**HELIUS Collaboration Policy** (version 2019)

This document describes the organization of the HELIUS (HEalthy LIfe in an Urban Setting) study, the opportunities for collaboration and the procedures for the use of research data.

**1. General**

1. HELIUS has been set up to study health differences among the six largest ethnic groups in Amsterdam, with emphasis on cardiovascular disease, infectious disease and mental health. HELIUS is being carried out by the AMC and the Public Health Service of Amsterdam (*GGD Amsterdam*). Various departments of the AMC, of the Public Health Service of Amsterdam and other universities are participating in the study. The HELIUS team is open to proposals for collaboration with internal and external research teams.
2. Proposals regarding scientific collaboration should be submitted to the Scientific Coordinator, preferably after consulting the relevant Theme Leader (see below). The proposals will then be considered by the HELIUS Executive Board, on the basis of:1. compatibility with the general objectives of the HELIUS study, 2. the quality of the research proposal, 3. possible overlap with other cohort studies, 4. the use of biological material, 5. logistical feasibility and 6. the (financial) contribution to be made. See **appendix 1** for details on the types of research question HELIUS can be used for. See **appendix 2** for a summary of the study design and an overview of the HELIUS data collection.
3. Scientific collaboration is possible only after approval of the proposal by the HELIUS Executive Board and subject to agreement being reached regarding the matters referred to in this document.
4. Each research team is separately responsible for obtaining approval from AMC’s Medical Ethical Review Committee (METC) for the team’s research proposal (where relevant). No proposal for further HELIUS-based research may be submitted to the METC without the prior approval of the HELIUS Executive Board.

**2. Organization**

HELIUS consists of the Executive Board, the Project Group, the Operational Management Team and a Scientific Advisory Board (see Figure).

1. The Executive Board (*Dagelijks Bestuur*, DB) has ultimate responsibility for HELIUS. The DB is made up of the Chair, Vice-chair, Theme Leaders (for each research theme), at least one representative of the Public Health Service of Amsterdam, the Scientific Coordinator and one representative of the Operational Management Team ( if applicable). The DB is responsible for progress and the day-to-day operations, acquisitions not covered by the normal scientific subsidy applications, the assessment of research plans and formulation of the budget. The Chair and the Financial Controller of AMC Medical Research (AMR) together undertake the financial management. The DB is part of the Project Group.
2. The Project Group (PG) is responsible for the scientific input, acquisition and output. The PG is made up of the DB, the Operational Management Team and researchers working on the three research themes, drawn from various departments of AMC and the Public Health Service of Amsterdam (*GGD Amsterdam*). The PG discusses (plans for) research in the PG meetings and draws up research proposals and publication proposals. The PG writes HELIUS publications or supervises the writing of publications by trainee research assistants/researchers. The PG also supports the Operational Management Team in matters such as the selection and sourcing of equipment and obtaining protocols.
3. The Operational Management Team (MT) is responsible for the day-to-day data collection activities. Its members are as follows: Scientific/General Coordinator (MT coordination, research coordination, biobank management, liaison between DB, MT and PG), Research Secretariat Coordinator (coordination of logistics at research secretariat, quality control), Fieldwork Coordinator (coordination of data collection during the physical research, quality control), Interview Coordinator (coordination of data collection interviews, quality control), Data Manager (maintenance of the ICT structure, data cleaning, data extraction for researchers), and the Communication Manager (responsible for communication regarding HELIUS). In the event of problems or disagreements within the MT or regarding the data collection, the DB has the final say.
4. The Scientific Advisory Board (*Wetenschappelijke Adviesraad*, WAR) issues advice on research policy and the scientific quality of research. The WAR is made up of people who have no involvement with the HELIUS study, but have considerable knowledge and expertise regarding the three medical research themes and regarding large-scale cohort studies. The WAR meets once a year and advises the DB both on request and of its own accord. The WAR assesses the content (scientific quality) of the plans, the implementation and progress of the research programme and the underlying projects. One month before the annual meeting, the DB informs the WAR in writing about the research plans, implementation and progress.



*Figure: HELIUS organization diagram*

**3. Researchers**

1. Scientific participation in HELIUS usually involves the appointment of a PhD student whose doctoral research is based at least partly on the HELIUS study data. The PhD student is an active member of the HELIUS PG for a period of three to four years.
2. A PhD student whose doctoral research is based exclusively on the HELIUS study data contributes to the general HELIUS activities (i.e. data collection) for one full-time year. The year’s work may be spread out over the first two or three years of the appointment. The HELIUS activities undertaken are not necessarily related to the student’s own research. We aim for a situation where, during the period of attachment, half of the student’s time can be devoted to his/her own research. However, priority is given to the general HELIUS activities.
3. If the PhD student’s doctoral research is based only partly on HELIUS data, the amount of time contributed to general HELIUS activities is adjusted on a pro rata basis.
4. If a disagreement arises regarding the contribution that a PhD student should make to general HELIUS activities, the final decision lies with the DB.
5. The general HELIUS activities undertaken by a PhD student are supervised by the Scientific Coordinator or an appointed MT member. Scientific supervision of the PhD student’s activities in connection with his/her own research project is provided by his/her thesis supervisor(s).
6. PhD students working within HELIUS participate in the general meetings and activities for HELIUS staff and researchers (HELIUS Project Group meetings).
7. Researchers (postdocs, PhD students, students) who contribute to the data collection are required to sign a HELIUS confidentiality statement, which is available from the supervising MT member.
8. In consultation with the DB, alternative means of scientific collaboration may be agreed.
9. Where scientific participation is agreed, the relevant research project is embedded within one of the three research themes (cardiovascular disease, infectious disease and mental health) by the DB. Each of the three research themes is supervised by the Theme Leader who represents the project within the DB. If there is any doubt regarding the compatibility of a research project with one of the research themes, the DB may be contacted and has the final say.

**4. Finance**

1. The costs associated with a PhD student’s participation in HELIUS are borne by the department that initiates the relevant project. The associated costs include both the personnel costs (PhD student, personnel for data collection) and materials costs not already covered by HELIUS or another department.
2. For each PhD project, HELIUS will additionally receive:

* €25,000 as a contribution to the general data collection infrastructure (if the PhD student does not contribute to the data collection in the manner described in section 3.)

c. The above contributions are treated as financial contributions to the cost of the infrastructure that is required for general data collection within HELIUS.

d. The contributions payable in respect of non-doctoral research undertaken on a part-time basis and doctoral research undertaken only partly within HELIUS are adjusted on a pro rata basis, subject to a minimum of €10,000 per research question or publication. The exact amount is determined by the DB on a case-by-case basis. It is also possible to contribute in kind to the data collection costs by providing equipment or personnel capacity of an equivalent value. For example, consideration would be given to a proposal to contribute to the data collection through an internship involving one or two days per week for the duration of the internship.

e. The contributions specified above are payable in respect of projects that utilize previously collected data. If additional data need to be collected or if use is made of stored biological material, additional costs may be payable.

**5. Procedures for the use of data**

In order to secure approval for a larger research project within HELIUS, a *research proposal* must be submitted:

* The research proposal is submitted for a proposal for a subsidy application, a proposal for a sub-study (additional data collection in HELIUS participants) or a proposal for a doctoral programme. Research proposals should be submitted using the HELIUS Research Proposal Form (**appendix 3**). The HELIUS DB assesses research proposals on the basis of the following criteria: compatibility with the general objectives of the HELIUS study, the quality of the research proposal, possible overlap with other cohort studies, the use of biological material, the logistical feasibility and the (financial) contribution to be made.

In order to secure approval for the *publication* of available HELIUS data, a publication proposal must be submitted:

* A publication proposal is required for *each* article to be written using HELIUS data (also if a related research proposal has already been approved). Publication proposals should be submitted using the HELIUS Publication Proposal Form (**appendix 4**). This allows for an overview of all HELIUS publications and avoids possible overlaps. The DB assesses all publication proposals. A HELIUS Publication Proposal Form should also be submitted for provisional analyses, presentations and internships that are not intended for (immediate) publication.

In order to specify the exact *data* to be used for a proposal, a data request is submitted:

* A data request should accompany a publication proposal, or a research proposal concerning a study that involves the collection of additional data on a selection of participants. Data requests are submitted using the HELIUS Data Request Form (**appendix 5**). On the basis of the data request, a data file is created after the approval of the proposal, which is then used for the analyses associated with the relevant publication or study. In principle, data can be used for a period of 1 year. However, no data are released until the HELIUS Data Transfer Agreement (**appendix 6**) has been signed, agreeing to this HELIUS Collaboration Policy and the data utilization conditions. Where relevant, those conditions may include agreements regarding any services in exchange (financial, staffing and/or substantive undertakings).

To obtain *stored biological material* for laboratory measurements a material request is submitted:

* A material request should accompany a research or publication proposal wherever the proposal involves the use of the stored biological material in the HELIUS biobank. Material requests are made using the HELIUS Biobank Material Request Form (**appendix 7**). After the approval of the research or publication proposal, any accompanying material request is forwarded by the Scientific Coordinator to the person who has physical control of the material in question. However, no material is released until the HELIUS Material Transfer Agreement (**appendix 8**) has been signed, agreeing to this HELIUS Collaboration Policy and the data and material utilization conditions. Where relevant, those conditions may include agreements regarding any services in exchange (financial, staffing and/or substantive undertakings).

Research proposals, publication proposals, data requests and material requests should be submitted to the HELIUS Scientific Coordinator ([HELIUScoordinator@amsterdamumc.nl](mailto:HELIUScoordinator@amsterdamumc.nl)), using the appropriate forms.

**6. Data**

* 1. Data on HELIUS participants collected in the context of the various research projects within HELIUS – including data collected and supplied by collaborators and stored at the AMC – are the property of the AMC.
  2. Data for scientific analyses is supplied in the form of SPSS files stripped of information about matters such as the participants’ names, addresses and places of residence and of any additional data that is traceable to personal data.
  3. In cases where information about participants’ names, addresses, places of residence and phone numbers is required for additional data collection (sub-studies), the information is provided in the form of address labels (names and addresses) or printouts (names and phone numbers). HELIUS participants must be approached and informed in writing about any sub-study and subsequently contacted by phone (if possible and necessary).
  4. Information about participants’ names, addresses and places of residence must be stored in a safe place and strictly separated from research data. HELIUS must be informed as to which participants have been contacted regarding participation in a sub-study and whether each of them agreed to participate.

**7. Publications and authorships**

1. In principle, the international guidelines for authorships apply (see inset text). Under those guidelines, neither acquisition nor involvement in data collection is on its own sufficient to support a claim of authorship.

***International guidelines for authorships***

*● Authorship credit should be based on 1) substantial contributions to conception or design of the work, or the acquisition, analysis, or interpretation of data for the work; 2) drafting the article or revising it critically for important intellectual content; 3) final approval of the version to be published; and 4) agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Authors should meet conditions 1, 2, 3, and 4.*

*● When a large, multicentre group has conducted the work, the group should identify the individuals who accept direct responsibility for the manuscript (3). These individuals should fully meet the criteria for authorship/contributorship defined above, and editors will ask these individuals to complete journal-specific author and conflict-of-interest disclosure forms. When submitting a manuscript authored by a group, the corresponding author should clearly indicate the preferred citation and identify all individual authors as well as the group name. Journals generally list other members of the group in the Acknowledgments. The NLM indexes the group name and the names of individuals the group has identified as being directly responsible for the manuscript; it also lists the names of collaborators if they are listed in Acknowledgments.*

*● Acquisition of funding, collection of data, or general supervision of the research group alone does not constitute authorship.*

*● All persons designated as authors should qualify for authorship, and all those who qualify should be listed.*

*● Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content.*

*Source: Uniform Requirements for Manuscripts Submitted to Biomedical Journals, International Committee of Medical Journal Editors (*[*www.icmje.org*](http://www.icmje.org)*)*

1. A possible co-author must be given sufficient time to make a substantial contribution (two weeks to read draft results or a draft article). The person in question must then actually make a substantial contribution in order to justify being credited as a co-author.
2. At least two members of the HELIUS DB must co-author every HELIUS publication:

* First, the Theme Leader for the research theme to which the publication relates (cardiovascular: Bert-Jan van den Born and/or Eric Moll Van Charante (shared Theme Leadership); infectious disease: Maria Prins; mental health: Anja Lok) must be a co-author. If the publication relates to two research themes, both the relevant Theme Leaders may be co-authors. If the publication is of a general nature, one Theme Leader or another DB member is selected on the basis of consultation. If the publication does not relate to any of the research themes, the DB selects one DB member to co-author the publication.
* Second, in principle the Scientific Coordinator must co-author the publication with a view to assuring consistency (e.g. appropriate general description of the HELIUS project and use of the correct methods).

1. Ideally, every HELIUS publication should be co-authored by a representative of the AMC and a representative of the Public Health Service of Amsterdam. If such co-authorship is not consistent with the above guidelines, someone from the Municipal Health Authority should be approached in consultation with the DB (where appropriate for the content of the publication).
2. No contribution may be submitted to a journal for publication unless and until a Publication Plan has been submitted and approved. HELIUS data is made available only where a publication proposal has been approved and a Data Transfer Agreement has been signed.
3. Every publication must include the standard HELIUS acknowledgements. The most recent version of the acknowledgements is available from the Scientific Coordinator on request.
4. Upon publication, HELIUS will receive the complete dataset (including derived variables) and syntaxes which document how the results of the publication were obtained. These will be archived by HELIUS for audit purposes.
5. In principle, the authorship guidelines set out above apply equally to HELIUS sub-studies. In the case of a sub-study in which HELIUS participant data were used only for participant selection (without HELIUS study data being used), in principle only one DB member needs to act as a co-author. That will usually be the Theme Leader for the research theme to which the publication relates.
6. The authorship guidelines set out above apply equally to publications whose principal author is not employed by the AMC or the Municipal Health Authority.
7. The authorship guidelines set out above apply equally to internships, posters and presentations, since such items normally constitute (draft) publications.
8. In the event of uncertainty or disagreement regarding authorships of HELIUS DB members and Theme leaders, the DB has the final say. Regarding the authorships of other co-authors, the applicant of the publication proposal has the final say.

**7. Parties responsible for HELIUS**

The members of the HELIUS Executive Board are:

Prof. K. Stronks, Chair

Prof. A.H. Zwinderman, Vice-chair

Dr. M.B. Snijder, Scientific Coordinator

Prof.dr. A.P. Verhoeff, Representative Public Health Service

Dr. B.J. van den Born, Cardiovascular Theme Leader

Dr. E.P. Moll Van Charante, Cardiovascular Theme Leader

Prof. M. Prins, Infectious Disease Theme Leader

Dr. A. Lok, Mental Health Theme Leader

**Appendix 1**: **HELIUS research question types**

*Introduction*

What sets HELIUS apart from other cohorts in the Netherlands is the way subjects’ ethnic origin is differentiated. In the Netherlands, ethnic origin is routinely determined from a person’s country of birth and that of his/her parents. In other words, geographical origin is the dominant factor in the conceptualization of ethnic origin in the Netherlands. However, country of birth is not an ideal indicator, because a given country is liable to contain several population groups of distinct ultimate geographical origin. So, for example, Surinam has several distinct prominent population groups, such as Hindustani (South-Asian origin) and Creole (African origin) ethnic groups. Distinction between such groups requires the collection of additional self-identification data (Stronks K., Kulu-Glasgow I., Agyemang C. The utility of ‘country of birth’ for the classification of ethnic groups in health research: the Dutch experience. Ethn Health. 2009 Jun;14(3):255-69).

The unique ethnic differentiation in the HELIUS data can be utilized for scientific research in two ways. First, it facilitates the explanation of ethnic differences in health (see below, section A). Second, the ethnic differences can be used as a starting point for researching the aetiology of medical conditions (section B).

*A. Explanation of ethnic differences in health and care*

The well-documented phenomenon of differences in diabetes incidence amongst ethnic groups serves as an example for studies concerned with ethnic differences in health and care. To understand the background to the phenomenon, it is necessary to utilize a conceptual model that specifies the relationship between ethnic origin and health (see figure below). The underlying assumption is that ethnic origin is a collective expression of various more specific health and care consumption determinants. In the literature, three types of determinant predominate:

1. Socio-economic factors

2. Cultural influences

3. Genetic factors

In addition to those determinants, there is increasing interest in influences deriving from migration history (e.g. things experienced in the ‘home country’, refugee experiences, being separated from family) and ethnic identity (i.e. perceived ethnic origin). Such determinants ultimately influence health through more specific health determinants (proximal risk factors), such as lifestyle and living conditions. This conceptualization is visualized in Figure 1. A similar rationale can be applied to the use of care consumption as an outcome indicator.

The findings made regarding ethnic differences in health or care consumption will to some extent be ethnically specific (e.g. the influence of discrimination, or living between two cultures), but will also have a universal dimension, i.e. be valid for the population as a whole. The role of communication processes in care is a good example. The knowledge obtained from research into such processes is often applicable in relation to the majority population as well. However, the circumstances of ethnic minority population groups will often magnify issues that exist within the population as a whole. An ethnic minority can therefore serve as a ‘magnifying glass’ for the study of more universal mechanisms.



*B. Aetiological questions*

HELIUS can be used not only for the explanation of ethnic differences in health and care, but also for the examination of aetiological questions in various ways:

1. Ethnic variation amplifies variations in underlying risk factors, facilitating the study of those risk factors. For example, Brewster et al. investigated the relationship between CK and hypertension: the variation in CK within the ethnically diverse research population in the SUNSET study (Surinamese Creoles and Hindustanis and Dutch people) can be used to quantify the relationship between CK and hypertension, without the ethnic variation in the risk factor itself being the object of study (Brewster L.M. et al. Creatine kinase activity is associated with blood pressure. Circulation 2006;114:2034-9).

2. Unexpected associations between risk factors and outcome indicators in particular ethnic groups can be used as a starting point for investigating the aetiology of the relevant outcomes. For example: hypertension is relatively uncommon in the Bangladeshi population in the UK, yet the mortality due to stroke is twice as high in that group as in the majority population. What light does that shed on the aetiology of strokes?

3. The investigation of associations between risk factors and outcome indicators in various ethnic groups can shed light on causality. For example: if the relationship between a given risk factor and a given outcome indicator differs from one ethnic groups to the next, that may suggest that other (unidentified) risk factors may additionally impact outcome or that the relation between risk factor and outcome is influenced by other aggravating or ameliorating factors.

4. Genetic-environmental interactions form a particular focus of attention for aetiological research. Ethnic minority groups tend to experience particularly marked changes in factors such as culture, living conditions and lifestyle from one generation to the next. Therefore HELIUS provides a unique opportunity to study such interactions.

Ultimately, the knowledge of risk factors/aetiology obtainable from HELIUS is potentially beneficial for the population as a whole, regardless of ethnic origin.

*See also: Stronks et al. Unravelling the impact of ethnicity on health in Europe: the HELIUS study. BMC Public Health 2013 Apr 27;13:402.*

**Appendix 2**: **Study design and basic data collection HELIUS**

HELIUS (acronym for HEalthy LIfe in an Urban Setting) is a multi-ethnic cohort study carried out in Amsterdam, including participants of Dutch, African Surinamese, South-Asian Surinamese, Turkish, Moroccan and Ghanaian ethnic origin. The objective of HELIUS is to unravel the causes of the unequal burden of diseases across ethnic groups. The emphasis is on cardiovascular diseases (including diabetes), mental health (i.e. depressive disorders and substance use disorders), and infectious diseases, all major causes of the global burden of disease. Important themes related to these diseases are nutrition, physical activity and health care utilization.

Participants aged 18 to 70 years were randomly sampled, stratified by ethnicity, from the municipal population register of Amsterdam (GBA). Participants’ ethnicity was defined according to the country of birth of the participant as well as that of his/her parents, which is the currently the most widely accepted and most valid assessment of ethnicity in the Netherlands (Stronks et al, Ethn Health 2009). Specifically, a participant was considered as of non-Dutch ethnic origin if he/she fulfilled either of the following criteria: 1) he/she was born abroad and has at least one parent born abroad (first generation); or 2) he/she was born in the Netherlands but both his/her parents were born abroad (second generation). A limitation of the country of birth indicator for ethnicity is that people who are born in the same country might have a different ethnic background, which in the Dutch context is applicable to the Surinamese population (Stronks et al, Ethn Health 2009). Therefore, after data collection, the Surinamese group was further classified according to self-reported ethnic origin into ‘African’, ‘South-Asian’, or ‘other’. For the Dutch sample, we invited people who were both born in the Netherlands and whose parents were born in the Netherlands.

Participating GBA subjects (index persons) were asked if they had parents, siblings, a partner, and children from the age of 18-70 years, who are living in Amsterdam. We included a maximum of three related persons per index person. If an index person had parents in Amsterdam, then both parents will be invited to participate as well as a sibling of the index person (Figure 1). In case an index person has no parents living in Amsterdam, but has one or more children from the age of 18 years living in Amsterdam, then a maximum of two children was invited as well as the partner of the index (Figure 2). In case an index person had no parents or children of 18 years onward living in Amsterdam, only the index person was included in HELIUS.



Figure 1 Figure 2.

Participants filled in a questionnaire (or were interviewed, if necessary) about their health and they underwent a physical examination (for specific topics see overviews below). Biological samples were obtained, analysed and stored (biobank, including DNA). After baseline examinations, follow-up examinations are be planned at 5 to 10 year intervals. In addition, data of participants may be and have been linked to registry data: routinely collected data on health outcomes and health care (e.g. mortality, hospital admission) at the individual level.

*For more details see: MB Snijder et al. Cohort Profile: the Healthy Life in an Urban Setting (HELIUS) study. BMJ Open 2017;7(12):e017873.*

**Overview variables in baseline HELIUS questionnaire**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **DETERMINANTS OR RISK FACTORS** | | | | | |
| **General** | **Infectious diseases** | **Mental health** | **Cardiovascular diseases** | **Health care** | **Nutrition** |
| - Sex, age  - Marital status  - Household composition  - Ethnic origin (incl. subgroups and province)  - Migration history  - Educational level  - Occupational status  - Work-related recovery opportunities  - Religion  - Cultural distance  - Smoking  - Alcohol intake  - Cannabis use  - Physical activity (SQUASH) | - Sexual behaviour  - Anti-conception use (women)  - HPV vaccination (women)  - Circumcision (men)  - Travel behaviour (incl. visited countries)  - Use of self-tests  - Blood transfusions  - Use of drugs by injection - Surgery in other country | - Perceived discrimination (Everyday discrimination scale, Forman et al 1997) - Perceived social support (Social Support Questionnaire for Satisfaction Emotional Support Subscale)  - Childhood trauma (NEMESIS-I)  - Parental psychiatric history (NEMESIS-I)  - Mastery (NEMESIS-I)  - Neuroticism (NEO-FFI)  - Extraversion (NEO-FFI)  - Stressful life events (NEMESIS-II)  - Psychological stress (2 items from INTERHEART) | - History of high blood pressure (incl. family history)  - History of dyslipidaemia (incl. family history)  - History of diabetes (incl. family history)  - Fainting  - Age of menarche  - Age of menopause  - Variables to link with LVR | - Difficulty understanding medical information  - Compliance to medication  - Perceived quality of GP | - Weight perception  - Fruit intake  - Vegetarian diet  - Dietary pattern (breakfast, lunch, meal)  - Coffee/tea and sugary drinks intake |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **OUTCOMES** | | | | | |
| **General** | **Infectious diseases** | **Mental health** | **Cardiovascular diseases** | **Health care** | **Nutrition** |
| - General diseases  - Quality of life (SF-12)  - Functional limitations | - Allergy/asthma (incl. family history)  - Rhinitis  - Food allergy  - Urogenital infections | - Cigarette dependence (Fagerström)  - Alcohol dependence (AUDIT)  - Lifetime alcohol dependence  - Cannabis dependence (CUDIT)  - Lifetime cannabis dependence  - Current depression and depressive disorder (PHQ-9)  -Lifetime depression  - Post-traumatic stress disorder | - Angina pectoris (Rose)  - Myocardial infarction  - Intermittent claudication (Rose)  - Heart failure  - CVA/TIA  - Family history CVD and sudden death | - Visit to GP  - Visit to specialists  - Psychological help  - Alternative health care  - Medication or care in other country/countries | - Self-reported weight and height |

**Overview measurements/variables baseline HELIUS physical examination**

|  |  |
| --- | --- |
| **Questions at physical examination** | |
| Time of latest meal (to check fasting state) |  |
| Time of latest cigarette |  |
| Currently breastfeeding |  |
| Normal dietary pattern for the last 3 days |  |
| Normal physical activity patterns for the last 3 days |  |
| Current/recent (past 2 weeks) health problems: | Fever |
|  | Head ache |
|  | Muscle pain |
|  | Pain in throat |
|  | Coughing |
|  | Shortness of breath |
|  | A cold |
| Part of twin |  |
| Medication | Name, dose, frequency, indication |
| Nutritional supplements | Name, indication |
| Health literacy test |  |
| **Measurements** | |
| Anthropometry | Weight |
|  | Height |
|  | Waist circumference |
|  | Hip circumference |
|  | Thigh circumference |
|  | Arm circumference |
|  | Calf circumference |
| Body fat percentage | (by bio-impedance) |
| Hand grip strength |  |
| Blood pressure | (sitting) |
| Ankle-arm index | (supine position) |
| ECG | Left ventricular hypertrophy, infarction, etc. |
| Nexfin | Cardiac output, peripheral resistance |
| Arteriograph | Arterial stiffness |
| **Collection biological material** | |
| Morning urine sample | Storage  Direct determination of: micro-albumin, creatinine |
| Fasting blood sample | Storage  Direct determination of: total chol, HDL, LDL, triglycerides, creatinine, glucose, Hb, HbA1c, CK |
| Throat swabs | Storage |
| Nose swab | Storage |
| Vaginal swab (women only) | Storage |
| Faeces sample | Storage |

**Appendix 3**: **HELIUS Research Proposal Form**

This form should be used to submit a research proposal – e.g. a proposal for a subsidy application, a proposal for a sub-study, or a proposal for a doctoral programme – to HELIUS.

NB for data use for publications, internships, or quality checks of the data, please use the Publication Proposal Form (appendix 4).

NB publication proposals still need to be submitted for each publication making use of HELIUS data, also if the related research proposal has already been approved by the HELIUS board.

For notes and guidance, please refer to the full HELIUS Collaboration Policy**.**

|  |  |
| --- | --- |
| **1. Applicant** | *Name*  *University / Hospital / Faculty / Department / Research institute*  *Type of appointment (position)*  *Street address*  *Postcode and city*  *Phone*  *E-mail* |
| **2. Title of the proposed study** |  |
| **3. Main subject** | *What is the main subject of the proposed study?*  *Does the proposal relate to an activity which is part of a larger research project? If so, give a brief description.* |
| **4. Keywords** | *Give up to eight keywords.* |
| **5. Background** | *Describe the background to and rationale for this research proposal (including key references) and the significance/relevance in relationship to ethnicity.* |
| **6. Research question(s)** | *Describe the exact research question or questions* |
| **7. Study design and methods** | *Describe the study design and study population:*   1. *What health outcomes and what exposures/risk factors/possible causes will be measured?* 2. *Will the study exclusively use cross-sectional baseline data, or also data on incidence over time?* 3. *In how many people will exposure be measured?* |
| **8. Use of HELIUS data** | *How does the applicant propose to use the HELIUS data?*  *Level 1: use of the existing basic data collection*  *Level 2: use of the biobank (use of biological samples for lab tests)*  *Level 3: addition of a parameter (measurement or collection of biological samples) to the basic data collection; please specify whether in a selection of the HELIUS study population or the whole population (sub-study during basic data collection)*  *Level 4: measurement of additional parameters other than at basic data collection time in a selection or all of the HELIUS study population (sub-study after basic data collection)*  *NB: If the proposed study involves the selection of participants for a sub-study on the basis of HELIUS data, this research proposal should be accompanied by a HELIUS Data Request Form. The information entered on the latter form will serve as a basis for the Data Transfer Agreement (collaboration agreement).*  *NB: If the proposed study involves use of the biobank, this research proposal should be accompanied by a HELIUS Biobank Material Request Form. The information entered on the latter form will serve as a basis for the Material Transfer Agreement (collaboration agreement).* |
| **9. Proposed approach to the handling of findings** | *If the proposed study involves the lab testing of stored materials or the measurement of additional parameters:*  *Do any of the lab tests or measurements have the potential to yield findings that warrant disclosure to the participant, due to their clinical significance?*  *If so, what approach to disclosure is proposed?* |
| **10. Anticipated results** | *What are the anticipated outcomes of the proposed study?* |
| **11. Innovative features** | *What innovative features does the proposed study have in relationship to the multi-ethnic population?* |
| **12. Funding** | *How will the proposed study be funded? What proportion of the cost will be funded by the proposing institute and/or what proportion has yet to be covered by sponsors?*  *Is funding to be applied for? If so, when and from whom?* |
| **13. Project group** | *What other researchers are associated with this research proposal?* |
| **14. Timing** | *What is the planned start date for the proposed study?*  *What is the planned end date for the proposed study?* |

**Appendix 4**: **HELIUS Publication Proposal Form**

This form should be used to submit a publication proposal making us of the HELIUS data.

This form should also be used to submit a proposal regarding the use of HELIUS data for activities that will not lead to a publication, such as an internship, data quality control activities, etc.

Up to two A4 pages (excluding tables, where relevant)

|  |  |  |
| --- | --- | --- |
| **Manuscript #** | **Date of submission** | **Date of approval** |
| **1. Applicant** | *Name*  *University / Hospital / Faculty / Department / Research institute*  *Type of appointment (position)*  *Street address*  *Postcode and city*  *Phone*  *E-mail* | |
| **2. Title / subject of the publication** |  | |
| **3. Proposed authors** | *Who is the proposed first author?*  *Who are the proposed co-authors? The authorship proposals should be consistent with the guidelines set out in the HELIUS Collaboration Policy.* | |
| **4. First author’s contact details (if not similar to applicant details)** | *Name*  *University / Hospital / Faculty / Department / Research institute*  *Type of appointment (position)*  *Phone*  *E-mail* | |
| **5. Background and rationale** | *Describe the background to and rationale for this research proposal (including key references).* | |
| **6. Research question(s)** | *Clearly state the main research question and sub-questions.* | |
| **7. Data and population** | *What inclusion and exclusion criteria are to be applied (e.g. age, ethnicity, etc.)?* | |
| **8. Analysis plan** | *Describe on a step-by-step basis the statistical analyses to be performed (type of analyses, regression, tests, etc.) in order to answer each research question (using what dependent and independent variables, what confounders, etc.). What tables will be produced? (Please provide unpopulated tables if possible.)* | |
| **9. Timing** | *When will the data analysis start?*  *When will the manuscript be written?*  *When is the manuscript likely to be completed?* | |

**Appendix 5: HELIUS Data Request Form**

This form is intended for specification of the data required in connection with the **publication proposal** or **research proposal**.

If you have questions regarding the available data, please contact the Scientific Coordinator ([HELIUScoordinator@amsterdamumc.nl](mailto:HELIUScoordinator@amsterdamumc.nl)).

No data are released until the **HELIUS Data Transfer Agreement** has been signed, agreeing to the HELIUS Collaboration Policy and the data utilization conditions.

|  |  |
| --- | --- |
| Name applicant: |  |
| Title research proposal or publication proposal: |  |
| E-mail applicant(s): |  |
| Reason for data request:  *(please tick)* | □ data-analysis for publication (or internship or preliminary analyses)  □ selection of participants for sub-study  □ quality control of specific data, description:  □ other, namely: |

**Explanation**

Please tick which data are requested. For data management reasons, the data are sorted by ICT-source of the data. If additional data from the questionnaire or the physical examination are needed, please describe them in the dedicated table.

|  |
| --- |
| **Standard variables** |
| *These variable will be available in each HELIUS dataset.* |
| ▪ Questionnaire completed (yes/no)  ▪ Physical examination completed (yes/no)  ▪ Date of physical examination  ▪ Sex  ▪ Age  ▪ Migration generation (based on countries of birth of participants and parents)  ▪ Ethnicity (based on countries of birth of participant and his/her parents:  Dutch, Surinamese, Ghanaian, Turkish, Moroccan)  ▪ Ethnicity including Surinamese subgroups (definition of ethnicity completed with  information from the questionnaire) |

|  |
| --- |
| **Already defined variables/composite variables** |
| *Please tick which variables you need for your proposal* |
| **General (questionnaire)**  □ Educational level (highest education obtained, either in the Netherlands or in the  country of origin, 4 categories) Deel G  □ Working status (4 categories) Deel G  □ Occupational level (5 categories) Deel G  □ Work-related recovery opportunities Deel G  □ Quality of life (SF-12, Physical and Mental Component Scores) Deel B  □ Physical activity (obtained by SQUASH questionnaire) Deel E  □ Smoking status (yes, no, ex-smoker) Deel E  □ Smoking (packyears) Deel E  □ Alcohol use in past 12 months (yes, no) Deel E  □ Body weight perception scores Deel J  □ Health literacy scores (SBS-Q and REALM-D) Sam  **Body composition and muscle strength (physical examination)**  □ Mean weight Blok 1  □ Mean height Blok 1  □ Body mass index (BMI) Blok 1  □ Mean waist circumference Blok 1  □ Mean hip circumference Blok 1  □ Waist-to-hip ratio (WHR) Blok 1  □ Mean thigh circumference Blok 1  □ Mean arm circumference Blok 1  □ Mean calf circumference Blok 1  □ Body fat percentage (estimated by bio-impedance) Sam  □ Muscle strength (mean and maximum grip strength) Blok 5  **Cardiovascular/medical (questionnaire and physical examination)**  □ Mean blood pressures Blok 5  □ Hypertension (based on self-report, blood pressure, and/or medication) Sam  □ Blood pressure lowering medication (ATC codes C02 C03 C07 C08 C09) (yes/no) B1  □ Diabetes (based on self-report, glucose levels, HbA1c, and/or medication) Sam  □ Glucose lowering medication (ATC codes A10) (yes/no) Blok 1  □ Self-reported CVD (according to Rose-questionnaire) (yes/no) Sam  □ Self-reported CVA (yes/no) Sam  □ Self-reported MI (yes/no) Sam  □ Lipid lowering medication (yes/no) Blok 1  □ Metabolic syndrome (including its individual components) (yes/no) Sam  □ Kidney function (Cockroft-Gault eCC, eGFR (MDRD/CKD-EPI), MA, KDIGO) Sam  □ Antibiotics (ATC codes J01) (yes/no) Blok 1  □ Antithrombotics (ATC codes B01) (yes/no) Blok 1  □ Corticosteroids (ATC codes D07 plus specific codes) (yes/no) Blok 1  □ Decongestants and allergy medication (ATC codes S01G) (yes/no) Blok 1  □ Nasal medication (ATC codes S01G) (yes/no) Blok 1  □ Astma/COPD medication (ATC-codes R03) (yes/no) Blok 1  □ Systemic antihistamines (ATC-codes R06) (yes/no) Blok 1  □ Systemic steroids (ATC-codes H02) (yes/no) Blok 1  □ Estimated CVD risk (based on SCORE) (yes/no) Sam  □ Estimated CVD risk (based on Framingham) (yes/no) Sam  **Use of psychotropic medication (physical examination)**  □ Anti-psychotics (ATC codes N05A) Blok 1  □ Anxiolytics (ATC codes N05BA and N03AE) Blok 1  □ Hypnotics (ATC codes N05C and R06AD02) Blok 1  □ Modern anti-depressives (ATC codes N06A and N06AX) Blok 1  □ Mood stabilizers (ATC codes N03AF, N03AG, N03AN and N05AX) Blok 1  □ Stimulants (ATC codes N06BA) Blok 1  □ Tricyclic anti-depressives (ATC codes N06AA) Blok 1  □ Medication for addiction (ATC codes N07B) Blok 1  □ Psychotropic medication (use of one of the above medications)  □ Anti-depressives (modern/tricyclic anti-depressives and mood stabilizers; ATC codes N06A, N06AX, N06A,A N03AF, N03AG, N03AN, N05AX)  **Mental health (questionnaire, for additional information see document ‘*Mental Health Instruments in HELIUS*’)**  □ Perceived discrimination (score Everyday Discrimination scale) Deel D  □ Cigarette dependence (score Fagerstrom) Deel E  □ Alcohol dependence (score AUDIT) Deel E  □ Lifetime alcohol dependence Deel E  □ Cannabis dependence (score CUDIT) Deel E  □ Personality: extraversion (score NEO- Five Factor Inventory) Deel H  □ Personality: neuroticism (score NEO- Five Factor Inventory) Deel H  □ Dealing with everyday problems (score Pearlin-Schooler mastery scale) Deel H  □ Negative life events (List of threatening experiences, NEMESIS questionnaire) Deel H  □ Psychological stress (at work and at home) (INTERHEART questionnaire) Deel H  □ Experiences during childhood (Childhood trauma; NEMESIS questionnaire) Deel H  □ Problems because of unpleasent experiences (Post-traumatic stress disord) Deel H  □ Depressive symptoms (PHQ-9) Deel I  □ Lifetime depression Deel I  □ Parental psychological history (NEMESIS) Deel I  □ Social support (scores Social Support Questionnaire for Satisfaction – Daily  Emotional Support Subscale) Deel I  **Acculturation (questionnaire, for additional information see document ‘*Acculturation in HELIUS*’)**  □ Residence duration (years)Sam  □ Age of migration (years) Sam  □ Difficulty with Dutch language (yes/no) Sam  □ Ethnic identity (Berry’s acculturation strategies) Sam  □ Cultural orientation (Berry’s acculturation strategies) Sam  □ Social network (Berry’s acculturation strategies) Sam  □ Cultural distance to Dutch health care system Sam |

|  |  |
| --- | --- |
| **Questionnaire (source Limesurvey application)** | |
| *Enter which additional questions from the questionnaire you need (section, and number and subject of the question(s), see questionnaire)* | |
| **SECTION** | **Number and subject of the question(s)** |
| .. | …. |
| .. | …. |

|  |  |
| --- | --- |
| **Laboratory measurements (source LAKC, LABTRAIN extract)** | |
| *Please tick which variables you need for your proposal* | |
| *Blood (fasting)*  □ Glucose  □ HbA1c (=IH1c)  □ Hb (=HEMO)  □ Triglycerides  □ Total cholesterol  □ HDL  □ LDL (calculated)  □ Creatinin  □ CPK | *Morning urine*  □ Micro-albumin  □ Creatinin  □ Micro-alb/creat ratio (calculated) |
| **Results urine dipstick (source Oracle Clinical application, Blok Afsluiting)** | |
| *Please tick which variables you need for your proposal* | |
| □ pH  □ Glucose  □ Ketones  □ Leucocytes  □ Nitrite  □ Protein  □ Erythrocytes | |

|  |  |
| --- | --- |
| **Physical examination (source Oracle Clinical application)** | |
| *Enter which additional data from the physical examination you need* | |
| **Blok** | **Questions or measurements** |
| .. | …. |
| .. | …. |

|  |
| --- |
| **Substudies** *(note: participants of different substudies may not overlap)* |
| *Subsample n~5800) (five ethnic groups, no Ghanaians)*  *□ Dietary intake (please specify:…………………………………………………………)* |
| *Subsample n=6000 (six main ethnic groups)*  □ D-dimer  □ fibrinogen  □ Lpa  □ ApoB  □ CRP |
| *Subsample n~6000) (six main ethnic groups)*  □ Fecal microbiome |
| *Subsample ~600 (vaginal swabs, six ethnic groups, women)*  □ Vaginal microbiome (swabs)  □ Vaginal human papillomavirus (HPV) (swabs) |
| *Subsample ~1200 (six ethnic groups, women)*  □ Vaginal Chlamidia trachomatis (swabs) |
| *Subsample n=1058 (five ethnic groups, no Ghanaians)*  □ Cholesteryl fatty acids  □ Carotenoids |
| *Subsample n=786 (Dutch and South-Asian Surinamese)*  □ Acylcarnitines  □ Amino acids  □ Sphingolipids |
| *Subsample n=500 (Ghanaians and African Surinamese with (pre)diabetes)*  □ Metabolomics |
| *Subsample n=476 (five ethnic groups, no Ghanaians)*  □ Physical activity by Actiheart |
| *Subsample n=4683 (six main ethnic groups, age 18-44 y)*  □ Antibodies against human papillomavirus (HPV)  □ Antibodies against human T-lymphotopic virus-1  □ Antibodies against Helicobacter pylori  □ Antibodies against Herpesvirus  □ Antibodies against Chlamidia trachomatis |
| *Subsample n=1199 (six main ethnic groups, age 18-44 y)*  □ Antibodies against hepatitis E |
| *Subsample n~2990 (six main ethnic groups, only first generation migrants)*  □ Hepatitis B infection (anti-HBc, anti-HBs, HBeAg, anti-HBe, HBV-DNA)  □ Hepatitis C infection (anti-HCV, HCV RNA) |
| *Subsample n~10000 Dutch, South-Asian Surinamese, Turkish, Moroccan)*  □ Whole genome SNP genotypes (GSA Illumina) |

|  |
| --- |
| **Geo-data (source: Geoscience and Health Cohort Consortium (GECCO))** |
| HELIUS data has been linked to environment data based on zip-codes. For an overview of which data have been linked and additional procedures and conditions to use these linked data, please ask the Scientific Coordinator (HELIUScoordinator@amsterdamumc.nl) |
| **Environment data** |
| ..…. |
| ..…. |

|  |
| --- |
| **Selection** |
| *Describe whether (and if so, how) participants should be selected (for example: participants of a certain age, ethnicity or sex, participants who have given permission for additional research / substudies, participants who have been examined in a certain period, etc)* |
|  |

**Appendix 6**: **HELIUS Data Transfer Agreement #......**

This agreement is made **……..(day) - ……..(month) - ……..(year)** between:

The Academic Medical Center (“**AMC**”) acting on behalf of the HELIUS Study ("HELIUS"), Meibergdreef 9, 1105 AZ, Amsterdam, The Netherlands, legally represented by the Chair of the Executive Board of HELIUS, **Prof. K Stronks**,

And

**…………………………………(institute)** (hereafter referred to as “the Recipient”)

Hereafter referred to collectively as “Parties” and individually as “Party”.

Example

BACKGROUND

The AMC, through HELIUS, has collected and owns certain data sets derived from information provided by participants in the HELIUS Study (“the Study Participants”). An employee of the Recipient (“Investigator”), wishes to use certain of the Pseudonymised data held by HELIUS (“Data”) for the research as set out in Appendix 1 (“the Research”) as approved by the HELIUS Executive Board. HELIUS is willing to supply the Recipient with a copy of the requested Data for a period of **12 months** (1 year) to conduct the Research under the terms and conditions of this Agreement.

DEFINITIONS

a) “Controller”, “Data subject”, “Personal data”, “Processing” and “Processor” shall have the meaning as in the General Data Protection Regulation (EU) 2016/679 (hereinafter: “GDPR”) where these terms appear in non-capitalized words.

b) “Pseudon ymised data” means Personal data which 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. This additional information will be stored by HELIUS, to which the Recipient will not have access.

NOW IT IS AGREED by Parties as follows:

1. This agreement does not affect the ownership of any Material and/or Data. No license to use any intellectual property is granted or implied by this Agreement except the rights expressly granted in this Agreement.
2. AMC will provide the Recipient with the a copy of the Data in the form of Pseudonymised data that the Recipient needs for the Research. Research Data shall be made available of the type and in the quantities as outlined in the Appendix 2 (“Research Data”). Parties acknowledge that the Research Data are Personal data. The Research Data shall be provided for the sole purpose of its use in the Research and in accordance with the terms of this Agreement.
3. AMC and the Recipient are considered joint Controller with regard to the Research Data to the extent processed by virtue of the present Agreement and for the period the Research Data are under the control of the Recipient. In addition, each Party may be considered an independent Controller in relation to its own processing of the Research Data. Therefore, in Processing the Research Data each Party will be bound to the provisions in the GDPR related to the Controller and abide to the additional data protection laws of the Netherlands. In addition, the Recipient warrants to Process the Research Data in accordance with its applicable national law, provided that in case of inconsistencies between the GDPR and national law, the provisions of the GDPR shall prevail.

Example

1. AMC warrants and undertakes:

a. the Research Data have been collected, processed and transferred in accordance with the GDPR and additional data protection laws in the Netherlands.

b. it has obtained any regulatory or ethics approvals necessary to collect the Data (including the Research Data) and to Process them for the purpose of HELIUS;

c. it has full authority to transfer the Research Data to the Recipient; and

d. informed consent of the Data subject has been obtained in accordance with applicable law.

1. All future correspondence pertaining to the Research Data and the Research should be addressed to the HELIUS Scientific Coordinator ([HELIUScoordinator@amsterdamumc.nl](mailto:HELIUScoordinator@amsterdamumc.nl)).
2. The Recipient will use the Research Data only to carry out the Research described in the Appendix 1 to this Agreement. The Recipient will not use the Research Data or any parts thereof for any commercial purpose or any purpose that is subject to consulting or licensing obligations to third parties. Recipient shall ensure that only those employees of Recipient shall have access to the Research Data, who are involved in the Research under direct supervision of the Investigator.
3. The Recipient will not try identify any Data subject nor link the Research Data to other HELIUS Data held by different recipients or by the same Recipient for different projects.
4. The Recipient will treat all Research Data strictly confidential and not transfer the Research Data in whole or in part to third parties. Consequently, Recipient shall not without first obtaining the consent of Provider:
   1. engage a (sub)Processor to process Research Data on behalf of the Recipient.
   2. transfer any (portion of) the Research Data to any affiliate of Recipient or third-party located outside the European Economic Area.

In case the Provider approves to any of the above, Recipient shall have in place procedures ensuring that any such (sub)Processors, affiliates and/or third-parties will respect and maintain the confidentiality and security of the Research Data and shall Process the Research Data in accordance with the requirements of the GDPR and be bound to provisions similar to those of this Agreement. Recipient shall be responsible to Provider for any acts of the such (sub)Processors, affiliates and/or third-parties as if Recipient had performed the Processing itself.

Example

1. Subject to Section 8, any person or organisation acting under the authority of the Recipient shall be obligated to Process the Research Data only on instructions from the Recipient and in accordance with the permitted use under this Agreement.
2. Recipient shall not be prevented to provide access to the Research Data to persons authorised or required by law or regulation to have access to the Research Data, provided it will without undue delay inform HELIUS of any projected or actual inspection.
3. Recipient shall be responsible to have an agreement in place with each of its employees who have access to the Research Data, which agreement binds them to provisions of confidentiality and to process any Research Data in accordance with the GDPR. The Investigator and other relevant employees of the Recipient involved in the Research have read and will abide by the “HELIUS Collaboration Policy”.
4. The Investigator will retain the Research Data in a secure location on its premises and warrants that it will have for the full duration the Research Data are in its custody, appropriate technical and organisational measures in place to protect the Research Data against accidental or unlawful destruction or accidental loss, alteration, unauthorised disclosure or access, and which provide a level of security appropriate to the risk represented by the processing and the nature of the Research Data to be protected.
5. The Recipient will use all reasonable endeavors to ensure that the Research Data in its possession, or under the control of the Recipient shall as soon as possible be returned or destroyed upon (i) the reasonable request of HELIUS; or (ii) on termination of this Agreement; or (iii) in the event that the Recipient is in breach of any of the conditions of this Agreement. If the Recipient is required to destroy the Research Data then it will ensure that this is done in compliance with all applicable laws and regulations and confirm in writing to HELIUS that the Research Data has been destroyed.
6. If the Recipient becomes aware of a (potential) personal data breach affecting the Data, or receives a request of a Data subject to exercise its rights under the GDPR, the Recipient shall promptly notify the AMC. In case of a personal data breach, Parties will fully cooperate with each other to remedy the personal data breach, fulfil their respective (statutory) notification obligations timely and cure the damages. A personal data breach shall have the meaning under articles 33 and 34 of the GDPR. In case of a request of a Data subject to exercise its rights under the GDPR, the Parties agree that HELIUS is most suited to handle such requests. However, the Recipient shall fully cooperate with HELIUS in handling such requests, if so requested by HELIUS.
7. The Recipient will keep HELIUS informed of the results of the Research (“Results”). All information (including the results of cleaned or derived variables) relating directly to Study Participants will be made available to AMC for the purposes of incorporation into HELIUS. All other results generated by the Research shall be the property of the Recipient save that the Recipient grants to the AMC royalty-free, irrevocable, perpetual non-exclusive right to use such Results for internal non-commercial research and teaching. The Recipient will provide HELIUS with a fully documented electronic copy of the full Results before publication in any form or within 6 months of the completion of the Research whichever is the sooner. In addition, for archival purposes, the Recipient will provide HELIUS with the complete dataset (including derived variables) and syntaxes which document how the Results of the publication were obtained.

Example

1. This Agreement does not affect the ownership of the Research Data. No license to use any intellectual property is granted or implied by this Agreement except the rights expressly granted in this Agreement.
2. HELIUS accepts no liability in connection with the Recipients use of the Research Data. HELIUS does not represent that (i) the Research Data is of satisfactory quality or fit for any particular purpose; or (ii) use of the Research Data is free from infringement of third party rights, including intellectual property rights. To the extent permissible by law the Recipient will indemnify and hold HELIUS harmless for any damages howsoever arising from Recipient’s use of the Research Data.
3. The rights and obligations as determined in the Agreement may not be assigned by a Party without the prior written consent of the other Party.
4. In return for using the Data, **……………………………. (*agreements regarding contribution to HELIUS data collection*)**
5. This Agreement shall be interpreted and governed by the laws of The Netherlands in any action. Any dispute relating to the interpretation or implementation of this Agreement which the Parties hereto have failed to settle amicably shall be exclusively referred to the competent courts of The Netherlands for settlement.
6. Modifications and changes to this Agreement are only binding after these have been agreed upon in writing between the Parties.

Each person signing this Agreement represents and warrants that he or she is duly authorized and has legal capacity to execute and deliver this Agreement.

AGREED BY THE PARTIES through their authorized signatories

SIGNED for and on behalf of AMC:

Signature: ………………………………………………..

Print Name: **K. Stronks** Date: ……………………………..

SIGNED for and on behalf of RECIPIENT:

Signatory of Recipient …………………………. …

Example

Printed Name: ………………………………. Date:………………………………

(1) Signature of Investigator ………………………………

Printed Name: ……………………………….. Date:………………………………

(2) Signature of Investigator ………………………………

Printed Name: ……………………………….. Date:………………………………

APPENDIX 1: **Research proposal** or **Publication proposal**

*Please note: A project specific appendix to be added here which must be approved by HELIUS.*

APPENDIX 2: **Categories of Data subjects and categories of Research Data**

Supplier shall make certain Research Data available to Recipient, including data that relates to human tissue samples.

1. The Research Data includes the following categories of Data subjects:

Participants of the HELIUS study

In the amount of [number] Data subjects

1. The Research Data includes the following Personal Data:

[age, sex, etc.]

1. Research Data is Pseudonymised data, to ensure data minimalisation under the GDPR.

**Appendix 7**: **HELIUS Biobank Material Request Form**

This form is for use in conjunction with a **publication proposal** or **research proposal**, in cases where the proposed activity involves the use of material from the HELIUS biobank. The Biobank Material Request Form will be considered by the Scientific Coordinator following approval of the associated publication proposal or research proposal. A **Material Transfer Agreement** will then be drawn up regulating all matters pertaining to the use of the biobank material. No material will be released until the signed Material Transfer Agreement has been received.

*Contents of the HELIUS Biobank*

If a HELIUS participant has consented to the storage of biological material, the following materials from the participant are stored in the HELIUS biobank:

*Blood and urine*

A fasting blood sample is taken and the participant is asked to bring a morning urine sample to the research location. If blood sampling is successful and the requested urine sample is provided, the following samples from each participant are stored in the biobank:

|  |  |  |
| --- | --- | --- |
| **Material** | **Max. number of test tubes\*** | **Max. quantity per test tube\*\*** |
| Citrate plasma (platelet-poor): | 3x | 0.75 ml |
| Serum: | 6x | 1 ml |
| Heparin plasma: | 7x | 1 ml |
| EDTA whole blood: | 3x | 1 ml |
| EDTA plasma: | 5x | 1 ml |
| DNA: | 1x | 1 pellet |
| Urine: | 2x | 1 ml |

*\* There may be fewer test tubes if blood sampling was not completely successful or insufficient material was present.*

*\*\* Individual tubes may contain less than the indicated quantity of material.*

The material is stored at -80 °C in 2D Micronic test tubes. The test tubes do not contain labels but bear a 2D code on the bottom. Blood and urine samples are stored at the Durrer Center at the AMC.

*Nose and throat swabs*

Nose and throat swab samples are taken from some participants, which are placed in a single test tube with transport fluid at the location where the participant is examined. Following transportation to the AMC (Medical Microbiology Department refrigerator), the test tube is vortexed the same day (or within 72 hours if delivered on a Friday or Saturday). Two 1.5 ml aliquots of the medium are then stored in a freezer at -80 °C.

*Vaginal swab*

All female participants are asked to provide a self-obtained vaginal swab sample. The swabs are dry-stored in a refrigerator at 4 °C until being sent by post (within two weeks) to the District Laboratory, Infectious Disease Cluster at the Amsterdam Municipal Health Authority. There the swabs are systematically stored in a freezer at -20 °C.

*Faeces*

If a participant has consented to additional tests, he or she is asked at the end of the physical examination to bring a faeces sample to the research location within six hours of its collection. Upon delivery by the participant, the sample is temporarily stored at the research location at -20 °C. It is then transported to the AMC (Vascular Medicine Department), where it is stored at -80 °C.

*Notes regarding procedures for and cost of supplying materials*

If the HELIUS DB has consented to the release of the HELIUS material, the Scientific Coordinator and the Data Manager, in consultation with the researcher, compile a list of relevant HELIUS numbers, which is sent to the institute that supplies the samples.

Where blood or urine samples are concerned, an analyst from the Durrer Center will take the relevant samples from the freezers, make them up (if necessary, in consultation) and dispatch them (if necessary, in consultation). Where vaginal swab samples are concerned, a Municipal Health Authority worker will take the relevant samples from the freezers and dispatch them. The cost of the necessary activities, the cost of the necessary materials and the cost of carriage are, in principle, all payable by the applicant. The costs in question depend on various factors, including the number of samples and the method of pipetting (manual or automated). A cost estimate may be requested from the Scientific Coordinator. Materials are normally supplied in 2D Micronic test tubes.

|  |  |
| --- | --- |
| **General applicant information (researcher)** | |
| Date of request: |  |
| Name of applicant: |  |
| Applicant’s e-mail address: |  |
| Applicant’s phone number: |  |
| Applicant’s postal address: |  |
| Title of associated publication proposal or research proposal: |  |

|  |  |
| --- | --- |
| **Details of the required material** | |
| What material is required? |  |
| What lab tests will be performed on the material? |  |
| What is the minimum quantity of material required (volume in microlitres)?\* |  |
| What test method will be used?  **Please append protocol** |  |
| From which participants is material required (number and selection criteria)? |  |
| In which laboratory will the tests be carried out and who is the contact person? |  |
| Where should the material be sent? |  |
| What will be done with remaining material? |  |

*\*Applicants are asked to state the absolute minimum quantity required, rather than the ‘standard’ quantity often requested as a matter of course, which usually includes significant excess. Applicants are also asked to indicate whether they are able to work with diluted material.*

**Appendix 8**: **HELIUS Material Transfer Agreement #......**

This agreement is made **……..(day) - ……..(month) - ……..(year)** between:

The Academic Medical Center (“**AMC**”) acting on behalf of the HELIUS Study ("HELIUS"), Meibergdreef 9, 1105 AZ, Amsterdam, The Netherlands, legally represented by the Chair of the Executive Board of HELIUS, **Prof. K Stronks**,

And

**…………………………………(institute)** (hereafter referred to as “the Recipient”)

Hereafter referred to collectively as “Parties” and individually as “Party”.

Example

BACKGROUND

The AMC, through HELIUS, has collected and owns certain biological materials and data sets derived from information provided by participants in the HELIUS Study (“the Study Participants”). An employee of the Recipient (“Investigator”), wishes to use certain of the Pseudonymised biological materials and data held by HELIUS for the research as set out in Appendix 1 (“the Research”) as approved by the HELIUS Executive Board. HELIUS is willing to supply the Recipient with a the requested materials and data for a period of **12 months** (1 year) to conduct the Research under the terms and conditions of this Agreement.

DEFINITIONS

1. “Controller”, “Data subject”, “Personal data”, “Processing” and “Processor” shall have the meaning as in the General Data Protection Regulation (EU) 2016/679 (hereinafter: “GDPR”) where these terms appear in non-capitalized words.
2. “Data” means copies of the data from the HELIUS database, which are made available by HELIUS to the Recipient under this Agreement for the purpose of the Research and including the data that are reduced from and/or otherwise accompanying or related to the Materials.
3. “Material” means the Material from the HELIUS biobank, which are made available by HELIUS to the Recipient under this Agreement, for the purpose of the Research.
4. “Pseudonymised” means the result of processing in such manner that the Data and Material 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. This additional information will be stored by HELIUS, to which the Recipient will not have access.
5. “Research Set” means the Material and Data jointly.

NOW IT IS AGREED by Parties as follows:

1. This agreement does not affect the ownership of any Material and/or Data. No license to use any intellectual property is granted or implied by this Agreement except the rights expressly granted in this Agreement.
2. AMC will provide the Recipient with the Research Set in Pseudonymised form and of the type and quantity needed by the Recipient for performing the Research and as outlined in the Appendix 2. Parties acknowledge that the Research Set contain Personal data. The Research Set shall be provided for the sole purpose of its use in the Research and in accordance with the terms of this Agreement.
3. AMC and the Recipient are considered joint Controller with regard to the Data to the extent processed by virtue of the present Agreement and for the period the Research Set are under the control of the Recipient. In addition, each Party may be considered an independent Controller in relation to its own processing of the Data. Therefore, in Processing the Data each Party will be bound to the provisions in the GDPR related to the Controller and abide to the additional data protection laws of the Netherlands. In addition, the Recipient warrants to Process the Data in accordance with its applicable national law, provided that in case of inconsistencies between the GDPR and national law, the provisions of the GDPR shall prevail.

Example

1. AMC warrants and undertakes:

a. the Research Set have been collected, processed and transferred in accordance with

- the GDPR and additional data protection laws in the Netherlands;

- any and all legislation applying in the Netherlands in respect to procurement, storage and use of the Materials.

b. it has obtained any regulatory or ethics approvals necessary to collect the Data and Materials for the purpose of HELIUS, including the purposes under this Agreement;

c. it has full authority to transfer the Research Set to the Recipient; and

d. informed consent of the Data subject has been obtained in accordance with applicable law.

1. All future correspondence pertaining to the Research Set and the Research should be addressed to the HELIUS Scientific Coordinator ([HELIUScoordinator@amsterdamumc.nl](mailto:HELIUScoordinator@amsterdamumc.nl)).
2. The Recipient will use the Research Set only to carry out the Research described in the Appendix 1 to this Agreement. The Recipient will not use the Research Set or any parts thereof for any commercial purpose or any purpose that is subject to consulting or licensing obligations to third parties. Recipient shall ensure that only those employees of Recipient shall have access to the Research Set, who are involved in the Research under direct supervision of the Investigator.
3. The Recipient will use the Material in accordance with good laboratory practice and shall ensure compliance with all applicable laws, regulations and research governance pertaining to the Research.
4. The Recipient will not use the Material in any experiments involving humans and will not use the Material in contact with any cells or other materials to be infused to humans. If animal studies have been proposed, the Investigator has considered in vitro approaches to the research and has followed the applicable guidelines for experimentation regarding such work.
5. The Recipient will not try to identify any Data subject nor link the Research Set to other HELIUS Data held by different recipients or by the same Recipient for different projects.
6. The Recipient will treat the Research Set strictly confidential and not transfer the Research Set in whole or in part to third parties. Consequently, Recipient shall not without first obtaining the consent of Provider:
   1. engage a (sub)Processor to process Data on behalf of the Recipient
   2. engage third parties to process the Materials
   3. transfer any (portion of) the Research Set to any affiliate of Recipient or third-party located outside the European Economic Area.

Example

In case the Provider approves to any of the above, Recipient shall have in place procedures ensuring that any such (sub)Processors, affiliates and/or third-parties will respect and maintain the confidentiality and security of the Research Set and shall Process all Data in accordance with the requirements of the GDPR and be bound to provisions similar to those of this Agreement. Recipient shall be responsible to Provider for any acts and/or omissions of the such (sub)Processors, affiliates and/or third-parties.

1. Subject to Section 10, any person or organisation acting under the authority of the Recipient shall be obligated to Process the Research Set only on instructions from the Recipient and in accordance with the permitted use under this Agreement.
2. Recipient shall be responsible to have an agreement in place with each of its employees who have access to the Research Set, which agreement binds them to provisions of confidentiality and to process the Research Set in accordance with the GDPR. The Investigator and other relevant employees of the Recipient involved in the Research have read and will abide by the “HELIUS Collaboration Policy”.
3. Recipient shall not be prevented to provide access to the Research Set to persons authorised or required by law or regulation to have access to the Research Set, provided it will without undue delay inform HELIUS of any projected or actual inspection.
4. The Investigator will retain the Research Set in a secure location on its premises and warrants that it will have for the full duration the Research Set are in its custody, appropriate technical and organisational measures in place to protect the Research Set against accidental or unlawful destruction or accidental loss, alteration, unauthorised disclosure or access, and which provide a level of security appropriate to the risk represented by the processing and the nature of the Research Set to be protected.
5. The Recipient will use all reasonable endeavors to ensure that the Research Set in its possession, or under the control of the Recipient shall as soon as possible be returned or destroyed upon (i) the reasonable request of HELIUS; or (ii) on termination of this Agreement; or (iii) in the event that the Recipient is in breach of any of the conditions of this Agreement. If the Recipient is required to destroy the Research Set then it will ensure that this is done in compliance with all applicable laws and regulations and confirm in writing to HELIUS that the Research Set has been destroyed.
6. If the Recipient becomes aware of a (potential) personal data breach affecting the Data, or receives a request of a Data subject to exercise its rights under the GDPR, the Recipient shall promptly notify the AMC. In case of a Personal data breach, Parties will fully cooperate with each other to remedy the Personal data breach, fulfil their respective (statutory) notification obligations timely and cure the damages. A Personal data breach shall have the meaning under articles 33 and 34 of the GDPR. In case of a request of a Data subject to exercise its rights under the GDPR, the Parties agree that HELIUS is most suited to handle such requests. However, the Recipient shall fully cooperate with HELIUS in handling such requests, if so requested by HELIUS.

Example

1. The Recipient will keep HELIUS informed of the results of the Research (“Results”). All information (including the results of cleaned or derived variables and laboratory results) relating directly to Study Participants will be made available to AMC for the purposes of incorporation into HELIUS. All other results generated by the Research shall be the property of the Recipient save that the Recipient grants to the AMC royalty-free, irrevocable, perpetual non-exclusive right to use such Results for internal non-commercial research and teaching. The Recipient will provide HELIUS with a fully documented electronic copy of the full Results before publication in any form or within 6 months of the completion of the Research whichever is the sooner. In addition, for archival purposes, the Recipient will provide HELIUS with the complete dataset (including derived variables) and syntaxes which document how the Results of the publication were obtained.
2. This Agreement does not affect the ownership of the Research Set. No license to use any intellectual property is granted or implied by this Agreement except the rights expressly granted in this Agreement.
3. HELIUS accepts no liability in connection with the Recipients use of the Research Set. HELIUS does not represent that (i) the Research Set is of satisfactory quality or fit for any particular purpose; or (ii) use of the Research Set is free from infringement of third party rights, including intellectual property rights. To the extent permissible by law the Recipient will indemnify and hold HELIUS harmless for any damages howsoever arising from Recipient’s use of the Research Set.
4. The rights and obligations as determined in the Agreement may not be assigned by a Party without the prior written consent of the other Party.
5. In return for using the Research Set, **……………………………. (*agreements regarding contribution to HELIUS data collection*)**
6. This Agreement shall be interpreted and governed by the laws of The Netherlands in any action. Any dispute relating to the interpretation or implementation of this Agreement which the Parties hereto have failed to settle amicably shall be exclusively referred to the competent courts of The Netherlands for settlement.
7. Modifications and changes to this Agreement are only binding after these have been agreed upon in writing between the Parties.

Each person signing this Agreement represents and warrants that he or she is duly authorized and has legal capacity to execute and deliver this Agreement.

Example

AGREED BY THE PARTIES through their authorized signatories

SIGNED for and on behalf of AMC:

Signature: ………………………………………………..

Print Name: **K. Stronks** Date: ……………………………..

SIGNED for and on behalf of RECIPIENT:

Signatory of Recipient …………………………. …

Printed Name: ………………………………. Date:………………………………

(1) Signature of Investigator ………………………………

Printed Name: ……………………………….. Date:………………………………

(2) Signature of Investigator ………………………………

Printed Name: ……………………………….. Date:………………………………

APPENDIX 1: **Research proposal** or **Publication proposal** with accompanying **Material Request Form**

*Please note: A project specific appendix to be added here which must be approved by HELIUS.*

APPENDIX 2: **Categories of Data subjects and categories of Research Set**

Supplier shall make certain Research Set available to Recipient, including data that relates to human tissue samples.

1. The Research Set includes the following categories of Data subjects:

Participants of the HELIUS study

In the amount of [number] Data subjects

1. The Research Set includes the following Personal Data:

[age, sex, etc.]

1. Research Set is Pseudonymised data, to ensure data minimalisation under the GDPR.

Example