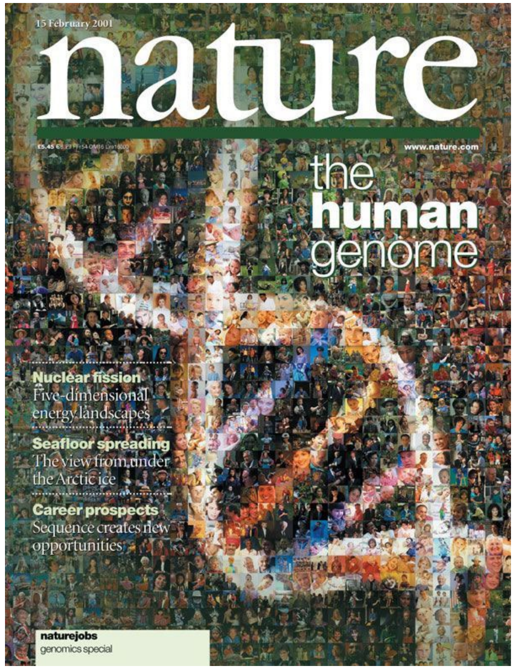
Ethische und rechtliche Herausforderungen im Umgang mit genetischen Daten im Rahmen des Projekts „Genome of Europe“

Julia GROTH, Barbara BOHN, Leo PANRECK, Olga TZORTZATOU, Davit CHOKOSHVILI, Monika KRAUS, Harald GRALLERT, Wolfgang LIEB, Christian GIEGER, Annette PETERS, Bettina LORENZ-DEPIEREUX

GENOME OF EUROPE

Die EU Genom Initiative „1+ Million Genom“ (1+MG)


15 February 2001

nature

the human genome

www.nature.com

Nuclear fission Five-dimensional energy landscapes

Seafloor spreading The view from under the Arctic ice

Career prospects Sequence creates new opportunities

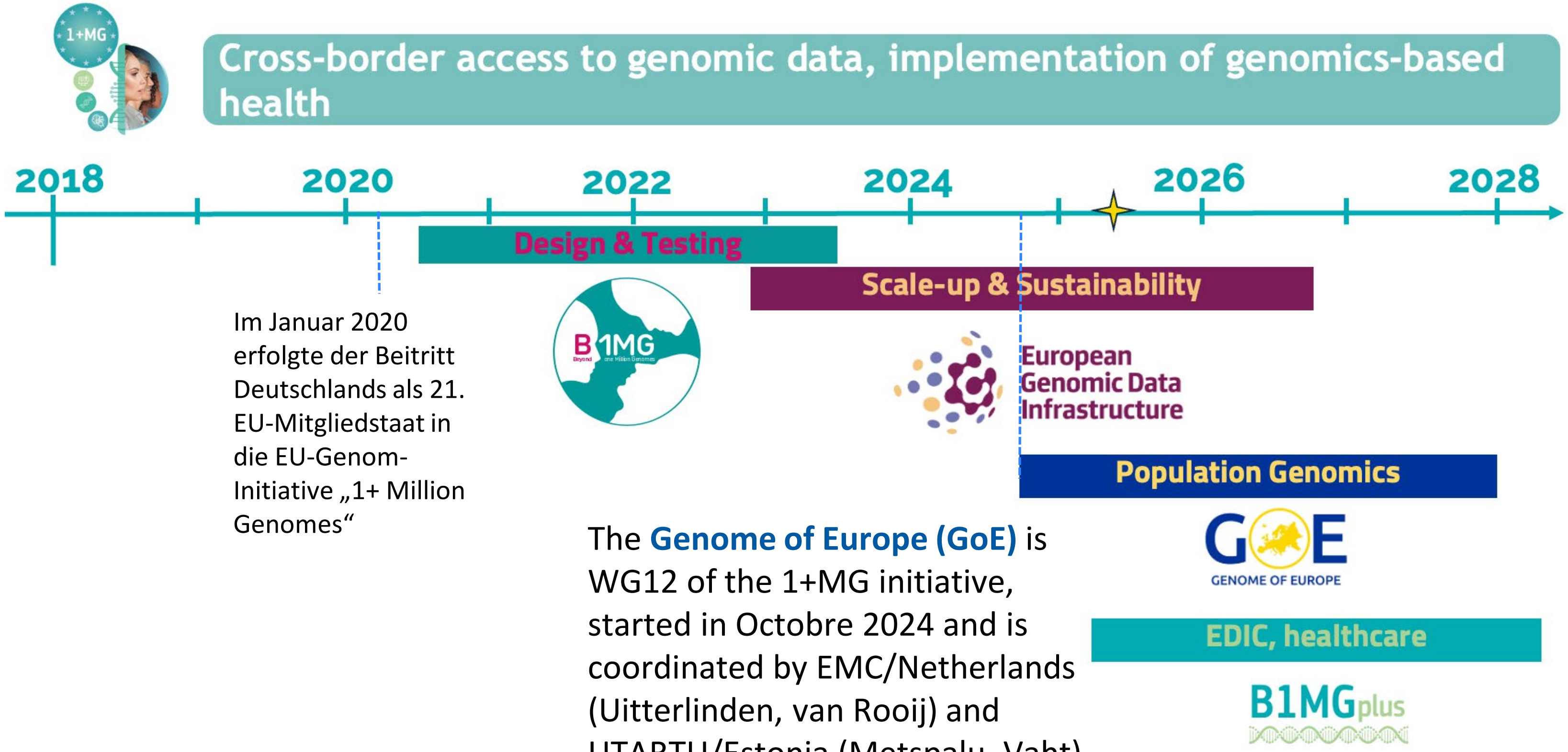
naturejobs genomics special

Das Humangenomprojekt

1990 – 2001 (2003)

Sequenz der ca. 3 Milliarden Basenpaare (DNA) des menschlichen Genoms

Ziel - über eine Million Genome zu sequenzieren und damit die Gesundheitsversorgung zu verbessern



Im Januar 2020 erfolgte der Beitritt Deutschlands als 21. EU-Mitgliedstaat in die EU-Genom-Initiative „1+ Million Genomes“

The **Genome of Europe (GoE)** is WG12 of the 1+MG initiative, started in Octobre 2024 and is coordinated by EMC/Netherlands (Uitterlinden, van Rooij) and UTARTU/Estonia (Metspalu, Vaht).

https://framework.onemilliongenomes.eu/population-genomics

GENOME OF EUROPE

Mission / Vision

Aims of the project

- Generate representative genomics data
- Made available for research through GDI infrastructure
- Harmonize QC and workflows
- Jointly tackle ELSI
- Long-term planning for using genetic data in health care and prevention
- Conduct a series of pilot studies that illustrate the utility of the GoE dataset.

Contribute 100 000 samples to **1+ Million Genomes (1+MG)**

Demonstrate **scientific and clinical value** trough pilots and use-cases

Benchmark & guide **ethical and legal issues**

GENOME OF EUROPE

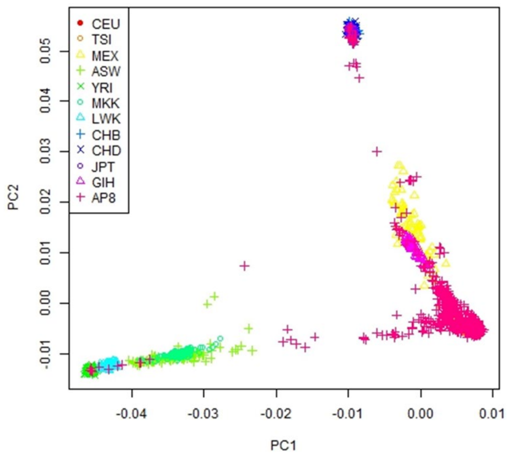
Engage with stakeholders through **communication and dissemination**

Provide an **accessible and secure** genetic dataset

Synergize with multiple **EU Data and Health** initiatives

GoE Use Cases
- Look-ups of individual variants
- Creating a Principal Component Analysis of genetic variation
- Generating reference panels for ancestry-specific imputation
- Providing population distributions for polygenic risk scores

Population structure of the NAPKON cohorts

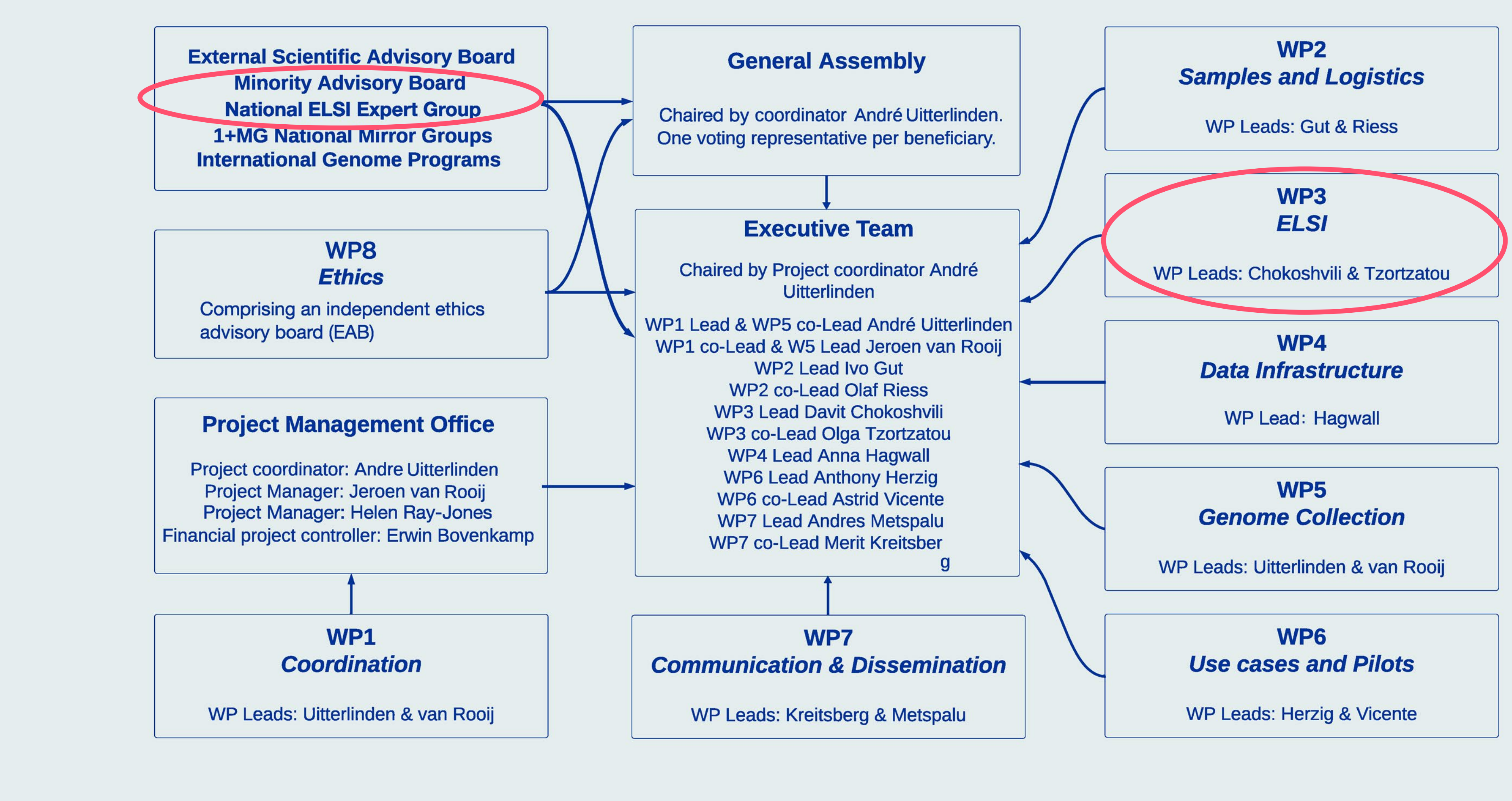


provided by B. Fösel

https://framework.onemilliongenomes.eu/population-genomics

Funded by the European Union's Digital Europe Program,
Grant agreement #101168231 || Part of 1+MG Initiative

Managementstructure / Workpackages



External Scientific Advisory Board
Minority Advisory Board
National ELSI Expert Group
1+MG National Mirror Groups
International Genome Programs

WP8
Ethics
Comprising an independent ethics advisory board (EAB)

Project Management Office

Project coordinator: Andre Uitterlinden
Project Manager: Jeroen van Rooij
Project Manager: Helen Ray-Jones
Financial project controller: Erwin Bovenkamp

WP1
Coordination
WP Leads: Uitterlinden & van Rooij

General Assembly

Chaired by coordinator André Uitterlinden.
One voting representative per beneficiary.

Executive Team

Chaired by Project coordinator André Uitterlinden

WP1 Lead & WP5 co-Lead André Uitterlinden
WP1 co-Lead & W5 Lead Jeroen van Rooij
WP2 Lead Ivo Gut
WP2 co-Lead Olaf Riess
WP3 Lead Davit Chokoshvili
WP3 co-Lead Olga Tzortzatou
WP4 Lead Anna Hagwall
WP6 Lead Anthony Herzig
WP6 co-Lead Astrid Vicente
WP7 Lead Andres Metspalu
WP7 co-Lead Merit Kreitsberg

WP7
Communication & Dissemination
WP Leads: Kreitsberg & Metspalu

WP2
Samples and Logistics
WP Leads: Gut & Riess

WP3
ELSI
WP Leads: Chokoshvili & Tzortzatou

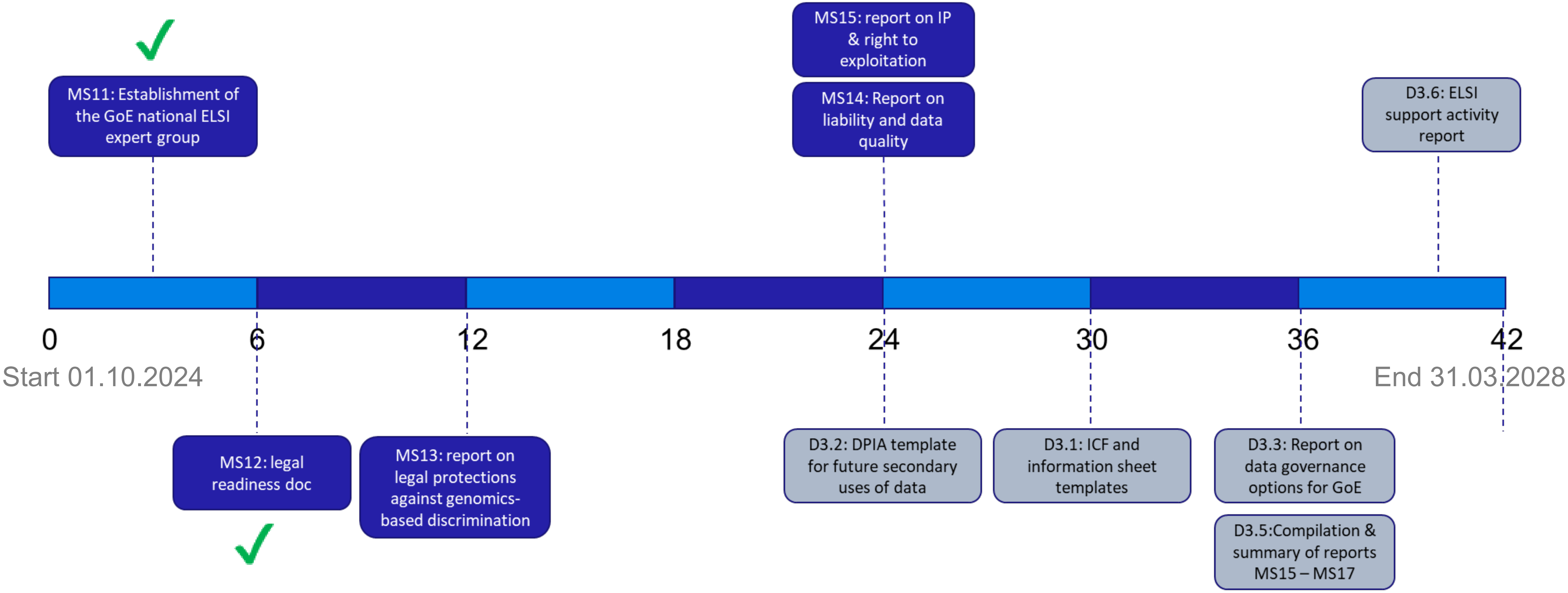
WP4
Data Infrastructure
WP Lead: Hagwall

WP5
Genome Collection
WP Leads: Uitterlinden & van Rooij

WP6
Use cases and Pilots
WP Leads: Herzig & Vicente

https://genomeofeurope.eu/

Timeline of milestones and deliverables WP3



✓

MS11: Establishment of the GoE national ELSI expert group

MS15: report on IP & right to exploitation

MS14: Report on liability and data quality

D3.6: ELSI support activity report

0
Start 01.10.2024

6

12

18

24

30

36

42
End 31.03.2028

MS12: legal readiness doc

✓

MS13: report on legal protections against genomics-based discrimination

D3.2: DPIA template for future secondary uses of data

D3.1: ICF and information sheet templates

D3.3: Report on data governance options for GoE

D3.5:Compilation & summary of reports MS15 – MS17

Challenge 1 / German part / Projektpartner - Koordination

- Repräsentative Abbildung der nationalen Gesamtbevölkerung (Ethnizitäten)
- Qualitativ hochwertige Bioproben / DNA (A. Hörlein, E. Rodriguez)
- Whole Genome Sequencing mittels Illumina NovaSeq X 30x coverage (O. Rieß)
- Ethik und Regularien GoE (J. Groth, B. Lorenz-Depiereux)

NAKO GESUNDHEITS-STUDIE

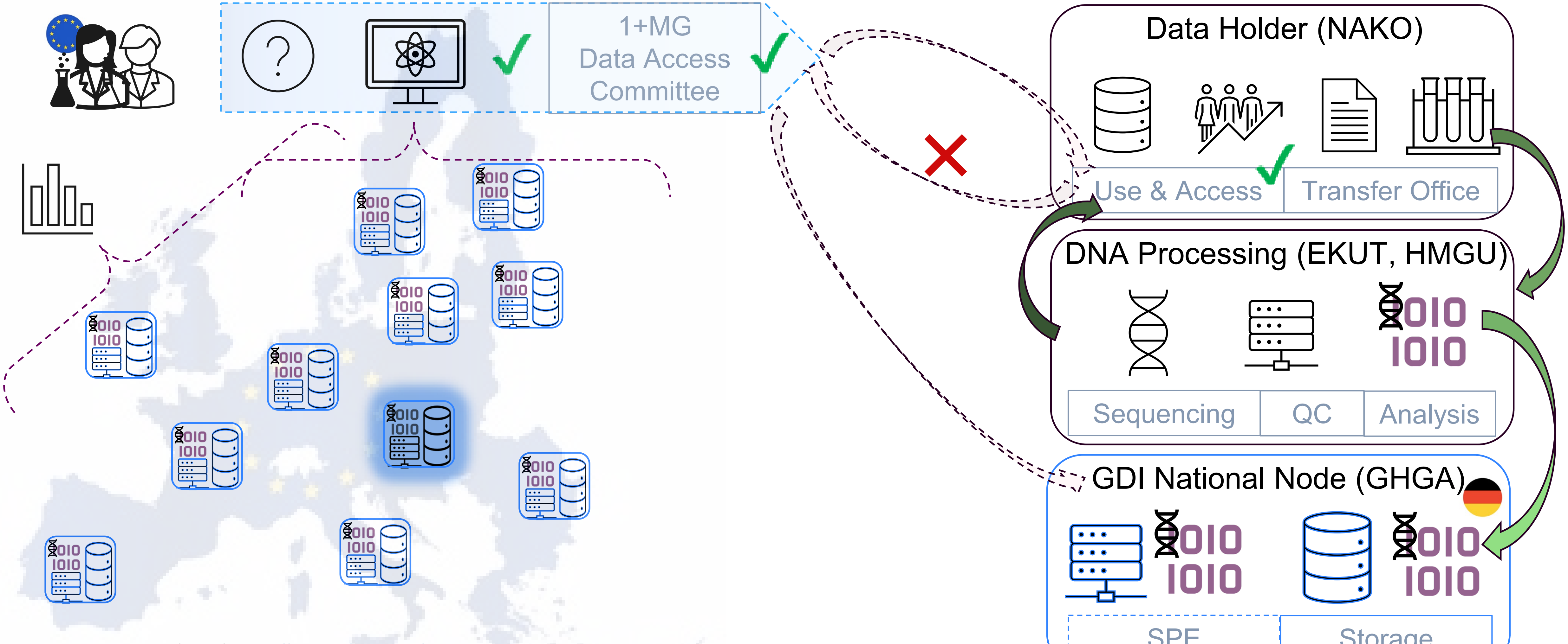
MAX DELBRÜCK CENTER
HELMHOLTZ MUNICH
dkfz. GERMAN CANCER RESEARCH CENTER IN THE HELMHOLTZ ASSOCIATION
HZI HELMHOLTZ Centre for Infection Research

NAKO-Nutzungsantrag (Forschungsprojekt):

Generierung von ca. **10.000 Gesamtgenom-Datensätzen aus NAKO DNA-Proben der Basisuntersuchung** und deren Verwendung für Ziele des GoE Projekts (Genome of Europe). (H. Grallert, C. Gieger)

GENOME OF EUROPE

Challenge 2 / Datenfluss / GoE / 1+MG data life cycle



1+MG Data Access Committee

Data Holder (NAKO)

Use & Access | Transfer Office

DNA Processing (EKUT, HMGU)

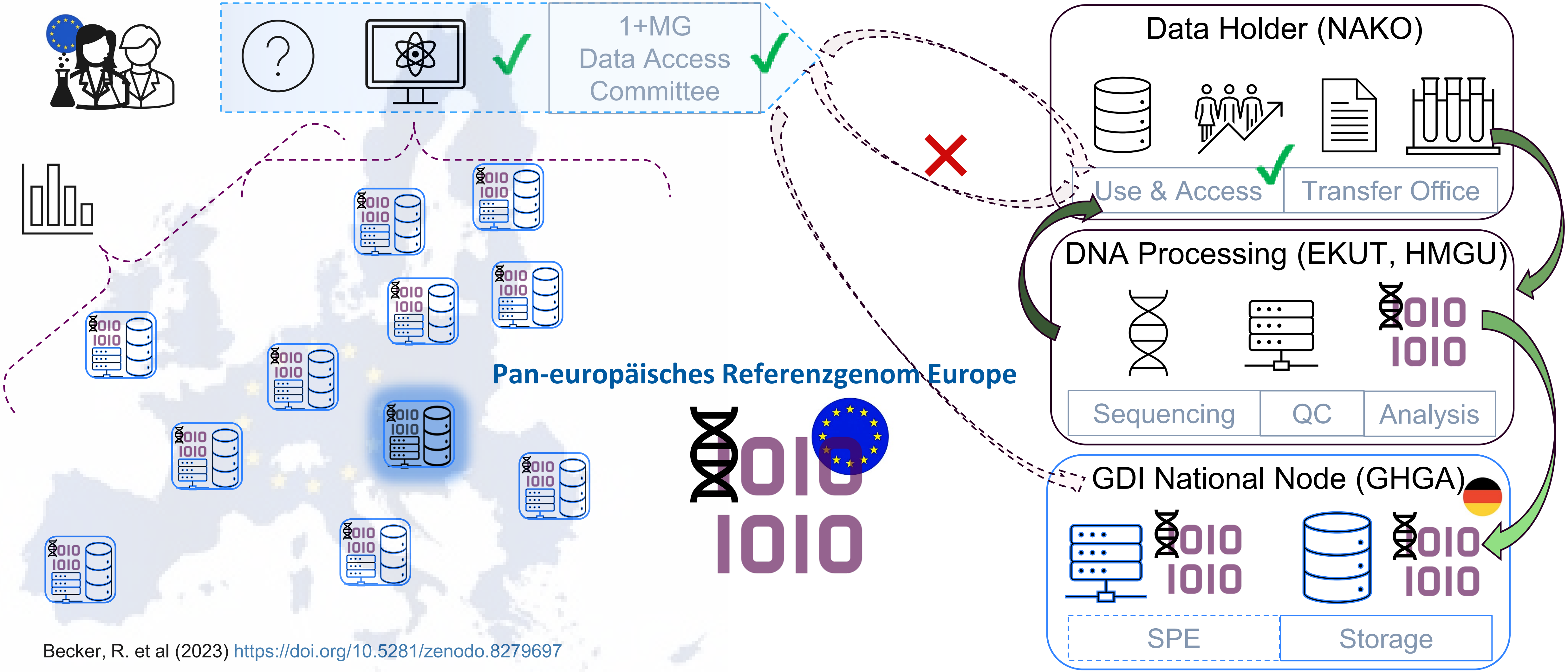
Sequencing | QC | Analysis

GDI National Node (GHGA)

SPE | Storage

Becker, R. et al (2023) https://doi.org/10.5281/zenodo.8279697

Challenge 2 / Datenfluss / GoE / 1+MG data life cycle



1+MG Data Access Committee

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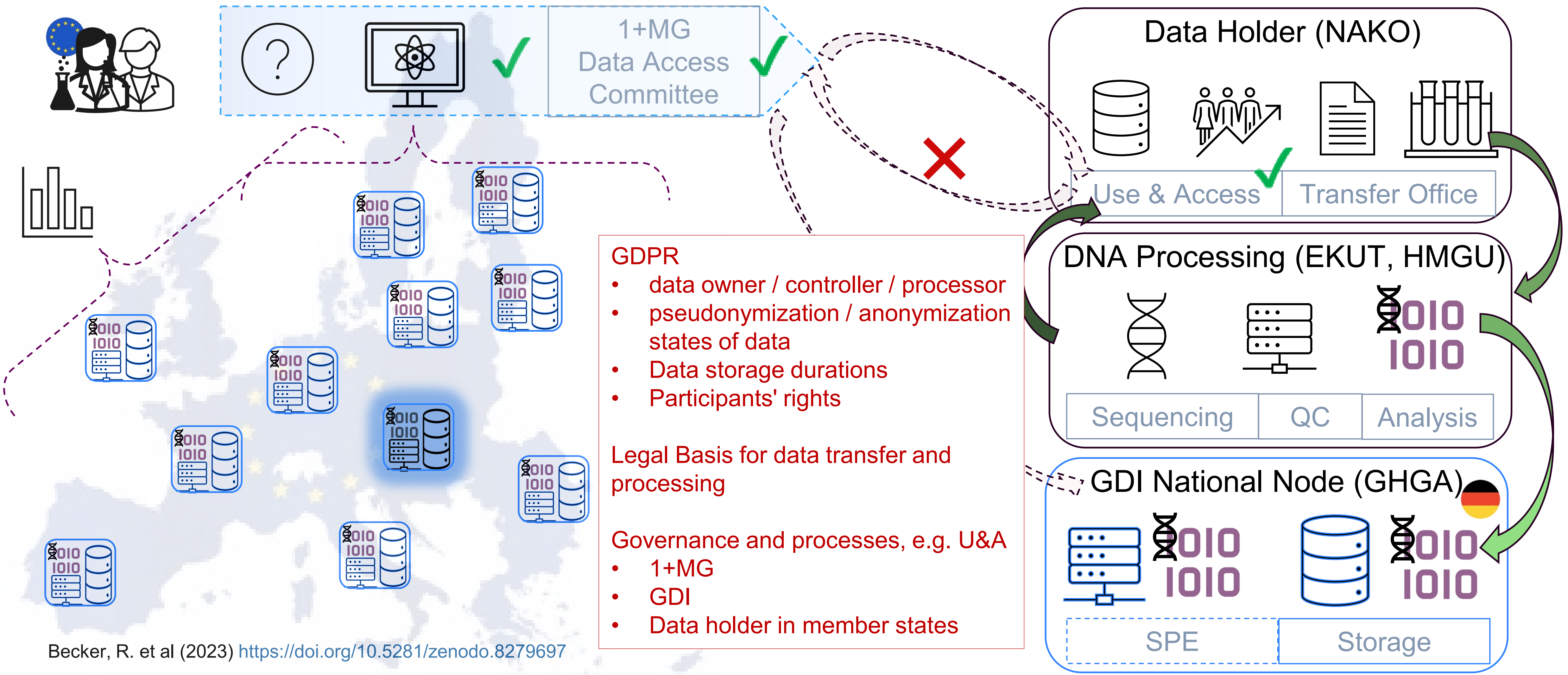
Pan-europäisches Referenzgenom Europe

Becker, R. et al (2023) https://doi.org/10.5281/zenodo.8279697

Challenge 2 / Datenfluss / GoE / 1+MG data life cycle



1+MG
Data Access
Committee

Data Holder (NAKO)

Use & Access | Transfer Office

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Sequencing | QC | Analysis

GDI National Node (GHGA)

SPE | Storage

GDPR
- data owner / controller / processor
- pseudonymization / anonymization states of data
- Data storage durations
- Participants' rights

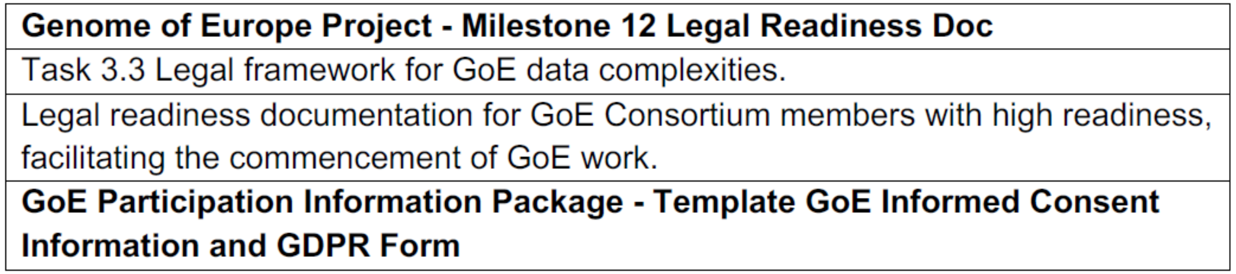
Legal Basis for data transfer and processing

Governance and processes, e.g. U&A
- 1+MG
- GDI
- Data holder in member states

Becker, R. et al (2023) https://doi.org/10.5281/zenodo.8279697

Challenge 3 / NAKO / Ethik und Recht / **ICF**

- Prüfung der NAKO-Einwilligungsunterlagen der Basis – Drittuntersuchung und entsprechende Anpassungen auf Basis des **WP3 Legal Readiness Document (working draft)**



Genome of Europe Project - Milestone 12 Legal Readiness Doc
Task 3.3 Legal framework for GoE data complexities.
Legal readiness documentation for GoE Consortium members with high readiness, facilitating the commencement of GoE work.
GoE Participation Information Package - Template GoE Informed Consent Information and GDPR Form

  - Einwilligungserklärung der **NAKO-Drittuntersuchung (Genetik)**
  - Eigenständige Einwilligungsunterlagen zum Projekt „Genome of Europe“ notwendig?

- Personenbezogene Daten (Geschlecht, Alter, Ursprungsland)

- Abstimmungen mit der **NAKO-Geschäftsstelle** (L. Panreck, B. Bohn), **NAKO-Geschäftsführung** und dem **NAKO-Vorstand** (W. Lieb, A. Peters)

- **Umfassende Information der Teilnehmenden zum Projekt „Genome of Europe“**

Challenge 3 / NAKO / Ethik und Recht / **AI**

WP 3 Legal Readiness Document

Potential Risks

Specifically, the use of Artificial Intelligence (AI) will enable unanticipated forms of research that may turn out to be controversial. We will seek to mitigate any negative impact that may arise therefrom, in particular by complying with the protection measures set forth in the EU AI Act.

Processing of your data

We and our partners of the Genome of Europe Project will take special attention to the potential role of Artificial Intelligence (AI), which is in strong development and may aid our research but also bring forth novel challenges and risks in (genetic) data sharing and interpretation. We will seek to mitigate these risks by complying with the protection measures set forth in the EU AI Act.

In addition,
☐ YES, I agree to my genomic data to be included in analyses for the purposes of the Project using Artificial Intelligence (AI).
OR: ☐ NO, I do NOT agree to my genomic data to be included in analyses using Artificial Intelligence (AI).

‘AI Act’ VERORDNUNG (EU) 2024/1689, 13.06.2024, https://eur-lex.europa.eu/eli/reg/2024/1689/oj/eng

Art. 3: Ausdrucksbezeichnung

(1) "KI-System": ein maschinengestütztes System, das so konzipiert ist, dass es mit unterschiedlichem Grad an Autonomie betrieben werden kann und nach seiner Einführung Anpassungsfähigkeit zeigt, und das für explizite oder implizite Ziele aus den Eingaben, die es erhält, ableitet, wie es Ausgaben wie Vorhersagen, Inhalte, Empfehlungen oder Entscheidungen generieren kann, die physische oder virtuelle Umgebungen beeinflussen können;”

Challenge 3 / NAKO / Ethik und Recht / **IF**

WP 3 Legal Readiness Document

RIGHT TO RETURN OF INCIDENTAL FINDINGS

"Customised text to be inserted by GoE Partner. The answer to this question may vary across Genome of Europe Partners and will be source specific (research, screening or clinical). Therefore, each GoE Partner should insert its Partner specific answer here (e.g. your national/institutional local Incidental Findings Policy) here."

"In order to align your local Incidental Findings (IF) Policy as much as possible with the Incidental Findings Policy of the other GoE partners across the project, we recommend that you seek to inform your IF policy by the 1+MG Recommendations on Incidental Findings."

"Please note that reporting incidental findings becomes obligatory under the European Health Data Space Regulation ("EHDS")."

"Example information text:
As stated above, pursuant to the GDPR your right to have your data erased shall not apply if, after your withdrawal of your consent, there is another legal ground for the processing, or if the processing is necessary for research purposes. To the extent your data has not been erased upon either your withdrawal of your consent or upon the end of the project, we will become obliged, as health data users under European law, to inform you about "significant findings" in your DNA."

"Your DNA sequence data that you receive from us and any other information that you may receive from us, is not intended to replace in any way professional medical advice, diagnosis or treatment. We cannot make any guarantees about the accuracy or completeness of our analysis or research of your DNA.
You may not use any information you receive from us or other GoE Project Partners for any medical or clinical purpose, unless the relevant DNA sequence or other data, including any preliminary research interpretations or findings are first confirmed by a licensed healthcare professional."

In addition,
☐ YES, I agree to be informed about Incidental Findings in my DNA. OR:
☐ NO, I do NOT agree to be informed about Incidental Findings in my DNA.

NB: GoE partners who do not allow for opt-out of, e.g., actionable incidental findings or who make different choices available for actionable versus nonactionable findings, should adjust this part according to their specific policy

Challenge 3 / NAKO / Ethik und Recht / **EHDS**

WP 3 Legal Readiness Document

‘Under the European Health Data Space Regulation ("EHDS"), we will become under the obligation to make your genomic data (and any other health data we may hold about you), available for use by academic researchers, government bodies, international organisations and commercial parties ("Health Data Users"), subject to your opt out, or, as may be the case in your country, your opt in.’

- **Upcoming public consultations on DRAFT guidelines** 30 SEPT – 30 NOV 2025, e.g.
    - Draft guideline for data holders on making personal and non-personal electronic health data available for reuse
    - Guideline for Health Data Access Bodies on **data minimisation, pseudonymisation, anonymisation and synthetic data**
    - Draft guideline for Health Data Access Bodies on implementing **opt-out from the secondary** use of health data
    - Draft guideline for Health Data Access Bodies on implementing the **obligation of notifying the natural person on a significant finding from the secondary use of health data**

https://tehdas.eu/public-consultations/

Challenge 4 / Secondary Use of Genomic Data Beyond the GoE Project

Uses of GoE data

The use cases of GoE WP6

🟩 T6.1. Population structure analysis	✓
🟩 T6.2. Single variant lookups	✓
🟩 T6.3. Imputation server infrastructure and testing	✓
🟩 T6.4. Polygenic risk score distributions	✓
🟩 T6.5. Investigate the added value of lrGS compared to srGS	✓
🟩 T6.6. Plan for future GoE applications	⚠
🟨 Any other research/medical/etc use of GoE data	N/A

Making GoE data available for future reuse

🟩 Through the infrastructure and governance established under the 1+MG initiative	⚠
🟨 Through the infrastructure and governance of the GoE partner that collected the data	N/A
🟨 Through the infrastructure and governance of any other platform/repository/hub/etc	N/A

🟩 = Within the scope of the GoE Project*

🟨 = Outside the scope of the GoE Project*

✓ = the purpose and its associated data processing activities are sufficiently well-defined to enable most GoE partners to comply with their legal obligations.

⚠ = the purpose and its associated data processing activities are not yet well-defined, making full compliance challenging (as of mid-2025)

** As of mid-2025. (Could change in the future, subject to the Consortium Agreement and/or DoA amendments)*

Summary / Acknowledgement

Vielen Dank für Ihre Aufmerksamkeit!

Pan-europäisches Referenzgenom Europe

GENOME OF EUROPE

Olga TZORTZATOU
Davit CHOKOSHVILI

GESUNDHEITS-STUDIE

Leo PANRECK
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Wolfgang LIEB
Annette PETERS

Universitätsklinikum Tübingen

Olaf RIEß

HELMHOLTZ MUNICH

Julia GROTH
Monika KRAUS
Harald GRALLERT
Christian GIEGER

Nationales Referenzgenom Germany

2028

Bundesministerium
für Forschung, Technologie
und Raumfahrt

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