Federal Institute
for Drugs
and Medical Devices

24th DGRA Annual Congress

The New Health Ecosystem: Medicinal Products, Devices and Big Data – are Regulators prepared?

Prof. Dr. Karl Broich, President BfArM

27th June 2022

Overview

- The growing eHealth ecosystem
- From Real World Data to Real World Evidence – examples from regulator`s perspective
- European Network Regulatory Strategy – Fostering Innovation and future-proofing system
- „Data Initiatives“ at BfArM and on EU level: „Health Data Lab („FDZ“), DiGA, DARWIN, EHDS,…
- Interoperability: Key connector in a growing eHealth World
- Conclusion

Federal Institute
for Drugs
and Medical Devices

“Health care can become more resilient, agile and innovative by shifting to digitally enabled business models with data at the core”

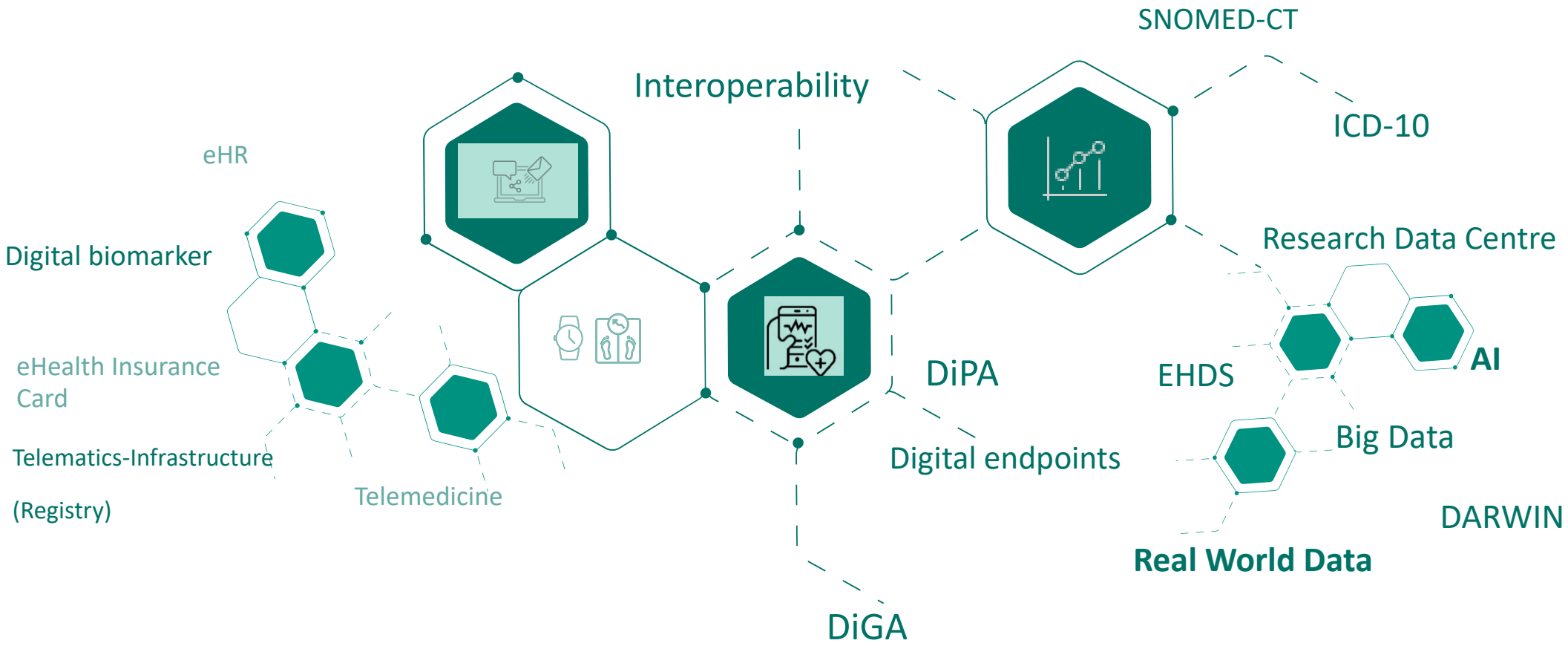
- How do we use the data that is generated in safe and meaningful ways?
- What is the right data strategy to ensure that operations will be data and AI-driven, for predictive models of care?
- What opportunities exist for partnerships with technology players to build out the necessary technical capabilities for greater data tractability and to take advantage of enabling data sets?

clinical information

care workers, at the point of care

https://www.ey.com/en_gl/smart-health/five-trends-shaping-health-care-s-data-driven-future

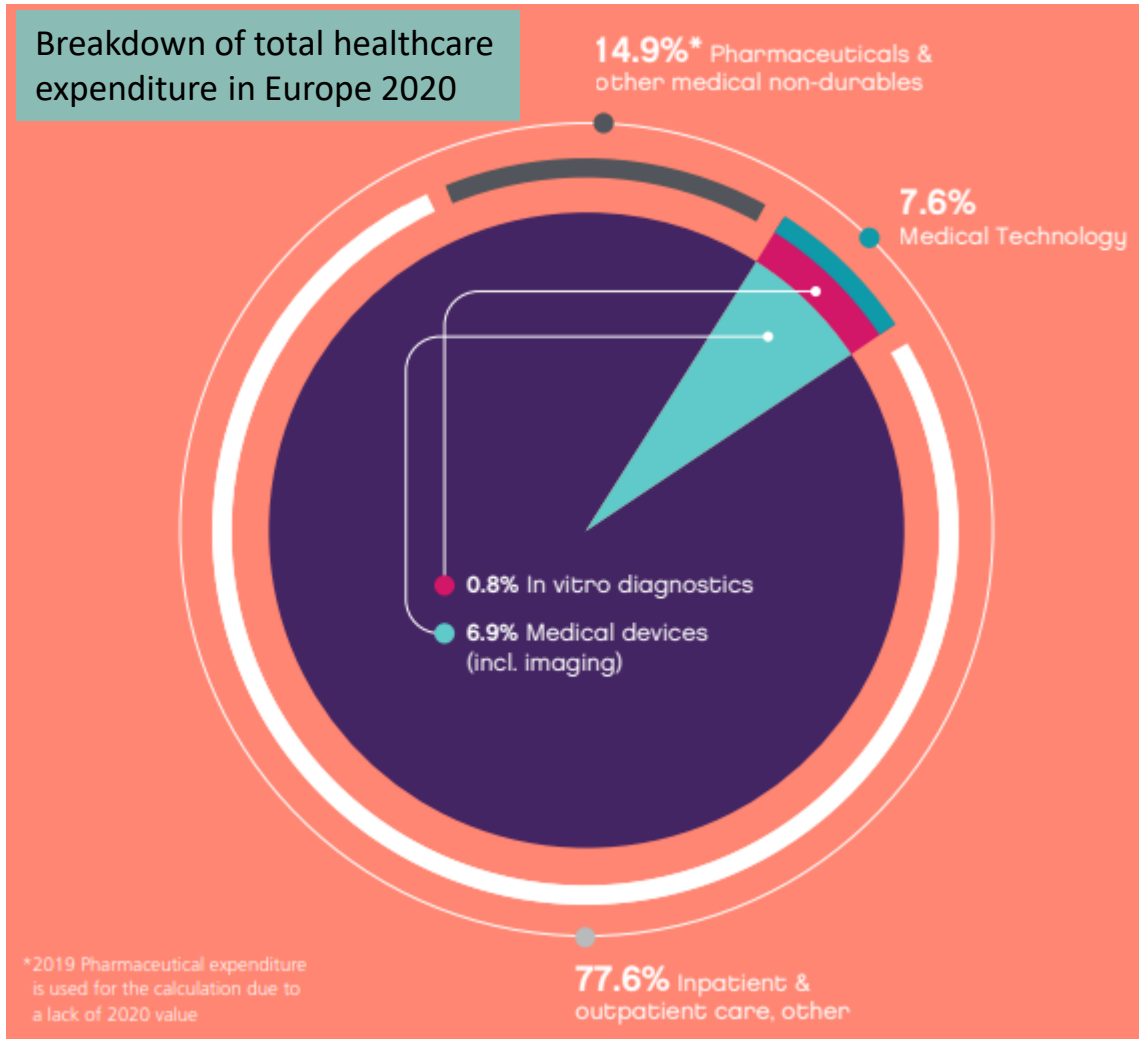
A world moving from „1 product – 1 indication“ to a growing connected **e-health ecosystem**



Federal Institute for Drugs and Medical Devices

...with an increasing (digital) device market...

- New MDR/ IVDR in implementation
  - Notified Bodies
  - New Risk Classifications
  - Certification of New Products
  - Renewance of CE Mark
- Borderline Products



MedTech Europe's Facts and Figures 2021; https://www.medtecheurope.org/resource-library/medtech-europes-facts-and-figures-2021/

Real World Data (RWD) in Regulatory-decision making

(Inter)national collaboration

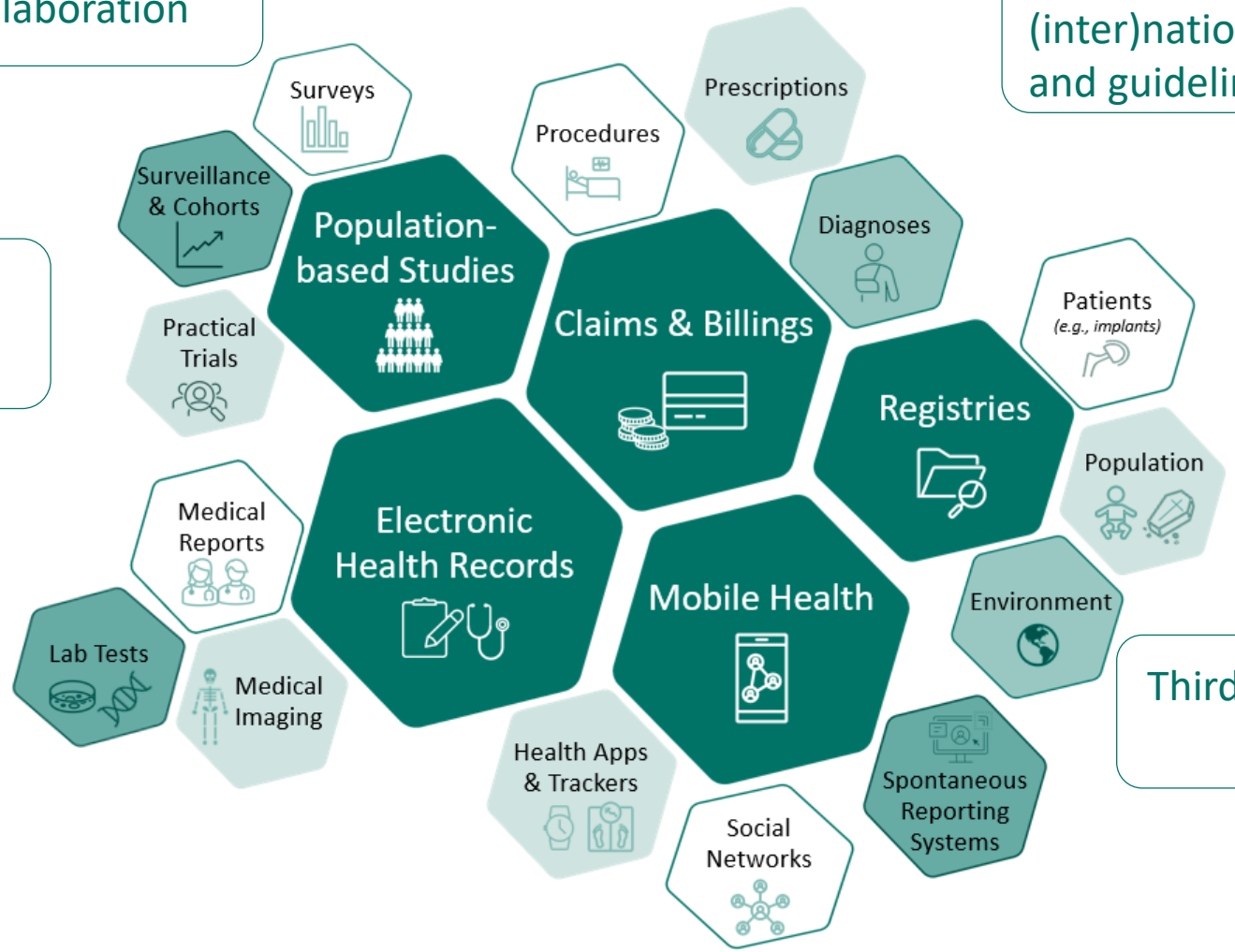
Involvement in (inter)national committees and guidelines

New methods for use of RWD

BfArM Workstream RWD

AI infrastructure at BfArM

Third-party funded projects



Federal Institute for Drugs and Medical Devices

RWD/ RWE- Working definition by EMA and applications

- Real-World Data (RWD): “routinely collected data relating to patient health status or the delivery of health care from a variety of sources other than traditional clinical trials”
- Real-world evidence (RWE): “information derived from analysis of real-world data”
- Analysis of RWD can inform regulatory decision-making throughout the product lifecycle, including scientific advice, authorization, and effectiveness and safety, e.g. Project DARWIN EU®

Example: RWE can provide different benefits to CHMP depending on the nature of the regulatory procedures

Committee	Procedure	High potential questions to be addressed	Example Use Case
CHMP	Initial MAA	• Disease epidemiology • Current clinical management • Support the planning & review of applicant studies	• Standard of Care in Europe and more ambitiously an analyses of the prognoses with current standard of treatment • Natural history of disease • RWE could support the decision making around submitted and/or mandated post-approval studies.
	Variations Type II Extension of Indications (90-days TT)	• Disease epidemiology • Current clinical management	Generate evidence on the actual clinical standard of care in different populations ○ How patients are diagnosed and treated ○ Treatment patterns ○ Characterisation of real-world drug use ○ Amount and duration of exposure ○ Changes over time and across Member States ○ Current indications and off-label use

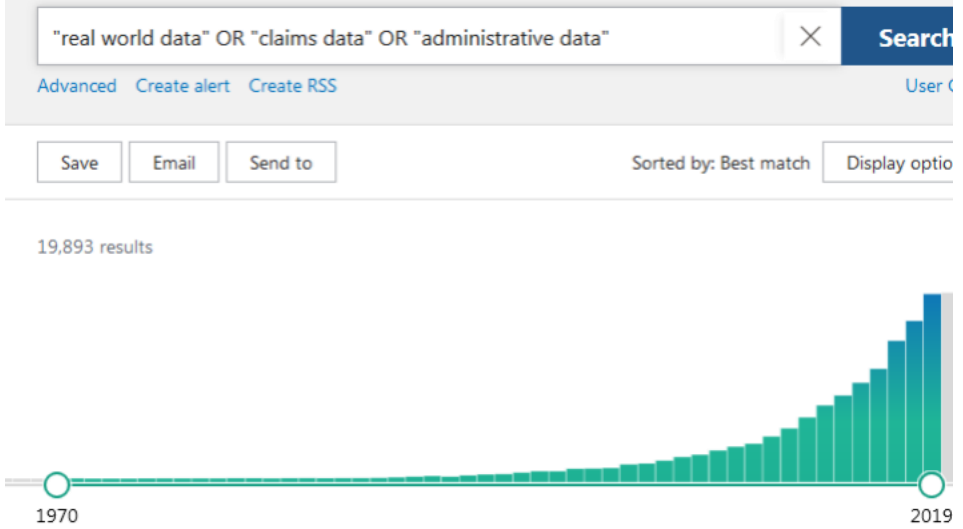
Federal Institute for Drugs and Medical Devices

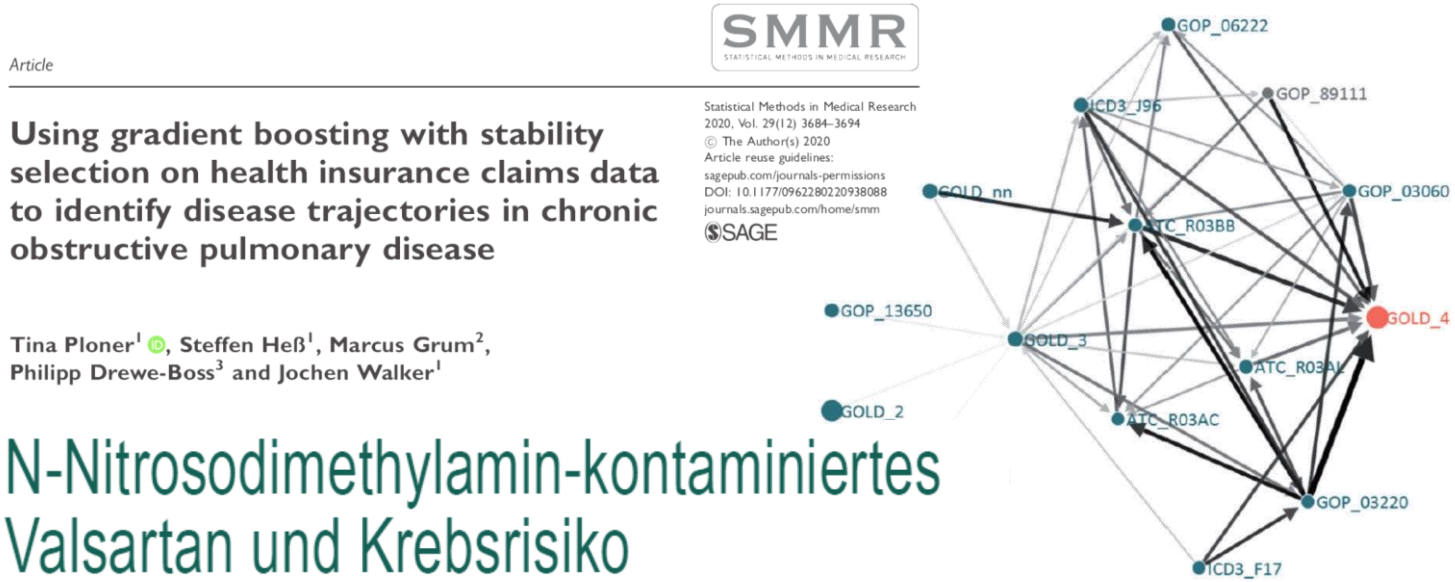
RWD - from Public Health Insurance

- Population-based, administrative, longitudinal cohorts
- Information from different health care sectors
- Established code systems, e.g. ICD, ATC, OPS
- Information including,
  - Personal information (e.g. gender, date of birth/ death, insurance status, residence [PLZ])
  - Prescriptions (e.g. ATC, PZN, date)
  - Outpatient data (e.g. quarterly diagnoses [ICD, OPS], costs)
  - Inpatient data (e.g. daily diagnoses, admission/ discharge date, procedures, treatment, costs)
  - Further data (e.g. level of care, doctor ID, region)

Usability of Real World Data - e.g. data from health insurance

- As the **volume of data increases**, so does the scope and usability of secondary data
- **Strongly increasing** research with health insurance data
- **Increasing impact** of secondary data
- **Modern methods** allow data-driven insights





N-Nitrosodimethylamin-kontaminiertes Valsartan und Krebsrisiko

Eine longitudinale Kohortenstudie mit deutschen Krankenkassendaten

Willy Gomm, Christoph Röthlein, Katrin Schüssel, Gabriela Brückner, Helmut Schröder, Steffen Heß, Roland Frötschl, Karl Broich, Britta Haenisch

Federal Institute for Drugs and Medical Devices

Regulatory research with RWE – another example

Project Covid-risk

- Pharmacoepidemiological analyses on medication and morbidity-associated risk factors on the progression of COVID-19 (e.g. disease severity, duration of inpatient stay, mechanical ventilation, morbidity, mortality)

- Collaboration between BfArM + Techniker Krankenkasse, funding: BMG

Insurants with COVID-19 without hospitalization

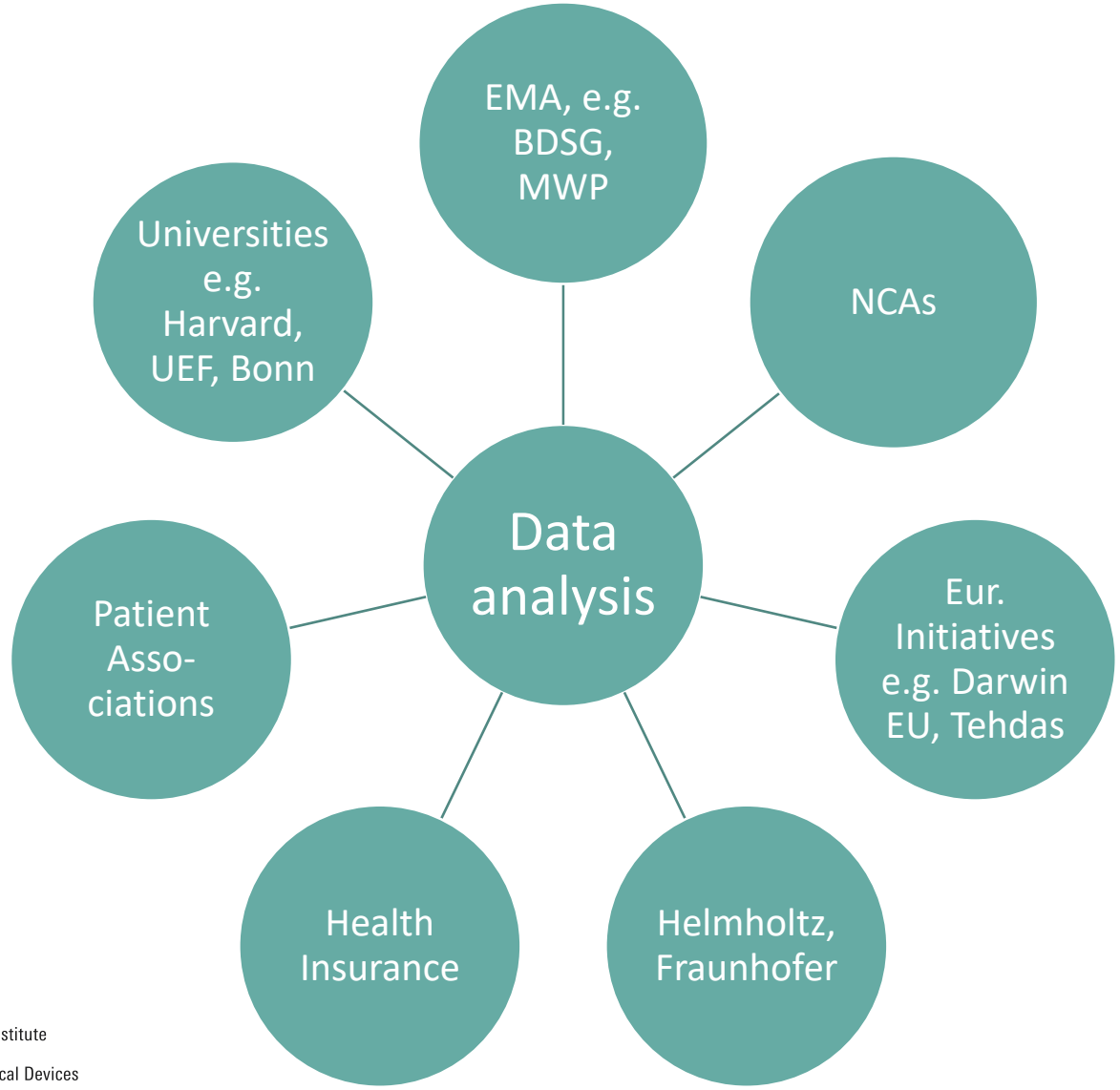
Insurants with COVID-19 with hospitalization

Control group (Insurants without COVID-19)

Pre-existing conditions (ICD-10), Medication (ATC)

COVID-19 diagnosis, inpatient stay, mechanical ventilation, mortality

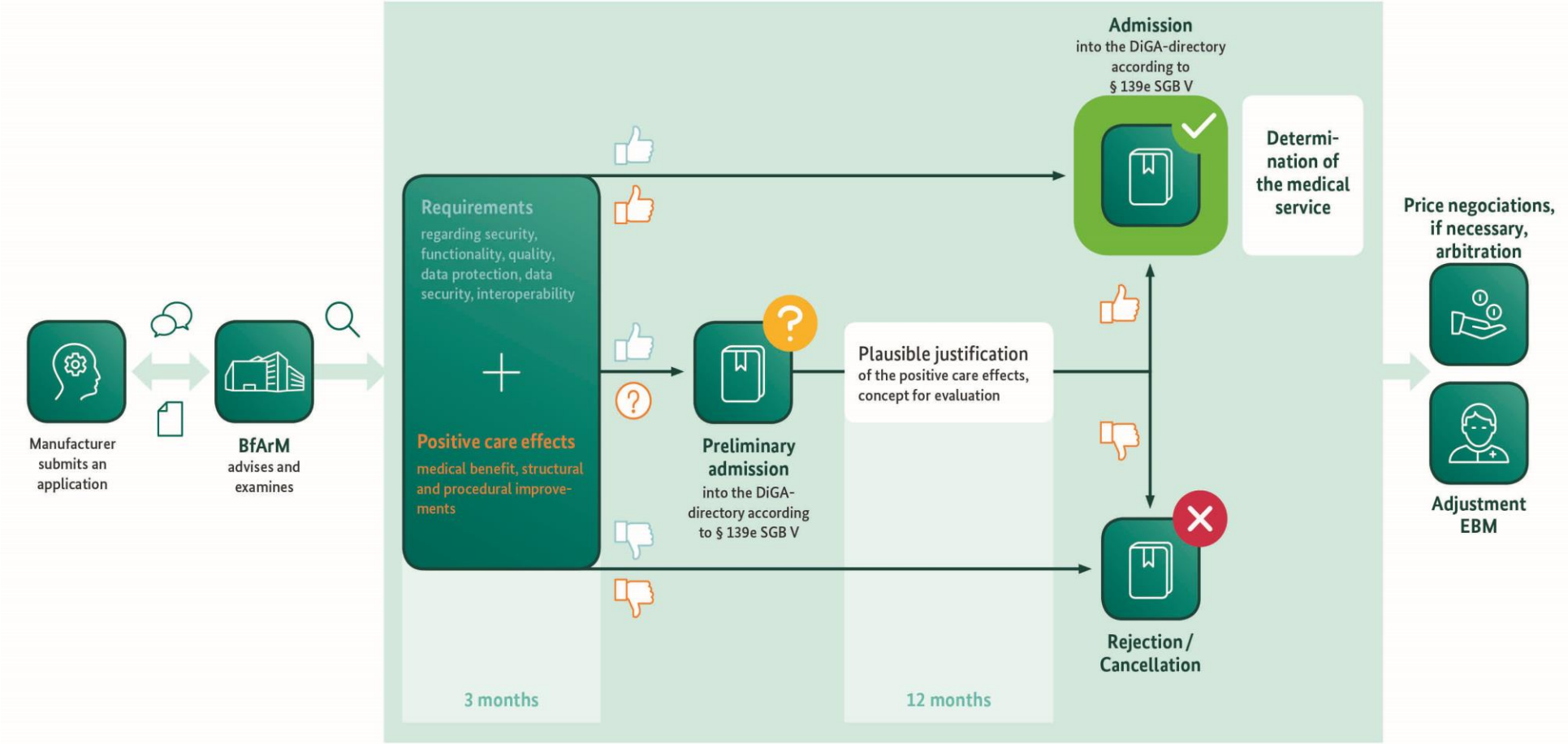
External capabilities - Overview



The BfArM collaborates with numerous external national and international partners in the course of data analytics, including RWD analysis and AI methods development!

Federal Institute for Drugs and Medical Devices

Usability of RWD (2) - Data from DiGA (and DiPA)



The DiGA-Directory: **Transparency** and **Guidance** for Users, Health Care Professionals, Statutory Health Insurances…

https://www.bfarm.de/EN/MedicalDevices/DiGA/_node.html

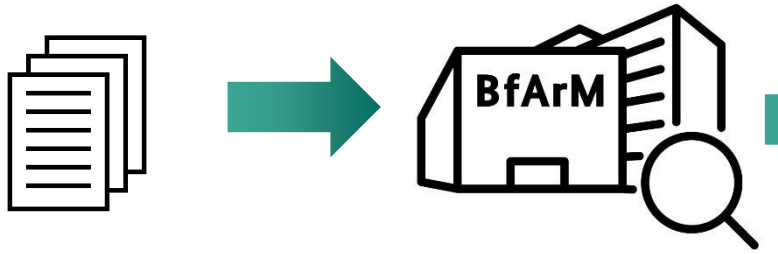
https://diga.bfarm.de/de

https://diga.bfarm.de/de/verzeichnis/316

Federal Institute for Drugs and Medical Devices

Results of the assessment by the BfArM

Results of the assessment by the BfArM up to now



Applications submitted by manufacturer

Assessment by the BfArM

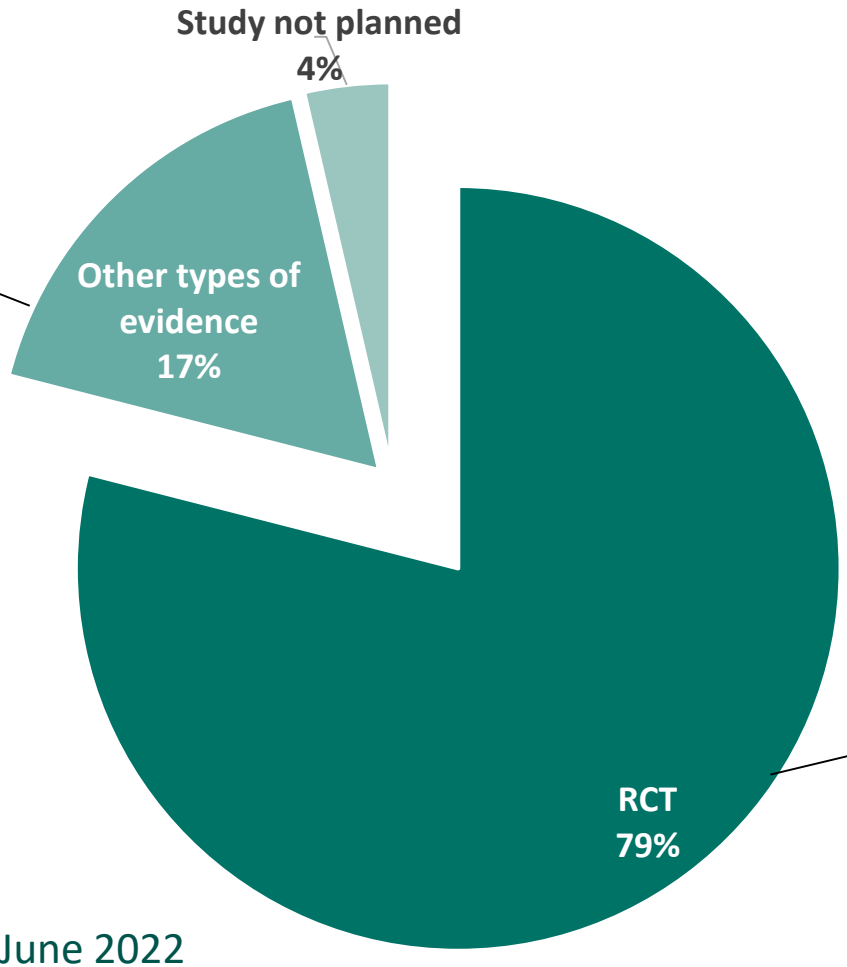
- Positive decisions: 31
- Negative decisions: 12
- Withdrawn: 75
- Currently being processed: 18
- Deleted from Directory: 2

Federal Institute for Drugs and Medical Devices

Status: 23 June 2022

Overview evidence ("study types")

The type of the evidence of the 138 applications is as follows:



24 Applications with other forms of evidence

- Surveys
- Intraindividual comparisons
- Prospective controlled studies
- Retrospective comparative study
- Register study with propensity score matching

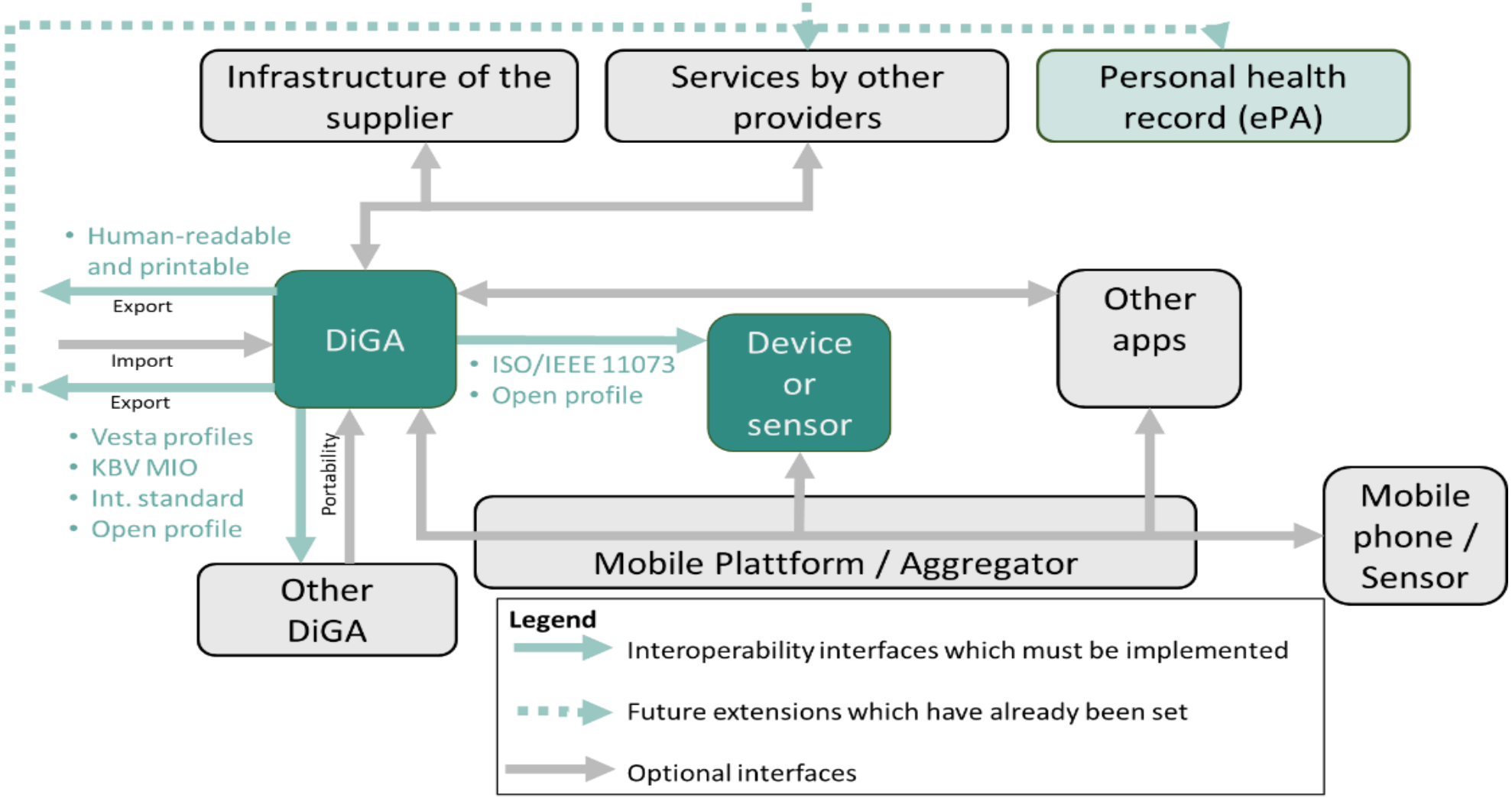
109 Applications with Randomized Controlled Trials (RCT)

- One RCT
- Multiple RCT
- Combinations of RCT and additional retrospective study
- Multiple RCT and meta-analysis

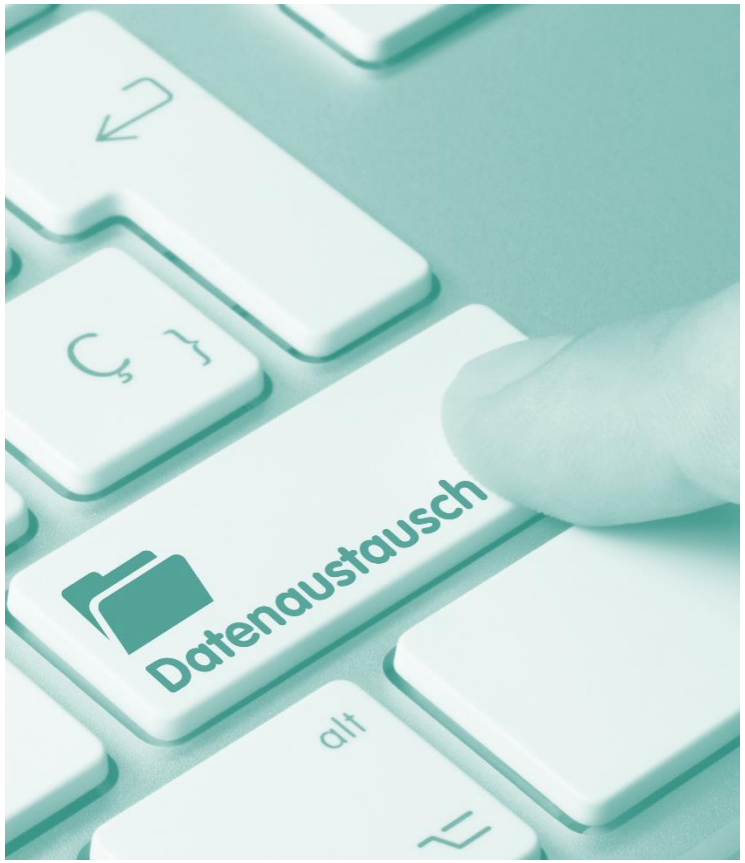
Status: 23 June 2022

Federal Institute for Drugs and Medical Devices

DiGA as Part of German e-Health Structure: **Interoperability**



Why do we need Interoperability?



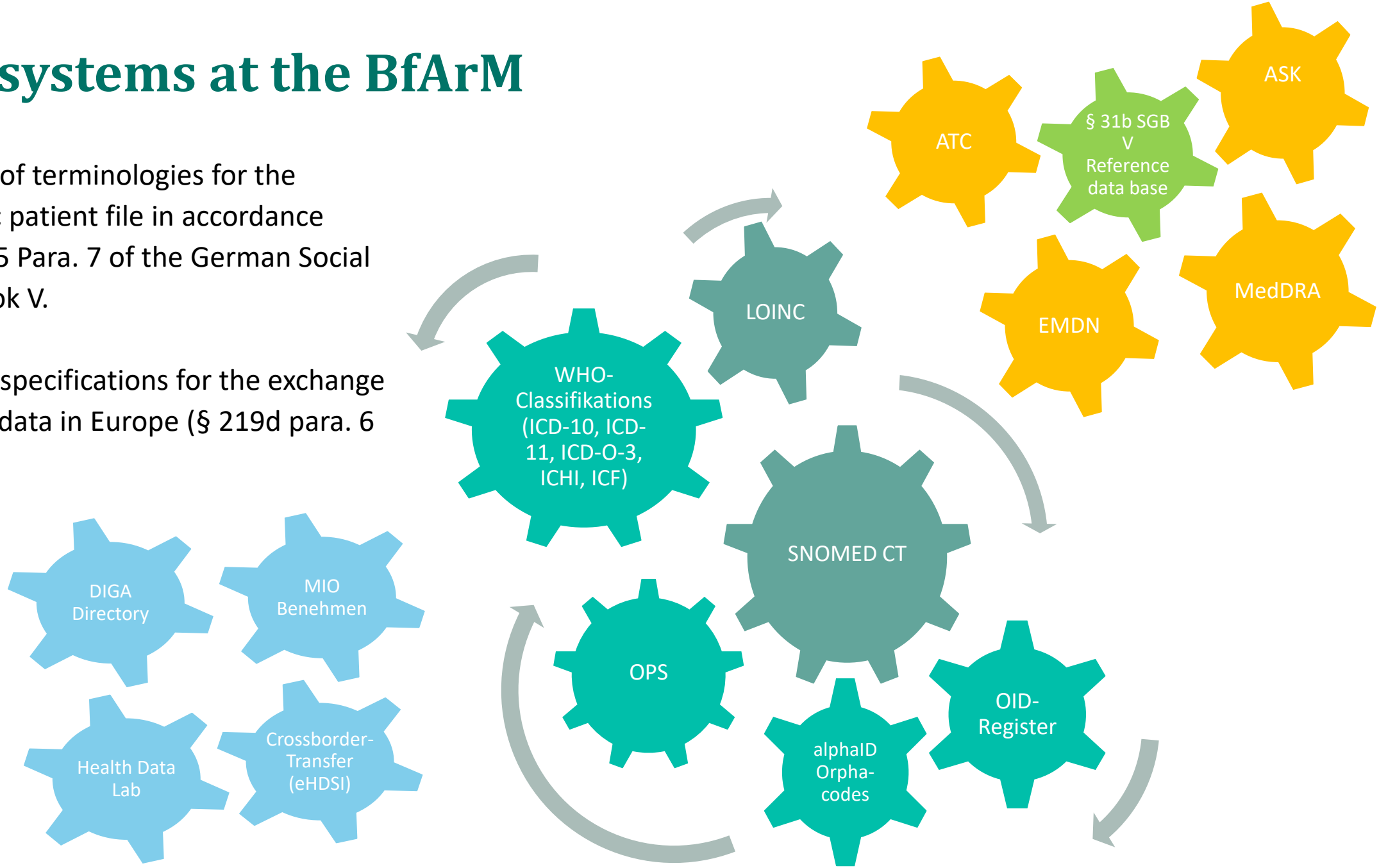
Prerequisite for efficient data exchange:

- Zero-loss communication of data
- Uniform interpretation of data across systems
- High-quality further processing of data

Federal Institute
for Drugs
and Medical Devices

Coding systems at the BfArM

- Provision of terminologies for the electronic patient file in accordance with § 355 Para. 7 of the German Social Code, Book V.
- Semantic specifications for the exchange of health data in Europe (§ 219d para. 6 SGB V)



Federal Institute for Drugs and Medical Devices

The Health Data Lab at the BfArM

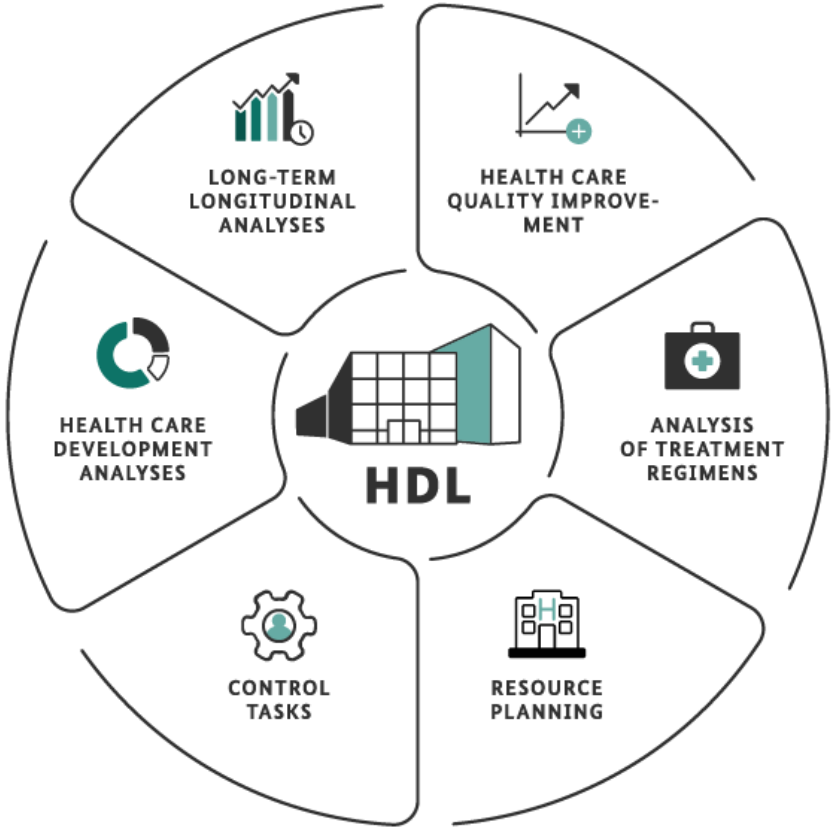
✓ Scope: The Health Data Lab (HDL) provides existing health data pursuing the following objectives:

Research orientation

- **Facilitate access to health data**
- **Close collaboration with data users**

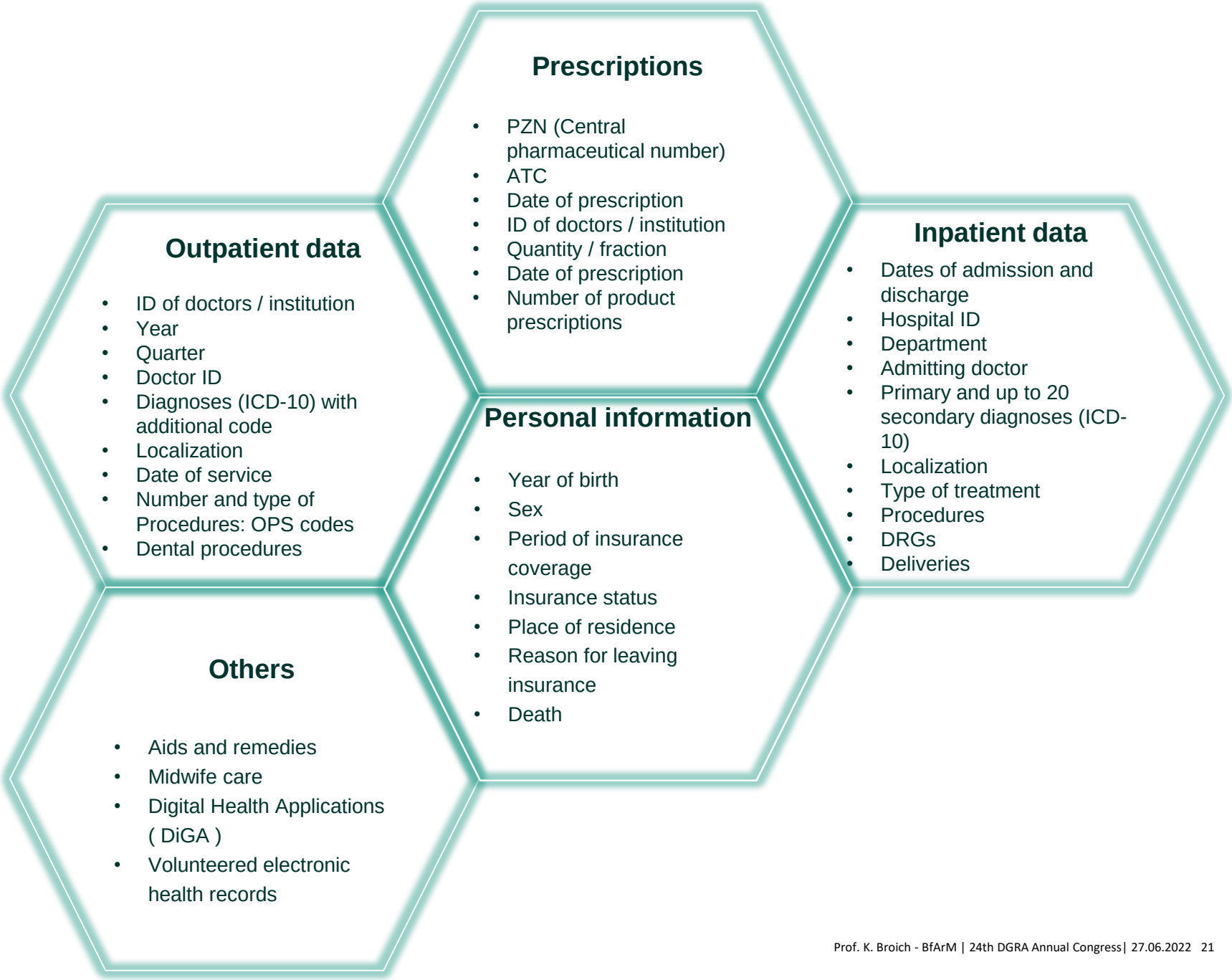
Security

- **Consideration of data sensitivity**
- **Close collaboration with information security and data protection authorities (BSI, BfDI)**



Types of data

- 72 million people with statutory health insurance in Germany
- Information from all health care sectors linked on the indiviudal level
- Longitudinal data starting from 2009
- Interoperability with established code systems (e.g. ICD10, ATC)



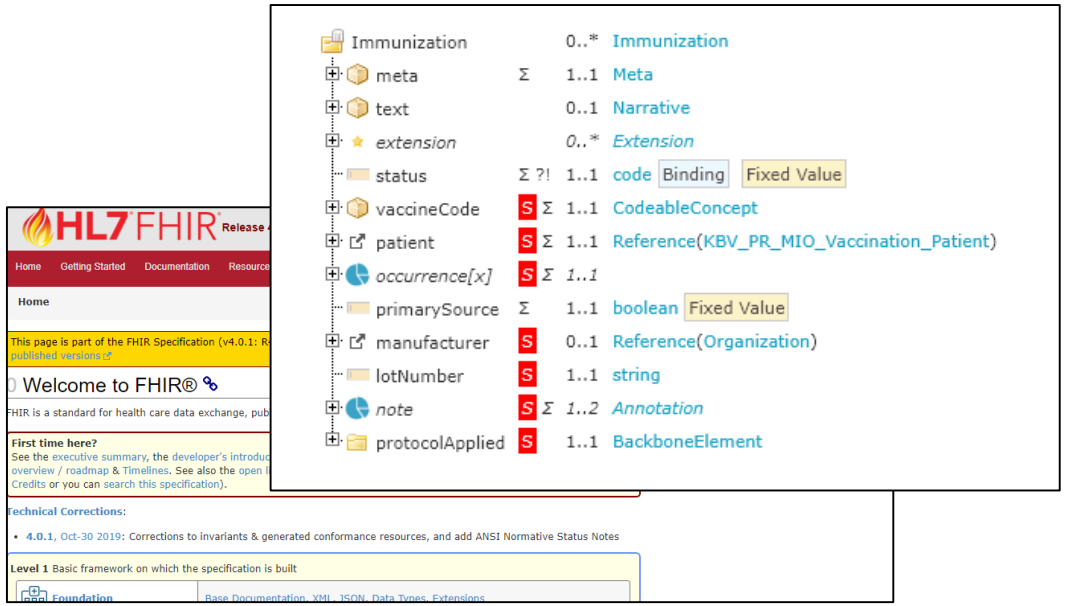
Federal Institute for Drugs and Medical Devices

Electronic patient record (ePA)

Voluntarily shared electronic health records:

- 2023: Structured medical information objects (MIO) in HL7/FHIR®

  - ➢ e-certificate of vaccination
  - ➢ e-dental bonus booklet
  - ➢ e-maternity record
  - ➢ e-child examination booklet



https://mio.kbv.de
https://www.hl7.org/fhir/

Data users*

Health care provider organisations

Kassenärztlichen (Bundes-)Vereinigungen
Spitzenorganisationen der Leistungserbringer auf Bundesebene
Bundesärzte-, Bundeszahnärzte-, Bundespsychotherapeuten- und Bundesapothekerkammer
Deutsche Krankenhausgesellschaft

Patient organisations

Patientenbeauftragte des Bundes und der Länder
Deutscher Behindertenrat
Bundesarbeitsgemeinschaft der PatientInnenstellen
Deutsche Arbeitsgemeinschaft Selbsthilfegruppen e. V.
Verbraucherzentrale Bundesverband e. V.

Health insurance sector

Krankenkassen
Bundes- und Landesverbände der Krankenkassen

Research institutions/universities

Hochschulen
Hochschulkliniken
Institutionen der Gesundheitsversorgungsforschung
Öffentlich geförderte außeruniversitäre Forschungseinrichtungen
Andere unabhängige Forschungseinrichtungen

Public institutions

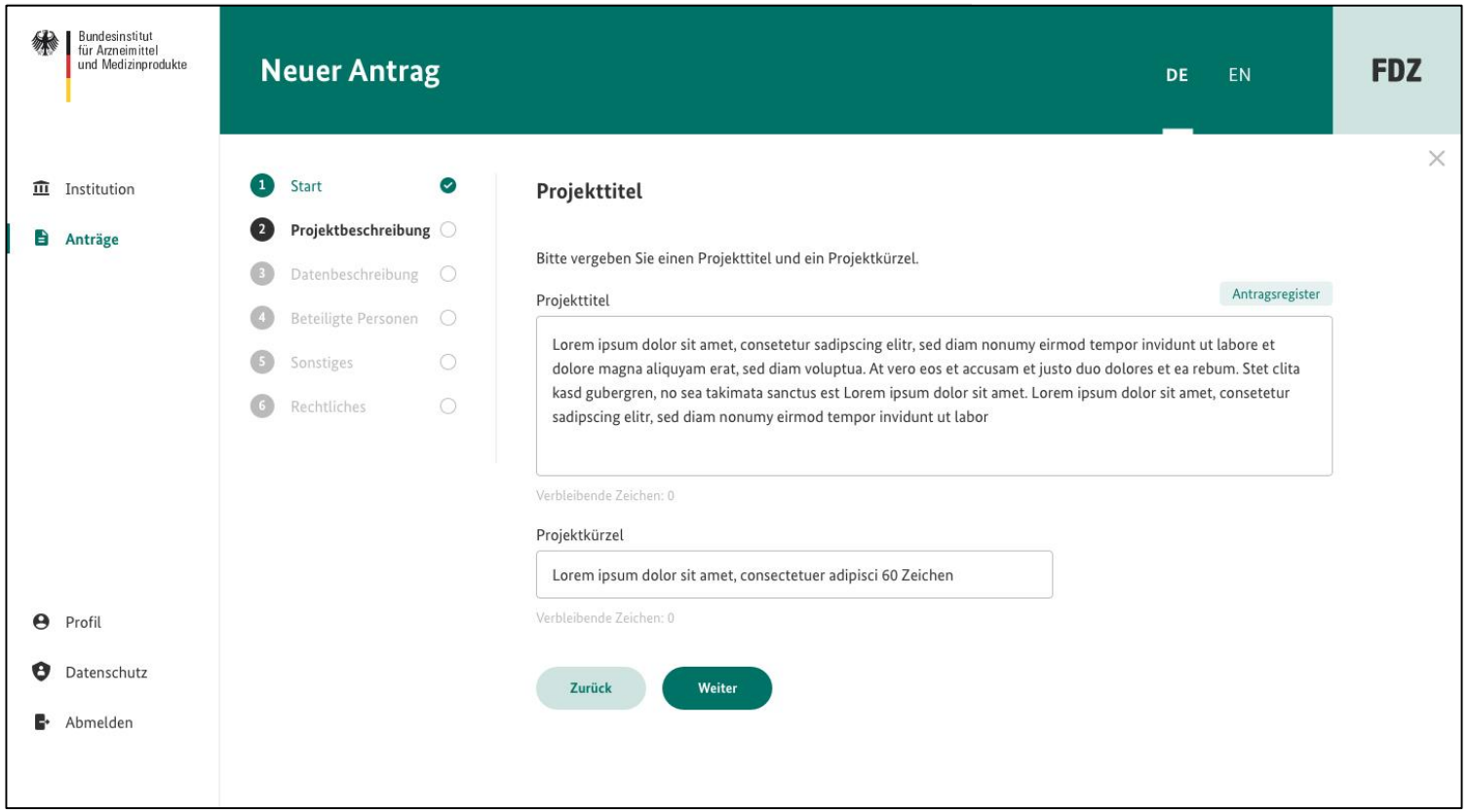
Institutionen der Gesundheitsberichterstattung des Bundes und der Länder
G-BA sowie IQWIG und IQTIG
Institut des Bewertungsausschusses
Institut für das Entgeltsystem im Krankenhaus

National agencies

Oberste Bundesbehörden, sowie Oberste Bundes- und Landesbehörden mit GKV-Zuständigkeit inkl. nachgeordneter Bereiche

* According to § 303e Abs. 2 SGB V

Fully digitalized data application process



Federal Institute
for Drugs
and Medical Devices

Synthetic data and AI-readiness

Gefördert durch:
Bundesministerium für Gesundheit
aufgrund eines Beschlusses des Deutschen Bundestages

KI-FDZ

Aims

- Creating synthetic data with AI-methods and comparing them with „classically“ anonymised data
- Evaluation of AI-readiness
- European connectivity

Duration

November 2021 - December 2024

Partners

- InGef – Institute for Applied Health Research Berlin GmbH
- Berlin Institute of Health at Charité (BIH)
- Fraunhofer Institute for Digital Medicine MEVIS

Blog article: https://www.bfarm.de/EN/News/Blog/_docs/2022-03-10-forschungsdatenzentrum.html

AI Infrastructure at the BfArM

Technical specifications of the AI/HPC network

- 2x IBM POWER SYSTEM AC922 server (8335-GTH)
- IBM FlashSystem 5100 NVMe Storage System
- IBM WATSON MACHINE LEARNING ACCELARATOR
- IBM Spectrum Virtualize Software
- (8 NVIDIA V100 GPUs, 512 GB DDR4, 50 TB ext. Storage)

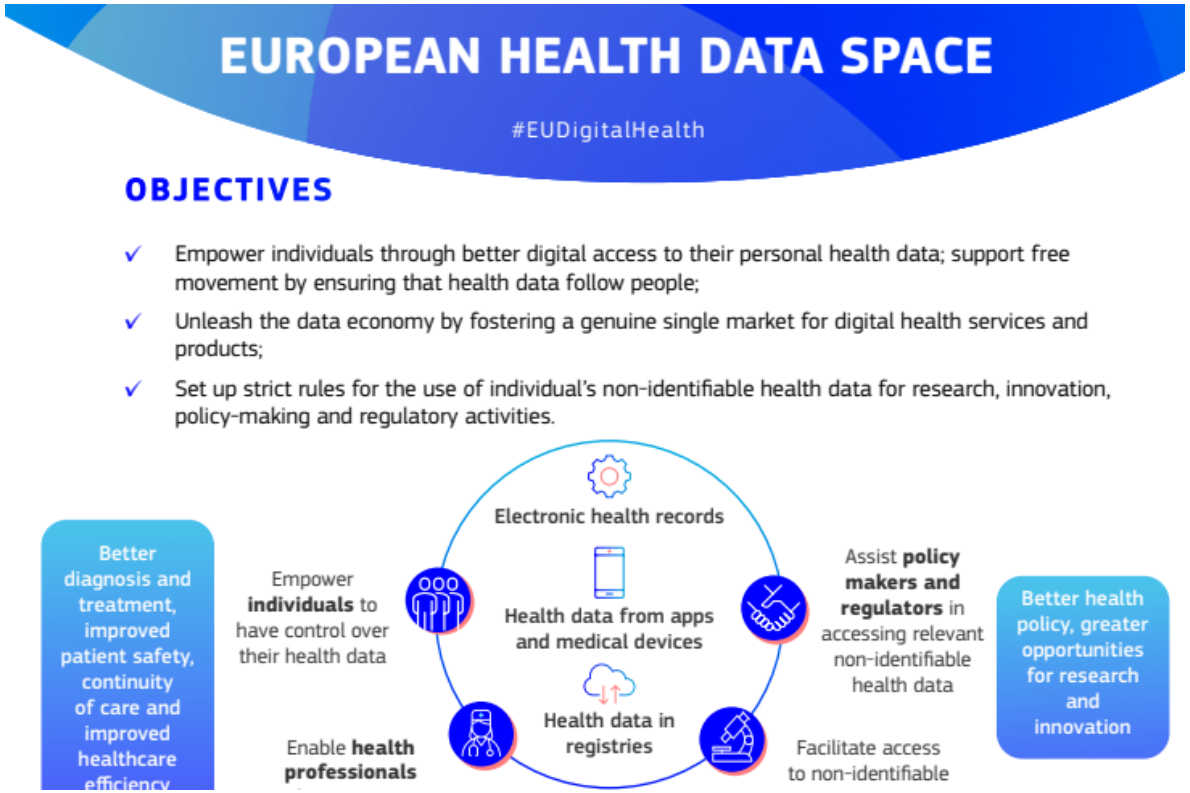
- NVLink 2.0 for fast bidirectional bandwidth between CPUs and GPUs
- Network: 10 Gb Ethernet, I/O architectures: PCIe gen4
- OpenPOWER Linux scale-out server (Red Hat Enterprise Linux operating system)

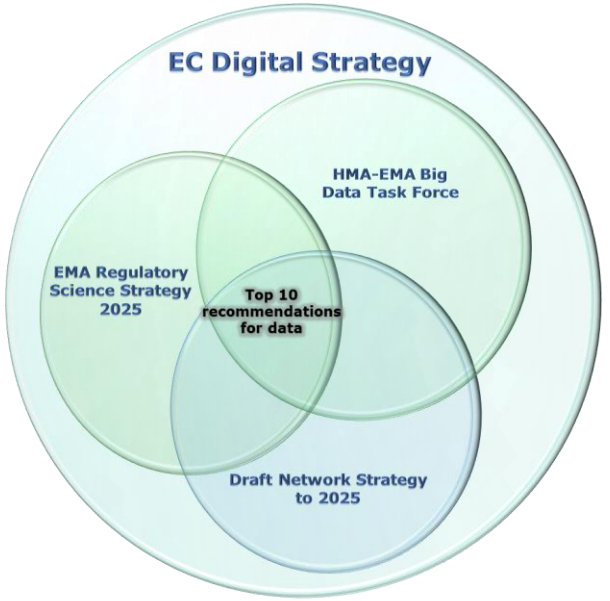
➢ System is especially designed for Deep Learning and AI, high-performance analytics, and high-performance computing

➢ **Projects including machine learning approaches**: EMPAR, ANKA, Covid-19 Risk; projects in progress for monitoring, mitigating and avoiding shortages and falsifications of medicinal products

Power System AC922 internal components

European Activities - BfArM Participation





EC supporting
digital "EU-Health Data Space"*
Pharmaceutical Strategy

EU **network strategy** 2025 + **DARWIN EU**

EMA Regulatory Science Strategy 2025

From HMA-EMA **Big Data Task Force to Big Data Steering Group**
(Top-Ten-Recommendations for data)

Federal Institute for Drugs and Medical Devices

* https://ec.europa.eu/health/ehealth-digital-health-and-care/european-health-data-space_en

HMA & EMA Network Strategy – Pillars Innovation & Digitization: Progress achieved

Data analytics, digital tools and digital transformation

- DARWIN EU
- Data quality & representativeness
- Data discoverability
- EU Network skills
- EU Network processes
- Network capability to analyse
- Delivery of expert advice
- Governance framework
- International initiatives
- EU stakeholder implementation forum
- Veterinary recommendations

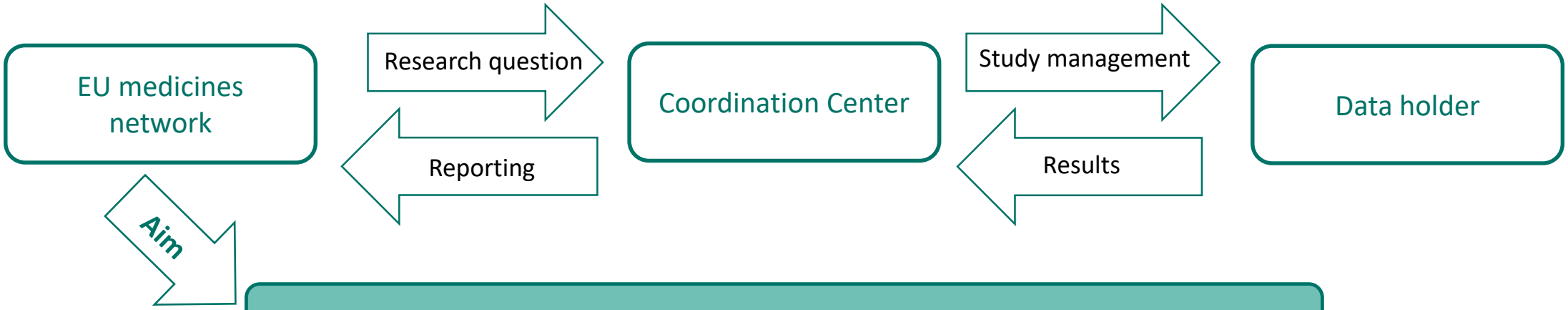
"By 2025 the use of Real-World Evidence will have been enabled and the value will have been established across the spectrum of regulatory use cases"

Big Data Steering Group; EU Telematics; EU Innovation Network, …

Federal Institute for Drugs and Medical Devices

Data Analysis and Real-World Interrogation Network (DARWIN EU®)

- **Network of data, expertise and services**
- **Supported by an Advisory Board**
- **Close collaboration with: TEHDAS joint action, EMA-HMA Big Data Steering Group, European Health Data Space Pilot project**



Federal Institute for Drugs and Medical Devices

Next steps…….

In process:
Point & Click UX, AI-readiness Automatisation with AI (Analysis, ETL, Performance)

Participation:
TEHDAS: "Joint Action Towards the European Health Data Space "

HDL

Funded by Federal Ministry of Health:
„Artificial Intelligence at the Health Data Lab - Investigation of anonymisation methods and AI-readiness "

EU grant application:
EHDS2 - Pilot project Co-Lead of WP5 IT-Infrastructure

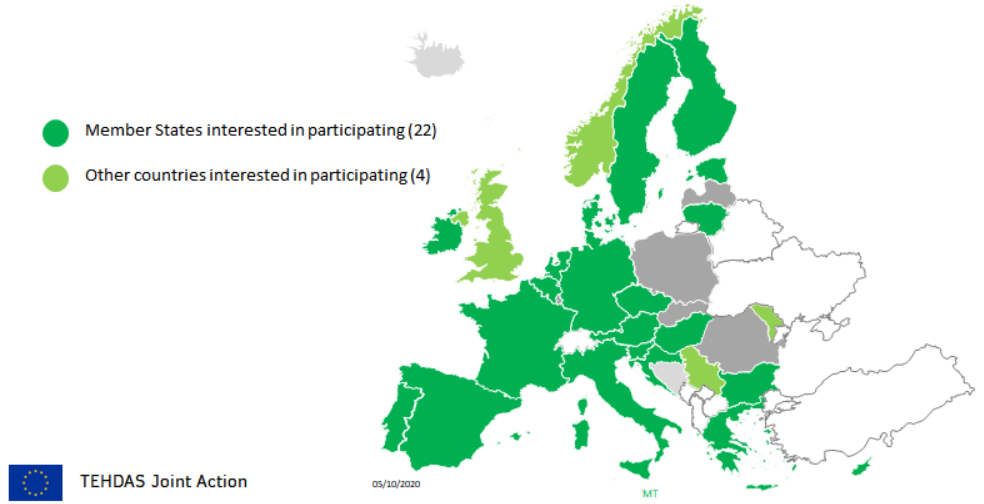
http://ehaction.eu/events/wp5-secondary-use-of-health-data-legal-aspects/
https://ec.europa.eu/health/ehealth/dataspace_de
https://tehdas.eu/

EHDS Initiative **TEHDAS**

Joint Action **T**owards the **E**uropean **H**ealth **Da**ta **S**pace with the following pillars:

- Reliable data governance system and priciples for cross-border data use
- Data quality
- Secure infrastructure und interoperability
- HDL supports TEHDAS as part of a delegation coordinated by Federal Ministry of Health

TEHDAS Towards European Health Data Space



http://ehaction.eu/events/wp5-secondary-use-of-health-data-legal-aspects/
https://ec.europa.eu/health/ehealth/dataspace_de
https://tehdas.eu/

EHDS Initiative **TEHDAS**

- Co-funded by EU Commission
- Duration: 01/02/2021 – 01/08/2023
- Aims: Develop and promote concepts for the EHDS
- Coordination: Finnish Innovation Fund Sitra
- Participants: Institutions from 25 European countries

TEHDAS Towards European Health Data Space

The work is divided into eight work packages:

1. Coordination
2. Dissemination
3. Evaluation
4. Outreach, engagement and sustainability
5. Sharing data for health
6. Excellence in data quality
7. Connecting the dots
8. Citizens

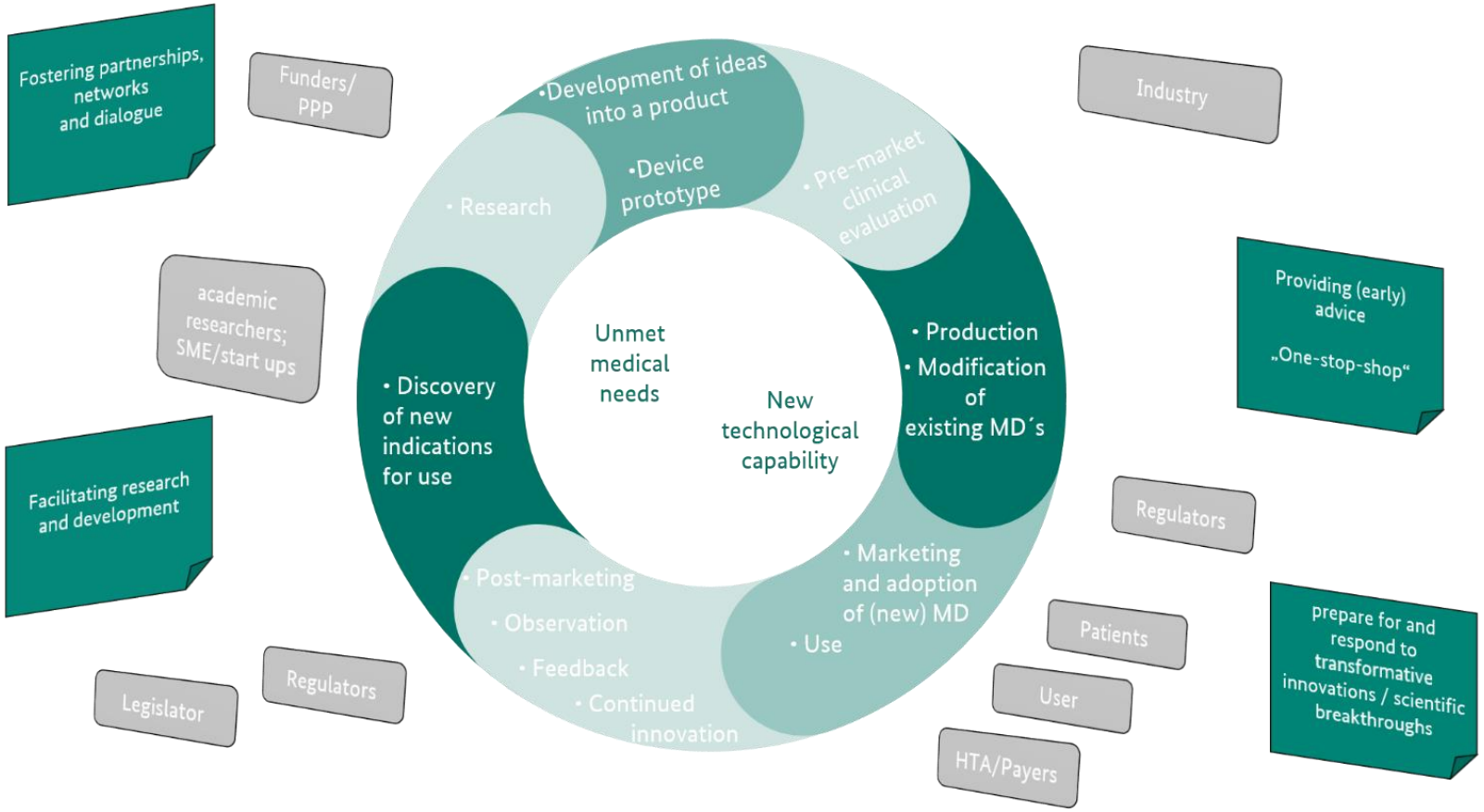
Federal Institute for Drugs and Medical Devices

EHDS2 Pilot

Pilot for a European Health Data Space on secondary use of health data

- Funding application submitted (EU4Health Programme)
- Time scale: January → submission, June → decision, September → possible project start
- Planned duration: 24 months
- Aim: Setup of a first version of the EHDS and testing of medical use cases
- Coordination: Health Data Hub, France
- Participants: 16 partners (national nodes, ERICs, European agencies and research institutions)

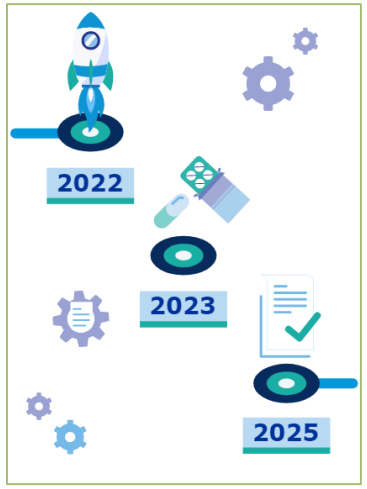
Regulators Perspective:
Joint efforts to support innovation in a modern (e)Health ecosystem



Federal Institute
for Drugs
and Medical Devices

Fostering a new health era – European Initiatives by NCAs, EMA and EC

- broad initiative from the regulatory network, e.g. to transform the EU/EEA clinical trials environment in support of large clinical trials
- to the benefit of medical innovation and patients



… supporting innovation and digitalization in clinical trials…

Clinical Trials Information System

…Bridging the translational gap..

Federal Institute for Drugs and Medical Devices

Are regulators prepared for the new Health Ecosystem of Medicinal Products, Devices and Big Data?

Federal Institute
for Drugs
and Medical Devices

... however, continuous change management and partnering with stakeholders necessary!

Good governance for digital enablement

At the enterprise level, those in a governance role must have a digital fluency and an intimate understanding of the health sector. This includes understanding the economics of technologies disrupting the health industry business and production of care models. A deep knowledge is required of health IT trends and expertise in applications appropriate to the enterprise.

Thank you very much for your attention!

Contact

Federal Institute for Drugs and Medical Devices
Prof. Dr. Karl Broich
President
Kurt-Georg-Kiesinger-Allee 3
D-53175 Bonn

www.bfarm.de
Phone +49 (0)228 99 307-3219

www.bfarm.de
www.bfarm.de/innovation
www.bfarm.de/diga
www.bfarm.de/digitalfuture
https://www.forschungsdatenzentrum-gesundheit.de/

Federal Institute for Drugs and Medical Devices