

Data management challenges and solutions in closing the loop from healthcare to research and back



eCLINICAL RESEARCH: GETTING VIRTUAL AND PERSONAL

Innovative solutions for the use of electronic medical data to serve research purposes

**30-31
May**

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Content

- Background
 - AIT
 - data protection regulations
 - Rare diseases
 - dimensions of data integration / record linkage
- Identity management & privacy preserving record linkage
- Examples for data integration in three dimensions
- Summary & Conclusion

AIT Austrian Institute of Technology

The largest applied research institute in **Austria**



Owner structure

50.46%

Republic of Austria

49.54%

Federation of Austrian Industries

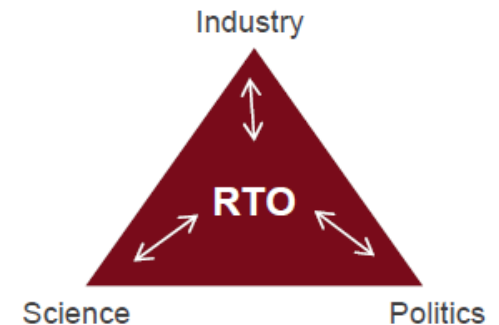
1300

Employees

Finance structure



Research and Technology Organisation



Health & Bioresources	Digital Safety & Security	Vision, Automation & Control
Low-Emission Transport	Technology Experience	Innovation Systems & Policy
Energy	Mobility Systems	

Digital Health Information Systems – Office Locations

- ~ 45 staff members at 3 locations



Graz



Hall in Tirol
(Innsbruck)



Vienna

The 4th dimension ...

- Sci-Fi
- Extra terrestrial
- Universal
- Relativity
- Time travel
- Confusing,
Unimaginable for 3D creatures like us
- ...

History of Regulations on data protection in research

- Declaration of Helsinki

- Privacy and Confidentiality

24. Every precaution must be taken to protect the **privacy** of research subjects and the **confidentiality** of their personal information.

- Good Clinical Practice (GCP)

- THE PRINCIPLES OF ICH GCP

2.11 The **confidentiality** of records that could identify subjects should be protected, respecting the **privacy** and **confidentiality** rules in accordance with the applicable regulatory requirement(s).

- General Data Protection Regulation (GDPR)

- Article 89 - Safeguards and derogations relating to processing for archiving purposes in the public interest, scientific or historical research purposes or statistical purposes

EU General Data Protection Regulation

- Regulation (EU) 2016/679
- **Article 4, Definitions**
 - *‘pseudonymisation’ means the processing of personal data in such a manner that the personal data can no longer be attributed to a specific data subject without the use of additional information, provided that such additional information **is kept separately and is subject to technical and organisational measures** to ensure that the personal data are not attributed to an identified or identifiable natural person;*



Privacy & Confidentiality

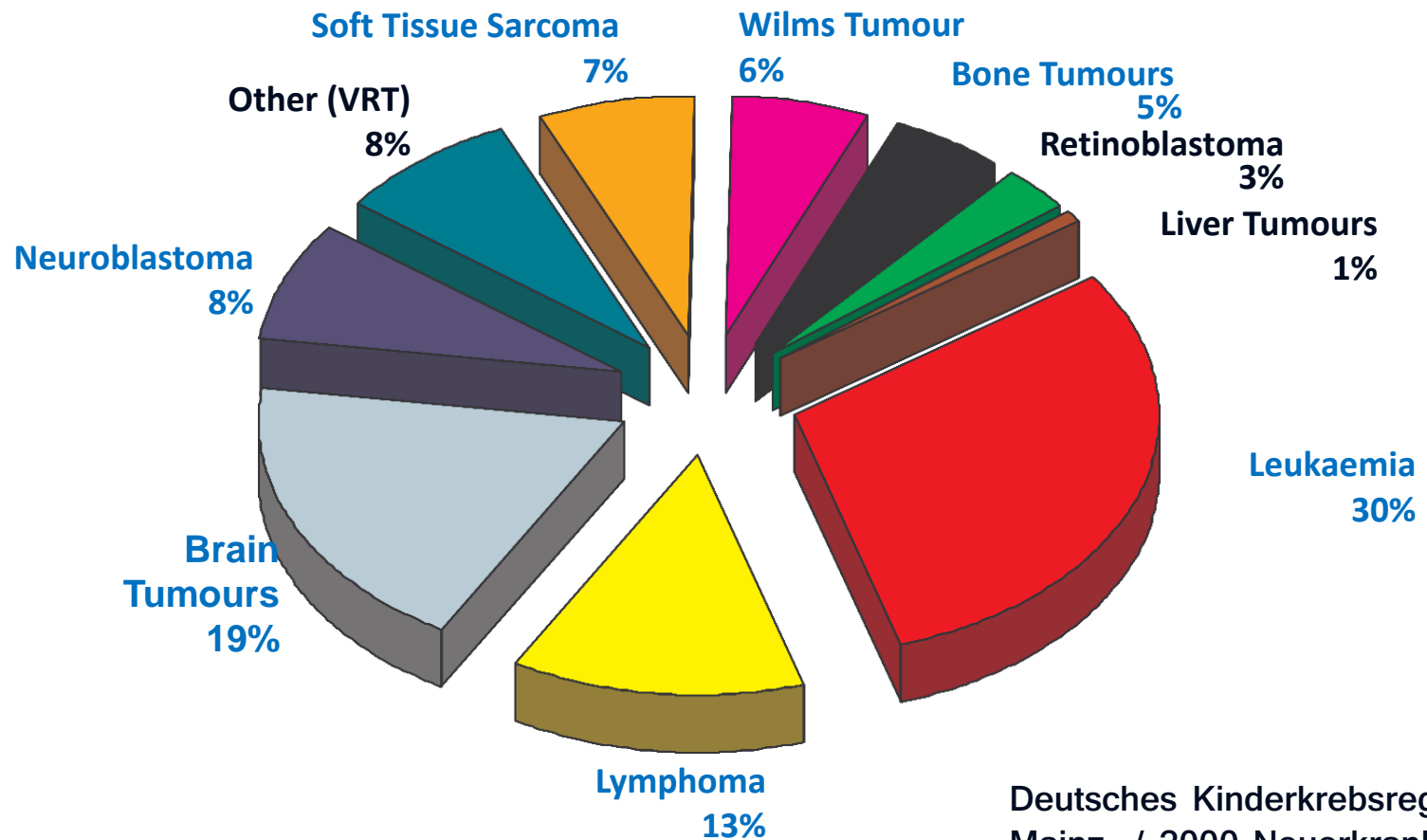
- Confidentiality is about the data
 - → one of the three dimensions in IT Security
- Privacy is about the subjects identity
 - De-identification
 - Pseudonymisation
 - Anonymisation
- Data Protection in 4 dimensions = management of
 1. Availability
 2. Integrity
 3. Confidentiality
 4. **Identity**

Dimensions of data management in clinical trials

1. Data Collection
2. Data Analysis
3. Data Archiving
4. **Data Protection**

Special Context - Rare Disease, e.g. Childhood Cancer

- Rare Disease Definition: Prävalenz < 1 in 2000 www.eurordis.org
- Childhood (< 15 years) Cancer Incidence in Europe: 1 in 6250
- Kaatsch et al. Cancer Treat Rev. 2010, 36(4):277-85. Epidemiology of childhood cancer.
- In Austria: ~ 185 cases per year (Statistik Austria)



Deutsches Kinderkrebsregister
 Mainz / 2000 Neuerkrankungen
 pro Jahr

What are European Reference Networks?

http://ec.europa.eu/health/ern/policy/index_en.htm

- Directive 2011/24/EU on patients' rights in cross-border healthcare
- Article 12 of the directive is concerned with supporting MS with the development of so called European Reference Networks (ERN)
- The European Reference Networks (ERNs) **bring together** highly specialised healthcare providers from different Member States. They help provide **affordable, high-quality and cost-effective healthcare** to patients with conditions requiring a **particular concentration of resources or expertise**.



ICT infrastructures for biomedical research networks



- **SIOPEN-R-NET** – Thematic Network (FP5)
 - SIOP European Neuroblastoma Research Network
 - AIT: design and operation of IT Infrastructure



- **ENCCA** - Network of Excellence (FP7)
 - European Network for Cancer in Children & Adolescents
 - AIT: Virtual Institute Information Portal



- **ExPO-r-Net** (European Reference Network – DG SANTE)
 - European Expert Paediatric Oncology Reference Network for Diagnostics and Treatment
 - AIT: ICT strategy and interoperability architecture

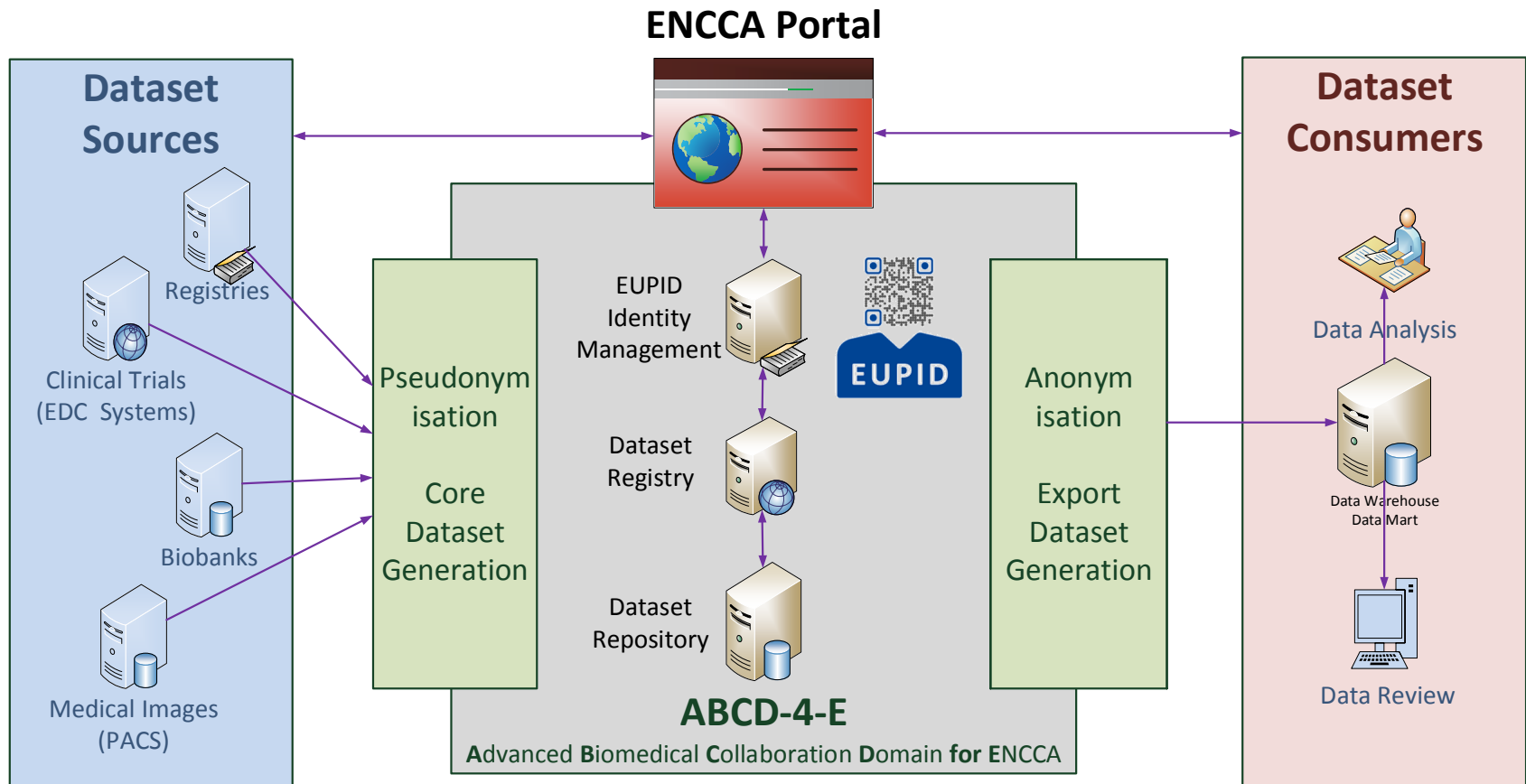
ENCCA

European Network for Cancer research in Children and Adolescents

- FP7 Network of Excellence
- 2011-2015
- Coordinator: St. Anna
Kinderkrebsforschung
(Prof. Ruth Ladenstein)
- AIT: ICT WP Lead:
„Establishing the Virtual
Institute“
- www.encca.eu

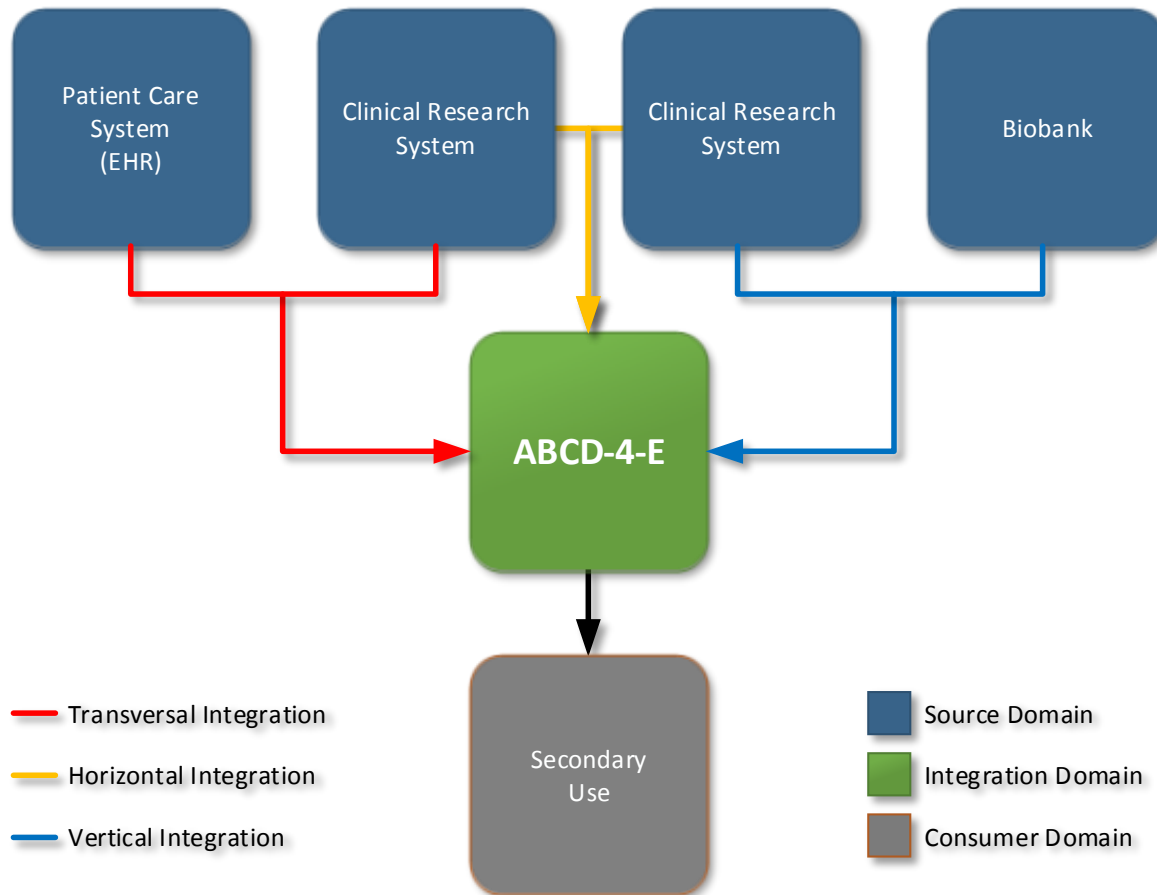


Advanced Biomedical Collaboration Domain 4 ENCCA



Nitzlader M, Falgenhauer M, Gossy C, Schreier G. Architecture for an advanced biomedical collaboration domain for the European paediatric cancer research community (ABCD-4-E). *Studies in health technology and informatics*. 2015;212:167-74. PubMed PMID: 26063273.

Different dimensions of data linkage



ABCD-4-E =

**Advanced
Biomedical
Collaboration
Domain**

For

ENCCA

M. Nitzlnader, M. Falgenhauer, C. Gossy, and G. u. Schreier, "Architecture for an Advanced Biomedical Collaboration Domain for the European Paediatric Cancer Research Community (ABCD-4-E)," in *Stud Health Technol Inform - Proceedings of the eHealth2015 - Health Informatics meets eHealth*, 2015, pp. 167-174.

Different dimensions of integration

- Horizontal integration
 - Linking different clinical trials
- Vertical integration
 - Linking clinical research and Biobanking
- Transversal integration
 - Bridging the gap between healthcare and research
- The 4th dimension
 - Reach out to the patient (electronic Patient Reported Outcomes)

EUPID ... a versatile acronym

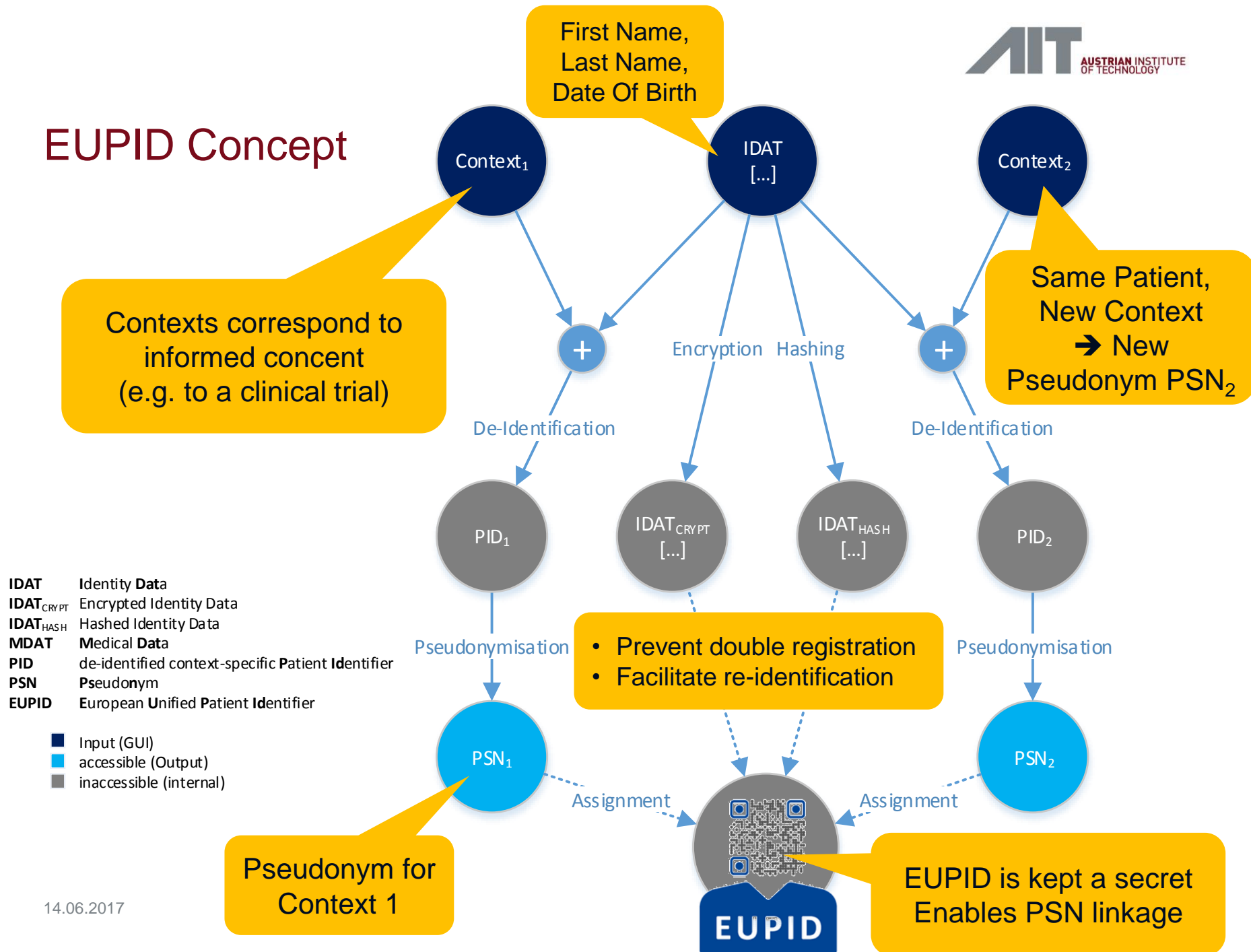
- **E**NCCA **U**nified **P**atient **I**Dentity
- **E**Uropean **P**atient **I**Dentity
- **E**lectronic **U**niversal **P**atient **I**Dentity



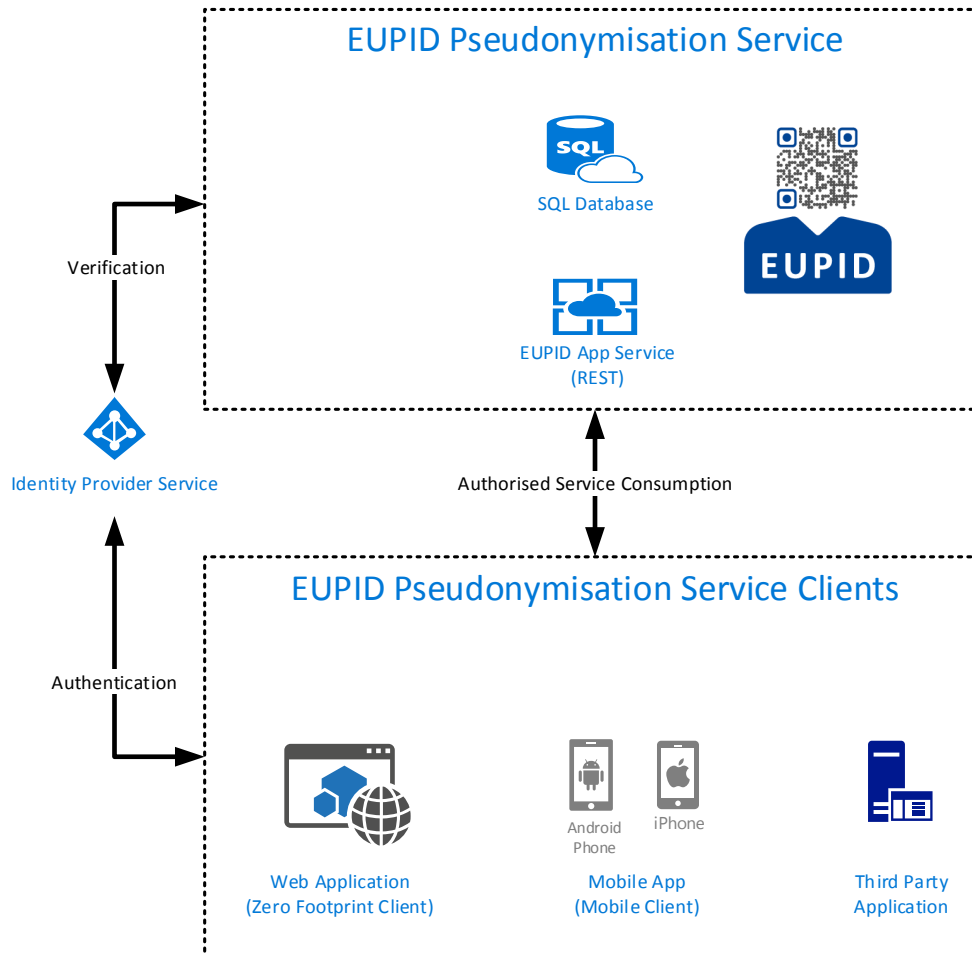
ENCCA → EUPID Core Requirements

1. Prevent duplicate registration of patients
2. Avoid publishing a transparent universal patient ID → use different pseudonyms for different contexts
3. Provide a method to link pseudonyms from different contexts, if needed
4. Preserve the possibility for re-identification by a trusted third party
5. Non-functional requirements:
Accessibility, Regulatory, Affordability, ...

EUPID Concept



EUPID Schema



*M. Nitzlnader and G. Schreier,
 "Patient identity management for
 secondary use of biomedical
 research data in a distributed
 computing environment," Stud
 Health Technol Inform, vol. 198, pp.
 211-8, 2014.*

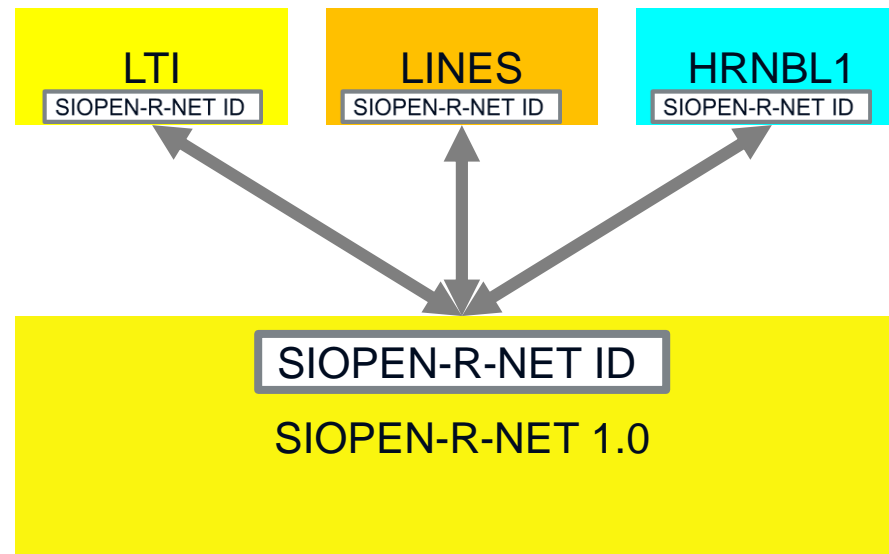
**No unencrypted personal data are
 stored anywhere in the system!**

**PRIVACY by DESIGN
 PRIVACY by DEFAULT**

Horizontal Integration

- Linking different clinical trials in a backward compatible way

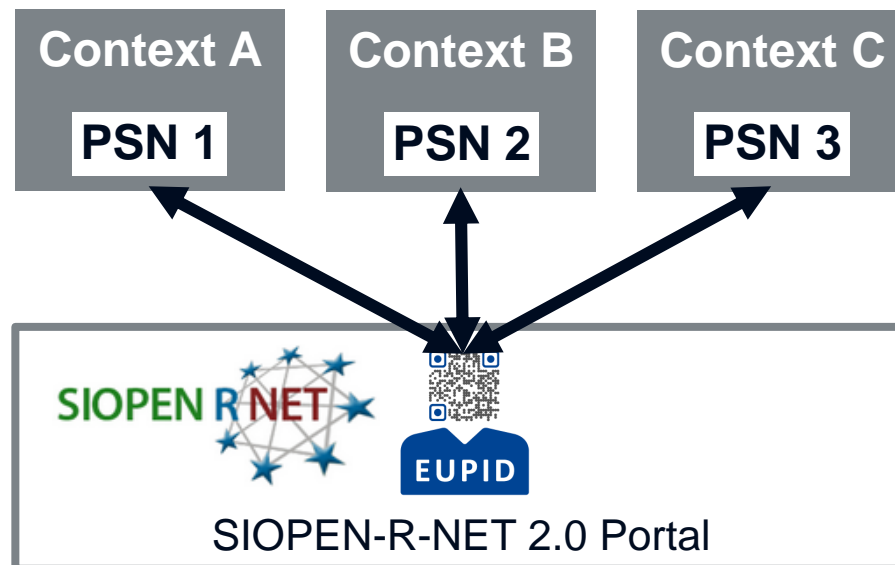
SIOPEN-R-NET Portal 1.0 –...



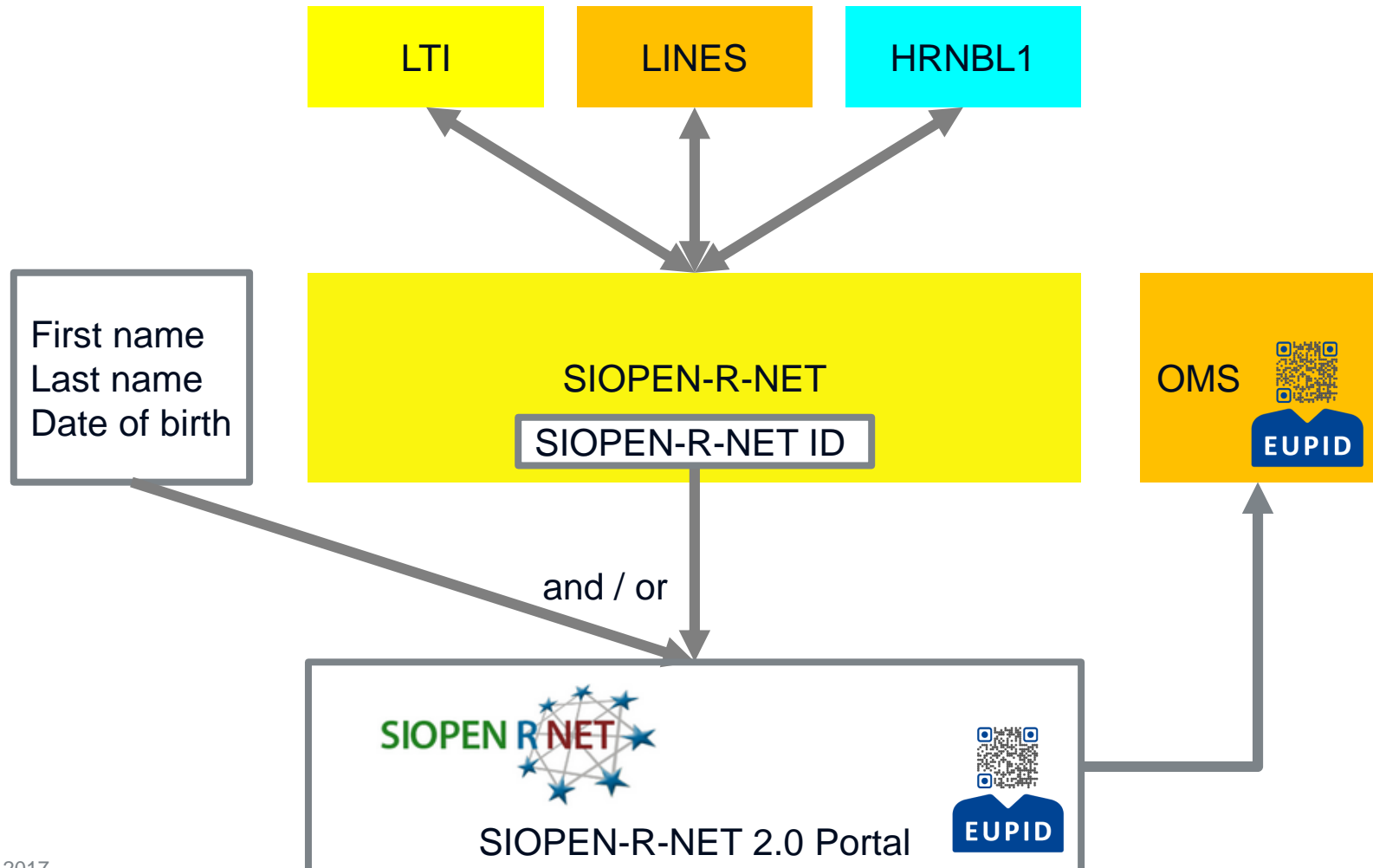
- Clinical Trials shared a unique identifier (SIOPEN-R-NET ID) for easy record linkage

SIOPEN-R-NET Portal 2.0

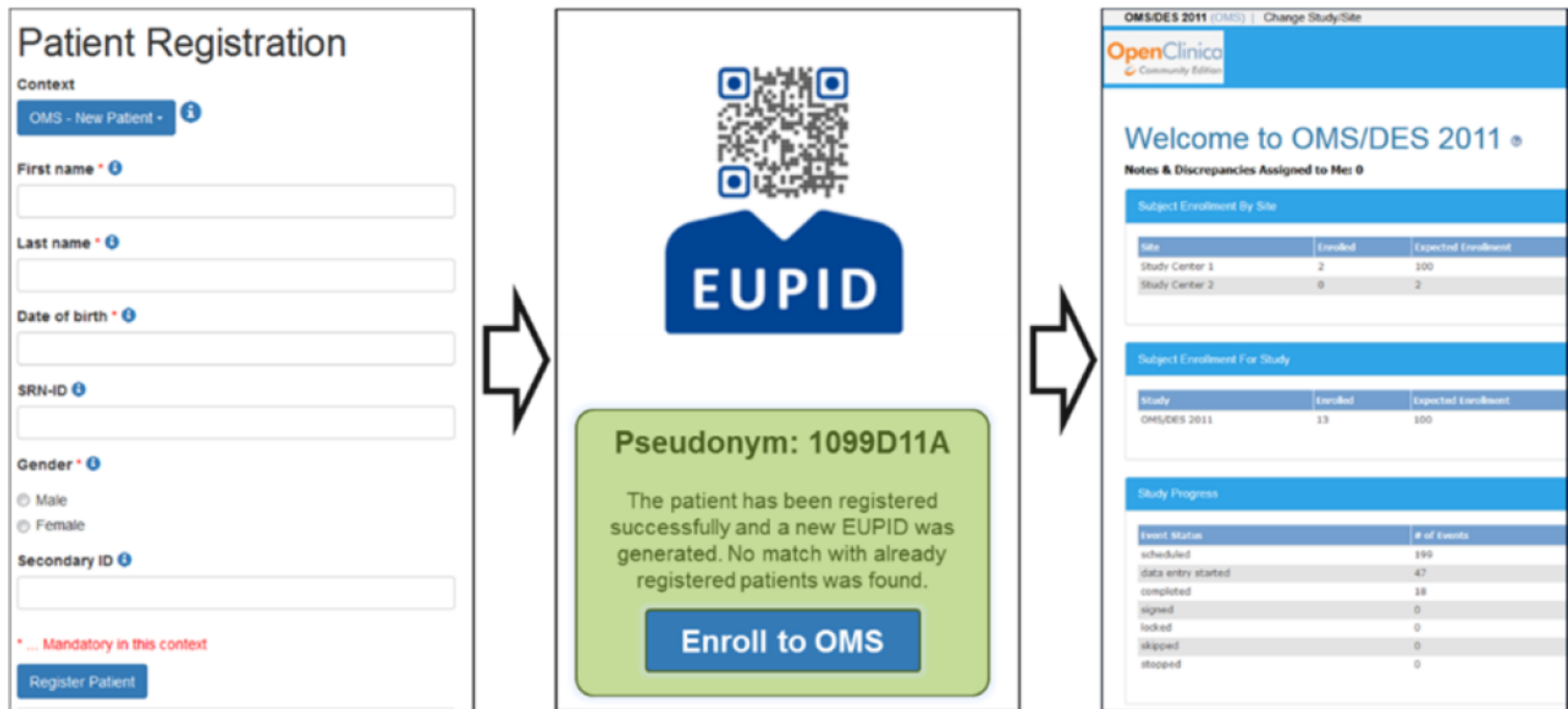
- SIOPEN-R-NET Portal 2.0 is based on EUPID
- Patients receive a unique ID for each clinical trial (data collecting project)



SIOPEN-R-NET Portal & Clinical Trials & EUPID



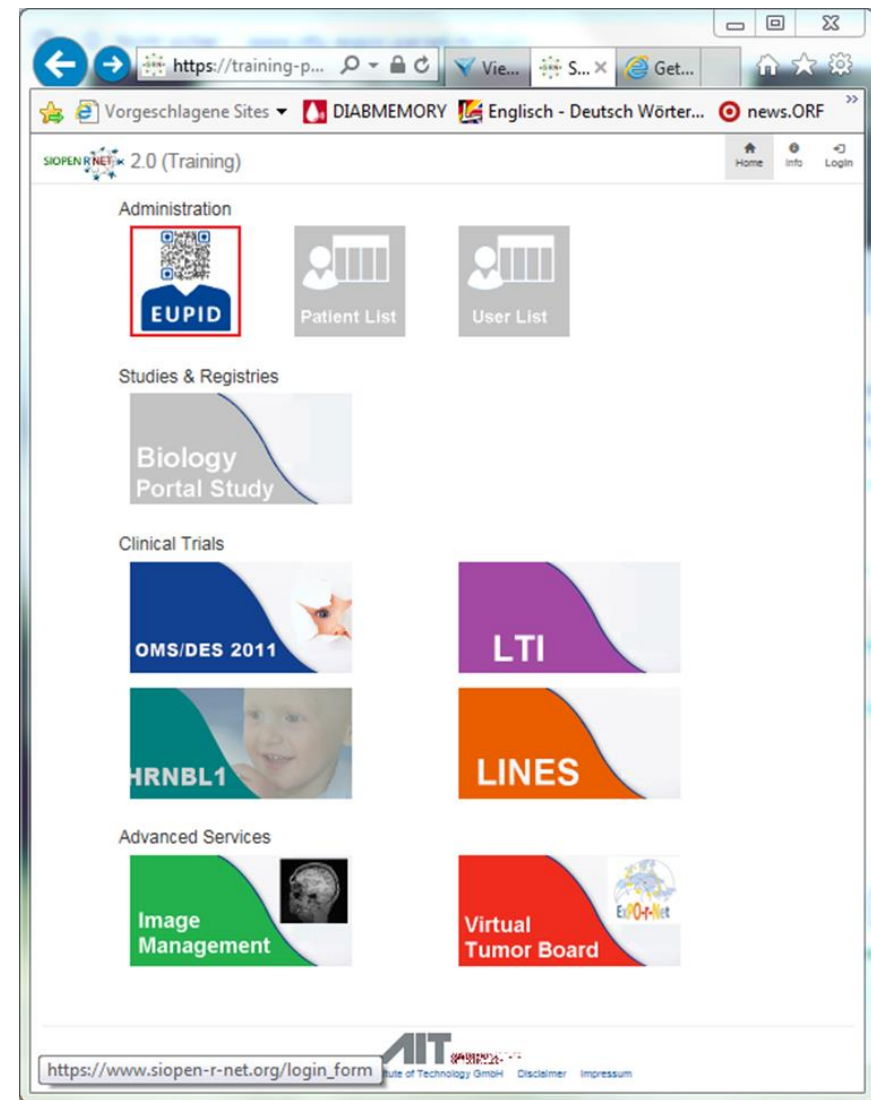
SIOPEN-R-NET Portal 2.0 & EUPID – link to clinical trial



Hayn D, Falgenhauer M, Kropf M, Nitzlnader M, Welte S, Ebner H, Ladenstein R, Schleiermacher G, Hero B, Schreier G. IT Infrastructure for Merging Data from Different Clinical Trials and Across Independent Research Networks. *Stud Health Technol Inform.* 2016;228:287-91

EUPID Demonstration

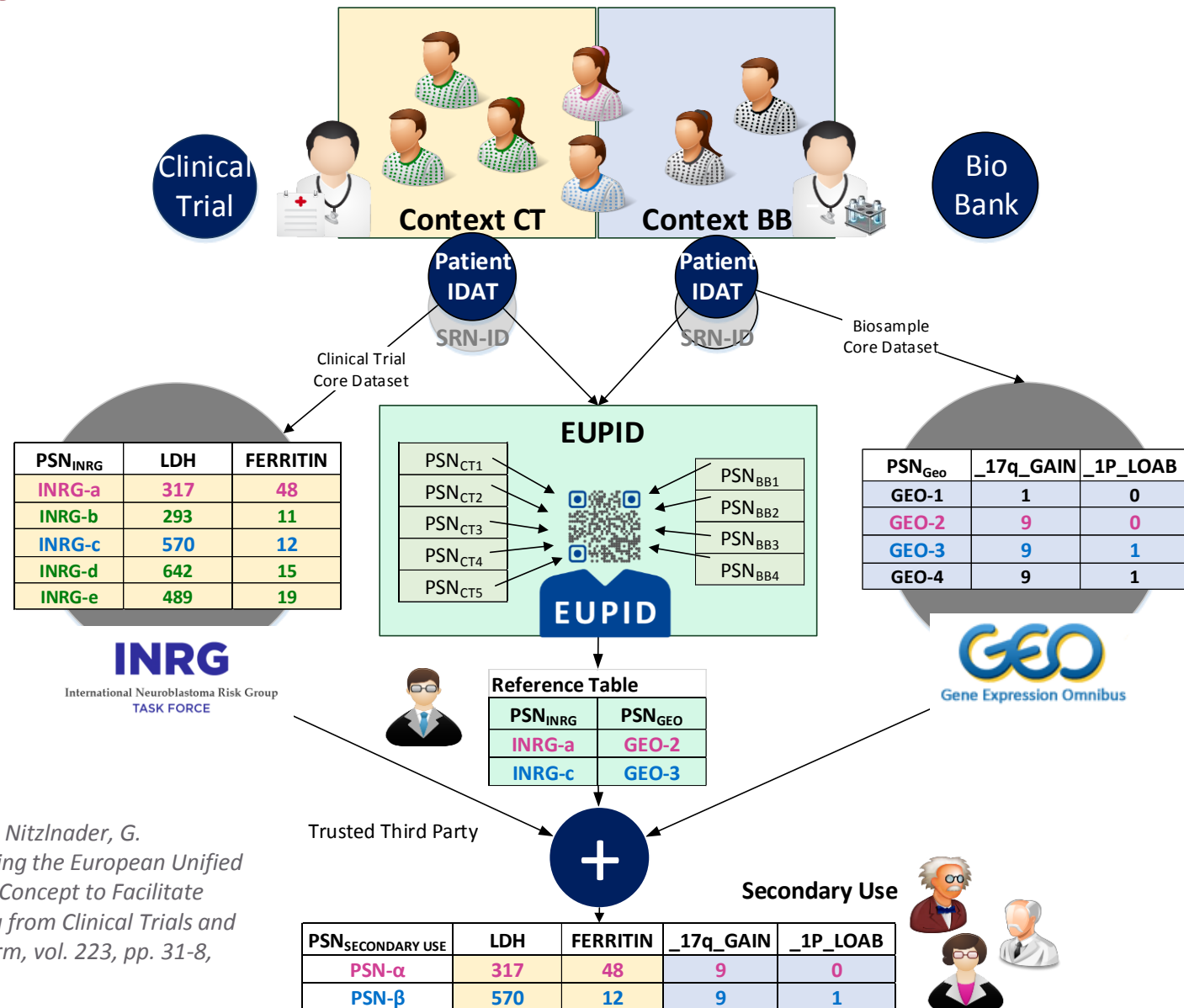
- Login as a registered user
- Register a patient to a clinical trial context
 - Using firstName, lastName, dateOfBirth
 - (Using an existing, unique ID)
- Enrolling the registered patient to a third party system (clinical trial)
- Adding a small typo – check system reaction



Vertical Integration

- Linking clinical trials and biobanking (clinical research and basic science)

Pilot data integration with EUPID



H. Ebner, D. Hayn, M. Falgenhauer, M. Nitzlnader, G. Schleiermacher, R. Haupt, et al., "Piloting the European Unified Patient Identity Management (EUPID) Concept to Facilitate Secondary Use of Neuroblastoma Data from Clinical Trials and Biobanking," *Stud Health Technol Inform*, vol. 223, pp. 31-8, 2016.

Transversal Integration

- Linking Clinical Research and Healthcare

Already available Tools from ENCCA

- EUPID – European Patient IDentity Management Service
 - <https://eupid.eu>
- Survivorship Passport – Patient Summary



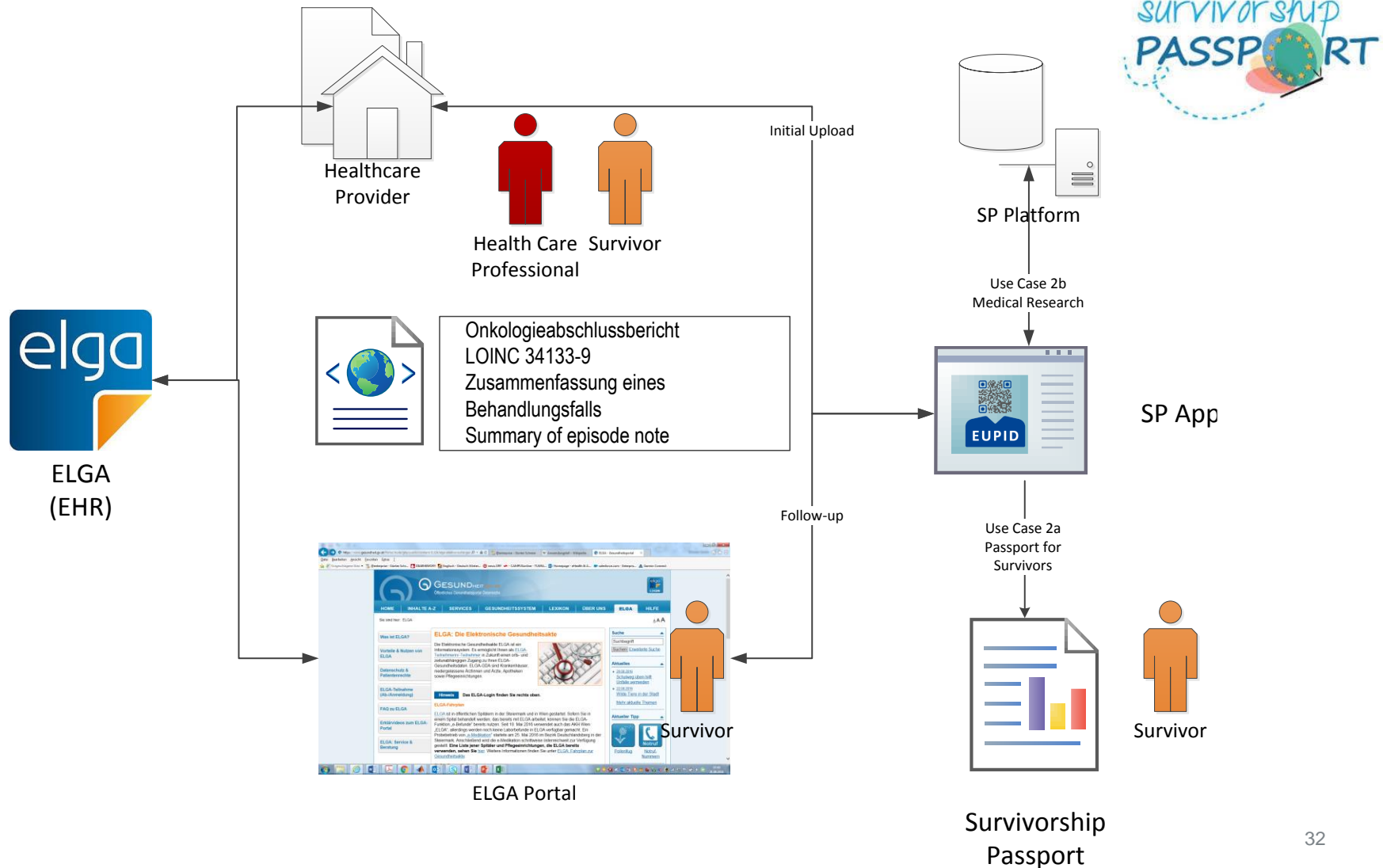
R. Ladenstein, M. Schrappe, K. Pritchard-Jones, Z. Dobai, S. Essiaf, P. Kearns, *et al.*, "ENCCA - EUROPEAN ACTIVITIES AND ACHIEVEMENTS WITH POTENTIAL INTEREST OUTSIDE OF EUROPE," *Pediatric Blood & Cancer*, vol. 62, pp. S202-S202, Nov 2015.

How to make the Survivorship Passport „fly“?

- Aim – better healthcare for children with cancer
 - Continuity of Care
 - Better management of long-term effects
 - Enhance „Late Effects“ research
- In Austria by leveraging the existing eHealth infrastructure
 - ELGA (Elektronische Gesundheitsakte)



From ELGA to Survivorship Passport



Survivorship Passport Concept

- ... how the Survivorship passport can be implemented in the Austrian Healthcare system, compliant with existing regulations (data protection, healthcare/ELGA)
- ... makes use of previously developed components
 - Survivorship Passport Platform
 - EUPID
- ... has been handed-in to the Austrian Ministry of Health



Ebner H, et al. A Concept to Bridge the Gap Between Health Care and Research in Pediatric Oncology based on EUPID and Survivorship Passport, Applied Clinical Informatics, submitted

Closing the virtuous cycle



Summary and Conclusion

- Data protection and privacy regulations pose increasing challenges to in Biomedical Research and Healthcare.
- Systems like EUPID allow for controlled identity management
 - privacy preserved record linking (PPRL) in different dimensions
 - featuring **privacy by design** and **privacy by default**.
- Identity Management ...
- the fourth dimension of data protection?