Biobanking quality control from the Shanghai Clinical Research Center perspective

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## Chinese Biobanks

<table>
<thead>
<tr>
<th>Year</th>
<th>Project</th>
</tr>
</thead>
<tbody>
<tr>
<td>1981</td>
<td>Chinese Human Sperm Bank</td>
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<tr>
<td>1992</td>
<td>The China Marrow Donor Program</td>
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<tr>
<td>1994</td>
<td>Immortalize Cell Bank of Different Chinese Ethnic Groups</td>
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<td>2003</td>
<td>China Kadoorie Biobank</td>
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<tr>
<td>2008</td>
<td>Shanghai Biobank Network (SBN)</td>
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<td>2009</td>
<td>Beijing biobank of Clinical Resources (BBCR)</td>
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<td>2011</td>
<td>China National Genebank (CNGB)</td>
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<td>2011</td>
<td>Clinical Specimen Repository in the context of Significant New Drugs Development</td>
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<td>2012</td>
<td>Shanghai Clinical Biobank for Major Diseases.</td>
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<tr>
<td>2012</td>
<td>Shanghai Birth Cohort</td>
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<tr>
<td>2016</td>
<td>Shanghai Brain Aging Study</td>
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*Gan RX, et al. Biopreserv Biobank 2015*
National Quality Infrastructure

Standardization Administration of the People's Republic of China (SAC)

China National Accreditation Service for Conformity Assessment (CNAS)

National Institute of Metrology (NIM)
SCRC Overview

- Founded in 2008, supported by the government

- Operating independently as a 3rd-party full service, assessment and resources platform

- Vision: To be one of the outstanding global clinical research centers by providing full services with international standard in China
The 3rd-Party Solutions

Platform
1. Standard
2. QA & QC
3. Ethics Guideline
4. Info. Construction
5. Networking & Sharing

Service
1. Tech. Consultant
2. Project Management
3. Centralized Storage
4. Sample Testing
5. R & D for Biobank

Translational Medicine
Knowledge Repository
High Quality Data & Biospecimen

$ BANK $
Quality Management System
<table>
<thead>
<tr>
<th>Works</th>
<th>This Stage</th>
<th>Next Stage</th>
</tr>
</thead>
</table>
| Quality Management System    | 1. Normative work flow  
2. Detailed SOP and forms  
3. Personal, Machine, Material, Environment and Method | 1. ISO 9001/17025  
2. CAP  
3. ISO 20387 |
| Quality Control              | 1. Attending ISBER PT program  
2. DNA Qualification  
3. RNA Integrity  
4. Cell Viability  
5. Temperature Monitoring & Alarms | 1. QC checkpoints  
2. Method Validation & PT  
3. Quantitative VS Qualitative  
4. Cell Viability  
5. Tissue Antigenicity & Histology |
| Quality Inspection           | 1. Professional team                                                       | 1. Documents Inspection  
2. Site Inspection |

Quality Manual

Procedure Files

SOP

Record Forms
QC for nucleic acid from tissue, blood and body fluid

Sample preparation

Nucleic acid Extraction

Quality Control Test

Quantitative & Qualitative Analysis
Technology Support

Over 800 Clinical & Bio-lab Tests

Clinical Laboratory Testing Division
- Clinical Immunology Lab
- Clinical Biochemistry Lab
- Clinical Microbiology Lab
- Clinical Molecular Biology Lab
- Hematology/Urianalysis Lab
- Flow Cytometry Lab
- Elemental Analysis Lab
- Cytogenetics Lab

Central Lab
CAP & ISO15189

Clinical Pathology Division
- Anatomic pathology
- Cytopathology
- Molecular pathology

Molecular Analysis Division
- Real-time PCR
- SNP analysis
- Gene sequencing

Analytical Chemistry Division
- Pharmacokinetics/dynamics lab
- Chemistry/Drug analysis
- LC-MS technologies
System Validation & Information Security

System Validation:
- The computer system validation strategy
- 21 CFR Part 11 plan
- Validation of the plan and the confirmation
- Risk assessment
- Software development
- Validation of the Database Room
- Quality Validation Plan
- Installation Validation
- Performance Validation
- Operation Validation
- Installation of hardware and software
- Validation of the standard computer configuration
- Business continuity plan
- Disaster recovery plan
- ... ...

ISO27001:
- Information Security management manual
- Corrective Action and Preventive Action
- Computer management
- Backup management
- Database management
- Visit control management
- Information security management system
- Business continuity management system
- Change management
- Server management
- ... ...
Method Validation of DNA Quantitation

Within-run

Between-run

Target Value

Precision

Accuracy

Reference material

Linearity

Limit of detection

Gradient dilution

Instrument limitation


National Institute of Metrology (NIM)
Internal & external QC (PT program)

1. Levey S, Jennings ER. Am J Clin Pathol. 1950
2. Westgard J.O. et al., Clinical Chemistry. 1981

'accurate' or 'very satisfactory'
Sampling Process for QC Program of Shanghai Biobank Network (SBN)

Reference:
A. 组织样本快速冷冻操作规程（SOP-SC-004-01）
B. 原始材料RNA检测用操作规程（SOP-SC-003-01）
C. 组织样本石蜡包埋及石蜡组织切片操作规程（SOP-SC-003-01）
D. 组织样本CT图像分析用操作规程（SOP-SC-005-01）
QC Program for Shanghai Biobank Network

1. Specimen pool
2. Sampling list
3. Reservation
4. Shipment
5. Sample reception
6. Sample testing
7. Report
**Temp. monitoring & Controls**

- **Temp. monitoring**
  - Dry ice (-80°C)
  - Shipment

PS: Positive controls were transferred and handled together with samples.

- **Positive control**
  - Blood
    Fresh whole blood (200μl/tube)
  - Tissue
    Hela cell line

![Graph showing temperature monitoring over time](image)
**CASE I Shanghai Birth Cohort (SBC)**

- Environmental pollution
- Disease causes remain elusive
  - Infertility, miscarriage, birth defects, childhood asthma, childhood obesity, and sexual prematurity
- Fewer children in each family
  - Raising serious public concerns
- China has a well-established maternal and child health (MCH) care system
  - Almost 100% coverage of women and children
- >5000 couples and >4000 new borns from 2013 to 2016


CASE II  Shanghai Brain Aging Cohort

- **Community-based recruitment**
  - 10-30% old people, easy to follow up
- **Disease-based**
  - Alzheimer disease, Parkinson’s disease
- **Clinical trial-based**
  - Drug/biomarker/behavioral intervention development
- **Multi-sites with data and biospecimen centralization**
  - Questionnaire, PET/MRI images, Clinic information access, biospecimen storage
- **Public Private Partnership (PPP)**
- **China Brain Project 2016-2030 (Ministry of Science & Technology)**
## SCRC’s Contribution

### Population based cohort study

#### Data Services
- Electronic questionnaire design
- Electronic data capture (EDC)
- Cognitive assessments administration
- Data validation

#### Biobanking
- Participant recruitment
- Informed consent
- Biospecimen collection, shipment, processing, storage and testing
- Method/procedure validation
- Lab-kit

#### Project Management
- Schedule control
- Training
- On site monitoring
- Quality assessment
- Others
In Summary

On Site
- ICH-GCP
- ...

Biobank
- ISO9001
- ISO17025
- ISO/DIS 20387

Central Lab
- ISO15189
- CAP
- ...

Data
- ISO27001
- ...

Birth Cohort
Chronic Disease
Brain Cohort
Thanks!

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