UNIVERSITY CHILDREN'S HOSPITAL ZURICH

University of Basel

MATERIAL TRANSFER AGREEMENT

FOR THE TRANSFER AND USE OF BIOLOGICAL MATERIAL

This agreement (hereinafter referred to as the "Agreement") is made and entered into by and between:

University Children's Hospital Zurich ("PROVIDER")
Steinwiesstrasse 75, 8032 Zürich

and

University of Basel ("RECIPIENT")
Klingelbergstrasse 50, 4056 Basel

Hereinafter jointly referred to as the "Parties" and individually as a "Party"

PROVIDER Authorized Signature(s)	**RECIPIENT Authorized Signature(s)**
(Duly Authorized Representative)	(Duly Authorized Representative)
Signature	Signature
Markus Malagoli, CEO	Torsten Schwede, Prof. Dr.
	Vice President Research
Date 29/6/2020	Date 18.6.2020

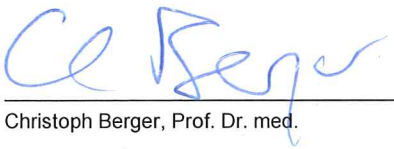
Universitäts-Kinderspital Zürich - Eleonorenstiftung
Dr. Markus Malagoli
CEO
Steinwiesstrasse 75
CH-8032 Zürich

PROVIDER Authorized Signature(s)	**RECIPIENT Authorized Signature(s)**
(Duly Authorized Representative)	(Responsible Scientist of Organization)
Signature	Signature
Michael Grotzer, Prof. Dr. med.	Henriette Meyer zu Schwabedissen, Prof. Dr. med.
Medical Clinic Director	Collaborator *SwissPK*^{cdw} Project (2018DEV21)
Date 30.6.2020	Date 12.06.2020

Prof. Dr. med. Michael Grotzer
Ärztlicher Direktor
Universitäts-Kinderspital Zürich
Steinwiesstrasse 75
8032 Zürich

PROVIDER Authorized Signature(s)
(Responsible Person of Project)

Signature



Christoph Berger, Prof. Dr. med.

PI *SwissPK*^{cdv} Project (2018DEV21)

24.06.2020

Date

PROVIDER AND RECIPIENT AGREE AS FOLLOWS:

Preamble

RECIPIENT wishes to conduct RESEARCH with ORIGINAL MATERIAL and DATA.

PROVIDER is willing to provide ORIGINAL MATERIAL and DATA to RECIPIENT under the terms and conditions as follows hereafter.

The effective date of this Agreement is the date of the last required signature obtained.

The biological material and preanalytical data as described in Annex 1 will be delivered by PROVIDER to RECIPIENT under the terms of this Agreement.

1 DEFINITIONS

For the purpose of this Agreement, capitalized terms, whether used in singular or plural form, shall have the following meaning:

BACKGROUND INTELLECTUAL PROPERTY (BACKGROUND IP) shall have the meaning set forth in Section 4 below.

DATA
Preanalytical data[1] provided by PROVIDER to RECIPIENT related to ORIGINAL MATERIAL as described in Annex 1.

FOREGROUND INTELLECTUAL PROPERTY (FOREGROUND IP) shall have the meaning set forth in Section 4 below.

INTELLECTUAL PROPERTY RIGHTS
All intellectual property rights throughout the world, whether existing under statute, at common law or equity, registered or unregistered, now or hereafter in force or recognized including trade secrets and know-how.

MATERIAL
ORIGINAL MATERIAL, any PROGENY and UNMODIFIED DERIVATIVES thereof, the ORIGINAL MATERIAL contained in MODIFICATIONS and DATA.

MODIFICATIONS
Substances created by RECIPIENT which contain/incorporate the MATERIAL in whatever form.

ORIGINAL MATERIAL
Biological material that is to be delivered by PROVIDER to RECIPIENT as described in Annex 1.

PROGENY
Unmodified descendant from the ORIGINAL MATERIAL, such as virus from virus, cell from cell, or organism from organism.

RESEARCH, RESEARCH PROJECT
Research project and experiments with the MATERIAL to be performed by RECIPIENT, as specified in Annex 2. Any use will be only for research purpose.

RESULTS
Any output of the RESEARCH, which are not PROGENY or UNMODIFIED DERIVATIVES, such as invention, data, software, algorithms, knowledge, know-how or information that is generated in the RESEARCH, whatever its form or nature, whether or not it can be protected, as well as any rights attached to it, including INTELLECTUAL PROPERTY RIGHTS.

UNMODIFIED DERIVATIVES
Substances created by RECIPIENT which constitute an unmodified functional subunit or product expressed by the ORIGINAL MATERIAL. Some examples include: subclones of unmodified cell lines, purified or fractionated subsets of the ORIGINAL MATERIAL, proteins expressed by DNA/RNA supplied by PROVIDER, or monoclonal antibodies secreted by a hybridoma cell line.

2 SCOPE

2.1 PROVIDER will provide RECIPIENT with MATERIAL under the conditions as set forth in this Agreement.

2.2 The MATERIAL may not itself be commercialized and is to be used solely by RECIPIENT and defined co-partner of RECIPIENT[2] under the direction of a qualified RECIPIENT's scientist at recipient's organization. The RESEARCH to be conducted by RECIPIENT is restricted to the RESEARCH PROJECT described in Annex 2. Restrictions of use of the MATERIAL, if applicable, are stated in Annex 1.

2.3 MATERIAL and MODIFICATIONS will be stored in a secure location and will only be used in laboratory animals or *in vitro* experiments. MATERIAL and MODIFICATIONS will not be used in human subjects, clinical trials or for diagnostic purpose involving human subjects without PROVIDER's prior written consent.

2.4 The RECIPIENT will ensure that RECIPIENT's scientist does not transfer the MATERIAL or MODIFICATIONS to anyone who does not work under his or her direct supervision and responsibility at recipient's organization or who is a defined co-partner of RECIPIENT[2] without the prior written consent of PROVIDER.

[1] Data related to the collection, processing, storage and usage of biological material (e.g. collection time, transport temperature, centrifuge speed, storing temperature, etc.).
[2] As listed in Annex 2.

3 COMPLIANCE WITH LAW, RULES AND REGULATIONS

3.1 The MATERIAL has been collected and processed by PROVIDER in compliance with all applicable laws.

3.2 In case of full or partial withdrawal of consent, the PROVIDER must inform the RECIPIENT of this revocation without delay. If applicable, the RECIPIENT ought to anonymize the MATERIAL according to the Human Research Ordinance *as per* the PROVIDER's request, unless one of the exceptions listed in Article 10 of the Human Research Ordinance applies. A written notification shall be sent to the PROVIDER upon receipt and after completion of the request.

3.3 RECIPIENT agrees to comply with all laws applicable to the research and the handling of biological material. In particular, RECIPIENT shall refrain from tracing or identifying the identity of any participants who provided the MATERIAL.

3.4 PROVIDER and RECIPIENT confirm that the RESEARCH PROJECT has been subject to review and approved by the [Kantonale Ethikkomission Zürich (BASEC Nr. 2019-01888)] as further described in Annex 2.

3.5 RECIPIENT is aware that the ORIGINAL MATERIAL and its PROGENY may contain infectious agents and that it should be handled accordingly. RECIPIENT confirms to perform the activity in accordance with local law before processing the ORIGINAL MATERIAL or its PROGENY in a way that infectious agents may be propagated.

3.6 PROVIDER and RECIPIENT warrant to each other that they will protect, in their respective areas of responsibility under applicable law and the present Agreement, the personality and the fundamental rights of the person providing the MATERIAL, including (i) the protection of privacy and (ii) the right to autonomy and informational self-determination.

3.7 The MATERIAL shall be used only (i) under the conditions, if any, specified by PROVIDER, including any conditions specified at the time of collection, as set forth in Annex 1 and (ii) as provided for by law.

3.8 PROVIDER confirms that a written consent covering the intended use has been signed by the relevant person providing the MATERIAL or by his legal representative. In case such consent is lacking and cannot be obtained, PROVIDER shall request lawful authorization from the competent Ethical Committee for the use of MATERIAL.

3.9 RECIPIENT agrees to protect MATERIAL against misuse through appropriate organizational and technical measures as described in Annex 3. Secure MATERIAL access and security shall be guaranteed at all stages of the process.

4 INTELLECTUAL PROPERTY RIGHTS

4.1 **BACKGROUND IP**. The Parties agree that each Party shall retain all title, right and interest in and to its respective INTELLECTUAL PROPERTY RIGHTS, as of the date of entry into force of this Agreement (the "BACKGROUND IP"). Unless otherwise agreed herein, nothing in this Agreement shall be construed as a transfer, license, and/or assignment by a Party to the other Party of ownership of, title, right or interest in and to its respective BACKGROUND IP.

4.2 **JOINT FOREGROUND IP.** All right, INTELLECTUAL PROPERTY RIGHTS, title and interest in and to the RESULTS shall be owned jointly by the Parties (the "JOINT FOREGROUND IP"). The Parties will set forth, by separate mutual agreement, their respective rights, duties and responsibility relating to the JOINT FOREGROUND IP. Such an agreement shall not cause a delay of publication of the RESULTS any longer than as defined in Section 7.2.

5 DISCLAIMERS

5.1 Any ORIGINAL MATERIAL delivered pursuant to this Agreement is understood to be experimental in nature and may have hazardous properties or contain infectious agents. PROVIDER makes no representations and extends no warranties of any kind, either expressed or implied. There are no express or implied warranties of merchantability or fitness for a particular purpose, or that the use of the MATERIAL or MODIFICATIONS will not infringe any patent, copyright, trademark or other proprietary rights of a third party.

6 LIABILITY AND INDEMNIFICATION

6.1 In no event shall PROVIDER be liable for any use by RECIPIENT of the MATERIAL and MODIFICATIONS, or any loss, claim, damage or liability, of whatsoever kind or nature, which may arise from or in connection with this Agreement or the use, handling or storage of the MATERIAL and MODIFICATIONS by RECIPIENT.

6.2 Each Party shall be solely liable for any loss, damage or injury to third parties resulting from its carrying out its parts of the Project.

6.3 **FOREGROUND IP**. The Parties use the FOREGROUND IP at their own risk. A Party using any of the FOREGROUND IP shall, to the fullest extent permitted by the applicable law, defend, indemnify and hold the other Party harmless against third party claims (including but not limited to claims based on mandatory product liability law) which are based on the Party's use of the FOREGROUND IP.

7 PUBLICATIONS

7.1 The most important purpose of biological resources' use is scientific research and RECIPIENT shall make every effort to publish its RESULTS related to the MATERIAL or MODIFICATIONS. RECIPIENT agrees to acknowledge PROVIDER either as co-authors of the publication or cite as the source of the MATERIAL in all written publications, posters or oral presentations. This applies to any publication on MATERIAL or MODIFICATIONS that discloses or relates in any way to RECIPIENT's use of the MATERIAL, unless otherwise agreed in writing by PROVIDER. The MATERIAL shall be cited at least in the methods and acknowledgement sections. RECIPIENT will acknowledge the name of the biobank and/or individual(s) who have collected the MATERIAL and/or created the biobank.

7.2 RECIPIENT agrees to submit written publications to PROVIDER in confidence for review and comment no later than thirty (30) days prior to submission for publication. RECIPIENT will use a reasonable effort to reflect into the proposed publication any reasonable comments made by PROVIDER no later than ten (10) days before the proposed submission. If no objection is made within the thirty days stated above, the publication is permitted.

7.3 All publications of the RESULTS must be compliant with the Authorship Guidelines of the Swiss Academies of Arts and Sciences, as updated from time to time.

8 RESEARCH RESULTS

8.1 RECIPIENT agrees, in accordance with its established practice, to keep complete and accurate accounts, notes, data and records of the RESEARCH.

8.2 Upon completion of the RESEARCH or on PROVIDER's request, RECIPIENT will disclose to PROVIDER all RESULTS obtained from conducting the RESEARCH, which relate to the use of the MATERIAL or MODIFICATIONS, including, without limitation, copies of relevant summaries and reports. PROVIDER agrees to keep these RESULTS confidential until they are published.

9 EXPIRATION AND TERMINATION

9.1 This Agreement will automatically expire the earliest of on 31.10.2023, unless the Agreement is extended in writing by the Parties. It is the responsibility of the collaborating PROVIDER and RECIPIENT to seek such an extension.

9.2 Either Party may terminate this Agreement through a 30-day prior written notice to this effect to the other Party stating one of the following grounds:

i. if the PROVIDER/RECIPIENT organization ceases, is likely to cease, or threatens to cease carrying on business;

ii. in case the other Party is in material breach of this Agreement and has not remedied such breach by the end of the notice period.

9.3 On expiration or termination for any reason, the grant of rights to RECIPIENT under the present Agreement will be automatically terminated. RECIPIENT agrees to discontinue use of MATERIAL. Recipient shall, in accordance with PROVIDER's directions, return or destroy any unused ORIGINAL MATERIAL.

9.4 RECIPIENT, at its discretion, will also either destroy the MODIFICATIONS or remain bound by the terms of this Agreement as they apply to MODIFICATIONS.

9.5 The provisions concerning publications, intellectual property, warranty and liability as well as those intended to protect the rights of participants shall survive the Agreement's expiration.

10 MODIFICATIONS AND AMENDMENTS

10.1 This Agreement constitutes the entire agreement and understanding of the Parties and supersedes any prior agreements or understandings relating to the subject matter hereof. This Agreement may not be modified except by a written instrument signed by all Parties.

10.2 If any portion of this Agreement is in violation of any applicable regulation, or is unenforceable or void for any reason whatsoever, it should be put in writing and discussed by the Parties. Such portion will be inoperative and the remainder of this Agreement will be binding upon the Parties.

11 FEES AND TRANSPORT

11.1 Transmittal fees to be reimbursed to PROVIDER for sample production, preparation and shipment costs are specified in Annex 4.

12 GOVERNING LAW AND JURISDICTION

12.1 This Agreement shall be governed by the laws of Switzerland. Any claim or controversy arising out of or related to this Agreement shall be submitted to the competent courts of the defendant party.

13 ANNEXES

Annex 1 Original Material and Data

Annex 2 Research Project/Purpose

Annex 3 Material Transfer Specification

Annex 4 Fees and Transport

All Annexes are integral part of this Agreement.

ANNEX 1
ORIGINAL MATERIAL and DATA

The following original material shall be provided from PROVIDER to RECIPIENT for genetic analysis

Patient materials as follows:

For the *Swiss Pharmacokinetics clinical data warehouse (SwissPK^{cdw})* SPHN Project here referred to as RESEARCH, polymorphism analysis will be performed at the RECIPIENT's Institute. In order to identify individuals eligible for the study and to select the BIOLOGICAL MATERIAL samples, the PROVIDER's SQL Data Base *Data Lake* queries for suitable samples, assigns a pseudonym and creates the pseudonymized 2D QR lables. Individuals are eligible for study entry if they obtained one of the study drugs of the RESEARCH and agreed to further use of their DATA and BIOLOGICAL MATERIAL in the general consent.

The BIOLOGICAL MATERIAL is gathered in the respective laboratory of the PROVIDER or biobank of PROVIDER and PROVIDER's collaborators. Here, an aliquot of the respective biological sample (EDTA blood, blood cake or DNA) from previous laboratory analyses is either transferred into tubes, which are labelled with the corresponding pseudonymized labels or relabeled in the previous storying tubes. The PROVIDER gets informed by the laboratory or biobank that samples are ready for transfer into the *Biopharmacy Biobank*.

Accordingly, with the entry in the *Biopharmacy Biobank* the biological samples are pseudonymized with the pseudonymization mapping key being kept by the PROVIDER.

ANNEX 2
RESEARCH PROJECT/PURPOSE

The RESEARCH shall be limited to use of the MATERIAL in connection with the following activities:

Project Name	*SwissPK^{cdw}*
Organization Name: Lab(s) and researchers names	PROVIDER: Prof. Dr. med. Christoph Berger and Dr. med. Paolo Paioni, University Children's Hospital Zurich RECIPIENT: Prof. Dr. med. Henriette Meyer zu Schwabedissen University of Basel
Project summary	*"To enhance access to clinical data from a high number of paediatric patients seen at the hospitals, the project will establish a clinical data warehouse (CDW). It will collect drug plasma concentrations from routine drug monitoring and clinical trials of paediatric patients together with clinical and prescription data as well as genetic information. CDW data are transferred to be analysed and shared on a connected platform. This data is essential to establish mathematic modelling, to eventually mirror the physiological processes that affect the drug in the developing and growing body of a child (pharmacokinetics). With this so-called pharmacokinetic modelling, dosage regimens for children can be optimized"* . Lay summary *SwissPK^{cdw}*, 2019
Project duration	01.05.2019 – 31.08.2020
Methods planned to be used	TaqMan Genotyping Sequencing Restriction Fragment Length Polymorphism (RFLP)
Ethical Committee Approval (name, ref number and date)	Kantonale Ethikkomisison Zürich BASEC-Nr. 2019-01888 15th October 2019
Co-partner(s) (if applicable, e.g. collaboration with other labs for analysis)	

The BIOLOGICAL MATERIAL samples are used for genetic analysis at the Biopharmacy Institute at the University of Basel. The genotyping is performed according to a validated protocol, either using TaqMan Genotyping, Sequencing or Restriction Fragment Length Polymorphism (RFLP). Analyzing the genetic variants defined in the RESEARCH. The processed samples are filled in the respective biobank processing file.

The genetic DATA generated in the RECIPIENT'S laboratory, summarizing information on multiple polymorphisms is gathered for submission to the RESREACH providing the individuals code naming the gene, the respective polymorphism (=single nucleotid polymorphism, or SNP) and the identified haplotype (homozygous or heterozygous and the respective Allele).

The genetic DATA (see export example below) is encrypted and transferred via the BioMedIT Node sciCORE. For the DATA transfer a DTUA was signed between all the involved DATA PROVIDER's and RECEIVER's of the RESEARCH.

E.g. of Genetics CSV [mock data]

data_provider_institute	subject_pseudo_id	genetics_gene	genetics_SNP	genetics_call	genetics_result	genetics_material	genetics_method
CHE-105.834.378[3]	ABCDFG123567	ABCB1	rs1045642	Homozygous Allele A / Allele A	Rs1045642A_rs1045642_A	Blood	TaqMan Genotyping

Figure 1: Export structure Genetic DATA from RECIPIENT to the RESEARCH.

ANNEX 3
MATERIAL TRANSFER SPECIFICATION

The peudonymized BIOLOGICAL MATERIAL (EDTA blood, blood cake or DNA) is transferred from the PROVIDER to the RECIPIENT's laboratory either by one person involved in the project or is delivered by a commercial delivery service.

After arrival, the pseudonymized samples are transferred to the *Biopharmacy Biobank*. Here, the procedure is following a standard operating procedure (SOP) for entry and processing. The *Biopharmacy Biobank* entry starts with the scanning of the code of each sample. With this, the sample is registered. Within the *Biopharmacy Biobank* entry file accessible to authorized personnel only, the accepting person will enter additional information such as the submitting collaborator, the respective ethical approval (EZKN number), the following procedures according to study protocol and the final handling of the respective sample (storage until notice by principal investigator or destruction after assessment and quality control of the data). Importantly, the laboratory personal has never access to the pseudonymization mapping key, which is hold by an elected key holder at the PROVIDER's Institute.

During their time in the *Biopharmacy Biobank,* the blood samples are stored in a continuously monitored -20 °C freezer, accessible to authorized persons only. Each following step in the sample processing (either sample preparation or data assessment) is entered in the respective biobank processing file.

Accidental loss, destruction or damage of the samples will be openly communicated to the PROVIDER in a written form.

ANNEX 4
FEES AND TRANSPORT

There are no FEES applied.