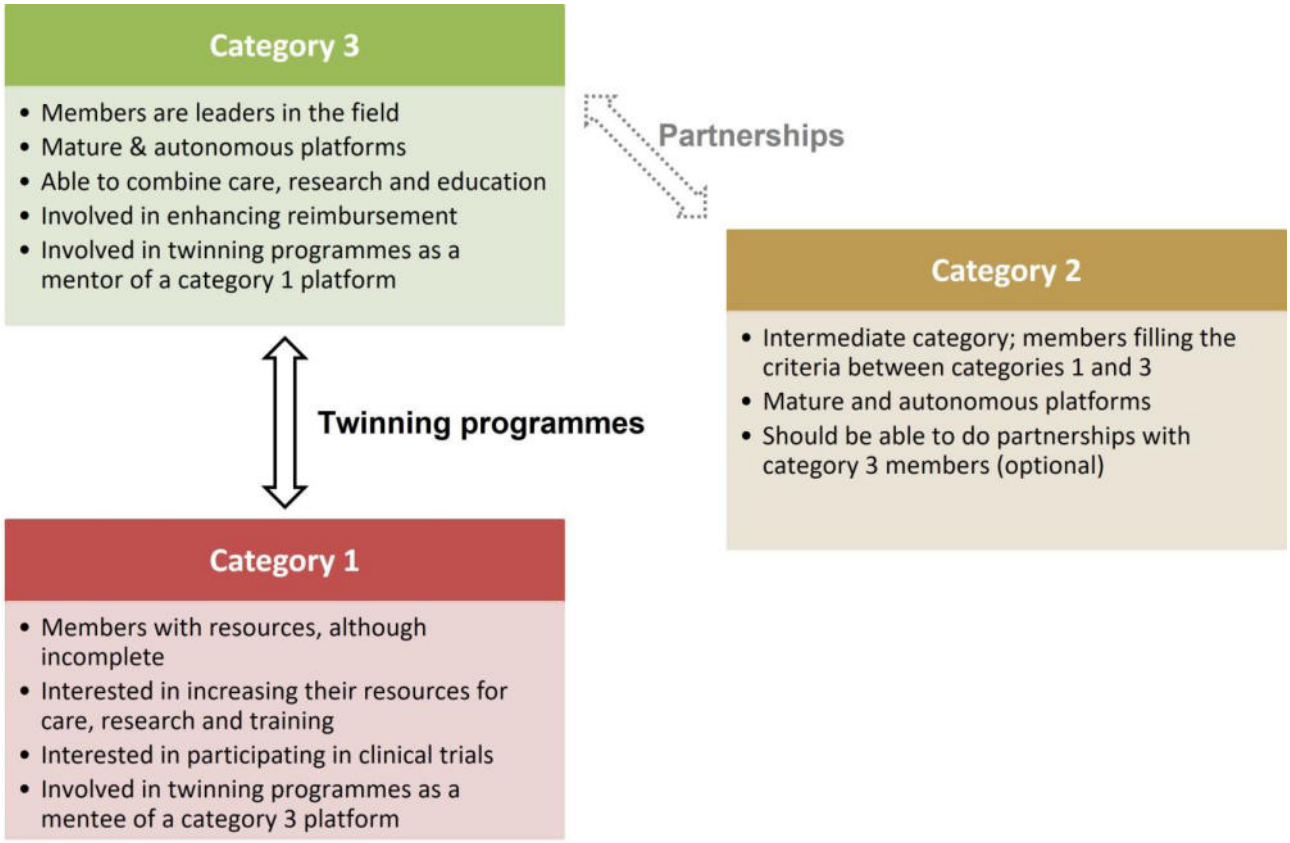

Figure 2: The 3 categories that were defined for members of the NoE on Omics. Members can be categorised based on the 13 identified endorsement criteria.

Thirteen different criteria were identified, which can be grouped into 3 main sets:

A: Type and volume of activity

1. Available resources
2. Field of application
3. Activity volume
4. Cancer types (very open criteria because of specialisation of some cancer centres, e.g. haematology, paediatric cancers…)

B: Infrastructure, resources, capability

5. Available infrastructure and core facilities
6. Human resources and expertise
7. Quality management (even though quality is a prerequisite, there are different levels)
8. Track record

C: Workflow, accessibility, collaboration

9. Integration into care
10. Accessibility
11. Connection with clinical cooperative groups, clinical trials, ERNs and other EU platforms
12. Clinical practice guidelines, training and education
13. Cost and NIHDI reimbursement (only category 3 has to facilitate and engage discussion for NIHDI reimbursement according to national regulations)

The endorsement criteria are detailed in Annex 4. They are useful for a capacity building exercise at the national/regional level. It is proposed that experts participating in the NoE represent category 3 omics platforms (or category 2 if not available). In countries having only category 1 platforms, a representative from one of these platforms will need to be involved in a twinning program with a category 3 platform from another country to join the NoE on Omics.

7. Use Cases consultations

Individual consultations of six use cases were organised to determine what they expect from the NoE on Omics, which interactions they foresee, how they could benefit from the provision of the NoE, what the priority activities of such NoE are, etc. This chapter provides a summary of the main topics as discussed in those consultations.

Omics preferably used

As expected, genomics and transcriptomics are the most used omics in the six use cases, followed by methylomics. The implementation of proteomics is currently only underway within the MASTER platform for clinical research purpose at DKFZ.

The AURORA clinical trial uses the results of the Comprehensive Genomic Profiling (CGP) performed in real time on DNA extracted from tumour samples, whole blood and baseline plasma samples. CGP on liquid biopsy and transcriptomics on tumour samples are performed by batch for research purpose. Biobanking storage is organised for methylomics for research purposes (not yet planned).

The activities of the both ERNs GENTURIS and EURACAN rely mostly on genomics, but also methylomics and transcriptomics and proteomics for the near future.

The MASTER platform developed at DKFZ mostly for rare and complex cancers relies on WGS, transcriptomics, and methylomics. The implementation of proteomics is currently underway.

The efforts against CUP mostly use genomics and transcriptomics (NoE on Complex and poor prognosis cancers; WP5).

Feedback on the organisation proposed for JANE 2 (see chapter 8)

All use cases validate the proposed organisation. Of course, the 4 **cross-cutting tasks** (*Figure **3***) will have to cross-talk between each other to avoid redundancies and overlaps. For example, the harmonisation of legal procedures will have to be done in collaboration with subtasks aiming to facilitate the implementation of Omics.

The use case consultations conclude that the subdivision of the different **domains** according to the clinical readiness makes sense. However, consultation of experts will have to be based not only on the omics types but also on the indications. And it is important to not only consider omics in the preclinical stage and curative care, but also to consult experts involved during the whole patient trajectory, including supportive care, palliative care and survivorship. For example, the domains should consider the use of omics for symptoms' control, the development of pharmacogenetics for anti-pain drugs. There is a need to improve the knowledge of omics at all steps of the patient journey. Clinical research has to be conducted so that omics technologies will be integrated into standard of care equally among Europe.

Endorsement criteria

The use cases express a need to identify existing omics platforms and their capacities, given the very large disparity across Europe. The endorsement criteria are considered useful to map omics platforms within the future European network of CCCs and assess the capacity building.

The 'molecular testing' is an integral part of the routine management of patients with cancers in the use cases. **Standard of care (SOC) omics** are ideally integrated within the pathology examination of the tumour sample. It should therefore be available in each cancer centre. The corresponding omics platforms should meet the category 1 endorsement criteria as explained in chapter 6. The criteria defined by JANE WP9 should be preferred, even if they cannot be imposed at the level of each MS.

It has been suggested by the use cases that **innovative omics** should be developed and supported by experts from an omics platform with category 3 endorsement criteria in a selection of comprehensive cancer centres that can conduct phase I clinical trials and that have a high level research infrastructure (e.g. CCCs belonging to the Cancer Core Europe, OECI, etc.). The objective of an approximate ratio of 1/5 members has been proposed. Then, these omics platforms should be able to provide services for other cancer centres in order to ensure equal access to all cancer patients. Collaborations at the European level are needed for innovative omics and for integrated omics.

Guidelines

For our use cases, existing scientific societies, mostly ESMO, but also EHA, SIOPE, ESHG…, provide the main useful guidelines. Also, EMQN and ERNs write (best practice) guidelines on what to test and how to report for specific diseases. There are no major gaps, and overlaps are relatively limited. The main issue is to have an overview of existing guidelines, to know where to find them. An index would be useful. It is also necessary to update them regularly, knowing that the omics fields are very dynamic and evolve rapidly (e.g., need for curation of the variant classification established by ESMO, ACMG/AMP or gene-specific guidelines being published by ClinGen Variant Curation Expert Panels).

Two areas were proposed where recommendations are missing: quality management systems, which is a hot topic for multi-omics, as well as randomised clinical trials.

Training, Twinning

There is a critical need for supporting the 'end users' to understand and correctly interpret the omics results within the reports. This literacy should be developed for medical oncologists, haematologists, paediatricians, organ specialists as well as, tumour biologists, pathologists and clinical biologists.

Two examples can inspire the way to disseminate expertise: ERN GENTURIS and DKFZ.

The training organised by ERN GENTURIS in partnership with ESHG and ESMO for cancer gene predisposition could serve as a model to organise trainings in other omics applications:

- **webinars available free of charge** on the GENTURIS website for healthcare providers as well as for patients:
- cancer genetics **courses** every 2 years (very broad target audience: medical oncologists, clinical geneticists, molecular geneticists, Bio-IT…).

Another example of training combining both theoretical and practical aspects is the **annual 2-day workshop** organized by MASTER platform at DKFZ and NCT as part of the NCT Molecular Precision Oncology Program:

- Across different institutions → different categories of interactions
    - To learn how to use Omics
    - To share experiences on different levels = Intermediate goal to disseminate knowledge and empower institutions
- Annual workshop (2 days)
    - Presentations by key opinion leaders, as well as established and junior investigators, covering scientific aspects, technology development, and implementation of multi-omics into clinical practice
    - Practical exercises
    - Participation in molecular tumour boards
    - Quality management
    - Data sharing

DKFZ also develops **partnerships** with various institutions in Germany and abroad, such as with high-level CCCs in Europe as partof Cancer Core Europe and in Canada, as well as less favoured countries, e.g., Jordan and Greece. The training programmes fostered by these bilateral partnerships are a success with mutual benefits, attracting juniors.

Ethical, legal and societal issues (ELSI)

All use cases highlight the need to facilitate the application of legal rules. Several examples illustrate the current difficulties:

- The CGP panel used for AURORA is for research purpose and cannot be officially used for standard of care: **how to implement the CGP panel used in this clinical trial into standard of care**?
- **GDPR issue** in cancer genetic predisposition: there is a need to facilitate the request for genetic data of relatives not seen for genetic counselling of a proband

- **IVDR issues**:
    - Most of the kits available for WES and WGS are for research purpose only, about 90% of the tests available in genetic centres are in-house tests: there is a need for training and support to comply with IVDR regulation
    - Belgian requirements by the Belgian federal agency for medicines and health products are more demanding regarding genetic tests than the European directive
- Need for **legal recognition** of molecular scientists, Bio-IT, technicians (MSc, PhD) working in molecular and genetic clinical labs (like in the USA or in rare European countries such as Denmark); molecular scientists also need an easier access to the EHR of patients to be able to elaborate reports
- Need to facilitate **data sharing** (cf. EHDS):
    - Complex legislation with too strong barriers: should have a compromise between patient protection and data re-use by researchers, need for simplification, especially important for rare cancers, need a common effort for clinical and biological data
    - Rare cancers raise the additional issue to facilitate cross boarder vs in boarder trials
    - Issue of different regulations between USA and Europe which limit the collaborations needed for rare cancers
    - And even different rules between institutions which not necessarily have the same application of GDPR and which complicate research and publications
    - Need for good registries: real world clinical studies are a useful complement to randomised clinical trials in the new area of precision cancer medicine.
    - Clinical trials should be open to all patients without age limits, but the authorization for younger patients (more difficult process) should not delay the inclusion of new adult patients.
    - Innovative models of clinical trials should be developed to facilitate the assessment of new drugs in small-size groups of patients having tumours with rare molecular events. Such trials have complex designs (e.g. assessment of combined drugs associated to molecular alterations, with AI tools).

Another highlight is the need to provide equity to patients throughout Europe. France's "Genomic Medicine Plan 2025" is setting an example by aiming to ensure equal access to novel technologies which improve diagnosis, prevention and treatment.

Health policy and reimbursements

The reimbursement of evidence-based omics tests, new drugs and even off label drugs (provided the presence of ample clinical evidence) should be improved, and the funding of corresponding clinical trials

should be facilitated in a proactive manner, including shared-risk models (e.g. DRUP, PRIME-ROSE studies). To illustrate; 2 out of the 3 drugs suggested by the MASTER molecular tumour board are not reimbursed.

Partnership with private sectors

All use cases consider it very important to find a way for private sector representatives to be involved in the network. They validate the principle of a matchmaker platform (e.g., call on public/private partnerships).

Two main areas were defined for the private sector:

- Technology and biotech companies (Illumina, PacBio, Nanopore, OncoDNA, etc.)
    - The NoE could test new kits/prototypes for free
    - The different use cases do not have enough experience in using demand-driven innovation tools (such as pre-commercial procurement or PCP), even if after explanations, they consider that it could be really useful to improve the development of such solutions
- Pharmaceutical companies (Pfizer, AstraZeneca, etc.)
    - Which are actively supporting the development of companion molecular testing (e.g., sponsor of masterclasses on variant classification by experts, EMQN, GenQA webinars).

Scope

There is a strong need to **extend the scope** of the NoE on Omics to other areas than cancers, in particular to rare diseases (ERN) and also in the near future to diseases with complex genetic determinants. This is in line with the evolution of genomics which is an integral part of medicine. The era of genomic medicine is only just beginning to take hold, yet we must already anticipate the era of omic medicine.

Collaborative stakeholders

- ESMO: Provides useful guidelines (very systematic, well organized) and training, but are limited by two factors: financing and human resources.
- Other Scientific societies: EHA (partnership with ESMO), SIOPE, ESHG
- ELIXIR
- ERNs
- EQA bodies: GenQA, EMQN, CAP, etc.
- EMA (companion diagnostic tests)
- Cancer Core Europe
- EORTC, EATRIS, ESFRI, ECRIN, Oncodistinct
- EACR
- BBMRI-ERIC

In summary, priority needs

- Legal aspects
    - Facilitate GDPR, IVDR applications
    - Facilitate data sharing (especially for rare cancers)
- Equity
    - Homogeneous access to omics technologies and to drugs in Europe (not the case for AURORA)
- Guidelines
    - Overview of existing initiatives (guidelines…)
    - Regular update of guidelines, training (very dynamic area)
    - Literacy for end users (oncologists, pathologists) (AURORA, WP5)
    - Recommendations for randomized clinical trials (WP5)
- Partnership public-private sector
    - Matchmaker platform: the mode of collaboration needs to be defined
- Need to design innovative pilot clinical trials, to test the utility and efficacy of the NoE on Omics (WP5, and collaboration with other NoEs, cf. WP10…)
- Facilitate and promote the development and research of omics in other areas of cancer treatment, such as symptomatic treatment

8. Organisation & Governance

Organisation

The NoE on Omics will operate as a service provider offering comprehensive guidance and recommendations to address challenges related to the implementation of omics in clinical practice by catalysing a community, by building, training, and transferring learning and research findings between mature and emerging technologies. The organisational structure of this initiative is centred around a central **NoE secretariat** that will provide administrative coordination of the network and serve as the hub for core facilities that scientifically support crosscutting tasks across the four priority domains defined based on clinical readiness (*Figure 3*). The data servers hosting this hub will preferentially be cloud-based (within the EU) rather than a physical infrastructure, to facilitate easy transfer of the governance should the secretariat move to a different host institute.

The EU NoE on Omics will be composed of EU expert partners in the different domains and tasks and will rely on national/regional networks. The NoE secretariat will organise **pluriannual consultations/workshops with experts** from the 4 priority domains to identify unmet needs and to prioritize the activities that must be

addressed by the cross-cutting tasks. The partners from each member state will be responsible for cascading these resources nationally.

The **four priority domains** are as follows:

1. **Established omics in the standard of care** – the domain emphasises the need for a homogeneous and widespread implementation of omics technologies with high quality and equality across EU MS;
2. **Omics in clinical research** – this domain focuses on demonstrating the added value of omics technologies for specific indications via use cases identified in WP5 and via other NoEs or ERNs;
3. **Omics in translational research** – this domain seeks to facilitate the validation pathway and provides access to high-potential omics technologies that are far beyond the clinical application;
4. **Integrated Omics** – innovative IT tools (machine learning/Artificial Intelligence) to foster the use of multi-omics in clinical research and ultimately clinical practice.

These four priority domains are supported by **four cross-cutting tasks** in close interaction with WP5-11:

1. **Omics technical and clinical support** from research setting to standard of care implementation
2. **Legal and ethical aspects**
3. **Training Centre**
4. **Stimulating synergies, collaborations** and looking for funding opportunities to ensure sustainability

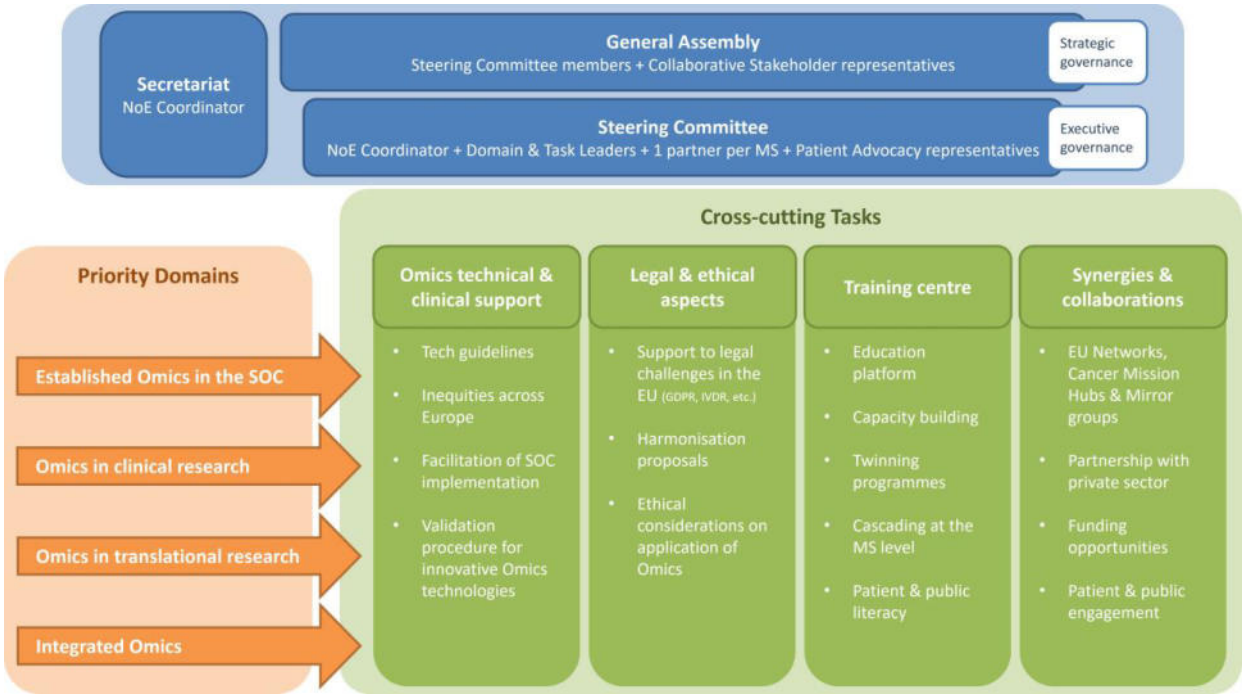

Figure 3: Proposed organisation and governance of the future NoE on Omics. MS = Member State; SOC = Standard Of Care

Governance

The first year of JANE 2 will aim to validate and finalize the governance of the NoE, which should be launched at the beginning of the 2nd year with the first pluriannual expert consultation/workshop. The proposed governance is adapted from the governance model of ERNs, and more precisely from ERN EURACAN[32] that also has a matrix organisation with domains and transversal task forces. The governance will include the following bodies (*Figure 3*):

1/ Leaders of domains and cross-cutting tasks

2/ NoE Secretariat

This activity will be ensured by the NoE coordination team.

3/ NoE steering committee

This is the executive body for daily management of the NoE. The steering committee will be composed of:

- the domain and crosscutting task JANE WP9 leaders;
- one representative per MS that is not already represented by a domain or task leader, from a category 3 platform (if not available category 2 or even category 1 if involved in a twinning program with a platform category 3);
- patient advocacy representatives;
- the NoE coordinator (JANE WP9 leader)

A restricted steering committee, consisting of the NoE coordinator and domain/task leaders, can be assembled for urgent operational meetings if needed.

4/ NoE General Assembly

In addition to the members of the steering committee, representatives of the collaborative stakeholders participate in the NoE general assembly which meets at least once a year to review the activities of the past year and define a strategic plan.

9. Synergies and integration in the EU Cancer landscape

Both WP9 and WP10 worked closely together to identify synergies between their future NoEs and the other European stakeholders and networks (*Table 3***Errore. L'origine riferimento non è stata trovata.**). The goal of this exercise is to elaborate the **future NoEs' position within the general cancer landscape**, in order to clarify their missions and to avoid duplication.

It is also crucial to consider the **synergies with other European projects** as part of the EU4Health, HORIZON Europe, and DIGITAL Europe programmes, such as:

- Those aiming to support the implementation of the CCCs, the CCI and the European network of CCCs (JA CraNE, EunetCCC, CSA CCI4EU, …)
- Those linked to the implementation of the 1 Million Genome Project (Beyond 1MG, GA GDI, …)
- Those fostering the development of the precision medicine (GA Can.Heal, PCP OncNGS, …)
- Those supporting innovative technologies and research (e.g. European Cancer Imaging Initiative (EUCAIM), Understanding Cancer platform (UNCAN.eu))
- Those supporting data governance and data sharing (e.g. health data authorities and agencies such as EHDS)

	NoE	Cancer ERNs	CCI/CCC/CCN	EU Scientific Societies (ESMO, EHA, SIOPE, ESO, ESH, …)	EU Official Bodies (EUnetHTA, EMA, …)	National/Regional Decision-making Bodies	Private Sector
Healthcare organisation model	Recommendations on the integration of innovative tools in the HCS Continuous discussion with national bodies	Services directly to healthcare professionals	Operational target: infrastructure, human resources (the NoE support their organisation and functioning)		Health technology assessment Access to innovative medicines	Funding & legal framework for sustainability	Support with existing tools or the development of customised products
Clinical Practice Guidelines (CPGs)	Integration of existing CPGs Identification (and mitigation) of gaps/outdatedness/urgent needs in collaboration with scientific societies	Idem NoE with emphasis on rare cancers	Implementation of CPGs	Elaboration and publication of CPGs			
Education of healthcare professionals	Support through definition of the needs and programmes	Idem NoE with emphasis on rare cancers	Organisation, human resources for teaching	Resources for teaching			Support with existing tools or the development of customised products
Research promotion	Recommendations on the valorisation and facilitation of innovation Capacity building: input for CCI	Idem NoE with emphasis on rare cancers	Operational target: benefit from promotion of their research activities	Define research programmes Facilitate (inter)national collaborations Communication & dissemination of research outputs		Funding & legal framework for sustainability	Support with existing tools or the development of customised products Sponsorhip for clinical research which provides evidence for their tools
Definition of monitoring/audit criteria	Criteria definition for audits performed by external national/regional bodies			Publication of CPGs, norms and standards			Support with existing tools or the development of customised products
Advocacy / policy / awareness	Mapping inequalities Recommendations regarding urgent needs, biggest gaps and inequalities across EU Continuous discussion with national bodies					Funding & legal framework for sustainability Support for communication & dissemination	
Patient and public engagement	Enhancing patient and public literacy and empowerment	Idem NoE with emphasis on rare cancers	Organisation, human resources for teaching	Resources for teaching		Develop literacy, mirror what is done by EU	Support with existing tools or the development of customised products
ELSI	Support, recommendations	Idem NoE with emphasis on rare cancers	Bioethics committees			Legal framework	

Table 3: Synergies in the EU Cancer Ecosystem

The participation of several partners of the JANE 2 WP9 in these projects will allow to be vigilant to ensure the complementarities and synergies of the NoE and to avoid the redundancies. Moreover, the NoE on omics should closely interact with the other NoEs (WP5-WP11). For these purposes, task 5 of JANE WP9 will have the specific mission of developing collaborations and synergies with existing initiatives, with the private sector, in addition to search funding and foster patient and public engagement (*Figure 4*).

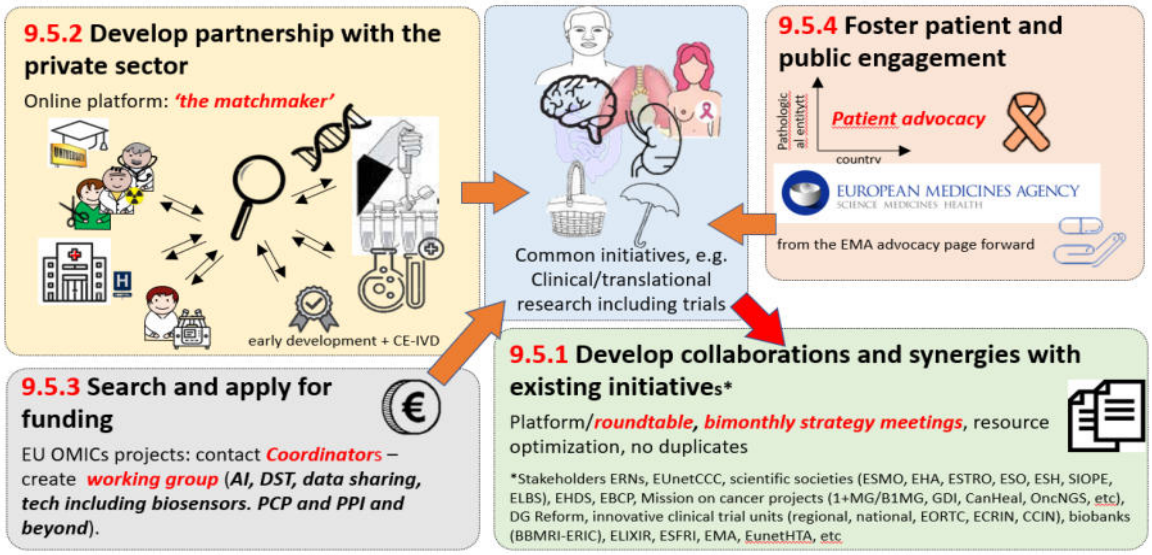

Figure 4: JANE 2 WP9 Task 9.5 on synergies, collaborations and funding opportunities

10. Collaborative stakeholders

The WP9 partners identified the following collaborative stakeholders :

- Omics technological platforms, national, regional or local (ex: NCT-Heidelberg, CurieCoreTech-I Curie, …)
- Innovative clinical trial units and infrastructures: EORTC, ECRIN, OncoDistinct
- Existing ERNs dedicated to cancer, GENTURIS, EURACAN, PAEDCAN, EUROBLOODNET
- European Scientific Societies which develop clinical practice guidelines, education and training of health care professionals and knowledge dissemination to patients and citizens: ESMO, EHA, ESO, ESH, SIOPE, ESHG, EAPM, EACR
- Life science infrastructures: ELIXIR (1+MG, GDI), ESFRI
- Biobanking to foster community engagement activities and leverage novel technology applications: BBMRI-ERIC
- National & regional decision-making bodies
- EU official bodies (EMA, EunetHTA, EQA bodies…)
- The European Institute of Innovation and Technology (EIT) Health
- Patient advocacy groups, with the complexity of there being a multitude of cancer patient organisations, especially for adults
    1. Cancer Patients Europe (CPE)
    2. Childhood Cancer International (CCI Europe)
    3. Data for Patients

4. European Patients Forum (EPF)

- DPO associations
    1. European Federation of Data Protection Officers (EFDPO)
    2. Professional Union of Data Protection Officers, Belgium (DPO-PRO)
- Private sector (priority for climate-neutral processes)
    1. Technology/biotech companies (possible collaboration with Biomedical Manufacturing Hub BiomedTech, Committee on Chemistry and Industry (COCI), ...)
    2. Pharmaceutical companies (possible collaboration with European Federation of Pharmaceutical Industries and Associations (EFPIA))
    3. Digital companies, including AI

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Annexes

1 - Partners involved in WP9		
2 - Meetings / Activities		
3 - Technology reviews on omics in cancer		
4 - Detailed endorsement criteria for expert members		

Annex 1 – Partners involved in WP9

Participants of JANE	
11 Countries	**24 Institutions**
Belgium	Sciensano HUB/IJ Bordet UGent
Germany	DKFZ
France	Unicancer INCa
Italy	INT-IRCCS CNAO IRST IOV ACC
Spain	IDIVAL HSJD Kronikgune ICO
Romania	IOCN
Greece	NHRF
Malta	MFH
Lithuania	NCI
Hungary	OOI
Norway	UIO
EU	OECI (ECPC)
Future task & domain leaders of JANE2 Participated in defining the NoE from February 2024.	
Belgium	Sciensano
France	Unicancer
Italy	ACC FPG
Poland	IBB
Portugal	I3S
Sweden	Karolinska Institute

Annex 2 – Meetings / Activities

13/12/22 (online)

- *Methodology*
- *Members of WP9*

11/01/23 (1 day F2F kick-off - Paris)

- *Scope definition with objectives*
- *Selection of 6 use cases*
- *Partners of the future NoE*
- *Synergies with other EU, international, national/regional, institutional initiatives*

24/03/23 (online)

- *Technology Readiness Assessment of the different omics (survey)*
- *Presentation of Elixir as a potential collaborative stakeholder*
- *Presentation of TTF3 AI/ML*

04/07/23 (online)

- *Methodology for endorsement criteria*
- *Agreement for working in close interaction with WP10 NoE on Hi-Tech Medical resources*
- *Presentation of BBMRI-ERIC as a potential collaborative stakeholder*
- *Mission and Vision*

15/09/23 (online between WP leaders of WP9 and WP10)

- *Methodology for endorsement criteria*

19/09/23 (1 day F2F joint meeting with WP10 - Paris)

- *Endorsement criteria and maturity levels*
- *Synergies of the NoEs Omics and High Tech Medical Resources in the Cancer Ecosystem*

15-16/11/23 (F2F mid-term meeting - Barcelona)

- *Presentation of the progress of the WP on Omics in tandem with WP10 on High Tech Medical Resources*

20/02/24 (online with JANE 1 partners and JANE 2 task and domain leaders)

- *Finalisation of the JANE 2 project (organisation)*
- *Presentation of JANE 1 achievements to JANE 2 Task/domain leaders*

- *Presentation of the JANE 2 project to JANE 1 partners*

08/04/24 (online with JANE 1 partners and JANE 2 task and domain leaders)

- *Consultation of the 6 use cases to know what they expect from the NoEs, which interactions, how they could benefit from having such an NoE available, what the priority activities are*
- *Request for a 7th use case: NoE on rare and complex cancers (CUP)*
- *Discussion on the deliverable Blueprint*

24/06/24 (online with JANE 1 partners and JANE 2 task and domain leaders)

- *Discussion of the output of the use case interviews*
- *Governance*
- *Stakeholders*
- *Blueprint*

Annex 3 – Literature review on omics technology applications in the cancer field

For the interested reader, we have compiled an extensive recommended reading list of recent scientific reviews and reports covering the state of the art on omics technologies in the cancer landscape, ranging from fundamental research applications to clinical care.

Omics in general

- Seminars in Cancer Biology. 2022. Volume 84
    - This edition of Seminars in Cancer Biology covers the topic of precision oncology and includes a range of interesting reviews on genomics, epigenomics and transcriptomics in precision medicine, as well as innovative AI applications.
- Orsini A, Diquigiovanni C, Bonora E. **Omics Technologies Improving Breast Cancer Research and Diagnostics.** Int J Mol Sci. 2023 Aug 11;24(16):12690. https://doi.org/10.3390/ijms241612690

Genomics

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Annex 4 – Detailed endorsement criteria for expert members

Endorsement criteria for experts and their corresponding Omics platform to participate in the NoE on Omics			
Criteria	**level 1**	**Level 2**	**Level 3**
A - Type and volume of activity			
1 - Available omics technologies: - **genomics**: small panel (Number of genes/targets), CGP (size), WES, WGS, ... - **transcriptomics**: RNA Seq, GEP, ... - **epigenomics/methylomics**: genome wide methylation analysis, ...	**Genomics: small gene panels (10-300 genes)** ***if germline testing (GL): MS-MLPA**	**CGP (>300 genes)** **MSI, HRD** **Targeted RNA-Seq panel**	**3 omics** **- Genomics: WES/WGS** ***GL: short/Long-read WGS** **- RNASeq, GEP** **- array/sequenced-based methylation analysis**
2 - Fields of application: - standard of care - clinical / translation research - fundamental research - public health...	**Standard of care**	**Level 1 + clinical / translational research**	**Level 2 + fundamental research**
3 - Activity volume: - Annual number of performed 'omics' tests (standard of care, clinical trials), covering the entire process from sample receipt to molecularly guided clinical decision -making prospective activity, minimal gene panel size >=10	**< 1000**	**1000-5000**	**> 5000**
4 - Cancer types: - common cancers - rare cancers - Paediatric cancers	Optional** (could be available through collaborations)	Optional** (could be available through collaborations)	**All cancer types of common, rare and paediatric cancers**
B - Infrastructure, resources, capability			
5 - Available infrastructure and core facilities: - Minimal equipment, resources - Autonomous platform for 1 or 2 or the 3 main omics, including secure data registration, biobanking - Continuous technological development	**Stand-alone platform** **Biobanking (sample conservation according to national rules)**	**stand-alone platform for al least 2 omics** **Biobanking (certified biological resource center according to national rules)** **Continuous technology development**	**Autonomous platform for the 3 main omics (cf 1-)** **Biobanking (certified biological resource center according to national rules, with participation in BBMRI-ERIC)** **Proactive technological development**
6 - Human resources and expertise: - On-site/network with scientists, bio-IT, pathologist, oncologist, hematologist, - On-site/network with geneticist, hemato-onco pediatrician - Continous professional development	**Sufficient multidisciplinarity required for standard of care (on site and/or within cross-institutional network**	**Level 1 + R&D/ translational researchers** **Continuous professional development**	**Medical expertise for all cancer types** **Fundamental researchers** **proactive professional development (share expertise)**
7 - Quality management: - In the process - Accredited for SOC tests (ISO15189 or equivalent)	**Accreditation completed for SOC tests or for the lab according to the national regulations (prerequisite)**	**Level 1 + Participation in external EQA**	**Level2 + interoperability with other EU platforms**
8 - Track record: - Number of peer-reviewed publications related to cancer multi-omics per year	Appreciated but not mandatory	**1 to 3**	**>3**
C - Workflow, accessibility, collaboration			
9 - Integration into care (MTB, DST, ...): - In the process of integration into MTB - Integrated into MTB - availability of DST	**Integration into care locally, with at least participation in an established local MTB (prerequisite)**	**Integrated into care with participation in a regional / national MTB**	**Participation in an international MTB**
10 - Accessibility - Provide part/full/assisted access to services (from the patient point of view)	**Provide full assisted access to genomic services, including clinical interpretation (prerequisite) at in house level**	**Provide full assisted access to omics services at regional / national level**	**Provide full assisted access to services for all 3 key omics at the international level**
11 - Connection with clinical cooperative groups, CT, ERNs, other EU Omics platforms - in the process of connection - connected - participation as a project leader	**Participation in a clinical/research cooperative omics-driven group at the national level during the last 5 years**	**Participation in a clinical/research cooperative omics-driven group at the international level during the last 5 years** **In the process of connection or minimally connected with other EU omics platforms**	**Participation in a clinical/research cooperative omics-driven group at the international level, including relevant ERN, during the last 5 years** **or Participation in a clinical/research cooperative omics-driven group at the national level as a leader during the last 5 years** **or Role as project leader in several projects with other EU Omics platforms over the last 10 years**
12 - Clinical practice guidelines, Training/Education: - Involvment in setting up international GCP, in (inter)national teaching program (for scientists, technicians, bio-IT...) - Involvment / Organisation of seminars, practical courses - Twinning program	**Participation in local training program(s)** **Need to follow GCP but don't need to be a leader** **Involvement in twinning program with a level 2 or 3 platform**	**Participation in or organization of regional/national training programs** **Need to follow GCP but don't need to be a leader**	**Involvement in setting up international CPG, teaching program** **Involvement in at least 1 twinning program with a level 1 platform as a leader**
13 - Cost, NIHDI reimbursement: - Involvement of the institution in the discussion with the healthcare decision policy maker for reimbursement of SOC Omics tests	Optional	Optional	**Facilitate and engage the discussion for NIHDI reimbursement according to national regulations**
GL: Germline CGP: Comprehensive Gene Panel GEP : Gene Expression Profiling SOC: Standard of Care GCP: Good Clinical Practices NIHD: National Insurance for Health and Disability MTB: Molecular Tumor Board DST: Decision Suport Tool			
*: in case of germline cancer predisposition			
**: Level 1 or 2: the platform may be dedicated to specific common cancers, or only for paediatric cancers			