Building genomics

genomDE : National and European initiatives

30th November 2020
DIGITAL EVENT

Supported by the European Union's Structural Reform Support Programme (SRSP) and implemented in cooperation with the European Commission's Directorate-General for Structural Reform Support (DG REFORM)

European Commission

Federal Ministry of Health

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The 1+Million Genome Initiative

Building genomics
genomDE : National and European initiatives
30TH NOVEMBER 2020

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Content

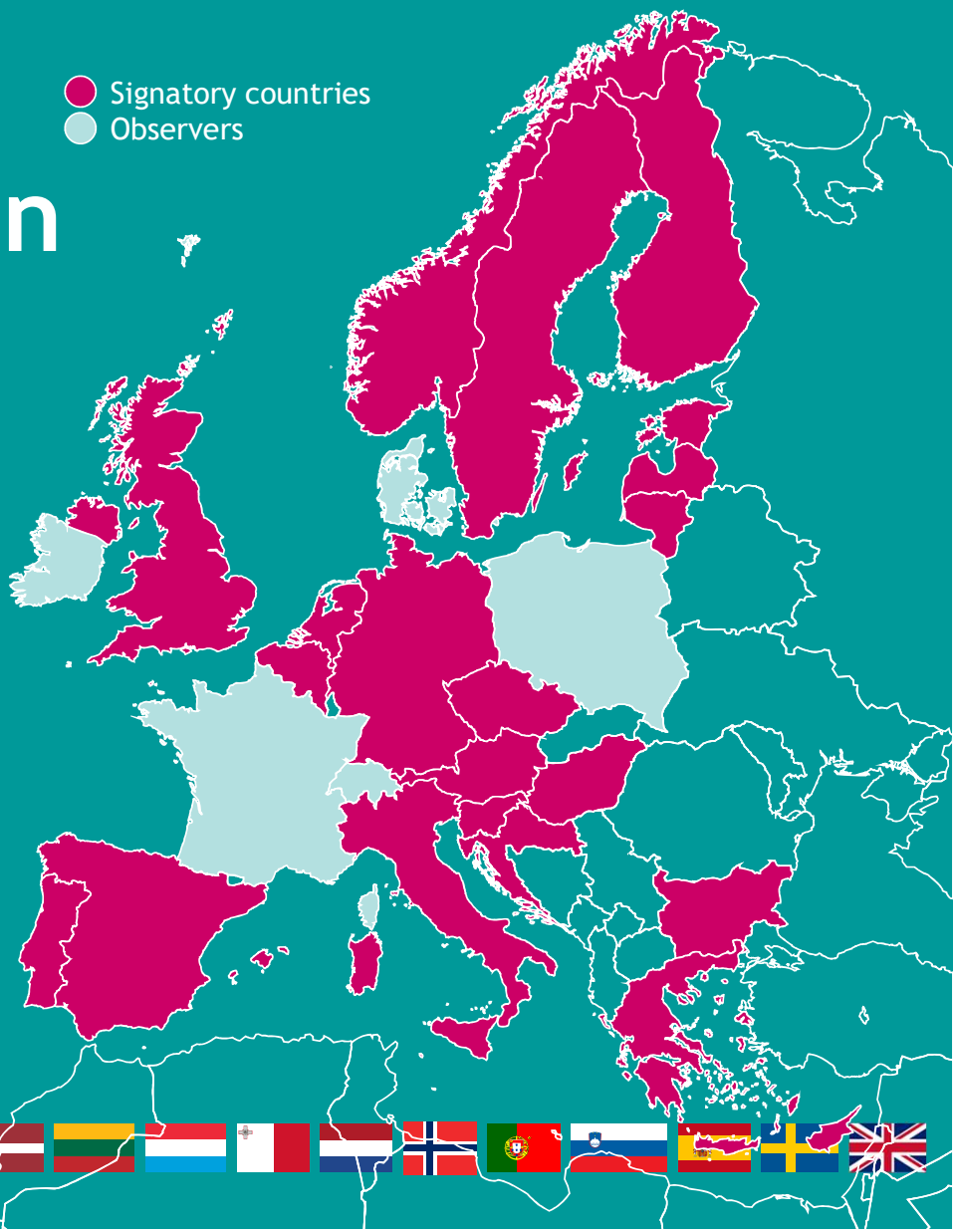
1. Overview of the 1+Million Genome (1+MG) Initiative
2. Organisational Structure
3. Beyond One Million Genomes – the B1MG project
4. 1+MG and B1MG – ongoing activities

01

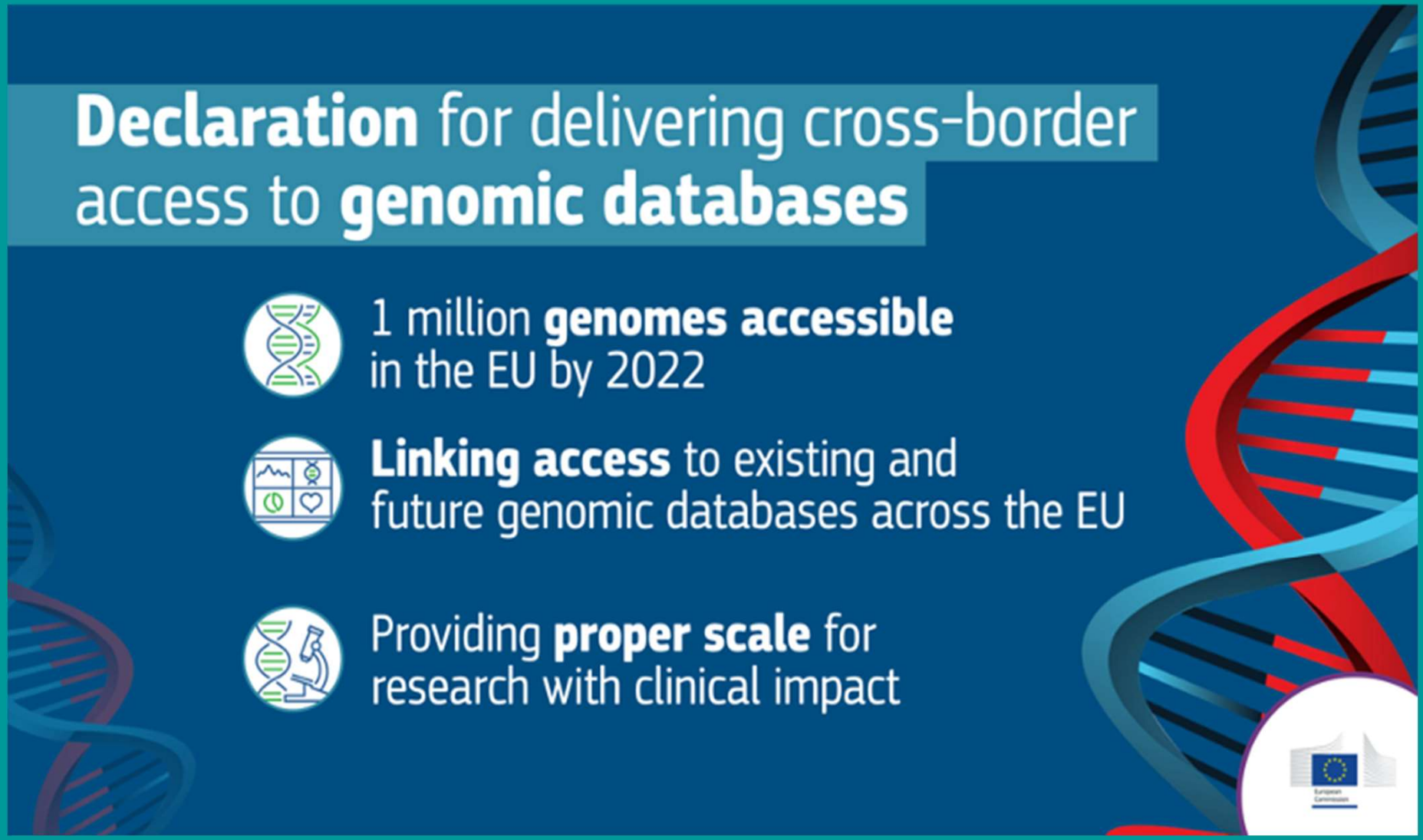
Overview of the 1+M Genome Initiative

1+Million Genomes Declaration of cooperation

23 countries and 5 observers



European Commission


Declaration for delivering cross-border access to genomic databases
1 million genomes accessible in the EU by 2022
Linking access to existing and future genomic databases across the EU
Providing proper scale for research with clinical impact

1+MG Working Groups

1. Organisation and governance	Coordination
2. ELSI aspects 3. Clinical data 4. Quality 5. Infrastructure 6. Health economics 7. Industry involvement	Technical Working Groups
8. Rare diseases 9. Cancer 10. Common Complex diseases 11. Infectious diseases (COVID-19)	Use cases Working Groups

1+MG Roadmap

Timeline & Objectives

Adopted in February 2020

2020

ENGAGE
Governance, cooperation and collaboration

Engage local, regional, national and European stakeholders to define the requirements for cross-border access to genomics and linked clinical data

1+ Million accessible genomes

1+MG Roadmap

Timeline & Objectives

Adopted in February 2020

2020

ENGAGE
Governance, cooperation and collaboration

2021

TRANSLATE
Infrastructure, guidelines and pilots

Translate requirements for data quality, standards, technical infrastructure, and ethical, legal and social issues (ELSI) into technical specifications and implementation guidelines that capture European best practice

1+ Million accessible genomes

1+MG Roadmap

Adopted in February 2020

Timeline & Objectives

2020

ENGAGE
Governance, cooperation and collaboration

2021

TRANSLATE
Infrastructure, guidelines and pilots

2022

DRIVE
Sharing, scaling and sustaining

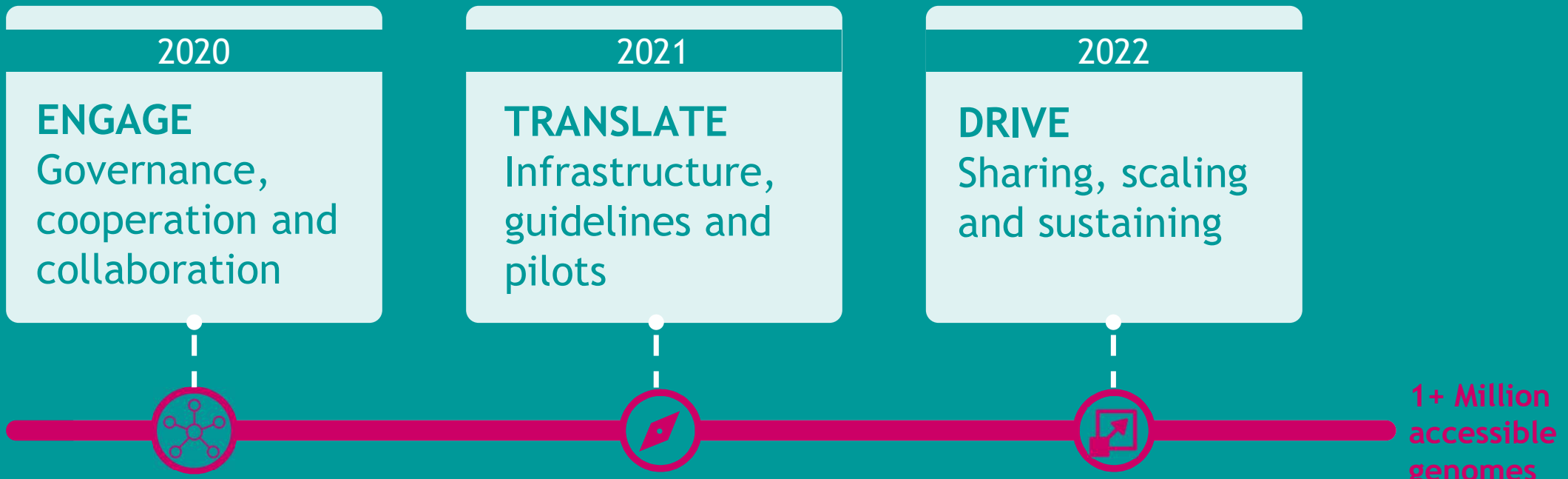
Drive adoption and support long-term operations via a maturity model and a methodology for economic evaluation

1+ Million accessible genomes

1+MG Roadmap

Adopted in February 2020

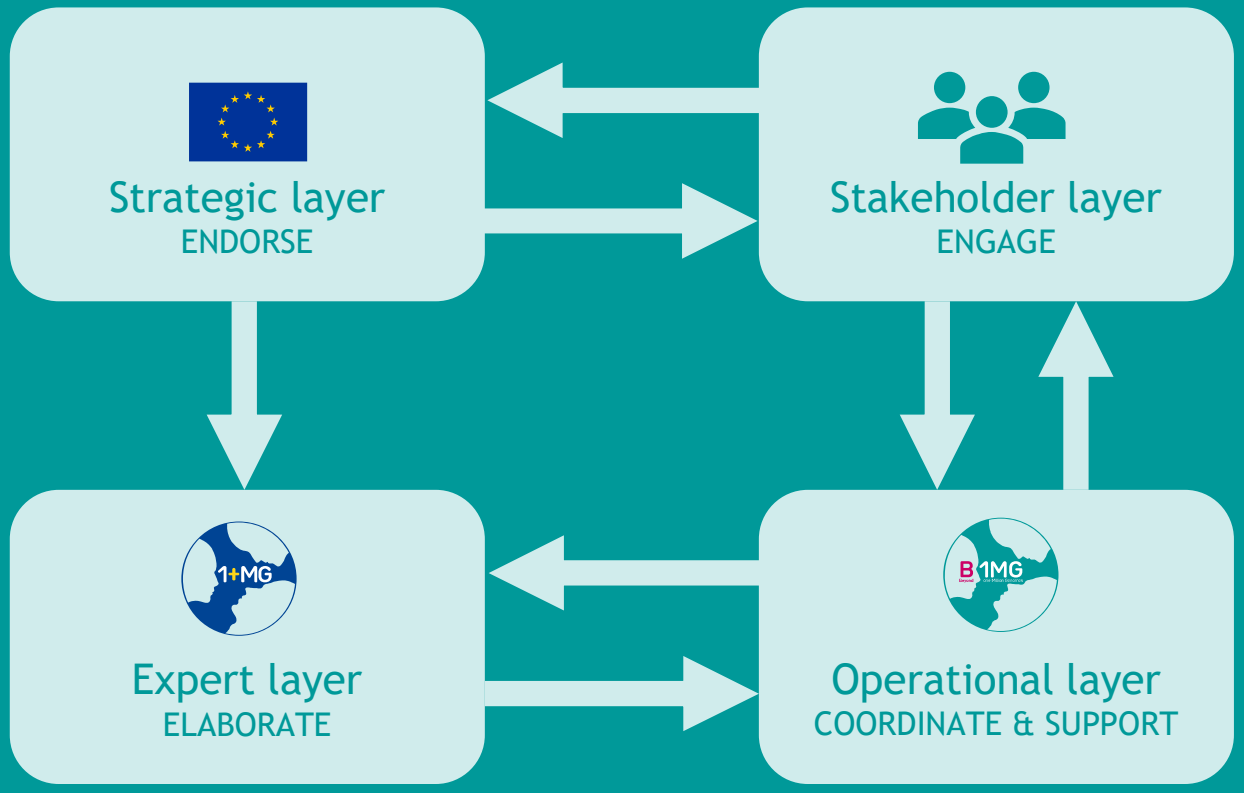
Timeline & Objectives



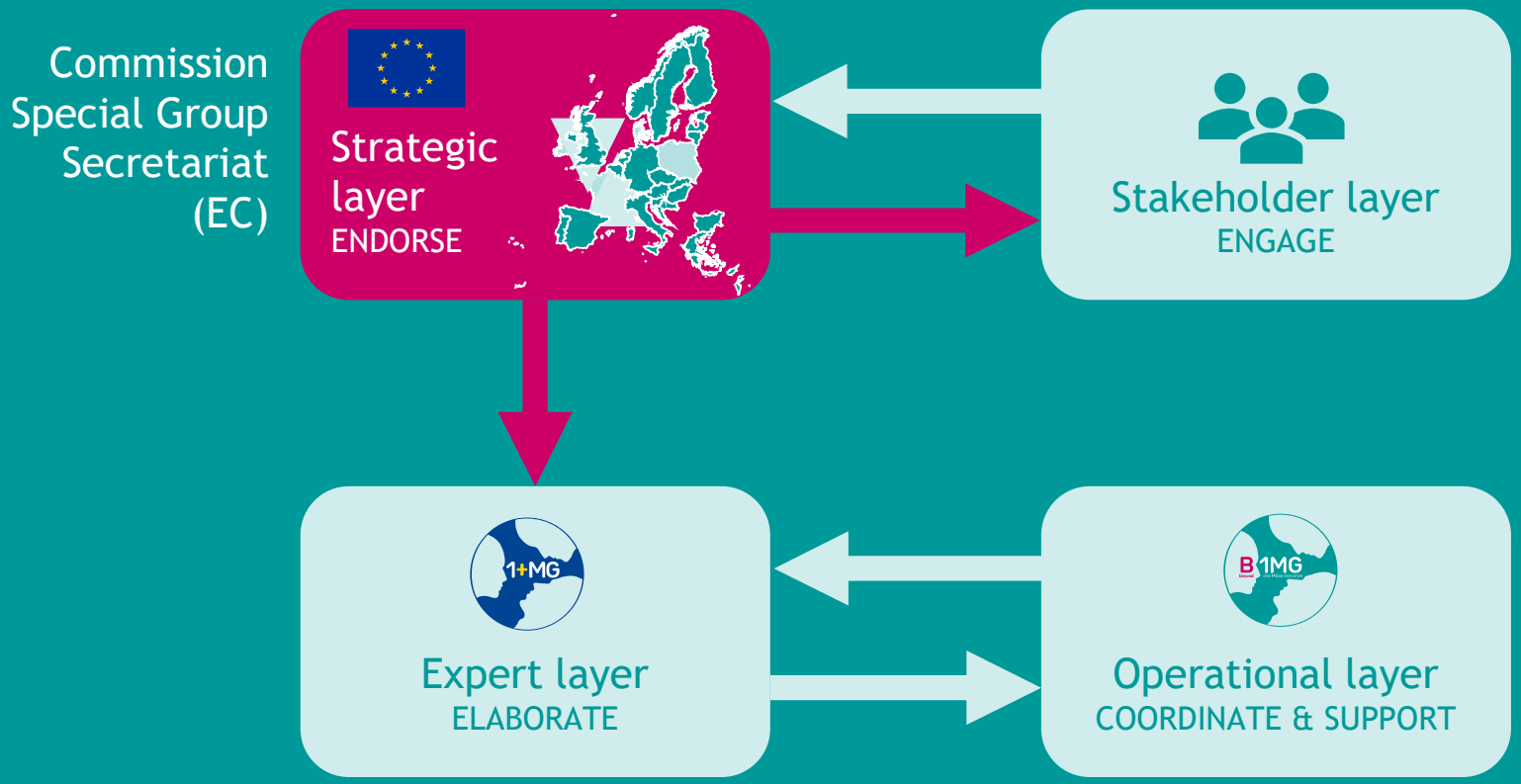
02

Organisational Structure

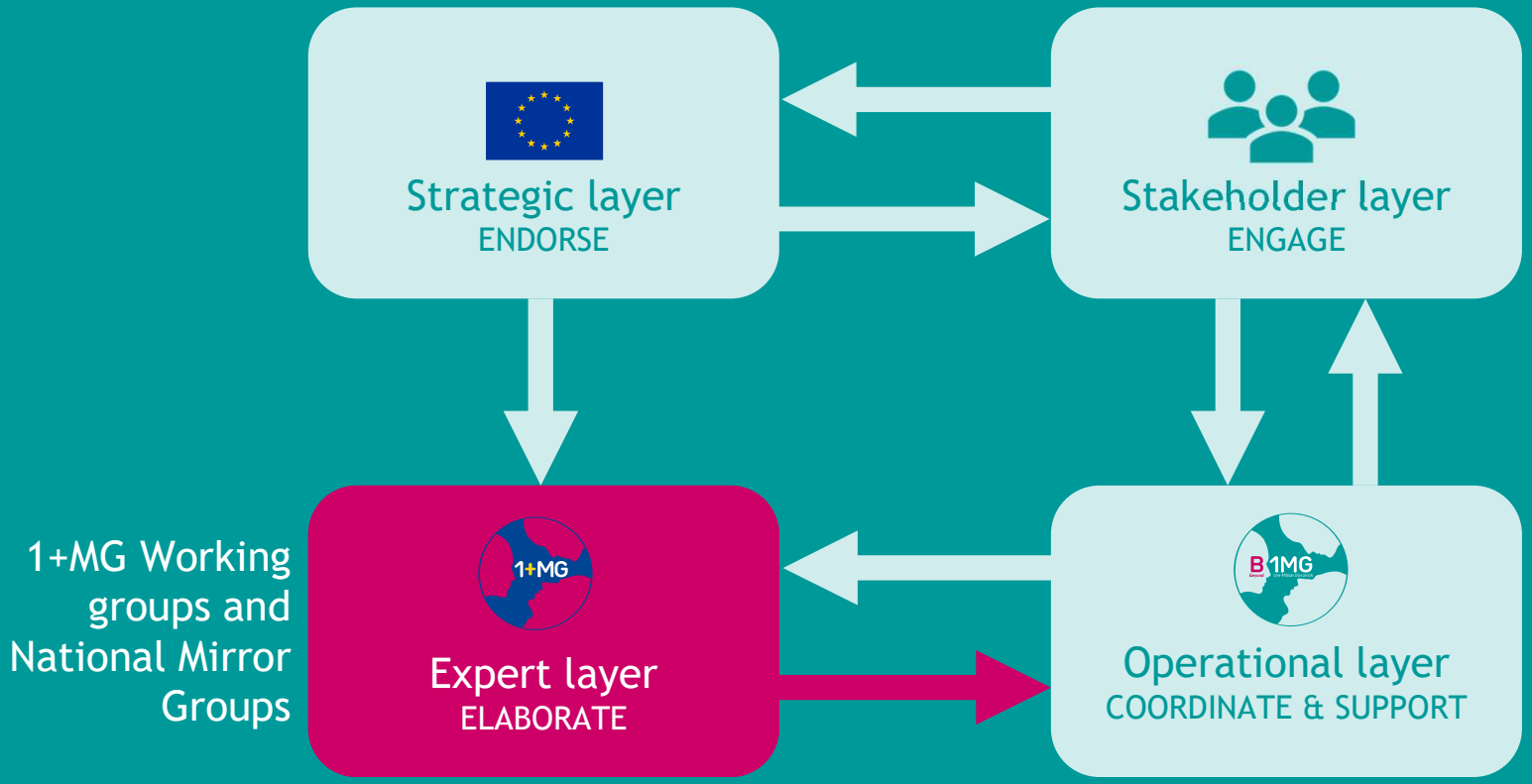
Organisational structure



Organisational structure



Organisational structure



Organisational structure

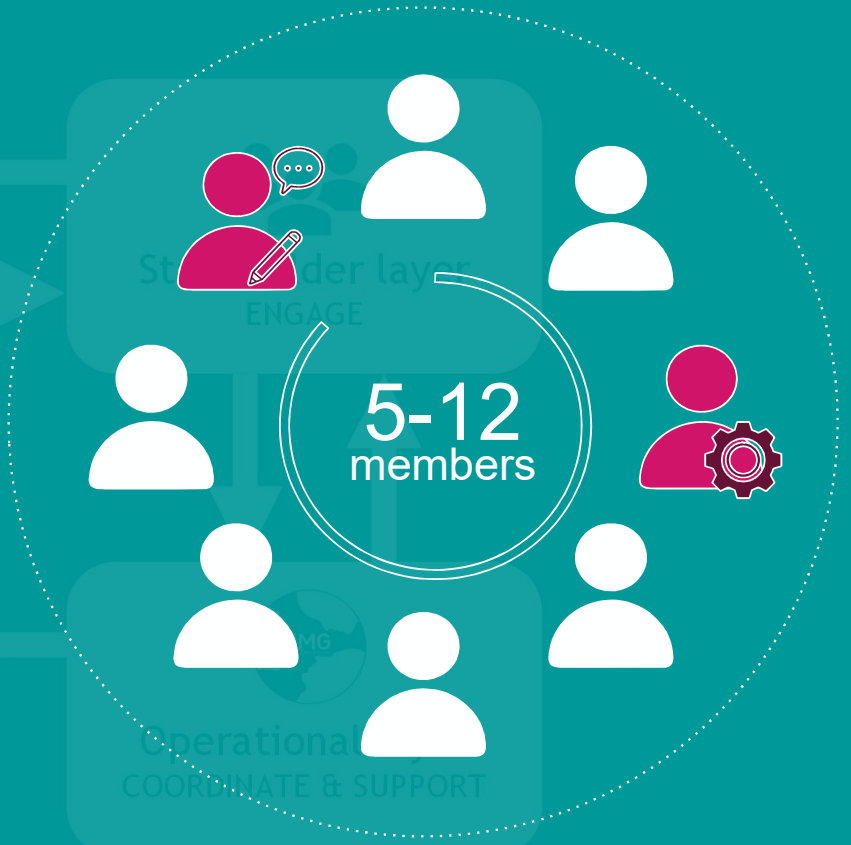
National Mirror Groups — NMG

Establishing a European learning framework

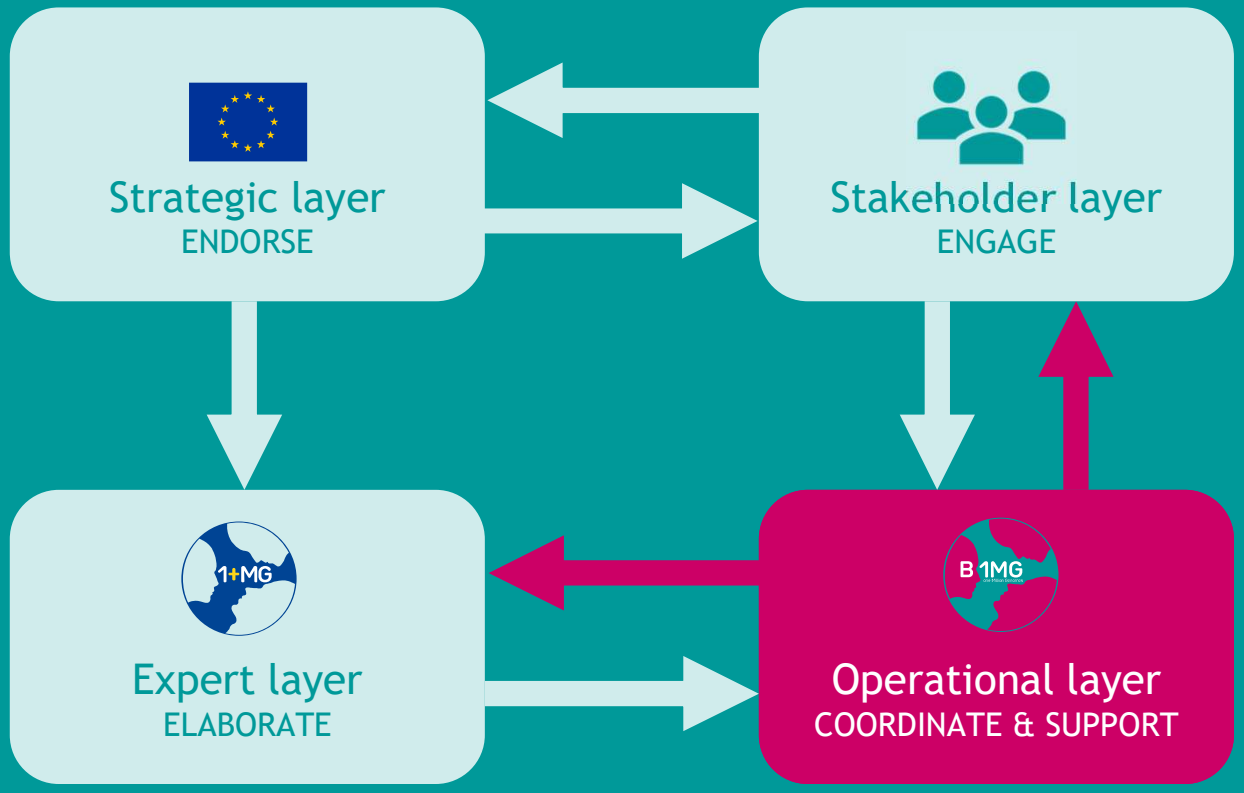
- 1 Scientific Coordinator
- 1 National Contact Point (NCP)
- 5-12 members

1+MG Working groups and National Mirror Groups

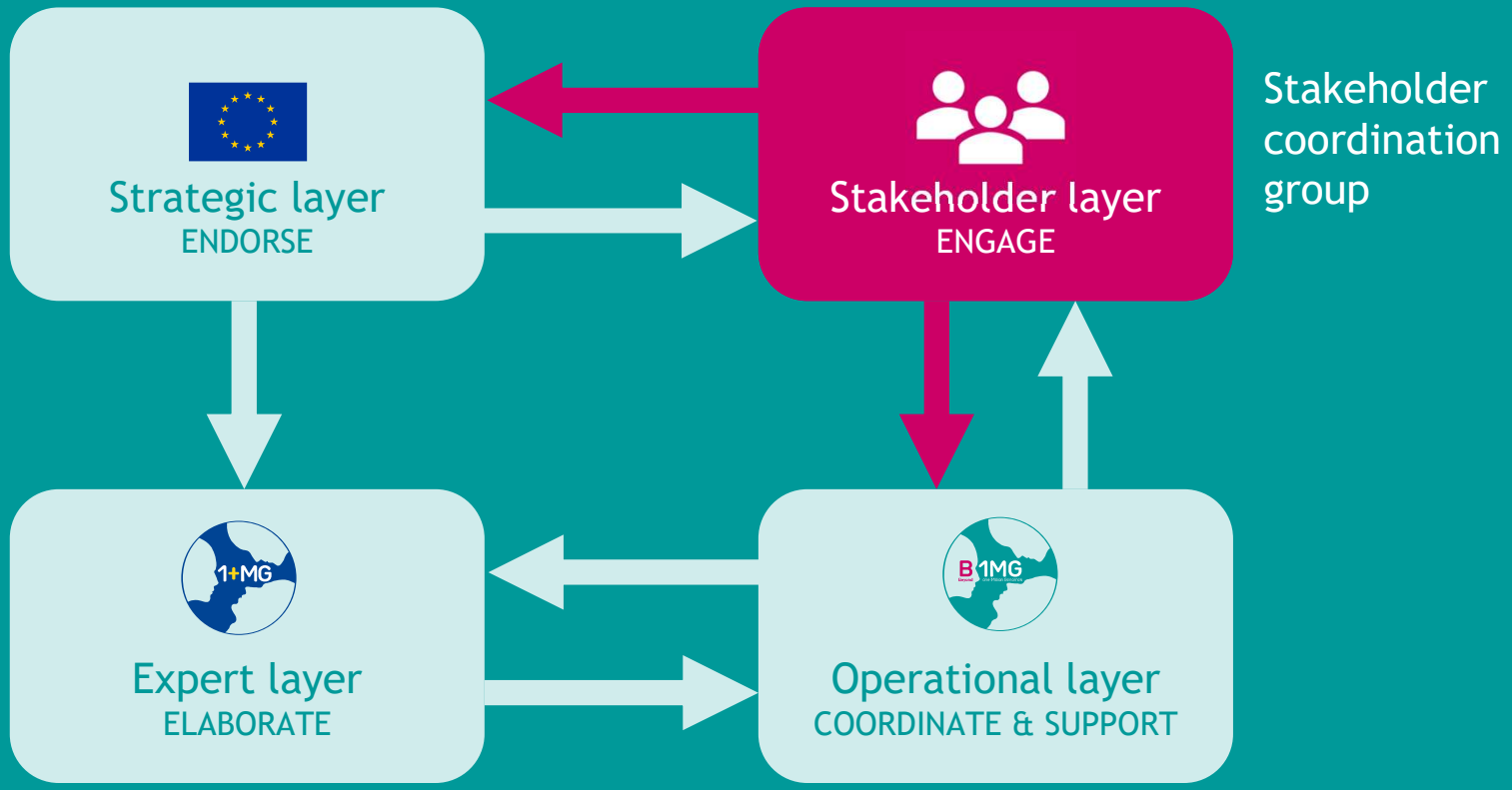
Expert layer
ELABORATE



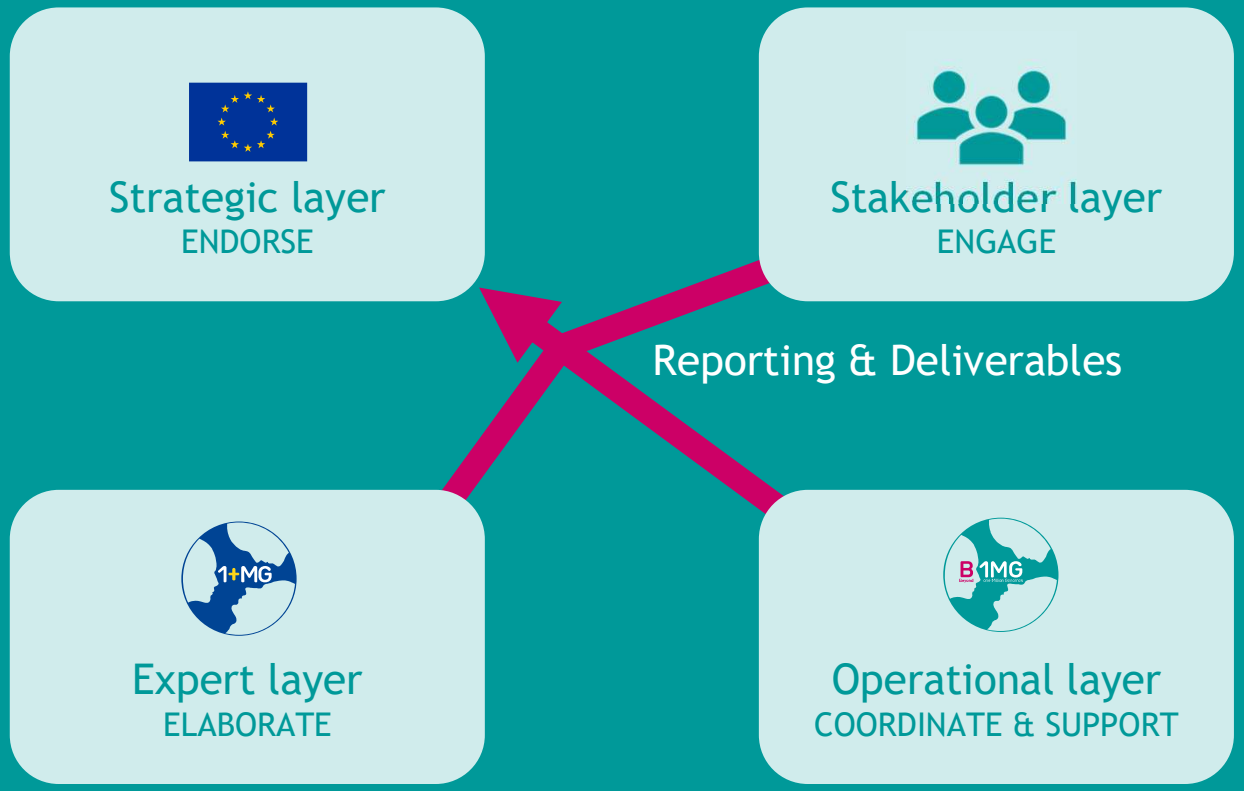
Organisational structure



Organisational structure

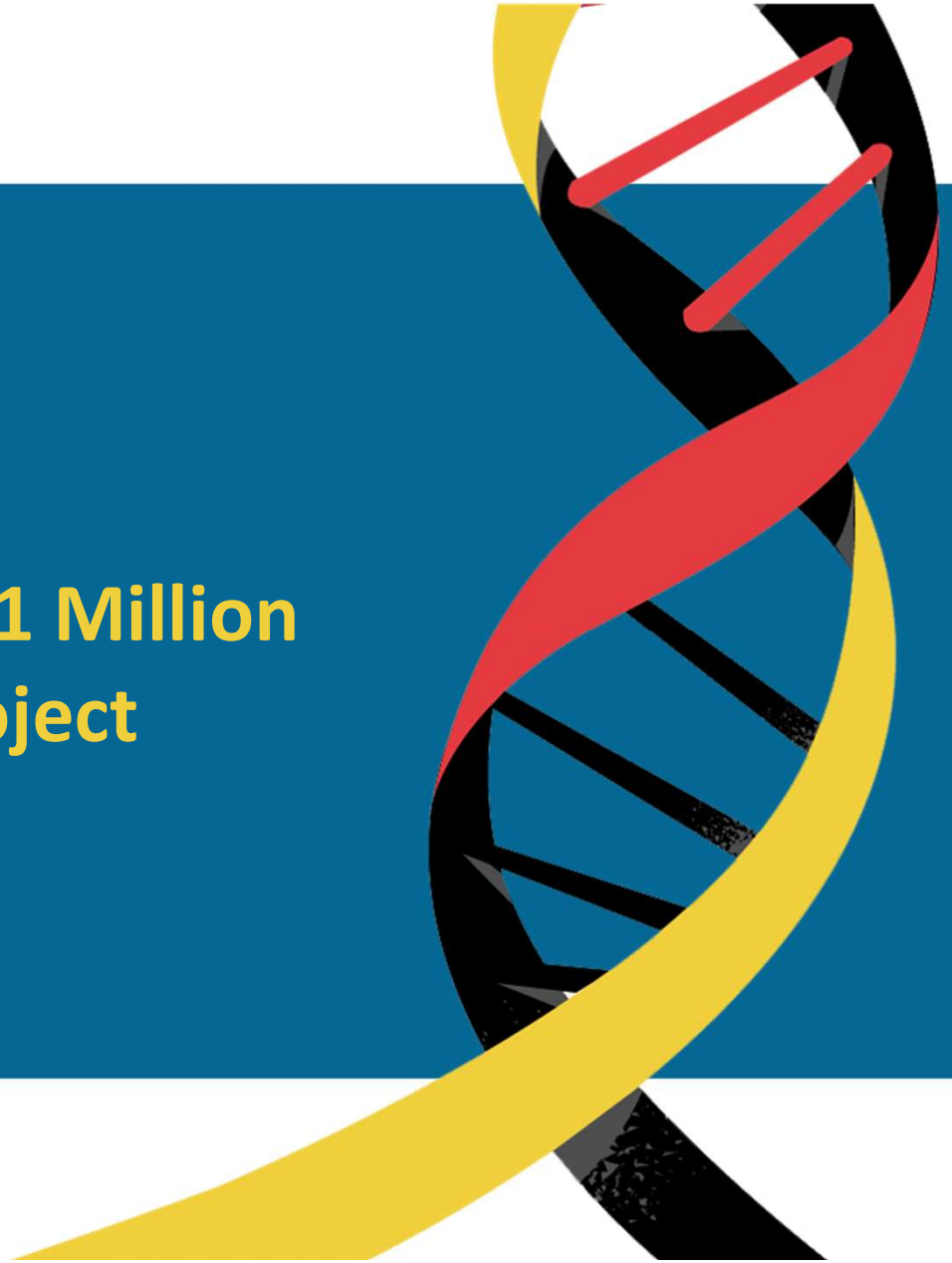


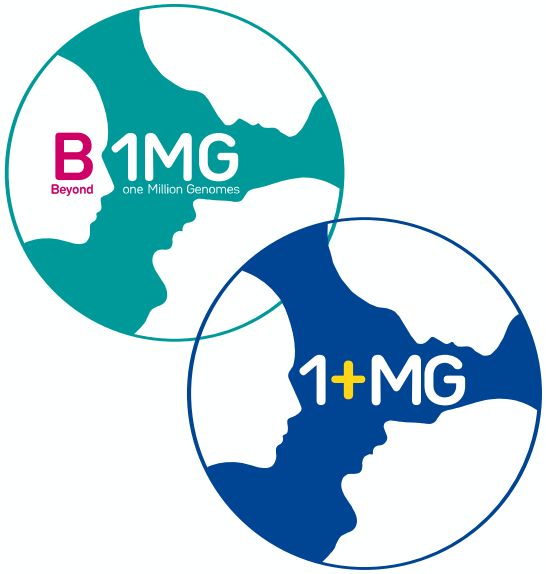
Organisational structure



03

The Beyond 1 Million Genomes Project B1MG





+ Beyond One Million Genomes (B1MG) aims to create legal guidance, best practices and recommendations to create infrastructure to enable the commitment of 22 European Member States and Norway to give cross-border access to one million sequenced genomes by 2022 **(1+ Million Genomes Initiative)**

The B1MG project

Started 1 June 2020

Coordination and support action of the 1+MG

Partners

Budget

Years

EU countries

The B1MG project

Coordination and support action of the 1+MG

Started 1 June 2020

29

Partners

B1MG objectives

Aligned to the 1+MG roadmap

2020

Engaging local, regional, national and European stakeholders

… to define requirements for accessing genomics and personalised medicine data.

2021

Translating requirements for data quality, standards, technical infrastructure, and ELSI

… into technical specifications and implementation guidelines.

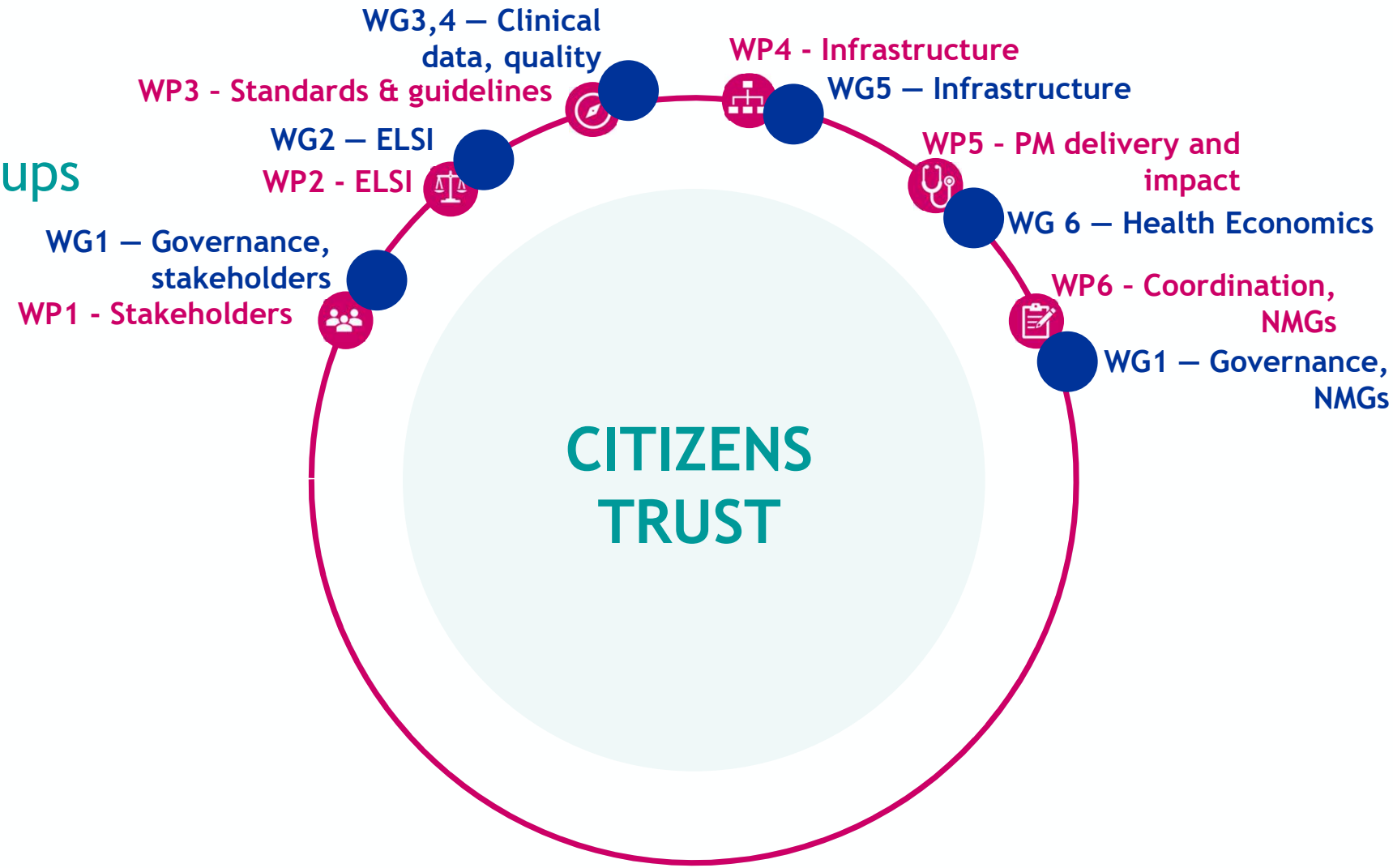
2022

Driving adoption and supporting long-term operations

… via the B1MG maturity level model and a methodology for economic evaluation.

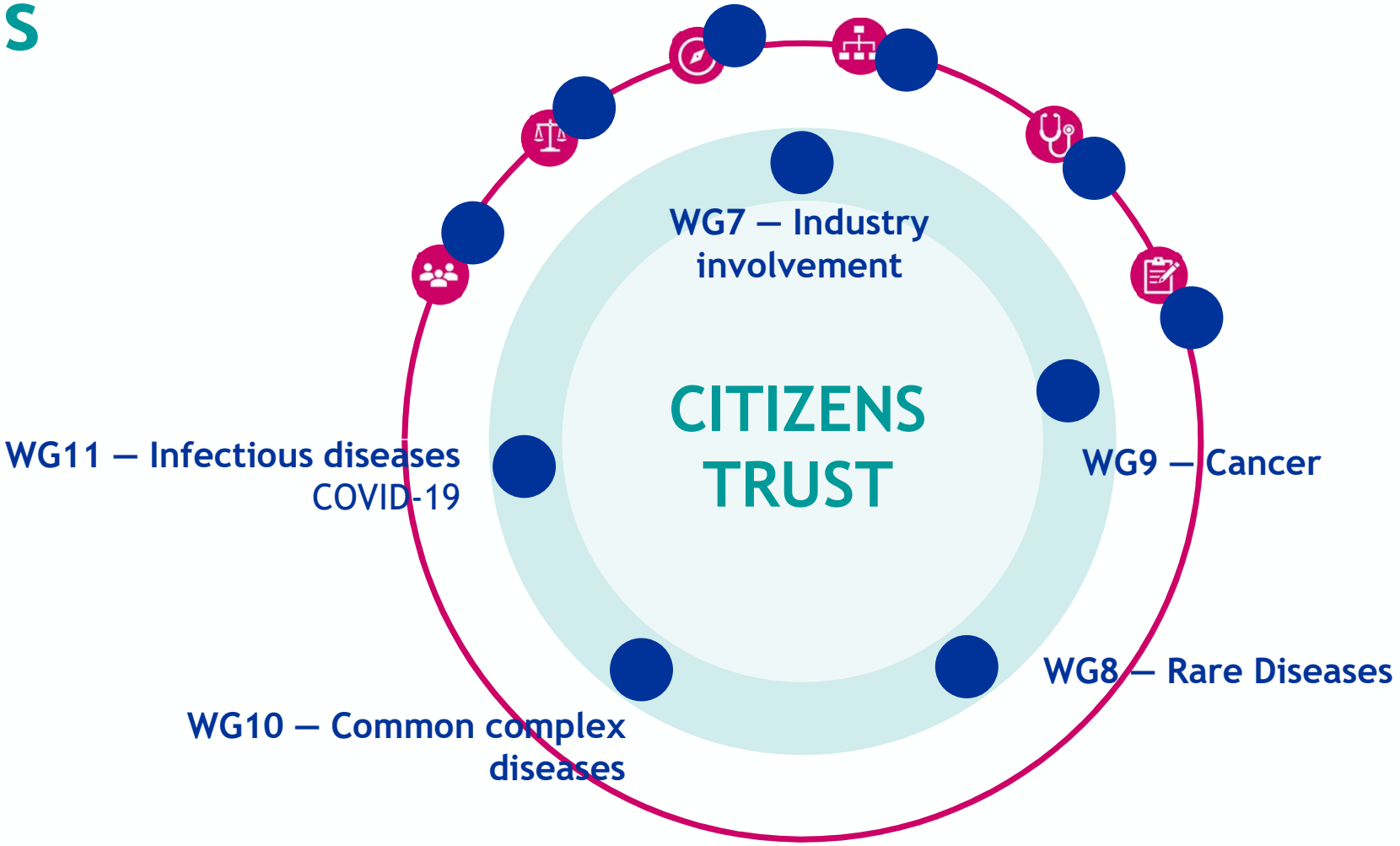
B1MG WPs / 1+MG WGs alignment

Technical Groups



B1MG WPs / 1+MG WGs

Use cases

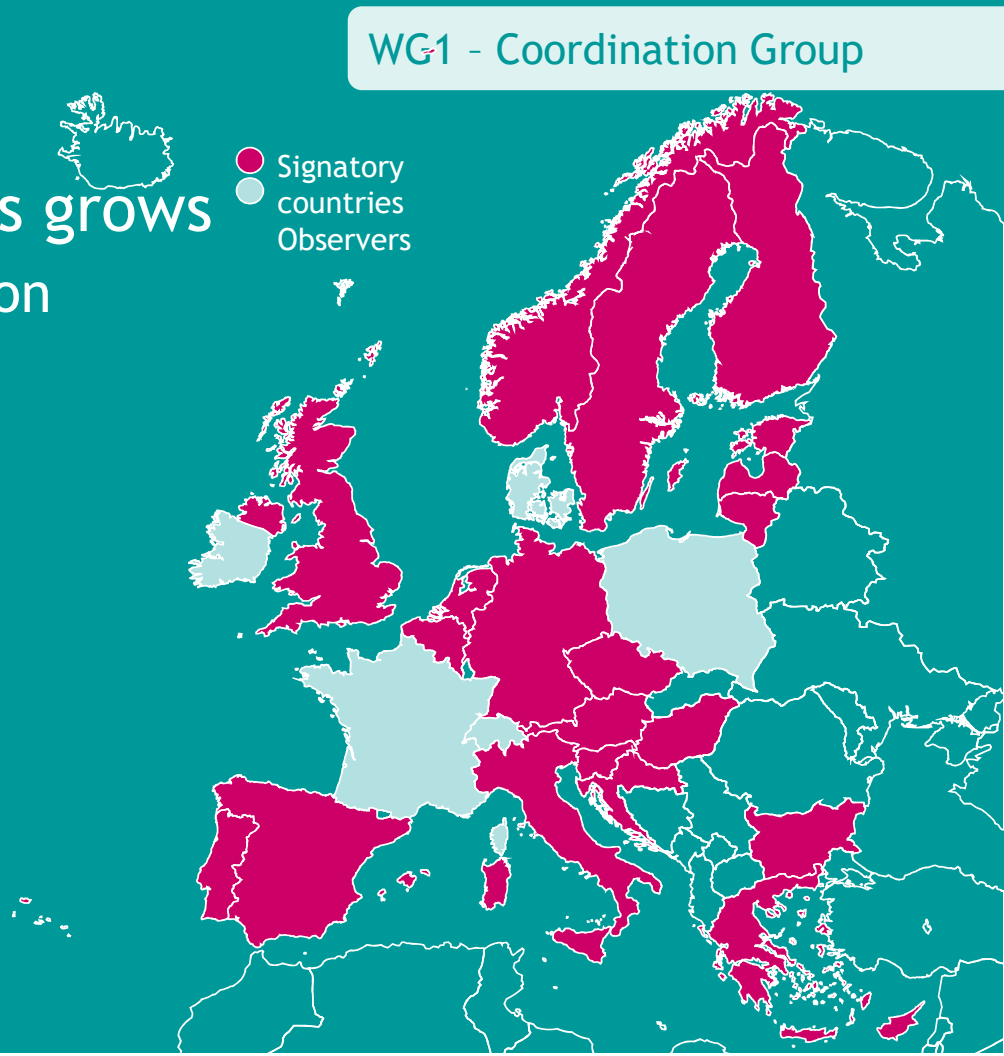


04

1+MG & B1MG
Ongoing activities

General Developments

- Alliance of 1+MG signatory countries grows
  - **Belgium** recently signed the declaration



1+MG Roadmap summary publication

- Translated the 1+MG Roadmap adopted February 2020 into a public brochure for the (educated) general public
- Editorial team with input from EC, 1+MG CG and WG/WP leads
- Supported through a Digital Health Europe Grant
- Published late Sept 2020

https://ec.europa.eu/digital-single-market/en/news/roadmap-1million-genomes-initiative-now-clearly-illustrated-new-brochure

1+MillionGenomes
Roadmap 2020-2022

1+MillionGenomes
Roadmap 2020-2022

LOUISE
IMPROVING CANCER TREATMENT

BREAST CANCER

Louise has a long family history of breast cancer. One day, she heard on TV that mutations in the BReast CAncer genes *BRCA1* and *BRCA2* increase the risk of breast cancer by up to 80%. Although it turned out that she doesn't have mutations in these genes, her risk of developing the condition is still high due to her family history.

CANCER SCREENING

In order to detect early potential breast cancer, she started breast cancer screening at age 35, much earlier than the usual recommended routine screening. A few years later, Louise indeed developed breast cancer. To determine the most suitable type of treatment, she underwent a genomic test assessing the utility of chemotherapy versus other treatments in her case.

TREATMENT

Test results showed that Louise would not benefit much from chemotherapy, so doctors opted for a more effective personalised treatment, which also prevented her from experiencing the unpleasant side effects of chemotherapy.

CHEMO

Developments in the sequencing of cancer genomes are rapidly improving insights and predictive power of genomic tests on risk, prognosis and treatment of cancer. The 1+MG network will greatly increase the availability of this knowledge to oncologists, improving the choices for patients and the reducing over-treatment.

MARTIN
IMPROVING PROGNOSIS FOR RARE DISEASES

MICROCEPHALY

In 2015 Martin was born in Dublin, Ireland. Doctors recorded an abnormally small head and face, as well as a slow development rate. Genome sequencing identified many possible candidates for the genes that were causing his slow development. However, a precise diagnosis would be needed to start treatment.

EUROPEAN PLATFORM ON RARE DISEASES REGISTRATION

EU RD PLATFORM

Launching a query through an EU federated platform that facilitates matching of cases with similar phenotypic and genotypic profiles allowed his doctors to find a second case in Spain with similar symptoms. Comparison of the sequencing results of the Irish and Spanish patients highlighted one mutation both had in common, which pointed to a defect that could be counteracted by supplying a specific metabolite.

Matching of cases with similar phenotypic and genotypic characteristics through an EU federated platform facilitates reaching an accurate diagnosis and treatment for rare disease patients with different backgrounds in separate countries. In this case this worked not only for Martin's condition but also for the Spanish patient.

JUSTYNA
PREVENTING COMMON AND COMPLEX DISEASES

POLYGENIC RISK SCORE

Justyna heard about the ongoing biobanking project in her country in the media, so she read more about the genetic risks of certain diseases.

Her healthcare provider recommended a genomic analysis to estimate her Polygenic Risk Score (PRS), a test for most common diseases which was just introduced as a new clinical trial in the university hospital.

CORONARY ARTERY DISEASE

This genomic analysis showed that she has a PRS in the top 5% for Coronary Heart Disease (CAD). Drugs such as statins and other preventive measures lower the cholesterol levels in the blood and reduce the CAD risk, so her doctor suggested to initiate statin treatment and make some lifestyle changes.

PREVENTION

Statin SIDE EFFECT

Now Justyna has to take statins. The genomic analysis also showed that one specific statin could increase her risk of muscle inflammation and should be avoided.
Justyna is now more aware of how to prevent CAD and make adjustments in her lifestyle, as well as receive the right treatment and regular check-ups, if needed.

Europe is currently developing PRS tests for early identification of risks factors for common diseases. The 1+MG project will yield genome sequences for many European citizens, in combination with phenotypic information, all collected with informed consent in biobanks across Europe. This will further the implementation of PRS testing in regular health care and will boost the availability of cheap prevention throughout Europe and elsewhere.

PABLO & PEDRO
TACKLING HIGH SENSITIVITIES TO INFECTIOUS DISEASES

COVID-19

Pablo (27 years old) develops severe COVID-19 symptoms. Shortly after, his brother Pedro (30 years old) is also tested positive. Both need to be treated in intensive care. The two brothers do not belong to any of the known risk groups, but their close family relationship suggests a genetic risk factor.

INFLUENCES

GENETIC

Genetic profiling of the brothers is undertaken and compared to other disease cohorts and population biobank resources. It turns out that Pablo and Pedro are carriers of a rare genetic mutation in TLR7 (Toll-Like Receptor 7). This gene on the X chromosome regulates the interferon level as a defensive response to viruses. Based on this finding, Pablo and Pedro receive a specific treatment to restore the natural capacity of their immune system to fight the virus.

DATABANK NETWORK

Imagine we would have the EU federated genomic data network of 1+MG in place offering European clinicians the possibility to receive alerts when they encounter patients with similar characteristics. Patients' increased susceptibility to life-threatening conditions caused by an infectious disease such as COVID-19 could be rapidly discovered and the necessary treatment adapted and personalised.

1+MillionGenomes
Roadmap 2020-2022

Which are the main areas of cooperation?

To create this framework with its focus on more than one million genomes, new ways of collaborating are needed. This is why the 1+ Million Genomes initiative was founded. The signatory countries are keen to move forward on accelerating developments in genomic science into enhanced healthcare. Various areas of activity are at the core of the initiative's work: work organisation; implementing personalised healthcare in health systems in cost-effective and efficient ways; ethical, legal, and social issues; health and phenotypic data; good genomic practice and standards; and infrastructure and interoperability.

Organisation of work

Strong coordination and collaboration of all the initiative's efforts have been put in place. This is happening through cooperation among the signatory countries, supported by expert working groups. One expert group focuses on governance and ensures overall coordination. It covers several aspects of activity, including stakeholder engagement, industry engagement, a learning framework, and education and communication.

Ethical, legal, and social issues

A number of ethical, legal, and social issues need to be brought into focus and resolved. Examples include the values and ethics underpinning this pan-European framework; the underlying legal framework and challenges of finding ways to process genomic data across borders despite legal differences; the contractual arrangements related to data use and data inclusion; and the societal implications, transparency, policies, and processes to govern data access.

An important priority is to address the implications of the 2018 General Data Protection Regulation (GDPR) in relation to questions about consent, privacy, and research uses of genomic data in Europe.

Genomics innovation in national healthcare systems

Embedding genomics expertise and research outcomes into personalised healthcare will lead to greater efficiencies and, thus, cost savings. Accelerating the transfer of research knowledge into improved and cost-effective healthcare is key (including improving disease prediction rates, diagnosis, and the tailoring of therapies and treatments to individuals). This requires innovation in healthcare systems across Europe; the 1+MG initiative will help the countries involved to learn from each other in this respect. Analysing the potential costs and benefits of the adoption of genomics in healthcare will be part of these steps. The 1+MG framework will thus assist in the analysis of economic viability, and in the harmonisation of cost assessment and economic evaluation models. This will help towards generating comparable evidence across European healthcare systems and facilitate countries to make informed policy choices about the implementation of genomics-based personalised medicine.

Clinical and phenotypic data

Agreeing on a minimal set of phenotypic and clinical data to be collected in each genomics study is crucial. This agreement will enable comparative studies across data collections that may have different backgrounds. The initiative will build consensus to implement this minimal dataset across European

Good genomic practice and standards

When sequencing genomic data, it is important to draw on good practice. As a result, guidelines and appropriate standards and forms of accreditation will need to be drawn up. Genome sequencing standards, benchmarking and metrics, as well as good quality control of data, are needed.

Infrastructure and interoperability

The initiative's proposed infrastructure uses a federated approach. Each country in Europe is invited to contribute to the endeavour, by bringing to the enterprise the strengths and qualities of its own national programme. The initiative is not centralised and will not pool genomic data in one place. Rather, through interoperability, it will bring data warehouses up to agreed standards and link them with a secure infrastructure. Users, like accredited research institutions, healthcare professionals, and health policy agencies, will be able to access this secure network to execute approved algorithms and analyse available data remotely.

1+MillionGenomes
Roadmap 2020-2022

What is the timeline and next steps?

The 1+ Million Genomes initiative has set up an intensive agenda of activities to reach its goals by 2022. Its signatory countries and expert groups are working together on many stepwise, concrete actions. By aligning the investments and advances expected in 2020-2022, the aim of creating a cohort of at least 1 million sequenced genomes can be achieved.

Laying out the 1+MG Roadmap 2020-2022

Between 2020-2022, three phases of activity will concentrate on engaging, translating, and driving the 1+MG initiative forward.

2020 – Engage – Engaging countries and other stakeholders in governance and collaboration

- Assemble **national, regional, and local public authorities** as well as a broad range of international stakeholders in the initiative. They will link together different genomic medicine resources in line with the initiative's declaration.
- Define **a governance model of coordination and cooperation**. The cooperation model will cover the terms and conditions needed for secure access to genomic data and associated health data across borders, and the use of national and regional data collections for research and improving healthcare.

2021 – Translate – Translating the mission into concrete infrastructure, guidelines, and pilots

- Pilot the technical infrastructure for **distributed, authorised and secure** access to national and regional genetic data, and facilitate the **interoperability of registries and databases.**
- Support the development of **an ethical and legal framework** for cross-border access to genomic datasets to advance research across Europe, while taking appropriate measures to **protect the privacy of individuals.**
- Test-run the secure infrastructure and legal framework to enable **cross-border sharing and analysis of genetic data and associated health datasets**, anonymised as appropriate. The datasets will come from multiple European countries, build on existing **initiatives in genomics and personalised medicine,** and focus on **four use cases.**

2022 – Drive – Moving forward on sharing, scaling, and sustaining the initiative

- Embed the coordinated data governance framework and infrastructure for **Europe-wide large-scale processing of genome and health data in national and regional science and healthcare systems.**
- Scale activities to enable distributed and **secure access to research cohorts of at least 1 million sequenced genomes.**

The underpinning aim of this three-year initiative will be to support a European data strategy that reinforces the creation of data spaces in key strategic sectors and domains of public interest. In the health sector, this will translate into **a European health data space,** essential for making advances in **preventing, detecting, and curing diseases** and for making informed decisions that will improve the **accessibility, effectiveness, and sustainability of health-care systems.**

A Horizon 2020 project "Beyond 1 Million Genomes" (B1MG) will provide support and coordination to the implementation of the roadmap.

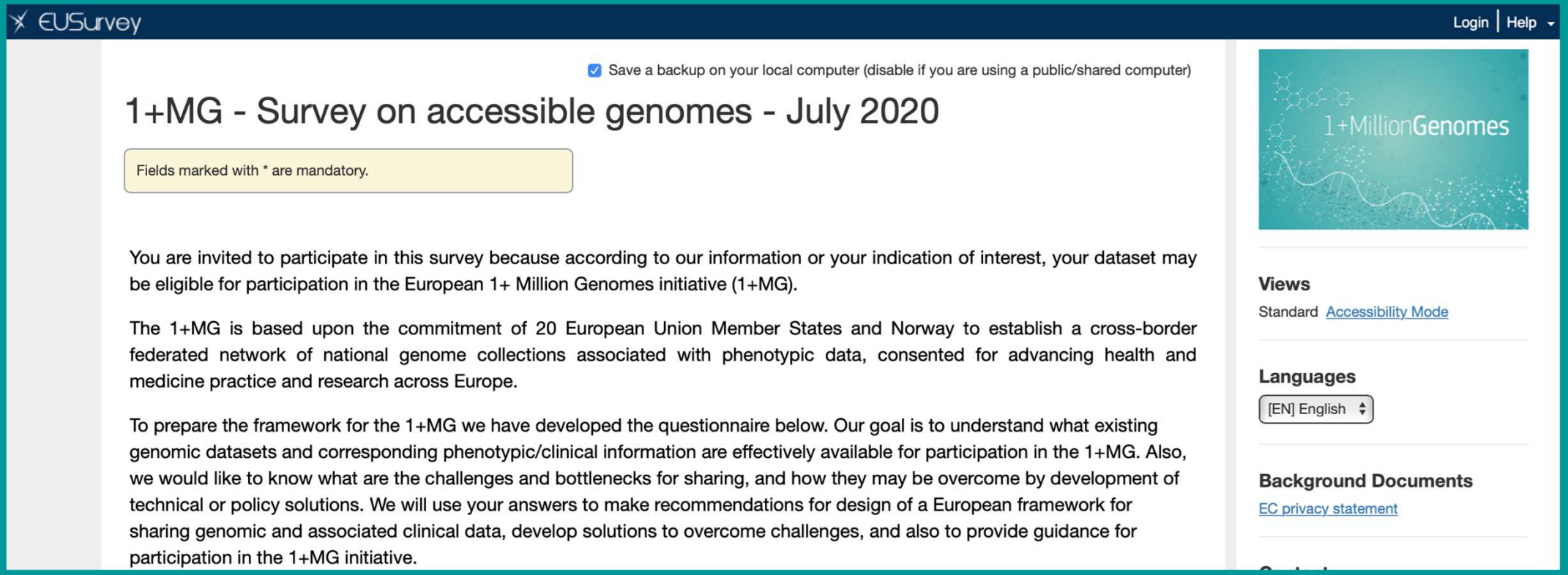
Engage
Governance, cooperation, and collaboration
- Governance model, national "mirror groups"
- Terms and conditions for distributed access
- Guidelines on good genomic practice
- Funding, communication

Translate
Infrastructure, guidelines, and pilots
- Distributed, authorised and secure access
- Legal guidelines for cross-border use
- Technical specifications, interoperability
- Secure infrastructure and tools

Drive
Sharing, scaling, and sustaining
- Coordinated data governance
- Plan for scale-up of the infrastructure
- Economic evaluation
- Roadmap for longer-term sustainability

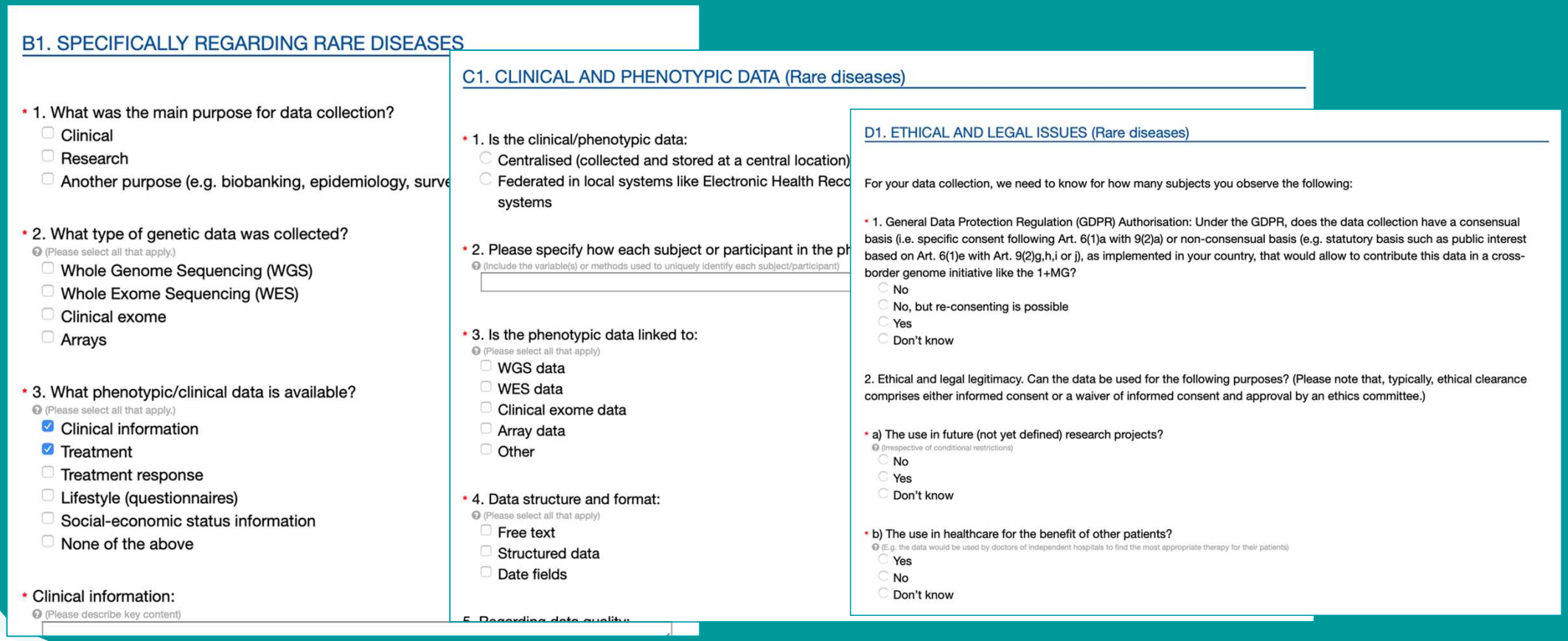
For more general information, the 1+ Million Genomes initiative encourages people to visit its website: https://ec.europa.eu/digital-single-market/en/european-1-million-genomes-initiative

Survey on accessible genomes



https://ec.europa.eu/eusurvey/runner/1plusMG_Survey2020

Detailed questionnaire to deepen our view on what can progressively be included in 1+MG



B1. SPECIFICALLY REGARDING RARE DISEASES

* 1. What was the main purpose for data collection?
- Clinical
- Research
- Another purpose (e.g. biobanking, epidemiology, surve

* 2. What type of genetic data was collected?
(Please select all that apply.)
- Whole Genome Sequencing (WGS)
- Whole Exome Sequencing (WES)
- Clinical exome
- Arrays

* 3. What phenotypic/clinical data is available?
(Please select all that apply.)
- [x] Clinical information
- [x] Treatment
- Treatment response
- Lifestyle (questionnaires)
- Social-economic status information
- None of the above

* Clinical information:
(Please describe key content)

C1. CLINICAL AND PHENOTYPIC DATA (Rare diseases)

* 1. Is the clinical/phenotypic data:
- Centralised (collected and stored at a central location)
- Federated in local systems like Electronic Health Reco systems

* 2. Please specify how each subject or participant in the ph
(Include the variable(s) or methods used to uniquely identify each subject/participant)

* 3. Is the phenotypic data linked to:
(Please select all that apply)
- WGS data
- WES data
- Clinical exome data
- Array data
- Other

* 4. Data structure and format:
(Please select all that apply)
- Free text
- Structured data
- Date fields

5. Regarding data quality:

D1. ETHICAL AND LEGAL ISSUES (Rare diseases)

For your data collection, we need to know for how many subjects you observe the following:

* 1. General Data Protection Regulation (GDPR) Authorisation: Under the GDPR, does the data collection have a consensual basis (i.e. specific consent following Art. 6(1)a with 9(2)a) or non-consensual basis (e.g. statutory basis such as public interest based on Art. 6(1)e with Art. 9(2)g,h,i or j), as implemented in your country, that would allow to contribute this data in a cross-border genome initiative like the 1+MG?
- No
- No, but re-consenting is possible
- Yes
- Don't know

2. Ethical and legal legitimacy. Can the data be used for the following purposes? (Please note that, typically, ethical clearance comprises either informed consent or a waiver of informed consent and approval by an ethics committee.)

* a) The use in future (not yet defined) research projects?
(Irrespective of conditional restrictions)
- No
- Yes
- Don't know

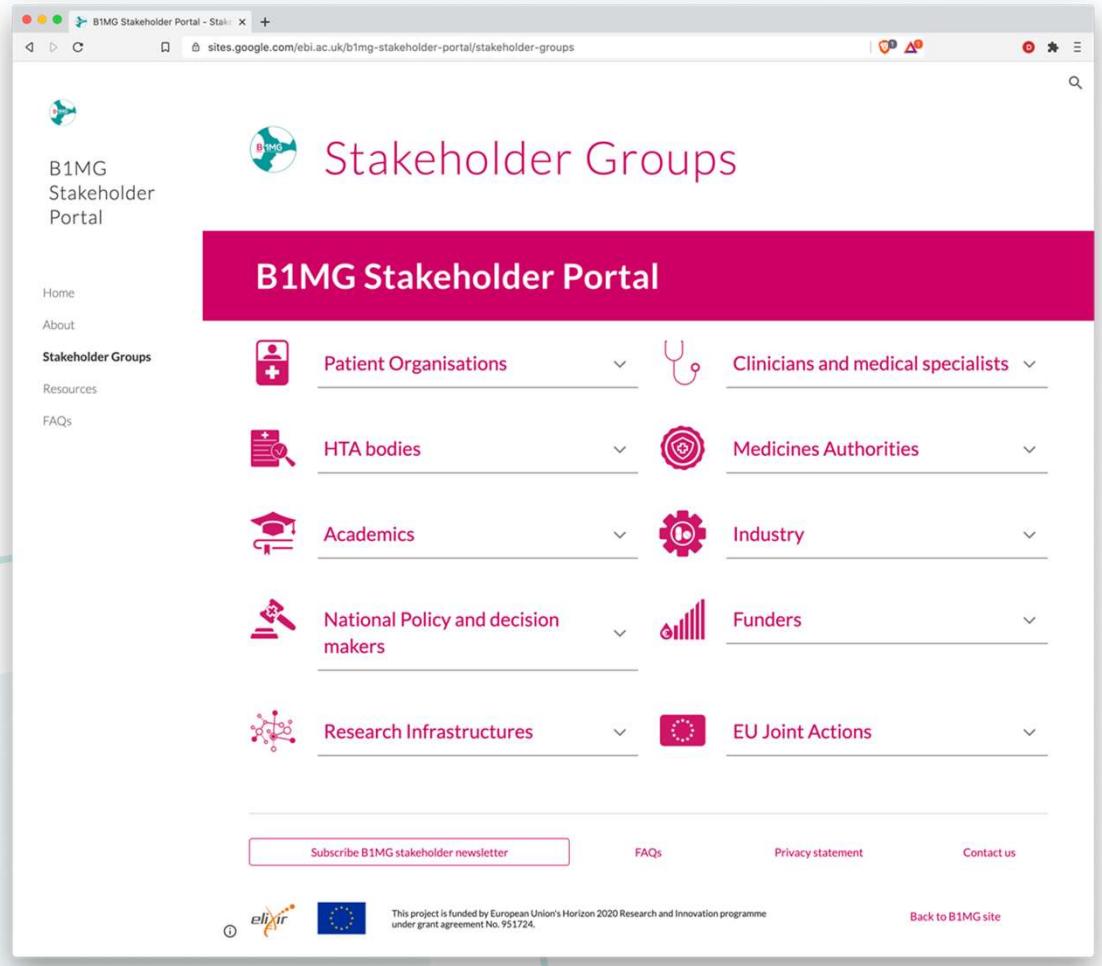
* b) The use in healthcare for the benefit of other patients?
(E.g. the data would be used by doctors of independent hospitals to find the most appropriate therapy for their patients)
- Yes
- No
- Don't know

B1MG Work Packages / 1+MG Work Groups activities

Workstreams

WP1 – Stakeholder

To contribute and shape outcomes



WP3

WP2

WP1 — Stakeholder Engagement

- Stakeholder portal now live, creating an interface between external stakeholders and project partners, to facilitate community participation and engagement, communication and collaboration
  - 21 registered so far (link to register)

Registration

Workstreams

WG2 & WP2 – ELSI

Provide ELSI Toolkit to:

- Consolidate national requirements, policies and recommendations
- Build upon good practice developed in EU projects and national genomic initiatives

Relevance of ELSI to 1+MG

- 1+MG aims to ensure “distributed, authorised and secure access … while taking appropriate measures to **protect the privacy** of individual data donors”. (Declaration, 2018)
- The Declaration places **notable emphasis** on addressing ethical, legal and societal issues (ELSI).
- The ELSI Working Group (ELSI WG) develops **recommendations** on how to responsibly provide cross-border access to genomic and related health data.
- **Ultimate decisions** rest with the 1+MG signatories.

Roadmap

- Collect existing **governance best practices**
- Review applicable **ethical guidelines** and **literature**
- Review **applicable EU** and **exemplar national laws** to define legal requirements
- Organise **use case workshops** to better understand ELSI challenges
- Engage with relevant **stakeholders** and related **initiatives**
- Prioritise aspects that are necessary **input of the work of other WGs**
- **Recommendations** relevant for **Signatory Member States**

Workstreams

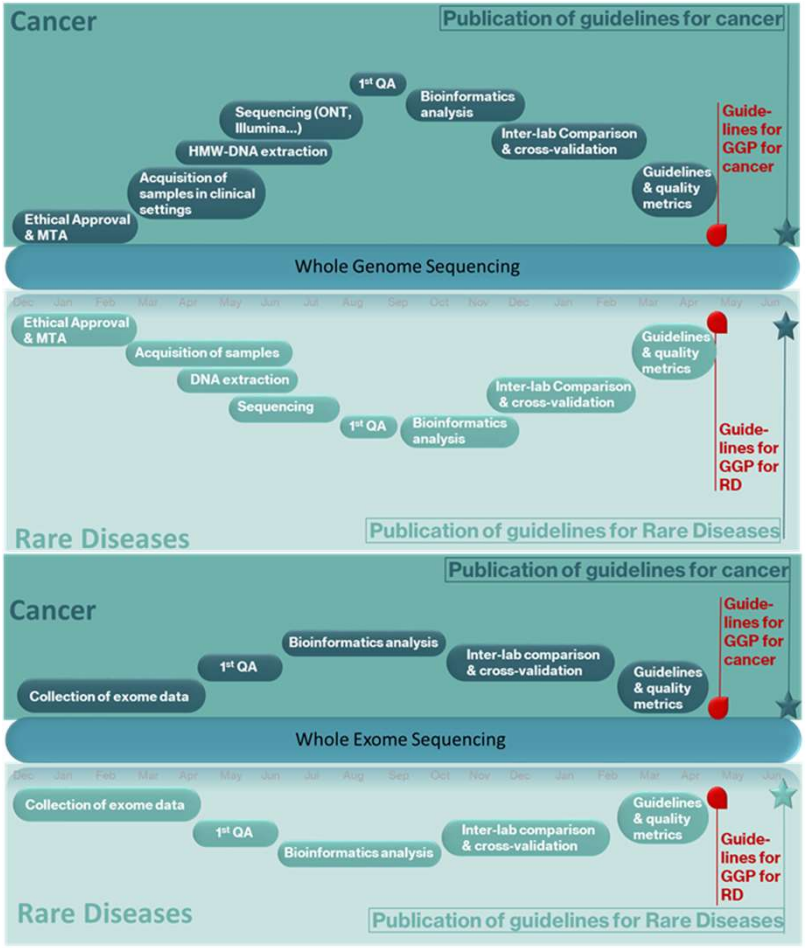
WG3, WG4, WP3– Clinical & Data Quality

Provide minimal requirements for:

- Sample source
- Bioinformatics analysis
- the description of patient-specific phenotype and clinical data

Consider national particularities, such as clinical systems and languages

WP3 - WG4 - Good Genomic Practice



Workstreams

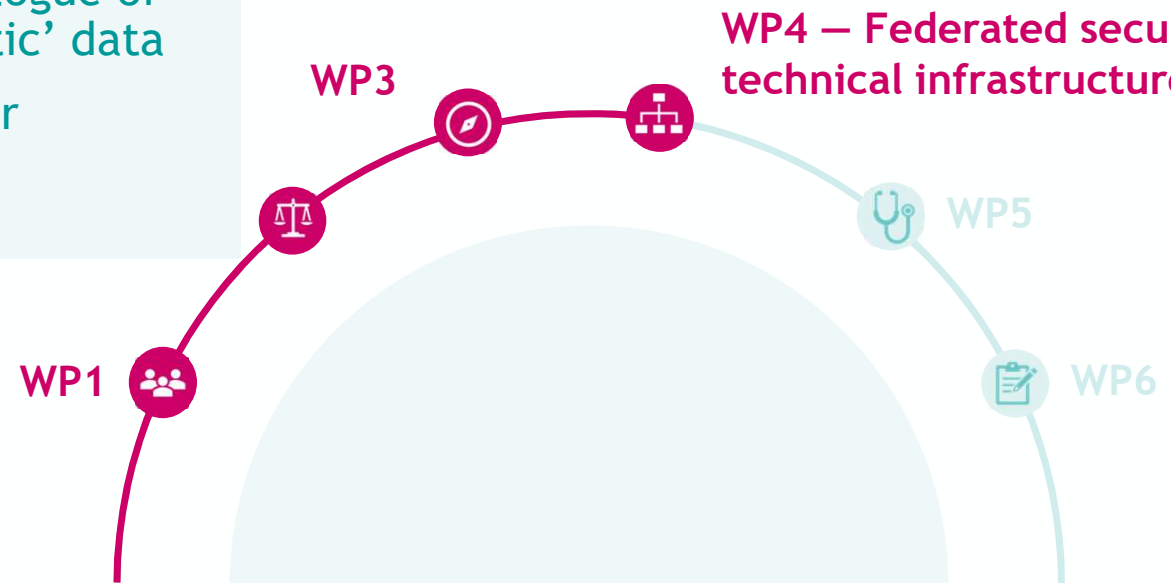
WG5/WP4 – Infrastructure

Provide infrastructure requirements for:

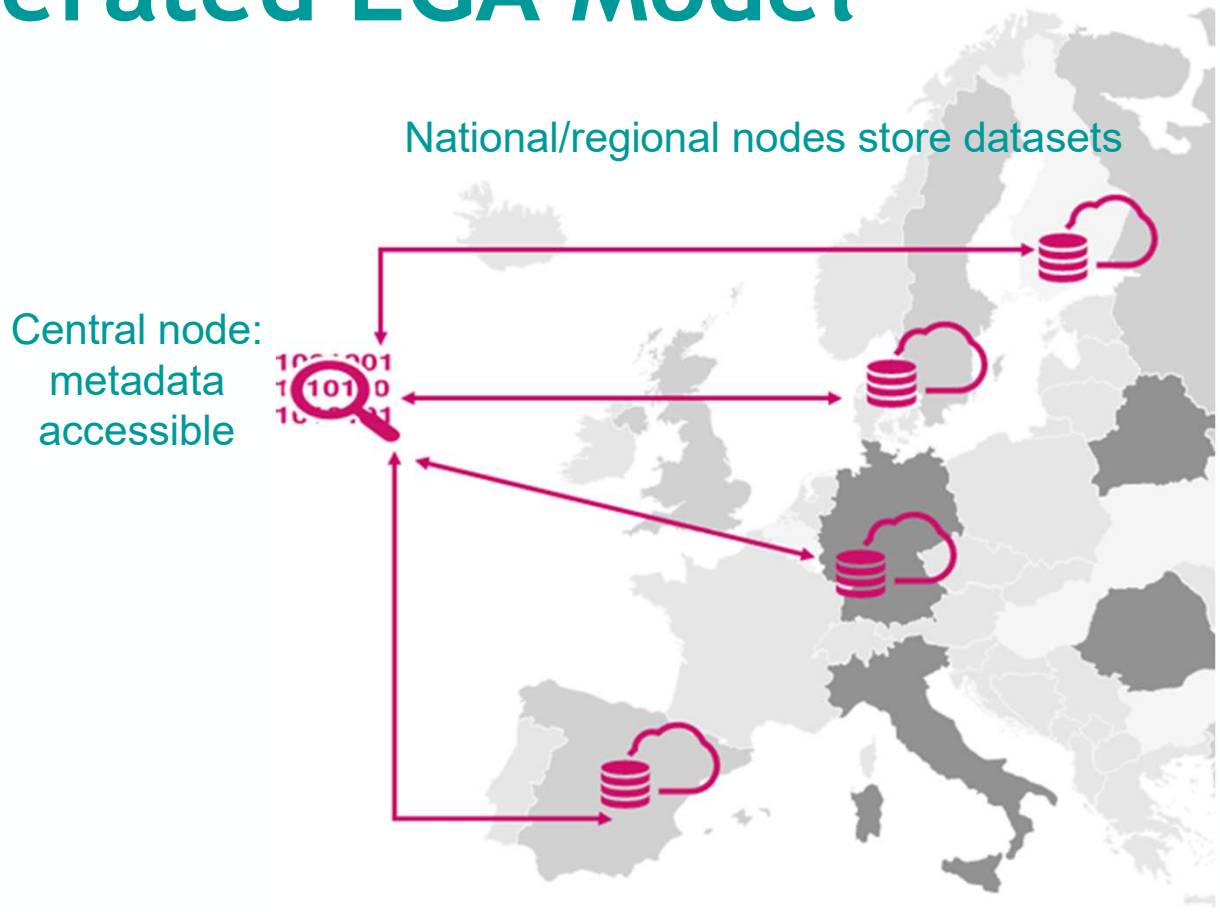
- Security and privacy
- Interoperability standards

Coordinate catalogue of existing ‘synthetic’ data

Test cross-border interoperability



Federated EGA Model

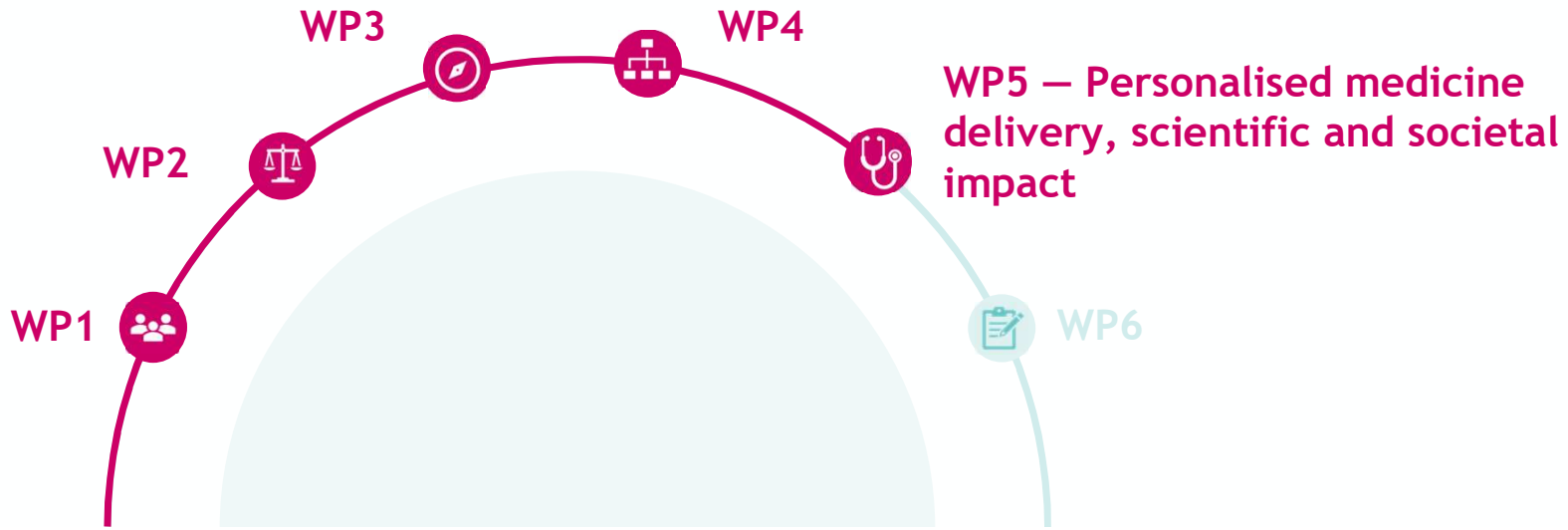


WG6/WP5 - Healthcare Implementation and impact

Workstreams

Implementation of:

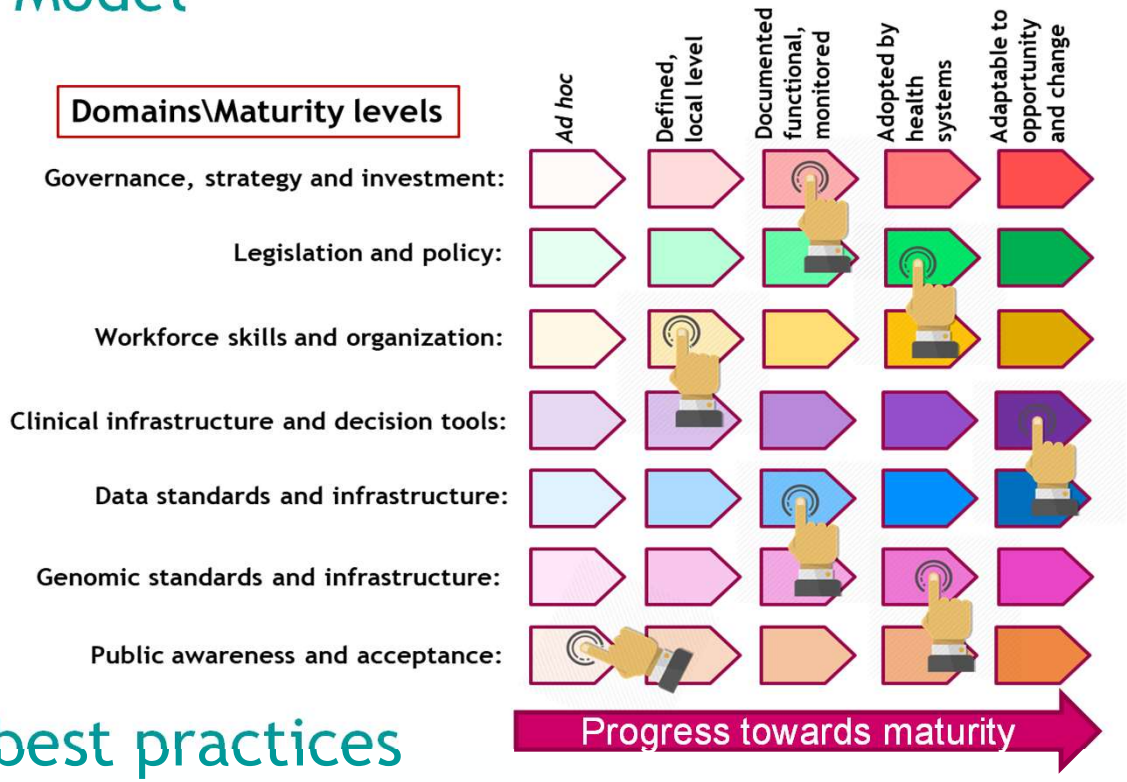
- Maturity level model
- Country visits for knowledge exchange
- Economic model for evaluating personalised medicine approaches



Tools

WG6/WP5 - Healthcare Implementation and impact

- Harmonised Health Economic Model
- B1MG Maturity Level Model

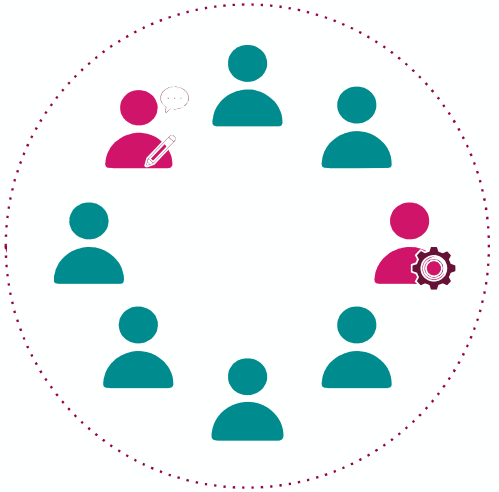


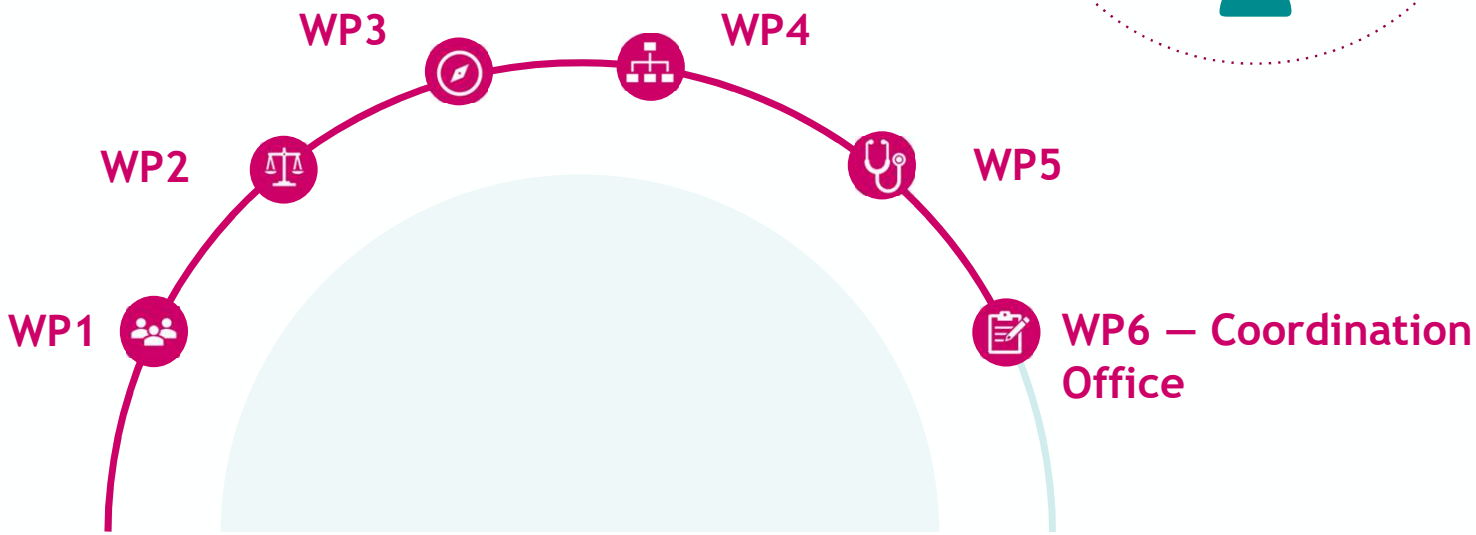
- Country Visits – exchange on best practices
  - UK, Estonia, Finland

Workstreams

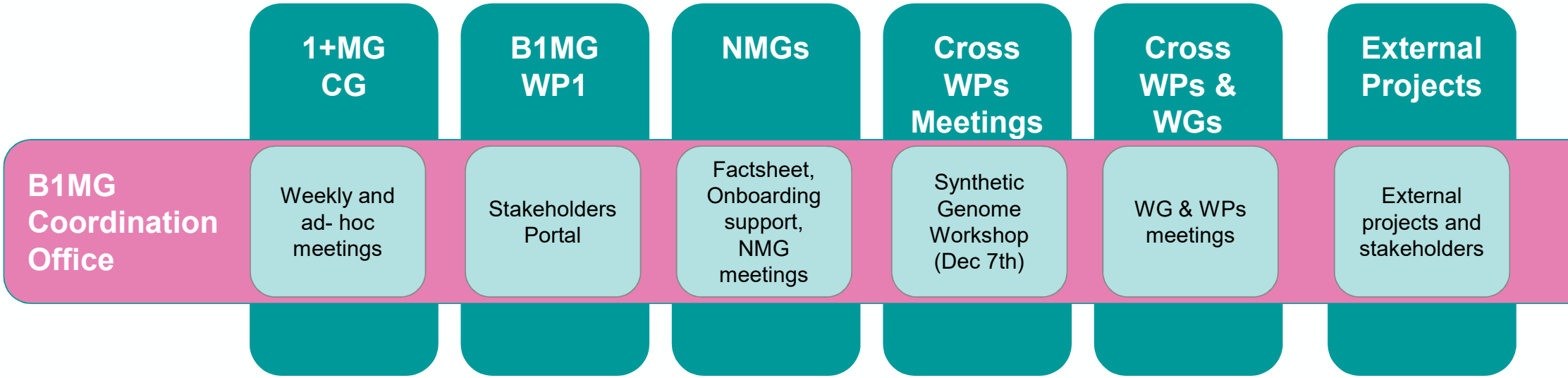
- Project management
- Communication
- Governance
- Sustainability

National Mirror Groups

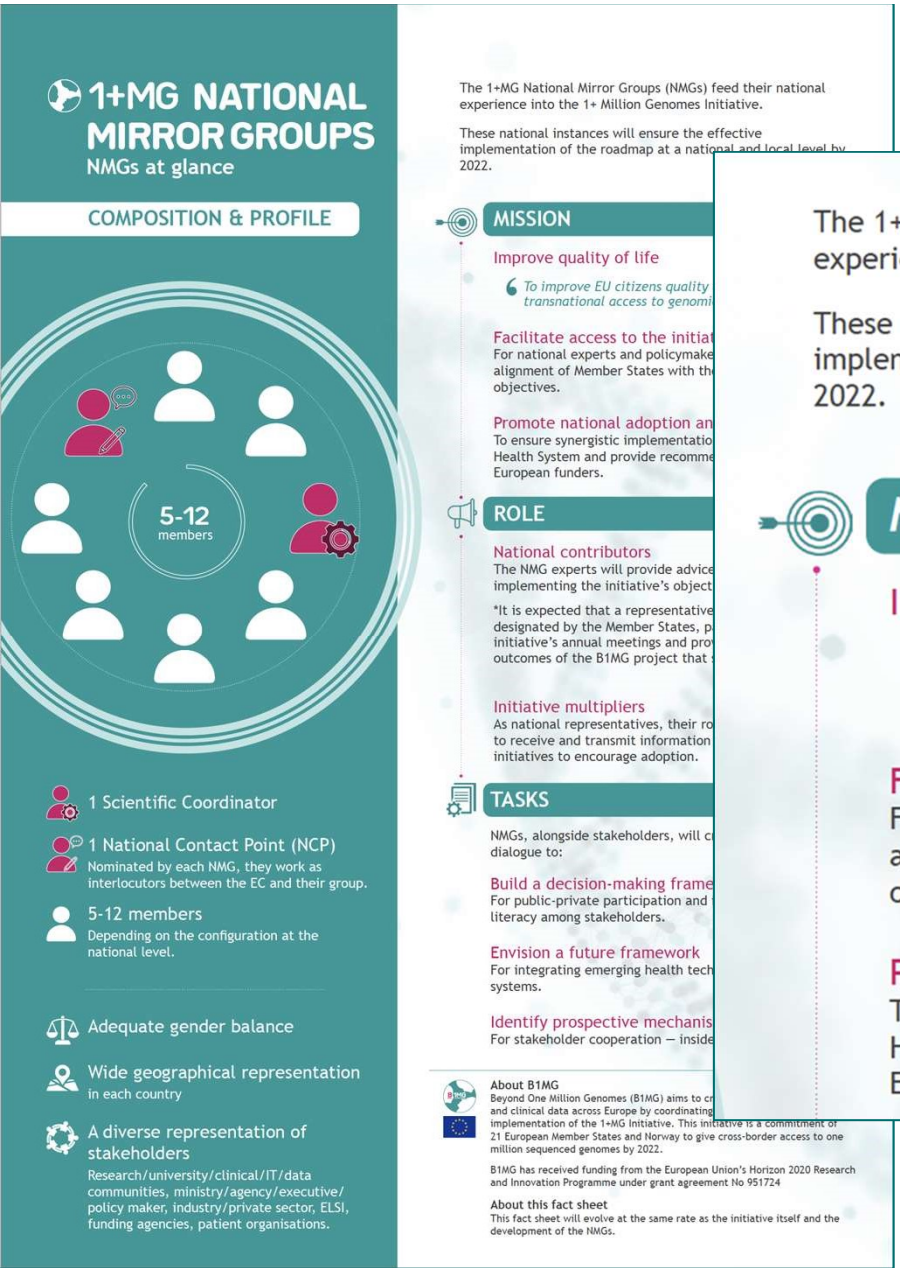




WP6 – Coordination Office



General support: b1mg-coordination@elixir-europe.org
NMG support : b1mg-nmg-coordinator@elixir-europe.org



The 1+MG National Mirror Groups (NMGs) feed their national experience into the 1+ Million Genomes Initiative.

These national instances will ensure the effective implementation of the roadmap at a national and local level by 2022.

MISSION

Improve quality of life

To improve EU citizens quality of life by enabling transnational access to genomics data

Facilitate access to the initiative's information

For national experts and policymakers to ensure the alignment of Member States with the initiative's objectives.

Promote national adoption and sustainability

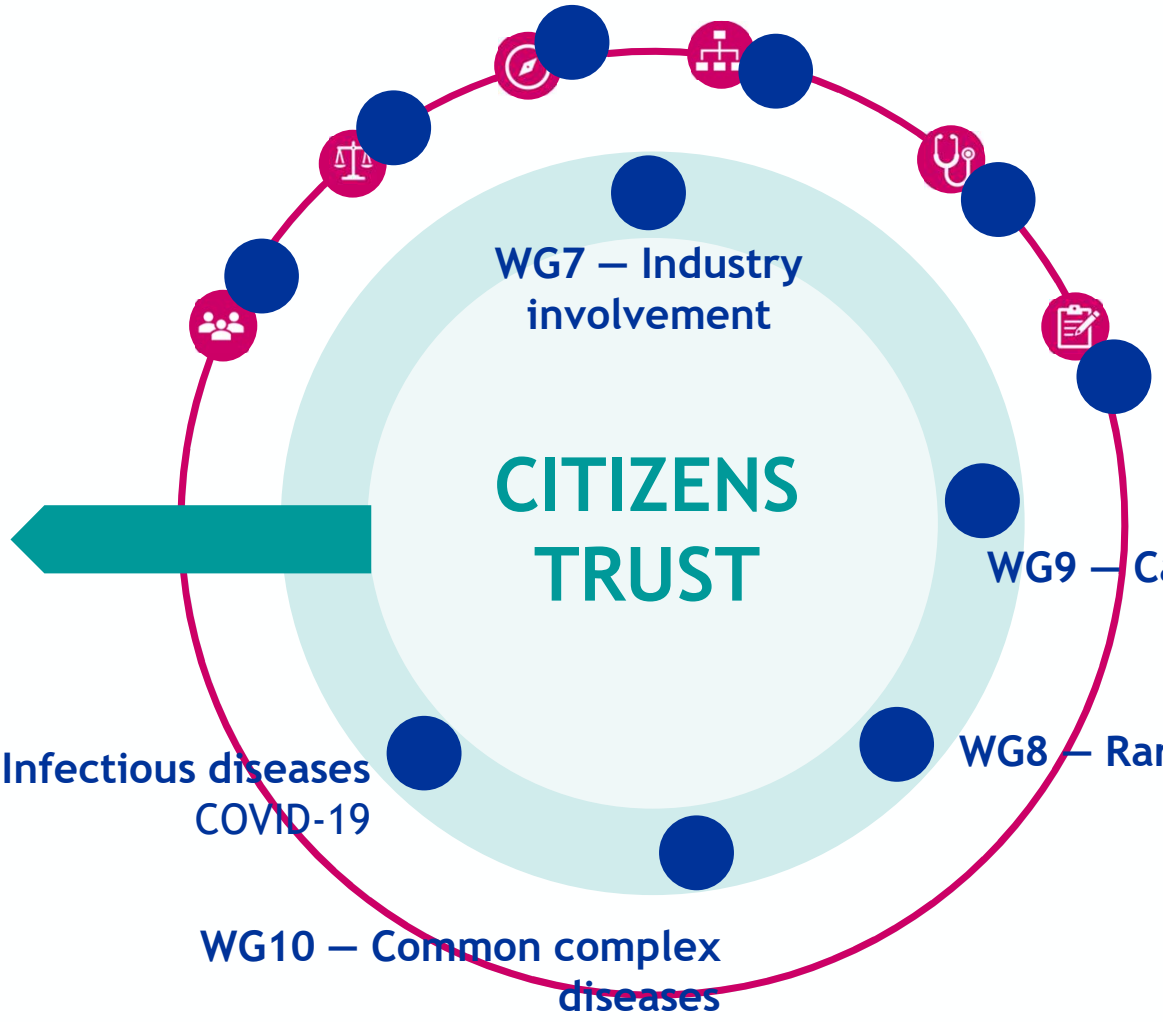
To ensure synergistic implementation in each National Health System and provide recommendations to local and European funders.

B1MG

Download

Workstreams

Personalised medicine a reality
across Europe



Develop Europe's future health data landscape

3 years

Maturity Model
ELSI toolkits
Technical recommendations and guidelines

European Health Data Space

Long-term strategy — Use Cases working groups
Cancer, infectious diseases, rare diseases, common complex disease

Thank you

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