



Biobanking in the German Centers for Health Research





P. Schirmacher

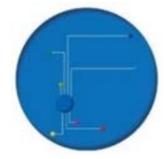
Institute of Pathology

University of Heidelberg

Coordinator Biobanking

DKTK, DZIF, DZG-Working Group Biobanking/IT













The German Centres for Health Research

- Fighting major disease challenges
- Coordination of competences → Translational Research, Core infrastructures
- Six centres:
 - Deutsches Zentrum für Neurodegenerative Erkrankungen (DZNE, 2009)



Deutsches Zentrum f
ür Diabetesforschung (DZD, 2009)



Deutsches Zentrum f

ür Herz-Kreislauf-Forschung (DZHK. 2012)



Deutsches Zentrum f
ür Lungenforschung (DZL, 2012)



Deutsches Zentrum f
ür Infektionsforschung (DZIF, 2012)



Deutsches Konsortiums für Translationale Krebsforschung (DKTK, 2012)



Different organisational and decision-making structures!





Aims of the DZGs

- Sustainable partnerships between Universities, University Hospitals and external Research Institutions (coordination by Helmholtz Center)
- Bundling of competences → Translational Research
- Development of infrastructures (IT, Biobanks, Data management etc.)



Cooperation of the DZGs:

- Public Relation
- Drug design
- Biobanking, IT & Data management

Reviewed by Joint Steering Board





DZGs

Common:

- One coordinating Helmholtz-Centre
- Incremental funding over 1st period
- Sustainability concept
- Review after 1st funding period (ongoing)
- Strong structural/core concept

Differences:

- Multiple partly overlapping locations (5-9)
- Different internal structures (governance)
- Different time lines (2009-12)
- Different challenges (entities)





Using (local) synergies and cooperative potential

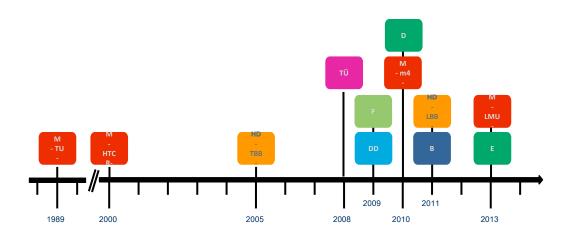




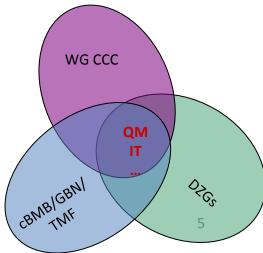
Positioning of DZG-Biobanking

- DZGs
- cBMBs/GBN, TMF (WG Biobanking)
- WG CCCs (WG Tissue banking),
- Other Research Networks (SFBs, Epidemiology (NatKo))

Most powerful supportive structure for biobanking (focus, user network/outreach, sustainability)









German Center for Lung Research (DZL)



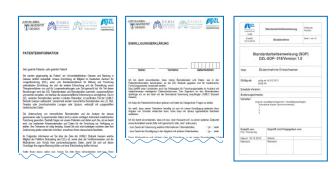
Achievements (2012-2015)

• Implementation of a DZL-biobanking portal: searchable data base for existing (retrospective) biomaterials

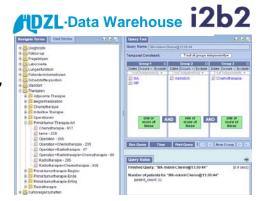


 Harmonization of documents and procedures related to biobanking:

broad IC form, SOPs, by-laws regulating use & access to biomaterials/data



Development of a data management structure:
 data protection concept, centralized DZL-data warehouse,
 software solutions for DZL centralized Pat- and Lab-ID generation,
 Data harmonization pilot projects



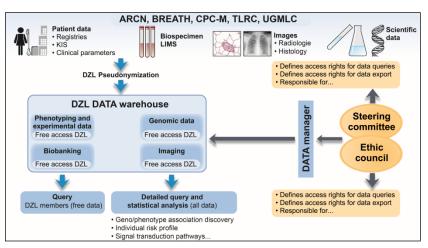


German Center for Lung Research (DZL)

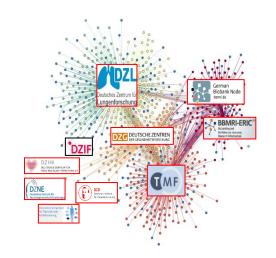


Goals (2016-2020)

 Full implementation of a centralized, automated, pseudonymized patient data warehouse and decentralized biospecimen repository



- Full setup and operation of the DZL central DWH
- prospective sampling of biospecimen from all types of pulmonary patient cohorts
- integration and harmonization of already existing phenotyping tools, clinical registries, cohorts and biomaterial collections
- integration of biomaterial-based ~omics data, linkage of imaging to phenotyping data
- Development and implementation of guidelines for quality management:
 - SOPs, QM measures/biobanking standard, site-specific teaching of biobank issues
- Network activities with other DZGs and biobank structures within Germany





The German Center for Heart and Circulation Research (DZHK)



Biobanking Challenges



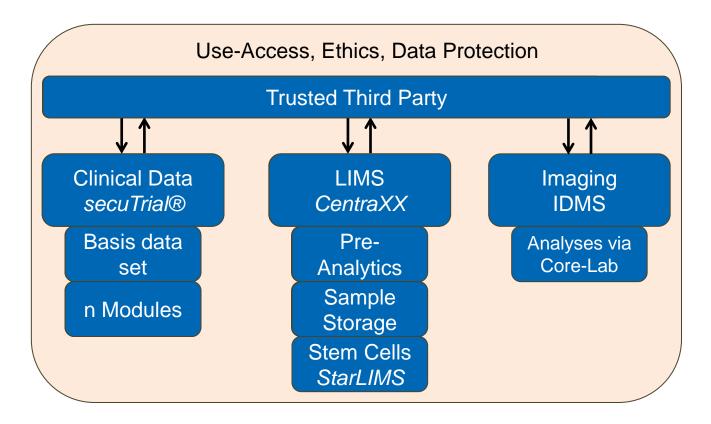
- Decentral (inhomogeneous) structures at the partner sites
- -> Standardization and Harmonization:DZHK Infrastructure
 - ► Use & Access Rules
 - ► Data Protection
 - ► Ethical approval
 - ► SOPs
 - ► IT-Infrastructure



The German Center for Heart and Circulation Research (DZHK)



Scientific Infrastructure for Clinical Research



- Post hoc concept (developed in first period)
- Strong central coordination; decentral storage
- Prospective/trial-based concept



The German Center for Heart and Circulation Research (DZHK)



DZHK: Basis Set Study Set (Transition CHF)









Research for a Future without Diabetes

- Founded 2009
- > 250 Scientists
- Excellently evaluated in 2014

Biobanking Activities

- Preexisting Biosamples > Biobanks in the BBMRI catalogue
- Novel study-derived Biosamples

IT Activities

Data and Knowledge Management



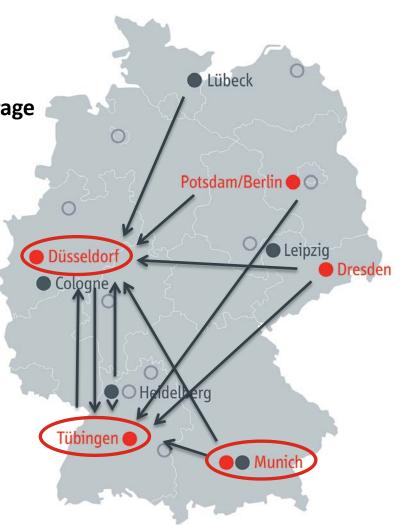




Novel Study-derived Biosamples

1st Phase: Centralized Management – Local Storage (Ongoing clinical studies)

- 1. Samples taken locally at DZD clinical study sites
- Storage and sample management (LIMS) at the leading study centers (Tübingen, Düsseldorf)
- 3. Project management of applications at the Head Office







Novel Study-derived Biosamples

2nd Phase: Centralized Biobank and Data Management

(Future clinical studies)

1. Samples taken locally at DZD clinical studies

- 2. Storage and sample management (LIMS) centralized at the Helmholtz Zentrum München (service provider)
- 3. Project management of applications at the Head Office in Munich

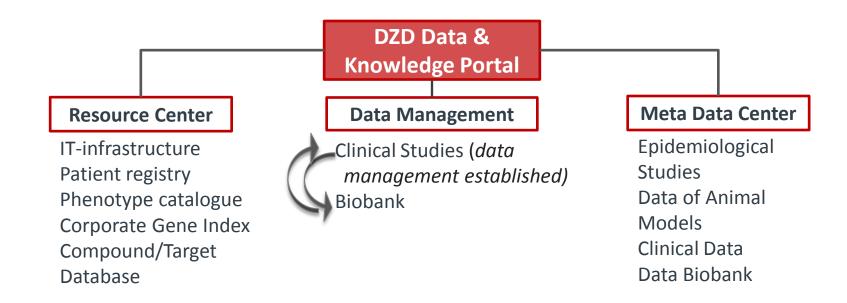






Data and Knowledge Management - Added value by sharing knowledge (under development)

Aim: building up knowledge management environment that offers the big picture of locally available data at DZD partner sites. Eestablished e-infrastructures and communication structures will be linked with novel IT solutions.





German Center for Neurodegenerative Diseases (DZNE)



| 2009 3 April: | Found | lation of | DZNE |
|----------------------|----------|-------------------------|------|
| Single Helmho | oltz cei | nter, 9 si [.] | tes |

Mission:

understand causes and risk factors leading to predisposition for neurodegeneration and develop new therapeutic and health care strategies.

Fields of research:

- major neurodegenerative diseases (Alzheimer and other dementias, Parkinson disease)
- rare conditions (prion or Huntington disease).





German Center for Neurodegenerative Diseases (DZNE)



Translational by design:

- Basic research
- Clinical research
- Population research: epidemiology
- Health care research

Biobanking activities: next steps

- Central storage (biorepository) for all research areas in DZNE
- Storage: liquid N₂

IT:

 DZNE-wide LIMS (Nautilus) for clinical and epidemiological biobanking

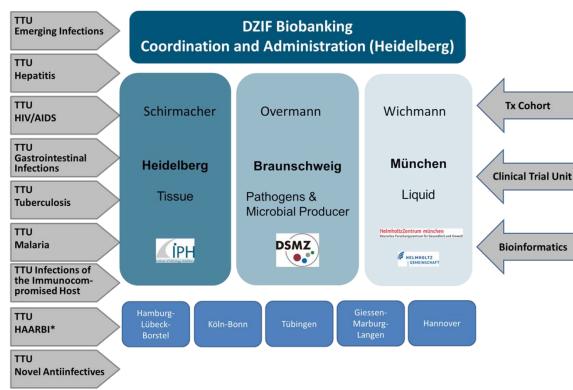




DZIF Biobanking platform (2013-2015)

- Translational Infrastructure (TI)
- Decentral storage
- 3 main locations
- 3 columns: tissue, liquid, pathogens & microbial producer (until 2015; separated in 2016 (pathogens in TTU EI))









Key Achievements TI Biobanking:

- Establishment of functional and active biobanking infrastructure within DZIF; fully integrated within the national (GBN, TMF, other DZGs) and international (BBMRI) biobanking community.
- Support of >100 projects
- Compilation of key disease collectives; integration of focussed preexisting collectives (e.g. hepatitis)
- Implementation of information platform (Biobanking website (www.dzif-biobanking.de), Biobanking catalogue with more than 31 biobanks, specific DZIF sub-catalogue on pathogens linked to the novel metadata in BacDive (http://bacdive.dsmz.de).
- Development of a cost-calculation model, and an ethical and data protection concept
- active support of DZIF Tx-cohort development.
- Selection of **central DZIF LIMS system** for DZIF-wide administration of common data sets for all prospective biomaterial collections (pilot project: Tx-cohort)
- Initiation and organization of the regular meetings within the **DZG Biobanking & IT working group**.





Ethical, Legal, and Social Issues (ELSI)

- Comprehensive votes (Heidelberg and Munich sites)
- Standardized Patient consent (informed, broad, retraction possible at any time)
- Standardized ethical vote(s)
 (Altruistic: no promise for further diagnostic use, feedback information, reimbursement)
- Data protection issues (see IT)
- Generic template for DZIF purposes available
 Cooperation with TX-Registry, TTU HIV,
 TTU Hepatitis
 Support & information
- → High effort to respect patient will
- → Basic frame for interchange of biomaterial (nationwide/international)

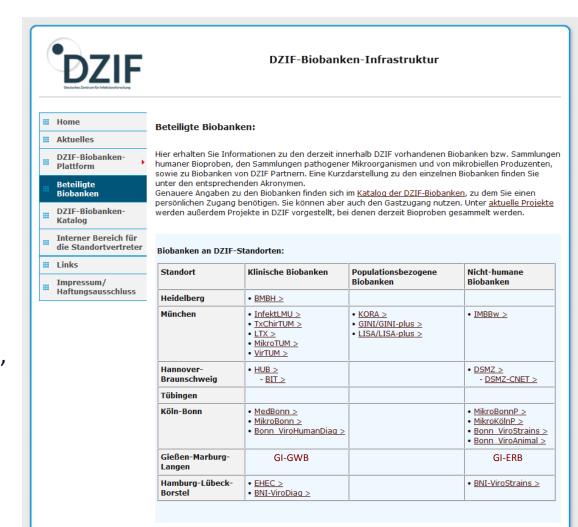






DZIF Biobanking Website:

- Representatives of partner sites
- Participating biobanks/partners
- Detailed information on available samples in biobanking catalogue
- Internal module of biobanking platform (exchange of information, protocols, quality management, ethical/legal issues)







Quality management Liquids

- Aim: harmonized SOPs for biomaterials in DZIF
- For liquids:

SOPs of German National Cohort:

- → worked out by expert group
- → used by other DZGs: DZL, DZHK, DZD



DZIF-Biobanken-Infrastruktur

Interner Bereich Qualitätsmanagement/ Ethische und rechtliche Themen:

Aktuelle SOPs der DZIF-Biobank: Liquids

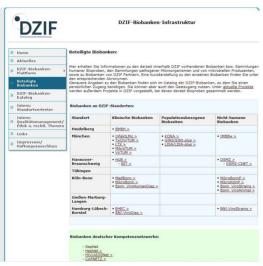
| Blutentnahme: | DZIF LIQ 2.2 01 Blutentnahme.pdf | |
|------------------------------------|---|--|
| Blutverarbeitung: | DZIF LIQ 2.2 02 Blutverarbeitung.pdf | |
| Bioprobenprotokoll Blut: | DZIF LIQ 3 01 Bioprobenprotokoll Blut.pdf | |
| | | |
| Uringewinnung: | DZIF LIQ 2.2 03 Uringewinnung.pdf | |
| Bioprobenprotokoll Urin: | DZIF LIQ 3 03 Bioprobenprotokoll Urin.pdf | |
| | | |
| Stuhlgewinnung: | DZIF LIQ 2.2 05 Stuhlgewinnung.pdf | |
| Bioprobenprotokoll Stuhl: | DZIF LIQ 3 05 Bioprobenprotokoll Stuhl.pdf | |
| | | |
| Speichelgewinnung: | DZIF LIQ 2.2 04 Speichelgewinnung.pdf | |
| Bioprobenprotokoll Speichel: | DZIF LIQ 3 04 Bioprobenprotokoll Speichel.pdf | |
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| Nasenabstriche: | DZIF LIQ 2.2 06 Nasenabstriche.pdf | |
| Bioprobenprotokoll Nasenabstriche: | DZIF LIQ 3 06 Bioprobenprotokoll Nasenabstriche.pdf | |





DZIF Biobanking Catalogue

- Website
- >30 registered biobanks
- Accessible collectives, representatives, features
- Promotion
- Project management (application)
- Conformity with German Biobank Catalogue and BBMRI



Project Work

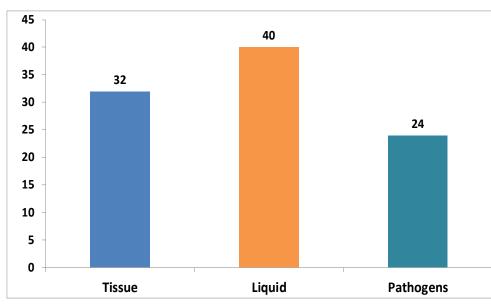
96 projects (8/2015):

Tissue: 32

Liquid: 40

Pathogens: 24

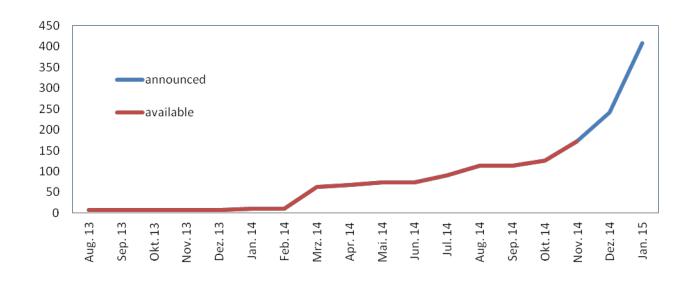
Key support of TX-cohort (ongoing)







Pathogen Repository – Deposits



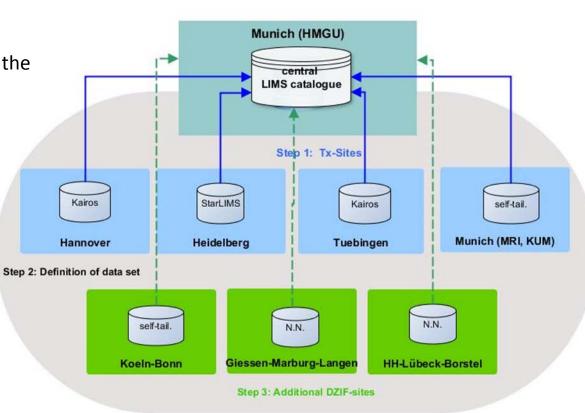
- 80 strains Mouse-Microbiome (Thomas Clavel, TUM) \(\square\) description of new taxa
- 50 *Clostridum difficile* strains (clinical isolates)
- Testpanel for compound screening (TI Natural Compound Library)
- key strains: MRSA, MRSE, Arthrobacter mysorens, Streptococcus suis (Gießen) ☐ genome sequencing
- key strains: Serratia marcescens, Enterobacter sp., E. coli (Gießen)
- pulmonary Microbiome: *Pseudomonas aeruginosa* strains (Hannover)





DZIF LIMS-next steps

- Fine-concept preparation with the provider and first test system ready by mid of 2016
- Definition of common minimal data set
- Interface to Tx-partner sites (blue) available in Q3 / 2016
- Catalogue and search function ready in Q4 2016
- Interface to residual DZIF partner sites with biosample collections (green) in Q1/2017



Provider: Kairos CentraxX





DZIF Biobanking -future

Priority project:

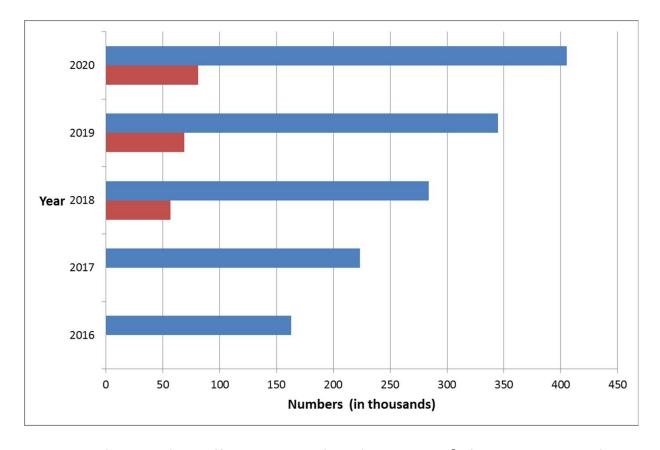
Support of **the Tx-cohort** with the focus on

- <u>Data management:</u> implementation of a central LIMS catalogue at the Munich site; Munich is in charge of the development of the infrastructure and implementation as well as the roll-out to the Tx-cohort sites; in a second step all other DZIF sites collecting biomaterials and the TTUs with cohort activities will be integrated
- Quality management: development of common and harmonized standard operating procedures (SOPs) and/or common minimal standards for sample retrieval especially avoiding pre-analytical artefacts, sample processing, transport and storage of biosamples
- <u>Tissue banking</u>: support of all biobanking activities and further set up special tissue specimen collections (annotation and ELSI support)



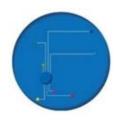


DZIF Biobanking -future



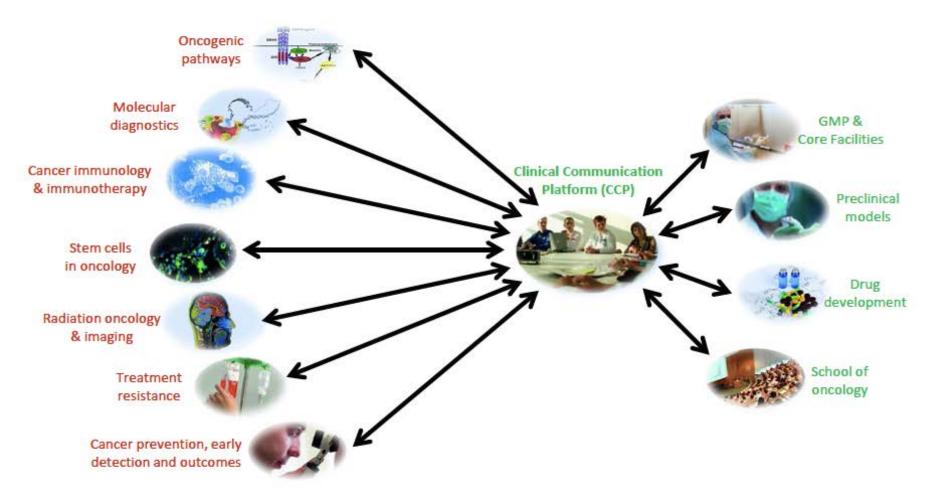
Estimated sample collection and utilization of the DZIF Tx-cohort 2016-2020





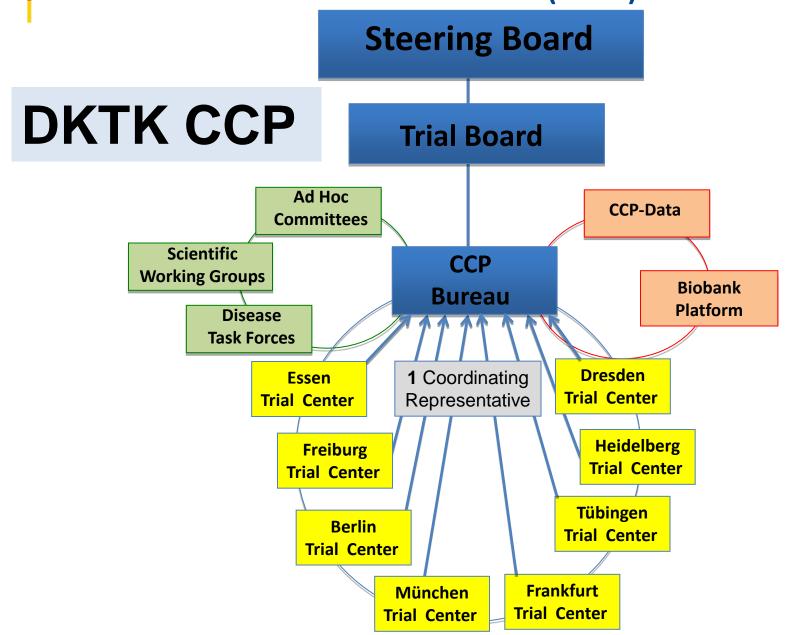
Translational research program

Structurcal platforms

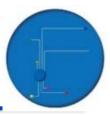


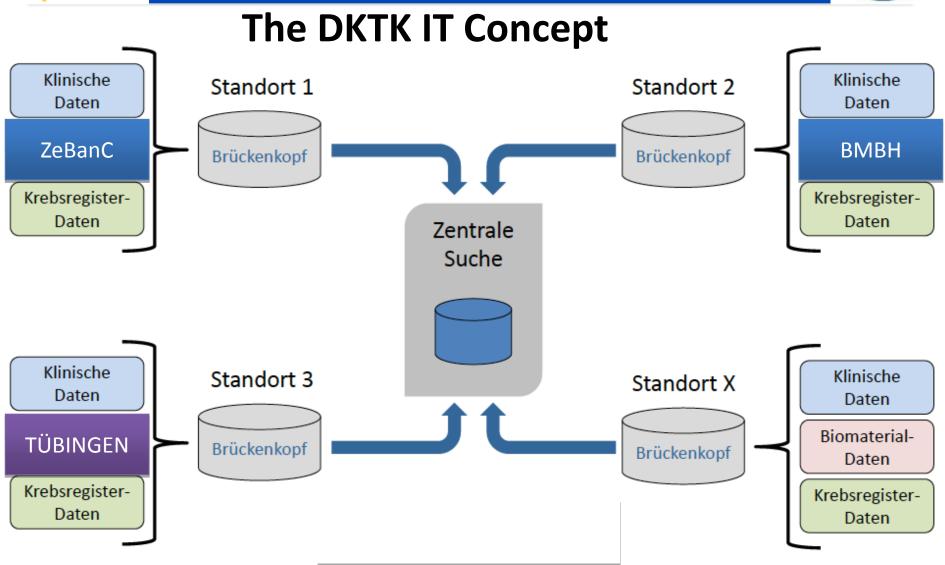




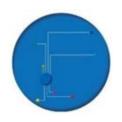


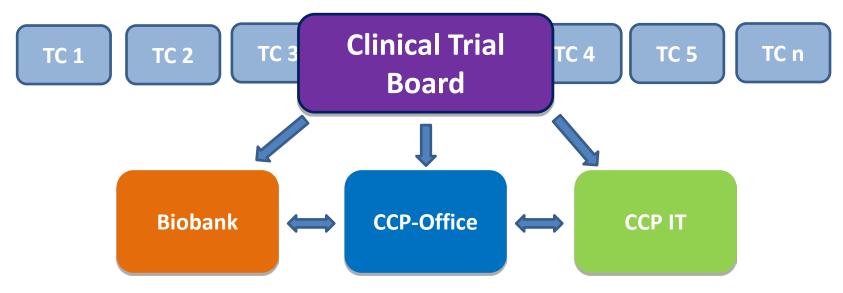








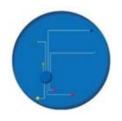




Mission of the biobanking platform:

- ☐ High quality biomaterials
- ☐ Enable research projects within DKTK
- ☐ Project quality and good scientific practice
- ☐ Trustee of users and partner biobanks





Biobanking Platform

Coordinative Activities

- Detailed site evaluations
- Biobanking-IT/Coordination with CCP-IT/ Integration in CCP concept
- Harmonization of DZGs Biobanking
- Biobank Catalogue (BBMRI & German Biobank Catalogue conformity)
- Interaction with other national and international activities





Detailed Site Evaluations

- Biomaterials: storage, degree of utilization, performance indicators, special collections...
- Datamanagement: Which data are available? How are they administered?
- Qualitymanagement: Is there an existing QMS?
 Which standards?
- Projectmanagement: Available? Standardized?
 Performance indicators?
- ELSI: ethical vote, informed consent & data protection rules

| Berlin | | |
|------------------------------|--|--|
| Dresden | | |
| Essen/ Düsseldorf | | |
| Frankfurt/ Mainz | | |
| Freiburg | | |
| Heidelberg | | |
| München | | |
| Tübingen | | |
| □= finished □= date fixed | | |



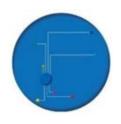


Biomaterial Availability

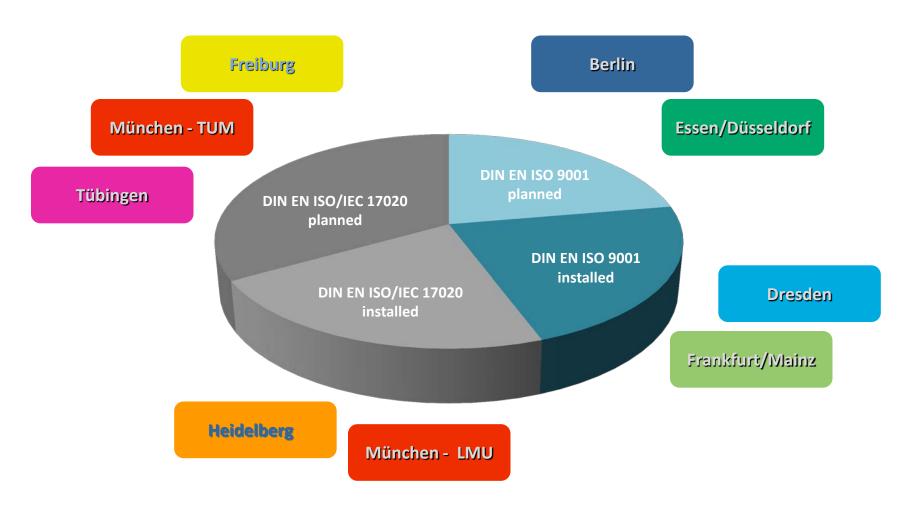
| | Tissue | Liquids | DNA/RNA |
|--|--------|---------|---------|
| ZeBanC Berlin | ✓ | ✓ | ✓ |
| TNTB UCC Dresden | ✓ | × | × |
| Biobank des Westdeutschen Tumorzentrums Essen | ✓ | ✓ | ✓ |
| UCT-Biobank Frankfurt (Allgemeine Tumorbank) | ✓ | × | ✓ |
| UCT-Biobank Frankfurt (Hämatologische Tumorbank) | × | ✓ | ✓ |
| UCT-Biobank Frankfurt (Hirntumorbank) | ✓ | × | ✓ |
| Tumorgewebebank Freiburg | ✓ | × | × |
| NCT-Gewebebank Heidelberg/(NCT Liquid Biobank) | ✓ | (✓) | (✓) |
| Gewebebank TU München | ✓ | × | × |
| LMU Biobank München | ✓ | ✓ | ✓ |
| Tumorbank CCC Tübingen | ✓ | × | × |

| Collection: | <u> </u> | = yes; | ⊨ nc |
|-------------|----------|--------|------|
|-------------|----------|--------|------|





Quality Management







Biobanking Platform - Future

- Reach sustainability (2nd funding period)
- Complete harmonisation of all sites
- Complete integration in CCP-IT concept (bridgeheads)
- Harmonisation with other activities (DKH-CCCs; joint board)
- Increase project work





The German Centres for Health Research – Coordinative Biobanking (and IT) Issues

- Common ground on biobanking and IT in DZGs
 - Need for local and Meta-IT-Systems
 - Need for coordinated DZG-adapted biobanking
 - Lack of respective preexisting structures need for implementation
 - Need for information and best practice exchange
 - Need for perception and sustainability
- Avoid conflicts and use synergies at multi-DZG sites
- Avoid unnecessary implementation work/mistakes learn from the others
- Coordinate similar activities (lobbying, PR, training)







DZG WG Biobanking & IT

- 1st coordination meeting in (Munich; Nov 13)
- DZG management board (Frankfurt; Dec 2013)
- Consent on biobanking structures and interaction
- Defined Activities:
 - QM/SOP collections
 - Biobanking Catalogue
 - PR
 - Regular communication
 - DZG Boards statements (Controlling and reviewing parameters)





DZG Biobanking Catalogue

- Good DZG-wide documentation /overview
- Individual but harmonized BBMRI-compatible format

Laboratory Information Management System (LIMS)

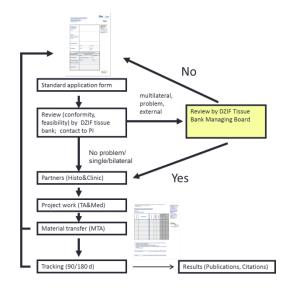
- Different systems → interoperability challenges
- Using/expanding local synergies

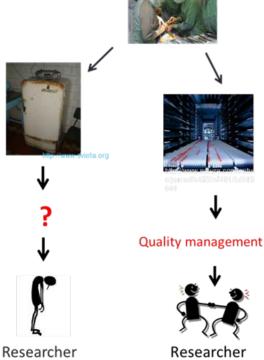




Quality management for Biobanking

- Indispensable: comprehensive and structured quality management considering future certifications/ accreditations
- SOP-collection
- Project management harmonisation









Statements of DZG WG Biobanking Example Controlling and Reviewing of Biobanks

- 2014/15 First draft statement by WG
- 4-11/15 Adaptation, evolution, and interdisciplinary consent by German Cancer Aid (DKH) working group biobanking
- 11/15-2/16 Acceptance by
 - CCC Board of DKH
 - All 13 CCCs
 - DKTK Board





The German Centres for Health Research – Differences in Biobanking

- Preexisting biobanking structures?
- Sufficient prospective probes and data acquisition?
- Need/acceptance of centralisation
- Extent of interaction/interference with clinical structures
- Need for human bioprobes
- Different DZG organisational structure
- Different core structures concepts



Different organisational and decision-making structures!





The German Centres for Health Research – Biobanking

- Most powerful and sustainable biobanking support network
- Efficient implementation of biobanking in all DZG
- Different structures and aims due to inherent DZG differences
- Efficient internal harmonisation and information activity (DZG WG Biobanking and IT)
- Efficient work share with other national activities (GBN, TMF, WG CCCs)
- Clear future perspectives





The German Centres for Health Research – Biobanking Perspectives

- Assure sustainability of biobanking in DZGs (organisational & financial)
- Harmonisation of assessment and controlling rules
- Harmonisation of IT solutions (limited)
- Maintain coordinative platform (biobanking & IT WG)
- Joint activities
 - Catalogues
 - Outreach
 - International networking









DZGs

Coordination Biobanking

DZG WG Biobanking&IT

BioMaterialBank Heidelberg (BMBH)

- L. Glück
- E. Herpel
- R. Kirsten