Faculty of Health Sciences Ethics Office

ETHICS OFFICE	Standard Operating Procedure		
Title	Standard Operating Procedure for data and biological sample collection, storage, management and transfer in research studies and HREC-registered Databases, Biobanks and Registries		
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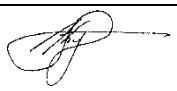
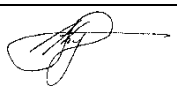
1 COMPILATION AND AUTHORISATION

Action	Designated person	Signature	Date
Compiled by:	Prof Minrie Greeff		10 March 2017 6 June 2018
Checked by:	Ethics Office		15 March 2017
	HREC		16 March 2017
	Faculty board		18 May 2017
Authorised by:	Prof Minrie Greeff as Head of the Ethics Office		19 May 2017 6 June 2018

2 DISTRIBUTION

Department/Unit	Name	Signature	Date
Ethics Office	Prof Minrie Greeff		6 June 2018
Chairperson on behalf of the HREC	Prof Wayne Towers		6 June 2018
Executive Dean of the Faculty of Health Sciences	Prof Awie Kotzé		6 June 2018
Faculty of Health Sciences	Mrs Leanie van Ronge		6 June 2018

3 DOCUMENT HISTORY

Date	Version No.	Reason for revision
10 March 2017	1	Formulated the SOP
6 June 2018	2	Change in university structure

4 PURPOSE OF THE SOP

A distinction is made between *data* and *human biological material* (see section 6 for definitions). This SOP covers both these aspects.

Databases and Biobanks are both collections of, respectively, data and biological samples from *individuals* and/or *populations,* collected within either *larger studies* or *HREC-registered Databases and Biobanks.* Both give rise to similar ethical concerns about:

- Dignity
- Autonomy
- Privacy
- Confidentiality
- Discrimination

The purpose of this SOP is to provide guidance to researchers about ethical issues during:

- Data or biological sample collection.
- Storage and management.
- Sharing and transfer.
- Registration of Databases and Biobanks with HREC.

This SOP is to support researchers using Databases, Biobanks or Registries within *larger studies* or for *HREC-registered Databases, Biobanks and Registries*.

5 SCOPE

Two documents form the basis for this SOP:

- Ethics in Health Research: Principles, Processes and Structures, with special reference to chapter 3 (Department of Health, 2015) (Referred to as DoH, 2015 in the rest of the SOP).
- Declaration on Ethical Considerations regarding Health Databases and Biobanks (World Medical Association, 2016). (Referred to as WMA, 2016 in the rest of the SOP).

The DoH, 2015 guidelines make reference to several aspects: the permitted usage of biological materials; data and biological materials for research purposes; identifiability of biological materials and data; collection of biological materials and data; restriction on collection of biological materials; special reference to informed consent in this context; and secondary use of materials or data. All these aspects are applicable to larger studies as well as HREC-registered Databases, Biobanks or Registries. The guidelines also more specifically refer to Databases, Registries and Repositories and the informed consent required for these processes. This SOP functions within these guidelines.

The National Health Act (2003) allows for biological material to be removed from both *living and deceased persons* (National Health Act of 2003 ss 55 and 62) for *diagnostic, therapeutic and health research purposes* (NHA s 64(1)). Once collected, data and biological material may be stored in a researcher's larger study Database, Biobank or Registry or a HREC-registered Database, Biobank or Registry as a future research resource.

Note: Although data and biological material are separate from their source, within the South African context they *symbolise that person* and should be handled with the necessary respect.

The ethical considerations concerning the use of data or biological samples involve:

- How to access these appropriately.
- How to use these appropriately.
- How to manage potential privacy concerns that may arise from information management.
- How to address the special status some segments of the population ascribe to the human body and its parts.

- How to demonstrate sensitivity to the values, beliefs and attitudes of the person/s from whom data and biological materials are derived (DoH, 2015).

The Declaration of Helsinki (2013) further lays down ethical principles for research involving human participants, including the importance of protecting the dignity, autonomy, privacy and confidentiality of research participants, and obtaining informed consent for using identifiable data and biological materials. However, since 2016 it also focusses on the ethical principles and governance of Databases and Biobanks. The World Medical Association, 2016 emphasizes the right to autonomy, privacy and confidentiality that entitle individuals to exercise control over the use of their personal data and biological material in Databases and Biobanks. They encourage all researchers using data or biological material in Databases and Biobanks to adopt the newly formulated ethical principles and governance guidelines. No national or international ethical, legal or regulatory requirement should reduce or eliminate any of the protections for individuals and/or populations set forth in the declaration.

6 ABBREVIATIONS AND/OR DEFINITIONS

Abbreviation/definition	Description
Data	Information collected from a research participant e.g. transcribed interviews, questionnaires, documents, health records, etc.
Human biological materials or specimen	Human tissue which includes blood and blood products, DNA, RNA, blastomeres, polar bodies, cultured cells, embryos, gametes, progenitor stem cells, saliva, sputum, gastric juices, urine, small tissue biopsies and growth factors (Adjusted from DoH, 2015). Biological material refers to a sample obtained from an individual human being, living or deceased, which provides biological information, including genetic information, about that individual (WMA, 2016).
Donor	The person (living or deceased) from whose body biological materials have been removed or withdrawn (DoH, 2015) with the appropriate permission.
Narrow consent	Donor permits single-use only of data and biological materials; no storage; no sharing of data or specimen; new consent required if further use wanted (DoH, 2015).
Tiered consent	The donor permits use of biological materials for the current study and chooses whether to permit storage for future use, as well as data and sample sharing (DoH, 2015). Each follow-up study has to obtain re-consent from the original donor.
Broad consent	The donor permits use of data and biological materials for future studies, *subject only to further prior ethics review and approval by the HREC.* It allows for storage and possible future use for research purposes, even though the precise nature of future research may be unclear at the time. In the informed consent documentation, the *nature of future use should be described as fully as possible* and *stipulate that further ethics review by the HREC of a new study or sub-study* is necessary. Consent can then be *waived and the HREC becomes the advocate for the participant.* Permission may also be sought by *re-consent* if the planned research is outside the scope of the current consent (DoH, 2015). Note: See Appendix A, Point 4 for an example of a template for storage and future use of unused samples of biological materials (Ethics in Health Research: Principles, Processes and Structures, DoH, 2015).
Blanket consent	Unrestricted use of data and collected biological material. NB: Not recommended in the South African context, as it becomes difficult to implement and sustain fundamental ethical principles - especially that of respect for persons (DoH, 2015).
Coded data or specimen	Identifiers are substituted by a number, symbol, or other method to provide a code; a key to the code exists that can link the specimen to its original source (DoH, 2015).

Identifier	Information such as a name, initials, address, folder numbers or biometric identifier (e.g. fingerprint) that can identify a particular donor (DoH, 2015).
Identifiable information	Reasonably expected to identify an individual on its own or in combination with other information. • **Directly identifying** – direct identifier e.g. name, identity number. • **Indirectly identifying** – combination of indirect identifiers e.g. date of birth, address, unique personal characteristics. • **Coded information** – direct identifiers removed; replaced with codes. • **Anonymised information** – *irrevocably stripped* of direct identifiers; no code. • **Anonymous information** – never had identifiers (DoH, 2015)
Anonymous data or specimen	Data or biological materials *without any overt identifying information or link* to a specific donor (DoH, 2015).
Database	A collection of information including images arranged in such a manner as to facilitate swift search and retrieval (DoH, 2015). A system for collecting, organizing and storing health information (WMA, 2016). A Database can consist of a large dataset collected for multiple studies under a *larger study* or can be for the specific purpose of populating an *HREC-registered Database* for which specific research studies will be developed to make use of the previously collected data in the Database.
Biobank/repository	A collection, storage and distribution system for *human biological materials* for research purposes including blood, urine, faeces, bone marrow, cell aspirates, diagnostic specimens, pathology specimens, and so on. Usually *demographic and/or medical information* about the donors is included in the repository, as are codes that link the material to the donors (DoH, 2015). A collection of biological material and associated data (WMA, 2016).
Virtual repository	A digitised system that manages distributed *bar-coded electronic versions* of material, data or images through shared data systems (DoH, 2015).
Registry	A *collection of information* (data) from multiple sources, maintained over time with controlled access through a gatekeeper organizer (DoH, 2015).
Secondary use	Data or biological materials originally collected for other purposes e.g. diagnostic, therapeutic, service delivery or work-integrated purposes.
Secondary analysis	Analysis of datasets or previously collected biological samples that have been analyzed for their original objectives but are now analyzed for new objectives.
IRERC	Institutional Research Ethics Regulatory Committee

7 RESPONSIBILITIES

7.1 Researchers

- Each researcher should consider the ethical, legal and regulatory norms and standards for Databases, Biobanks or Registries in South Africa as well as applicable international norms and standards.
- Whether for use in a larger study or for an HREC-registered Database, Biobank or Registry it has to undergo *prior ethics review by the HREC* as *no retrospective approval can be granted*.
- All researchers that want to use large Databases, Biobanks or Registries for larger studies or HREC-registered Databases, Biobanks or Registries must develop *procedural mechanisms* for secure collection, receipt, storage, management, sharing and transfer of information and specimens.
- The associated *informed consent documentation* should at all times be available to ensure that data or biological samples are used according to the original purpose for which consent was obtained.
- All research using Databases, Biobanks or Registries of larger studies or HREC-registered Databases, Biobanks or Registries, including that undertaken by a post-graduate student, require new ethical approval.

- The application can be done as *a sub-study under a larger study* or *a single new study application using the HREC-registered Database, Biobank or Registry by* following SOP_Ethics_1.4. The sub-study will receive its own HREC number which will be linked to the larger study, or a new number will be allocated if not part of a larger study.

7.2 THE HREC

The HREC must:

- Assess the extent to which data and/or human biological materials could be used in larger studies or HREC-registered Databases and Biobanks.
- Eliminate risks to dignity, autonomy, privacy, confidentiality and discrimination.
- Ensure the integrity of the data and/or biological samples.
- Carefully scrutinize informed consent documentation to ensure that the proposed research and its implications are adequately disclosed and explained.
- Ensure the appropriate dataset owners are involved or acknowledged.
- Register Databases, Biobanks and Registries.

8 PROCEDURE/S

8.1 Data or biological sample collection

Data and biological materials can be collected in a variety of ways:

- Specifically for *research* purposes.
- Incidentally during *diagnostic or therapeutic* procedures.
- For a *combination of purposes*, including future research.

Secondary use of data or biological materials:

Sometimes data or biological materials are collected and used for *diagnostic or therapeutic* purposes. In the *absence of broad consent that includes consent for research,* the following is recommended:

1. Use of existing or archived material collected for clinical or diagnostic purposes requires expedited review. The nature of the previously obtained consent should be determined to ascertain whether subsequent usage was envisaged and whether it falls in the scope of the current proposal. If so, new consent is not required.
2. If the scope is different, then new consent may be required.
3. If the samples are anonymous (no identifiers, and the results would not place any individual, family or community at risk), then new consent is not required.
4. The person who holds the code or link should sign an explicit written agreement not to release the identifiers to the research team.
5. If the samples can be linked to identifiers, the HREC must decide on a case-by-case basis whether expedited or full review is necessary.

There are, however, specific absolute restrictions on collection of certain biological materials that require ministerial permission.

The following biological materials have restrictions:

- Biological materials from a mentally-ill person (none permitted);
- Biological materials that are not naturally replaceable from a minor;
- Gametes from a minor (none permitted); and
- Fetal biological material except for umbilical cord progenitor cells (none permitted).

General informed consent requirements:

The requirements for *written informed consent* as set out in the DoH, 2015 guidelines are applicable.
Special attention should, however, be given to include important aspects like the type of consent (e.g. broad/narrow consent), the intended research objectives, whether the HREC will oversee any further research done in a larger study, whether data will be shared or transferred or sent overseas, and so on. It could be meaningful to see which of the aspects mentioned under section 8.4.2 might be applicable to the intended larger study.

Should data or biological samples specifically be collected for *research* use, **prospective** informed consent is required.

For larger studies, *tiered* or *broad consent* are the options. In the case of tiered consent, re-consent will have to be obtained for each new further study. With broad consent and specific review by the HREC, consent can be waived by the HREC as long as the intended new further study falls within the parameters of the obtained consent.

Specific informed consent requirements for gathering biological material:

- Written informed consent is required **prior to removal** of biological material from a **living** *donor* (NHA ss 56 and 62).
- In the case of a **deceased person** it can be found in:
  - The Will of the deceased person.
  - A written statement.
  - A witnessed oral statement may be provided by:
    The spouse, partner, major child, parent, guardian, major brother or major sister of that person in the specific mentioned order (proxy).
  - An **authorized person.**
- **Proxy consent** may be permissible if a donor is unable to provide informed consent.
- It should be made clear that biological materials cannot be completely anonymised.
- Participants should always understand clearly what is requested.
- The HREC must ensure that the nature (diagnostic, therapeutic or health research) is explained adequately so that purpose for which consent is being requested is completely clear.
- The HREC must also consider circumstances under which *re-consent* from donors would be sought.
- The HREC should bear in mind that careful deliberation is always necessary when considering future use.

Specific informed consent for genetic or genomic research:

The HREC must pay attention to multiple considerations, namely:

- The proposed social value of the intended study.
- The type of consent obtained.
- Privacy and confidentiality measures.
- Potential effect on the family or community.
- The proposal must include a plan on how information revealed by the research will be managed:
  - Participants must be able to choose whether they wish to receive the information personally especially if clinically significant results are determined.
  - It must ascertain whether it may be shared with biological relatives.
  - Genetic counselling must be available.

8.2 Data or biological sample storage and management

For ethical considerations, the various forms of data or specimen storage **(Database, Biobank or Registry)** are treated similarly.

Databases, Biobanks or Registries must be appropriately managed and safeguarded in order to protect individuals and populations.

Databases, Biobanks or Registries must be operated under the responsibility of an appropriately qualified professional assuring compliance with the set policies.

In order to foster trust, Databases, Biobanks or Registries must be governed by internal and external mechanisms based on the following principles:

- Protection of individuals and populations: Governance should be designed so the rights of individuals and the population prevail over the interests of other stakeholders and science.
- Transparency: Any relevant information on the Databases and Biobanks must be made available to the public.
- Participants and inclusion: The means of consultation and ongoing engagement with participants and their communities in the development of Databases and Biobanks must be detailed.
- Accountability: The use of Databases, Biobanks and Registries should be based on the respect of mutual obligations of all stakeholders.

Governance arrangement must include the following elements:

- The purpose of the Database, Biobank or Registry.
- The nature of the data and biological material that will be contained in the Database, Biobank or Registry.
- The length of time the data or material will be stored.
- Regulations for the disposal and destruction of data or material.
- How the data and material will be documented and traceable in accordance with participants' consent.
- How the data and material will be dealt with in the event of change of ownership or closure.
- Obtaining appropriate consent or other legal basis for data or material collection.
- Protecting dignity, autonomy, privacy and preventing discrimination.
- The criteria and procedures concerning access to and the sharing of the data or biological material, including the systematic use of a Material Transfer Agreement (MTA) when necessary.
- The persons/s who are responsible for the governance.
- The security measures to prevent unauthorized access or inappropriate sharing.
- The procedures for re-contracting participants, where relevant.
- Procedures for receiving and addressing enquiries and complaints.

Those researchers contributing to or working with the Databases, Biobanks or Registries must comply with the appropriate governance arrangements (WMA, 2016).

An annual progress report must be submitted to the HREC that reflects all new research undertaken by researchers or named co-investigators which used data or biological samples from the Database, Biobank or Registry, as well as general management practices.

8.3 Transfer or export of data or biological samples

In research, the need might exist to share or transfer data or biological samples to another collaborator/researcher/institution or another country (See paragraph 8.4.4 below).

To do this, participants must have given prior permission for data or biological samples to be shared or transferred.

For these purposes, collaborative agreements and/or Material Transfer Agreements (MTA) are put in place before any data or biological samples can be shared or transferred to another collaborator/researcher/institution or country. These agreements should have been set up by the researcher, authorized by the legal office of the NWU, and approved and signed by the correct level of authority.

The minimum requirements that should be stated in the MTA are:

- What is going to be transported?
- The quantities transferred.
- The number of participants and visits/frequency of exporting samples.
- Whether the substance will be stored overseas, or destroyed.
- Who the collaborator is.
- It should be signed by the appropriate signing authority and the collaborator.
- Export address that is the same as the MTA address (DoH, 2016).

To export biological samples and obtain an export permit from the DoH, three documents have to be in place:

- An HREC ethical clearance certificate based on the review of the proposal, the informed consent and the approved MTA.
- The material transfer agreement.
- A completed DoH application form (DoH, 2016).

8.4 HREC Registration of Databases, Biobanks or Registries

A researcher/group of researchers might decide to develop a Database, Biobank or Registry for future research purposes. In this case, they have to apply for *HREC registration* of such a Database, Biobank or Registry.

8.4.1 Proof of adherence to the ethical principles

- It should be clear that the ethical principles are adhered to at all times.
- The research should be conducted for the benefit of society.
- As stewards protecting information provided by participants, researchers have both ethical and legal obligations.

- The right to autonomy, privacy and confidentiality entitle individuals to exercise control over the use of their personal data and biological material.
- Confidentiality is essential for maintaining trust and integrity in Databases, Biobanks or Registries. Knowing that their privacy will be respected gives participants and donors the confidence to share sensitive personal data.
- Privacy is protected by the duty of confidentiality adhered to by all involved in handling the data and biological material.
- The collection, storage, use and reuse of data and biological materials from participants capable of giving informed consent must be voluntary.
- Participants have the right to request and be provided with information about their data and use, as well as to request correction of mistakes or omissions.
- Databases and Biobanks should adopt adequate measures to inform the participants about their activities.
- Participants have the right, at any time and without reprisal, to alter their consent or to ask for their identifiable data to be withdrawn from the Database and their biological material from the Biobank. This prevents future use of the data and biological materials.
- In the event of a clearly identified and immediate threat where anonymous data will not suffice, the requirements for consent may be waived to protect public health. The HREC should confirm that each exceptional case is justifiable.
- Beyond the need to protect the individual, the protection of the communities and populations concerned, in particular those that are vulnerable, must also be taken into consideration, especially in terms of benefit sharing.
- Special consideration should be given to the possible exploitation of intellectual property. Protections for ownership of materials, rights and privileges must be considered before collecting and sharing the material. Intellectual property issues should be addressed in a policy.
- The HREC must approve the establishment of Databases, Biobanks or Registries used for research and other purposes.
- The HREC must also approve use of data and biological material and decide on the type of consent required, taking into consideration risks and benefits of the activity.
- The HREC has the responsibility of monitoring ongoing activities (WMA, 2016).

8.4.2 Informed consent for data and biological samples being used in Databases, Biobanks or Registries

If the data or biological material are stored in a Database, Biobank or Registry for multiple and indefinite uses, consent is only valid if the participants have been adequately informed about and have understood:

- The purpose of the Database, Biobank or Registry; how it works and the type of research it supports.
- The nature of the data or the material to be collected.
- The procedure that will be followed in the case of incidental findings.
- Implications of genetic testing.
- The rules of access to the Database or Biobank.
- The governance arrangements (as stipulated in 8.4.3 below).
- The potential decision to anonymise data, and in the case of irreversible anonymization, the fact that the participant will not be able to know what is done with their data and biological material, nor will they have the option of withdrawing their consent.
- Their fundamental rights and safeguards established in the declaration.
- When applicable, commercial use and benefit sharing, intellectual property issues and the transfer of data or material to other institutions or other countries (WMA, 2016).
- How privacy and confidentiality interests will be protected.
- The nature and extent of specific risks of harm related to use and storage, especially if identifiers are retained.
- When human genetic research is anticipated, information about potential consequences of genetic testing (e.g. paternity determination, reproduction decisions, illness profiles) and associated confidentiality risks.
- Potential benefits.
- The conditions and requirements under which data or material will be shared.
- Where applicable, the material may be:
    - Used for future research not yet identified.
    - Shared with or transferred to other institutions or other countries.

- The freedom to withdraw consent and the assurance that material will be destroyed.
- Length of storage.
- When the current consent to use the data will expire.
- Information about possible secondary use of stored material.
- Possible creation of an immortalized cell line (DoH, 2015).

The HREC *may approve waiver of consent* for secondary use (see definition under section 6) of material or data if:

- There is no more than minimal risk of harm.
- The donor's rights and welfare interests are unlikely to be adversely affected.
- The research cannot be conducted if the waiver was not approved (DoH, 2015).

8.4.3 Governance requirements for HREC-registered Databases, Biobanks or Registries

HREC-registered Databases, Biobanks or Registries must be appropriately managed and safeguarded in order to protect individuals and the population.

In order to foster trust, Databases, Biobanks or Registries must be governed by internal and external mechanisms based on the following principles:

- Protection of individuals and the population: Governance should be designed so that the rights of individuals and the population prevail over the interests of other stakeholders and science.
- Transparency: Any relevant information on the Databases, Biobanks or Registries must be made available to the public.
- Participants and inclusion: The means of consultation and ongoing engagement with participants and their communities in the development of Databases, Biobanks or Registries must be detailed.
- Accountability: The use of Databases, Biobanks or Registries should be based on respect for the mutual obligations of all stakeholders.

As mentioned, the various forms of data or specimen storage **(Database, Biobank or Registry)** are treated similarly.

Governance arrangement must include the following elements:

- The purpose of the Database, Biobank or Registry.
- The nature of the data and biological material that will be contained in the Database, Biobank or Registry.
- The length of time the data or material will be stored.
- Regulations for the disposal and destruction of data or material.
- How the data and material will be documented and traceable in accordance with consent of the participant.
- How the data and material will be dealt with in the event of change of ownership or closure.
- Obtaining appropriate consent or other legal basis for data or material collection.
- Protecting dignity, autonomy, privacy and preventing discrimination.
- Criteria and procedures concerning the access to and the sharing of the data or biological material, including the systematic use of Material Transfer Agreement (MTA) when necessary.
- The person/s who are responsible for the governance.
- The security measures to prevent unauthorized access or inappropriate sharing.
- The procedures for re-contracting participants, where relevant.
- Procedures for receiving and addressing enquiries and complaints.
- Arrangement of storage to prevent storage at multiple sites across campus which could lead to risks in non-standardised practices (e.g. specimen and temperature maintenance, back-up generators and temperature alarms).
- A contingency plan for data disaster management/retrieval (e.g. hard and soft copies, multiple sites, backup).

Those researchers contributing to or working with the Databases, Biobanks or Registries must comply with the appropriate governance arrangements.

Databases, Biobanks or Registries must be operated under the responsibility of an appropriately qualified professional.

Databases, Biobanks or Registries will be monitored on a regular basis by the HREC to ensure that they are governed as required (e.g. on-site inspections).

8.4.4 Data sharing

Where data or materials are shared with researchers in other institutions:

- The recipient institution should agree to comply with the requirements of the donor institution.
- Use of the data or materials should comply also with any additional requirements of the recipient institution.
- Inter-institutional sharing agreements should be confirmed in writing (DoH, 2015). See section 8.3 for a detailed discussion.

8.4.5 Registration of a Database, Biobank or Registry

To register a Database, Biobank or Registry the following need to be clearly specified:

- The site of the database/registry/repository.
- The type of data/specimen.
- The physical process by which items will be accepted into the Database/Biobank/Repository, for instance:
  - Data transposed onto the datasheet by research assistant.
  - Data entered into the database.
  - Specimen collection and processing and storage.
- The process of informed consent (attach informed consent document).
- Procedural mechanisms (receipt, storage, information handling) to protect privacy and confidentiality.
- The conditions under which data/specimens may be shared with or released to researchers.
- Clarity on the period that data/specimens will be maintained in the Database/Registry/ Repository.
- How data/specimens will be destroyed.
- How participants will be able to withdraw their data/specimens.
- Who will be responsible for ensuring that any requests for sharing information meet the database/registry/repository specification?
- A proposal and ethical application must be made to the HREC to ensure that the informed consent covers what the researcher wants to do so that consent can be waived by the HREC.

9 REFERENCE DOCUMENTS

Ethics in Health Research: Principles, Processes and Structures. Second edition. Department of Health, 2015.

The Declaration on Ethical Considerations Regarding Health Databases and Biobanks of the World Medical Association, 2016.

10 ADDENDA

No	Document name
1	Appendix A: Application form to register a Database, Biobank or Registry

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