

Access to ADDRESS-2 biological samples

The biorepository

ADDRESS-2 participants who consented to donate a blood sample and for whom viable samples were received have the following stored at the Public Health England European Collection of Cell Cultures (ECACC) based in Porton Down, Wiltshire:

- Extracted DNA; pellet re-suspended with a default concentration of either 100 ng/ul or 50 ng/ul (yield provided in ng)
- Lymphoblastoid cell Line (Epstein-Barr virus transformation of cryo-preserved peripheral blood lymphocytes) – for samples received up to 31st March 2015 only
- Serum; stored at -80 °C in aliquots of 0.5 ml, 1-11 aliquots per participant
- Peripheral blood lymphocytes; up to 2 cryo-preserved vials if not used for Epstein-Barr virus transformation

Sample identifiers

Serum samples, cell lines and PBLs are stored under a sample identifier that is linked to the ADDRESS-2 participant identifier. This link is accessible by members of the study team at the recruiting site and the ADDRESS-2 Co-ordination Centre. DNA is stored under an identifier generated by the ECACC. This identifier is linked to the ADDRESS-2 blood sample identifier, but the link is accessible by the ECACC and two members of the team at the ADDRESS-2 Co-ordination Centre (the Study Co-ordinator and Data Manager), and not by other members of the central or local ADDRESS-2 study teams.

Participant consent

ADDRESS-2 participants give consent for their data and biological samples (including DNA), and the results from testing their samples to be used in diabetes research that has been approved by the ADDRESS-2 Management Committee and has been given independent ethical approval. Genetic testing is limited to diabetes-related genes. Participants understand that samples and data will be made anonymous before being used by researchers outside the study team unless further consent is sought. Participants understand that researchers could be from outside the UK, and specifically outside the European Union.

The application process

The principles by which access may be granted to researchers wishing to use biological samples collected in ADDRESS-2 are described in the document “Research access to the ADDRESS-2 resource”. The principles follow those of the NIHR Clinical Research Network in governing eligibility for NIHR CRN support (set out in the Department of Health policy document “Eligibility for NIHR Clinical Research Network Support, April 2013”). Applications should be made to the ADDRESS-2 Management Committee via the Study Co-ordinator using the relevant form:

ADDRESS-2 application for access to biological samples

Preliminary enquiries can be made to the Study Co-ordinator to check sample availability, obtain a list of available data fields and get an estimate of sample transfer costs (email: address2@imperial.ac.uk, or tel: 020 7594 1316).

The samples are linked anonymous. No ADDRESS-2 participant identifiers will be provided to researchers and no attempt should be made by researchers to identify participants. Applicants can request a data set of demographical and clinical information with the samples. If subsequent participant identification is required, for example, to offer the opportunity of participation in a type 1 diabetes research study, a separate application for use of ADDRESS-2 to identify research candidates must be made. The processes for identifying and contacting candidates are described in the document "ADDRESS-2 identifying and contacting T1D research candidates".

Applicants must describe the purpose of the request for ADDRESS-2 samples and provide a summary of the research. To meet the conditions of consent under which the samples were donated, applicants must provide written confirmation from the Sponsor of the research that it has been approved by an independent research ethics committee, quoting the reference number for the ethical review. If the research is not included in the NIHR CRN portfolio of studies the funding stream will be assessed. If the funding stream does not have NIHR non-commercial partner status, applicants will be asked to provide written confirmation from the Funder and the Sponsor that the research meets the NIHR CRN criteria relating to funding and peer-review, specifically that

- a) the funding was awarded in open competition or the opportunity was available to all qualified researchers (written confirmation required from the Funder)
- b) was awarded subject to high-quality peer-review (written confirmation required from the Sponsor)

Applicants must describe the proposed arrangements for testing and storing the samples and data, including:

- A brief description of the testing methodology
- The location of the testing
- The location of sample storage (if different to above), including the individual and organisation taking responsibility for the samples and a description of the sample security arrangements/policy
- The location of data storage, including the individual and organisation taking responsibility for the data and a description of the data security arrangements/policy
- Participant sample selection criteria
- The sample volume required and any particular requirements for the preparation or transportation of the samples
- Any additional data requested, with justification regarding the necessity of the data fields selected

The application assessment process

Applications will be reviewed by the ADDRESS-2 Management Committee via email. The Study Co-ordinator will check applications for completeness. A member of the Committee will be assigned as lead reviewer for each application and will make a recommendation to approve or decline the application within 14 calendar days of receipt of a complete application. Committee members, with the exclusion of the Study Co-ordinator will be sent the application with the recommendation and justification of the lead reviewer and given a further 14 calendar days to respond in agreement or disagreement. A majority decision will stand. The Chairperson of the Management Committee will adjudicate if a majority decision is not reached. It is the responsibility of Committee members with a conflict of interest relating to an application to declare this and to not contribute to the assessment process unless the Chairperson judges it is appropriate to do so.

Applications shall be assessed against the following criteria:

- Is the research included in the NIHR CRN portfolio of studies?
OR
Is the research funded as part of an NIHR Biomedical Research Centre (BRC) / NIHR Biomedical Research Unit (BRU) / NIHR Collaboration for Leadership in Applied Health Research and Care (CLAHRC) or NIHR Patient Safety and Service Quality Research Centre (PSSQC) programme?
OR
Does the research meet the specific criteria used to assess eligibility for NIHR CRN support relating to funding and peer-review?
- Does the research meet the conditions of consent under which the samples were donated?
- Are there adequate security arrangements for storage of the samples and data?
- Is there sufficient justification for additional clinical and demographical data requested?

Consideration shall be given to the following:

- The risk of linking participants and their demographical and clinical data to the results of sample testing without participant consent to identify (de-anonymise) samples.
- Overlapping studies/requests, i.e. for biological samples for the same or a very similar purpose to the current application, such that the Committee would want additional justification for granting access to the samples in the current application.
- The number of remaining aliquots or vials or DNA yield (depending on presence of stored cell lines) for individual participants.

If the lead reviewer has concerns regarding any of the above and requires additional information before making a recommendation, the principal applicant will be asked to supply the extra information/further justification. The clock will stop from the time of the request and re-start when the additional information is provided.

The transfer of materials & researcher responsibilities

Materials shall be transferred to successful applicants under the terms of a Material Transfer Agreement (MTA) between Imperial College London, as Sponsor of ADDRESS-2, and the principal researcher's organisation (see Appendix 1 Material Transfer Agreement for biological samples). Samples will be transferred by courier. Researchers are required to cover the cost of the preparation and transport of samples and will be invoiced for these costs.

Researchers supplied with biological samples shall make available all results from analysis of the samples so that these data become part of the ADDRESS-2 resource. Associated clinical and demographic data requested with biological samples will only be released after results, and quality assurance data for the testing methodologies used, have been sent to the ADDRESS-2 Co-ordination Centre. Researchers will have exclusive use of the results for a period of 6 months, after which, such data may, on approval of a valid access request, be released to other researchers.

Researchers using ADDRESS-2 materials and/or data must comply with the Human Tissue Act 2004, the Data Protection Act 1998 and any other applicable regulations, and they must conduct research within the terms of ethical approval given for that research. Researchers must store samples in a secure location. Data must be stored in a secure system and handled as would reasonably be expected for sensitive and confidential data (e.g. use of encryption for transfer of data via email and temporary storage of data on portable storage media).

Appendix 1: Material Transfer Agreement**Imperial College**
London**MATERIAL TRANSFER AGREEMENT**

Imperial's Ethics Approval Number: 10/H0505/85

This Agreement is made this [] day of [] between

Imperial College of Science Technology and Medicine, Exhibition Road, London, SW7 2AZ, UK (the "Supplier") and

[INSERT NSAME AND ADDRES OF RECIPIENT] (the "Recipient")

WHEREAS the Supplier, through the project entitled an incident and high risk type 1 diabetes research cohort – After Diabetes Diagnosis REsearch Support System-2 (the "Project"), funded jointly by Diabetes UK and the Juvenile Diabetes Research Foundation, has produced as a result the Materials.

WHEREAS the Supplier, through its employee Prof Desmond Johnston (the "Supplier's Scientist"), is willing to provide the Recipient with the Material as defined below and such Materials shall include any and all biological samples as well as any and all progeny and derivatives thereof on the terms and conditions shown below, and the Recipient and Investigator agree to comply with these terms and conditions.

WHEREAS [INSERT NAME OF INVESTIGATOR] (the "Investigator"), who is an employee of the Recipient, wishes to acquire the Materials for non-commercial academic research relating to [INSERT TITLE/DESCRIPTION OF THE RESEARCH] (the "Research Programme") as detailed in the application for access to biological samples produced in the Project.

Description of the Material: [INSERT DESCRIPTION]

Recipient's Designated Individual: [INSERT NAME OF INDIVIDUAL]

Location of the Material: [INSERT LOCATION]

Duration of the Agreement: [INSERT DURATION]

- 1 The Recipient and Investigator shall keep the Materials secure at the Recipient's premises and ensure that no one other than the Recipient and authorised co-workers under the direct supervision of the Recipient (the "Co-workers") have access to the Materials.
- 2 The Recipient and Investigator shall use the Materials only for the Research Programme. The Recipient and Investigator shall not use the Materials for any commercial purpose or commercially sponsored research even if those purposes are being pursued in the Recipient's laboratory, without the prior written consent of the Supplier.
- 3 With the exception of providing the Materials to a subcontractor ("Subcontractor"), who will perform [INSERT DESCRIPTION OF WORK TO BE PERFORMED BY SUBCONTRACTOR] for the purposes of the Research Programme, the Recipient and Investigator shall not supply the Materials to any other party. The Materials shall not be used in humans.
- 4 In the event of the Supplier making available to the Recipient, whether directly or indirectly, confidential information relating to its business, scientific or other activities or intellectual property in relation to the Materials (the "Confidential Information"), the Recipient shall maintain the confidentiality of such information, and shall not disclose it to third parties or members of its staff or students outside the team working on the Research Programme without the prior written consent of the Supplier. Further, the Recipient shall not include any such Confidential Information in the published results without the prior

written permission of the Supplier.

- 5 The Recipient and Investigator shall make available to the Supplier all results generated using the Materials and quality assurance data for the testing methodologies used. These data will become part of the study resource for "an incident and high risk type 1 diabetes research cohort – After Diabetes Diagnosis REsearch Support System-2 (ADDRESS-2).
- 6 The Recipient and Investigator shall acknowledge the Supplier (and any grant funders that contributed with the Supplier with the obtention of the Materials) as the source of the Materials and for any other contribution in any publication that mentions the Materials, using the following wording: "[Researchers acknowledge/Organisation acknowledges] the support of Imperial College London, Diabetes UK, the Juvenile Diabetes Research Foundation and of the National Institute for Health Research via the Clinical Research Network." Before submission of any such publication the Recipient shall send to the Supplier a copy of any proposed reports or publications which describe work carried out using the Materials, and shall make available all results generated using the Materials at least thirty (30) days prior to submission to a journal editor or conference or other third party if not made available prior to that. The Recipient and Investigator agree that the Supplier shall have thirty (30) days to object to such publication and request amendments to ensure that information regarding the Materials is in accordance with applicable laws and regulations. If the Supplier makes such objection, the Investigator and Recipient agree to delay publication for a maximum of thirty (30) days or to amend the publication as reasonably requested by the Supplier. The Supplier shall be entitled to use and make available all such data, reports and publications for further non commercial research and academics purposes.
- 7 The Materials and any copies made thereof shall at all times remain the property of the Supplier. No licence under any Supplier intellectual property is granted or implied by this Agreement.
- 8 The Materials are supplied without cost but the Recipient shall reimburse the Supplier for any reasonable shipping and related costs that may be incurred when preparing and sending the Materials to the Recipient.
- 9 In the event that the Recipient or Co-workers make or observe any new discovery, improvement or invention ("Invention") relating to the Materials or as a direct result of the Research Programme then the Recipient will bring this promptly to the attention of the Supplier. The Recipient and Investigator shall not make or seek to make actual commercial gain from such an Invention, nor make any patent application or secure any other proprietary rights to legally protect any such Invention except with the prior written consent of the Supplier, which shall not be unreasonably withheld, and will be subject to any existing third party rights including but not limited to any obligations or commitments with any funders related to the development or use of the Materials.
- 10 Any arising intellectual property resulting of the Research Programme shall vest in the Supplier, who hereby grants the Recipient a non-exclusive, worldwide, fully paid, royal free license to use the results of the Research Programme for non-commercial purposes The Parties will separately negotiate the terms for any commercial exploitation of the arising intellectual property resulting from the Research Programme.
- 11 The Recipient and Co-workers shall use the Materials in accordance with good laboratory practice and the highest standards of skill and care and shall ensure compliance with any applicable laws and regulations governing the transportation, keeping, tracking, use and disposal of the Materials in particular the provisions of the Human Tissue Act (2004) and the Human Tissue Authority Codes of Practice. Unless instructed otherwise by the Supplier, the Material shall be disposed of in accordance with the Act at the end of the project period.
- 12 (a) The Supplier warrants that the Materials (i) have been collected with informed consent, and (ii) will be sent to Recipient's contractor in pseudo-anonymised format.

(b) Subject to Clause 12 (a) above, the Supplier makes no representation and gives no warranty or undertaking, in relation to the Materials. As examples, but without limiting the foregoing, the Supplier gives no warranty:- (i) that it owns all necessary property and other rights in the Materials and that their use will not infringe any patent, copyright, trade mark or other right owned by any third party; or (ii) that the Materials are of merchantable or satisfactory quality or fit for any particular purpose, have been developed with reasonable care and skill or tested, for the presence of pathogens or otherwise, or are viable, safe, or non-toxic. The Investigator and Recipient shall ensure that any person who has access to the Materials is aware of this Agreement and that Co-workers shall deal with the Materials in accordance with the provisions of this Agreement and solely for the purposes of conducting the Research Programme in accordance with the law and regulations.

- 13 The Supplier shall have no liability to the Recipient or Investigator, whether in contract, tort or otherwise, in relation to the supply of the Materials to the Recipient or their use or keeping by the Recipient or by any other person, or the consequences of their use, to the maximum extent permitted under applicable law. The Recipient shall indemnify and hold harmless the Indemnified Parties from and against all Claims and Losses arising from such supply, use or keeping, including without limitation Claims and Losses arising from:- (i) injury to the Recipient's employees and third parties; (ii) infringement of third party intellectual property rights; and (iii) use of the Materials within or outside the scope of this Agreement. The Recipient shall procure and maintain insurance cover with a reputable insurance carrier to cover its potential liability hereunder.
- 14 For the purposes of this Agreement:- (i) "Indemnified Parties" shall mean the Supplier, its associated undertakings, and their respective directors, officers, employees and representatives; (ii) "Claims" shall mean all demands, claims, proceedings, penalties, fines and liability (whether criminal or civil, in contract, tort or otherwise); and (iii) "Losses" shall mean all losses including without limitation financial losses, damages, legal costs and other expenses of any nature whatsoever but shall not extend to any special, consequential or indirect losses, including loss of profits, business, opportunity, reputation or goodwill no matter how arising.
- 15 The Recipient agree to be bound by the terms of this Agreement in consideration of the Supplier making the Materials available to the Recipient. The Investigator also also to be bound by those terms of the Agreement that apply to the Investigator.
- 16 This Agreement shall take effect from the date first written above (the "Effective Date") and shall remain in full force and effect for the duration written above (the "Term") unless terminated earlier by any Party with thirty (30) days written notice. Upon the termination of this Agreement, the Recipient shall cease to use the Materials and Confidential Information and, upon request by the Supplier, the Recipient shall return to the Supplier all of the Confidential Information and Materials.
- 17 The Recipient shall not assign, transfer, mortgage, charge or otherwise dispose of any or all of the rights, duties or obligations granted to it under this Agreement without the prior written consent of the Supplier.
- 18 This Agreement shall be governed by and construed in accordance with the laws of England and the Parties submit to the exclusive jurisdiction of the English courts.

AGREED by the parties through their authorised signatories:

For and on behalf of
Supplier

By the
Recipient

Signed

Signed

Print name

Print name

Title

Title

Date

Date

Undertaking by the Investigator

I have read the above terms and conditions of contract and understand that they apply to me in my use of the Material and any Confidential Information.

In consideration of the Provider making the Materials available to me and the Recipient, I agree to be bound by this Agreement and to use the Material and any Confidential Information on the same conditions that apply to the Recipient in this Agreement, except where they apply solely to the Recipient as an institution, and I shall use all my reasonable endeavours to enable the Recipient to fulfil its obligations under this Agreement.

.....
(the Investigator)

.....
(Date)