NETHERLANDS CANCER INSTITUTE
ANTONI VAN LEEUWENHOEK

MATERIAL TRANSFER & COLLABORATION AGREEMENT

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

(1) Stichting Het Nederlands Kanker Instituut – [redacted] having its principal office at Plesmanlaan 121, 1066 CX Amsterdam, The Netherlands, represented by its legal representative, [redacted], hereinafter referred to as "NKI-AVL";

and

(2) Masaryk University, Faculty of Science having its principal office at Kotlarska 2, 611 37 Brno, represented by its legal representative, Tomáš Kašparovský, dean of the Faculty of Science, hereinafter referred to as "Recipient".

Hereinafter jointly referred to as "Parties" and individually as "Party".

WHEREAS

a) NKI-AVL has certain human samples ("Samples") and associated data ("Data") at its disposal specified in the Schedule to this Agreement, and as indicated and approved under Institution Review Board application IRBm23-082 ("IRB Application").
b) Recipient, through [redacted], hereinafter referred to as "Recipient's Scientist", has requested NKI-AVL, through [redacted], hereinafter referred to as "NKI-AVL's Scientist", to provide Recipient with the Samples and Data for use by Recipient's Scientist for the purpose of the Research as specified in the Schedule;
c) NKI-AVL is willing, subject to the terms and conditions of this Agreement, to provide the Samples and Data to Recipient.

1. **Definitions**

In this Agreement the following words and expressions shall have the following meanings:

Confidential Information	all information, know-how, data and experience of NKI-AVL regarding the Samples and Data, its characteristics, NKI-AVL's research concerning the Samples and Data, whether of a scientific, technical, engineering, operational, or economic nature, supplied to or obtained by Recipient in written form and identified as 'confidential', in the form of drawings or in the recording of oral conversation, or samples, which is reasonably required by Recipient for performance of Research.
Data	associated data to the Samples being transferred under this Agreement as specified in IRB Application.
Effective Date	the date of last signing of this Agreement.

End Date	the 'End date project as specified in the Schedule to this Agreement.
Results	all results arising out of the Research performed using the Samples and Data.
Samples	the human samples being transferred under this Agreement as specified in the Schedule to this Agreement.

2. The Samples and Data and any other information provided is and remains under the custodianship of the NKI-AVL. Recipient agrees in its use of the Samples and Data complies with all applicable international and national laws, statutes, regulations and guidelines and the Recipient agrees that the Samples and Data:

    a. are to be used only for the purposes as described in the Research not for any other purpose;
    b. shall not be used in human subjects. Research using the Samples shall be carried out under appropriate containment conditions and in accordance with all applicable laws and regulations regarding human samples.
    c. will not be used for any commercial purposes; and
    d. will not be transferred to any third party.

    Recipient shall not carry out the Research with any third party or entity without prior written approval of NKI-AVL (for the avoidance of doubt, sub-processing of the Samples and/or Data by a third party is not allowed without prior written approval of NKI-AVL).

3. The Data will be coded and will not contain directly identifying personal data. Under no circumstances will the identity of the patient or any means to derive such identity be provided to Recipient. Recipient shall not carry out any procedures with the Data (linking, comparison, processing) through which the identity of the patient could be derived. As the Data is coded, this will be regarded as personal data and Recipient and NKI-AVL are both considered controllers for the processing of the personal data and will both act in accordance with the applicable privacy laws and any (additional) applicable national law. Recipient shall safeguard the Data received with a degree of care which is no less than Recipient uses to protect such Data, and shall have in place appropriate technical and organizational measures hereto but always in compliance with applicable privacy laws and regulations. Any accidental or unauthorised access to the Data or loss of Data must be reported to NKI-AVL immediately, and Parties agree that both Parties may contact the supervisory authority, but NKI-AVL will be the party to contact the patients concerned in accordance with the applicable data privacy law and regulations.

    Should Recipient become aware that the Samples have fallen into the possession of a third party, or that they are being used for any purpose other than the Research, Recipient will promptly notify NKI-AVL and provide NKI-AVL with full particulars thereof.

4. Both Samples and Data are collected in accordance with the informed consent form (ICF) and/or the applicable (Dutch and international) rules and legislation including but not limited to protection of privacy aspects of the medical and personal data of the patients. Recipient acknowledges that the patients shall at all times have the right to request NKI-AVL to destroy their Samples and Data. In the event a patient files such a request with NKI-AVL, Recipient shall – upon first request by NKI-AVL – promptly destroy the Samples and Data in an approved manner, or return the Samples and Data to NKI-AVL upon NKI-AVL's first written request. Any Results already obtained through the use of the Samples and the Data shall remain at the disposal of Recipient. The Parties further acknowledge that in case of a finding (an unsought and

unsuspected patient related result of the research), NKI-AVL shall be promptly informed about such finding ('toevalsbevinding').

5. Except as provided in this Agreement, no express or implied licenses or other rights are granted to the Recipient under any intellectual property rights of NKI-AVL.

6. Recipient shall obtain acceptance of the terms of this Agreement of all persons under its control and supervision who have access to the Samples and Data.

7. All Samples, Data and Confidential Information are made available "as is" and Parties understand and agree that all Samples, Data and Confidential Information are experimental in nature and are made available without any representation or warranty, express or implied, including any implied warranty of merchantability, satisfactory quality or fitness for any particular purpose or any warranty that the use of the Samples, Data and/or Confidential Information will not infringe or violate any patent or other proprietary rights of any third party.

8. Recipient accepts liability for any loss, claims and damages which may arise from the use, storage or disposal of the Samples, Data and Confidential Information or the use of the Results by the Recipient. Recipient shall hold harmless, defend and indemnify NKI-AVL and its employees, directors, agents and representatives against any loss, damage, liability, costs and expenses arising out of or in connection with third party claims relating to use, handling, storage or disposal of the Samples, Data, Confidential Information and/or Results by Recipient, except to the extent that such loss or damage are attributable to gross negligence or willful misconduct on the part of NKI-AVL.

9. Recipient shall treat all Confidential Information confidential for the duration of this Agreement including any extension thereof and thereafter for a period of five (5) years following termination or expiry of this Agreement. Excluded from this obligation of confidentiality shall be any Confidential Information of which the Recipient can reasonably demonstrate that it:

   a. was known by the Recipient prior to disclosure by the NKI-AVL;
   b. is developed independently and lawfully by Recipient;
   c. is obtained from a third party who is not under a confidentiality obligation to NKI-AVL; or
   d. is, and/or becomes, publicly available during said five (5) year period through no fault of Recipient.

   This obligation of confidentiality shall not apply to any disclosure required by law, provided that Recipient shall notify the NKI-AVL of any disclosure required by law in sufficient time so that the NKI-AVL may contest such requirement, if NKI-AVL so chooses.

10. The Results arising from the Research shall be owned by the NKI-AVL and the Recipient, and Recipient shall keep the NKI-AVL Scientist informed of these Results and shall provide updates of any such Results. Each Party hereby grants the other Party a worldwide, non-exclusive, royalty free, irrevocable license with respect to the Results for research purposes only. For the avoidance of doubt Parties will conclude a joint ownership agreement before commercialising any Results. Within thirty (30) days after the completion of the Research or the expiration or earlier termination of this Agreement, whichever occurs earlier, Recipient shall provide NKI-AVL with a written description of all Results.

11. Parties will jointly publish or otherwise publicly disclose the Results in accordance with the standards applicable to authorship of scientific publications. Both Parties agree to abide by the policies of journals in

which publications will appear as to such matters as the public release or availability of data or biological materials relating to the publication. Recipient shall acknowledge the NKI-AVL Biobank as the source of the Samples and Data in any disclosure of the Results.

12. This Agreement will become effective on the Effective Date and will terminate on the End Date. Parties can terminate this Agreement by giving a one (1) month prior written notice. Any clauses that will be expected or intended by its nature to survive the termination or the expiration of this Agreement, shall survive the termination or the expiration of this Agreement. Upon expiration or termination of this Agreement, the right to use the Samples and/or Data and Confidential Information will automatically end and within two (2) days after the End Date of the Research or the expiration or earlier termination of this Agreement, whichever occurs earlier, Recipient shall return the Samples and/or Data and Confidential Information received to NKI-AVL, or destroy the Samples and/or Data and Confidential Information received on NKI-AVL's request and send the NKI-AVL a written confirmation hereof.

13. The construction, validity and performance of this Agreement shall be governed by the laws of The Netherlands. All disputes arising out of or in relation to this agreement will be brought before the competent court in Amsterdam, The Netherlands.

14. This Agreement will be binding upon and inure to the benefit of the respective successors and assignees of the Parties hereto. However, Recipient may not assign this Agreement in whole or in part without the prior written consent of the NKI-AVL.

15. This Agreement represents this entire agreement among the Parties with respect to the subject matter hereof, and may only be altered or amended by an instrument in writing signed by all of the Parties.

16. All notices, reports, requests and other communications to NKI-AVL by Recipient will be delivered to the above mentioned address for the attention of the "Knowledge Transfer & Contracting" department of the NKI-AVL, email: [redacted]

In witness whereof, the Parties have executed this Agreement as of the Effective Date through their authorised representatives:

[redacted]

[redacted]

[redacted]

SCHEDULE

IRB Application Form and IRB Approval Letter:

Research description: CONCRETE – pilot study
Title: CONCRETE – pilot study

Acronym:

Short project description (max 250 words):

In this pilot project, we would like to test whether standard methodological procedures at RECETOX Research Infrastructure are applicable for the analysis of cohort mtFIT samples that are stored for different periods of time. Thus, we would like to obtain 10 samples stored for the short-time and 10 samples stored for the long-time from the Biobank, which should be analysed in the CONCRETE project.

Bacteriome analysis:

Application of 16S rRNA sequencing of DNA isolated from mtFIT samples will be evaluated. DNA from mtFIT samples (approx. 20 samples) will be isolated by selected kit. Internal standard (MOCK community) will be spiked into the DNA from samples. Library for 16S rRNA sequencing will be prepared using the Nextera DNA Flex Library Prep Kit V3 and deeply sequenced on an Illumina MiSeq instrument. All the generated metagenomic data will be subjected to strict quality control and to multiple profiling computational pipelines to obtain complementary features sets for secondary, statistical, and machine learning analysis. The proposed methods combine out in-development approaches and the state-of-the-art tools: Quality control, Taxonomic profiling (QIIME2 and DADA2), functional profiling and profiling of metabolic potential (PICRUST + PRMT), estimation of microbiome responsible for changes metabolic profiles (in house deconvolution based tool), estimation of crosslink between xenobiotics, host metabolism and gut microbiome (internal tool in development).

Chemical screening:

Application of a liquid chromatography – high resolution mass spectrometry (LC-HRMS) chemical screening of mtFIT samples will be evaluated. In brief, an initial dilute-and-shoot application of sample will be tested. If unsuccessful, sample preparation via solvent extraction will be tested. Analytes will be separated via reversed-phase / mixed mode chromatography, undergo electrospray ionization (ESI) and mass spectra acquired using Orbitrap technology. Annotation of detected signals will use reference spectral libraries and processing pipelines developed in-house.

Expected relevance:

The 16S rRNA sequencing is used for the characterization of bacteriome (diversity, relative abundance of bacterial genera), these can be used as potential marker for risk of colorectal cancer development or be an additional screening/predictive marker.

The LC-HRMS screening has potential to simultaneously detect endogenous metabolites and chemical exposure agents within the samples, providing a comprehensive characterisation of chemical composition with potential for candidate biomarker identification.

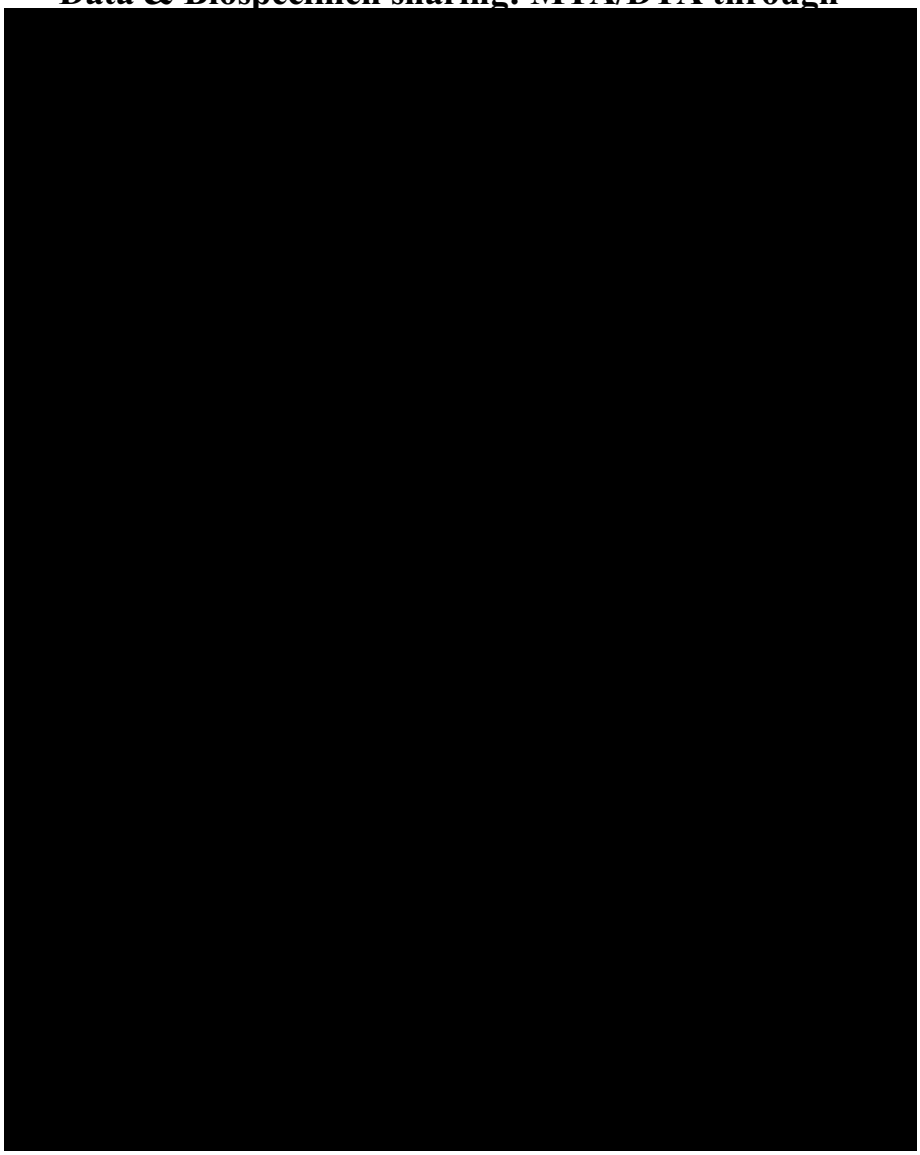
Start date: 011/10/2023
End date: 31/12/2025

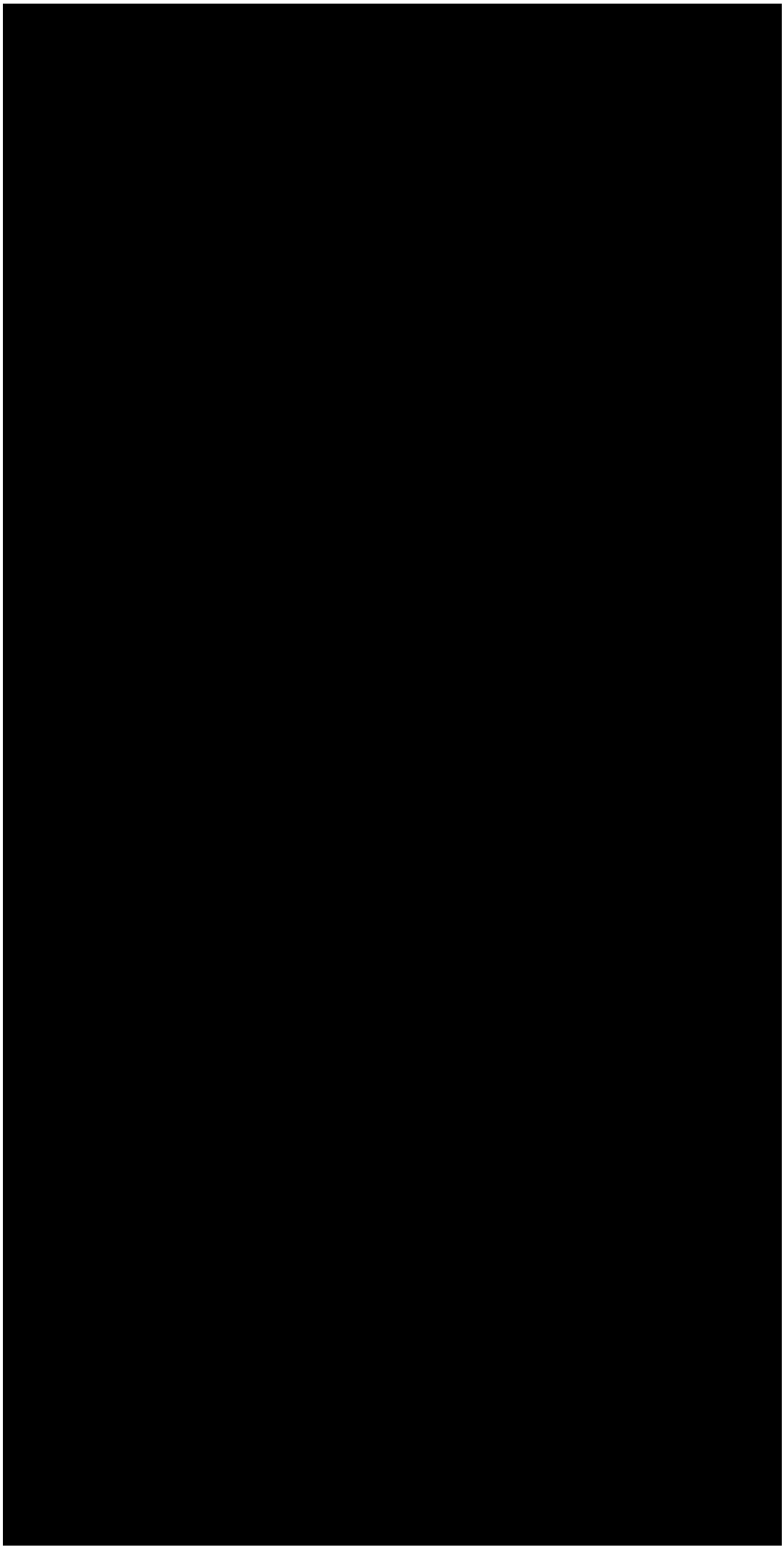
Mailing address MTA: *(execution by PDF is default, if not acceptable, please let us know)*

[redacted]

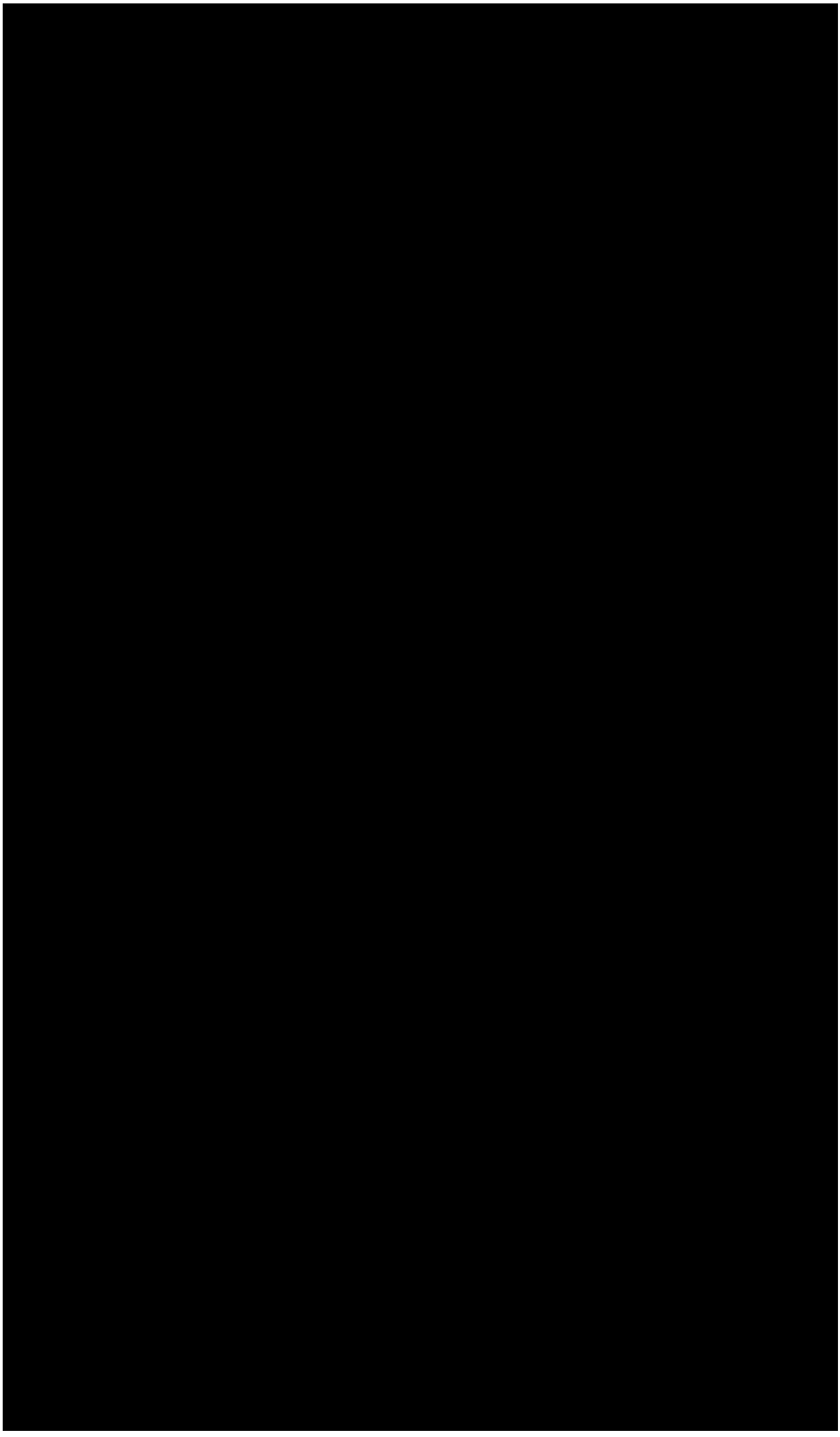
E-mail of Recipient Technology Transfer officer: [redacted]
Recipient principal scientist name, address and e-mail: [redacted] Integrative biostatistics and Bioinformatics RECETOX, Faculty of Science, Masaryk University Kamenice 34 625 00 Brno Czech Republic [redacted]
Address to send Sample(‘s) to: [redacted] Laboratoře analýzy mikrobiomu RECETOX, Faculty of Science, Masaryk University bud. D30/213 Kamenice 34 625 00 Brno Czech Republic
Fedex account number of Recipient:

Data & Biospecimen sharing: MTA/DTA through





3/31/2023



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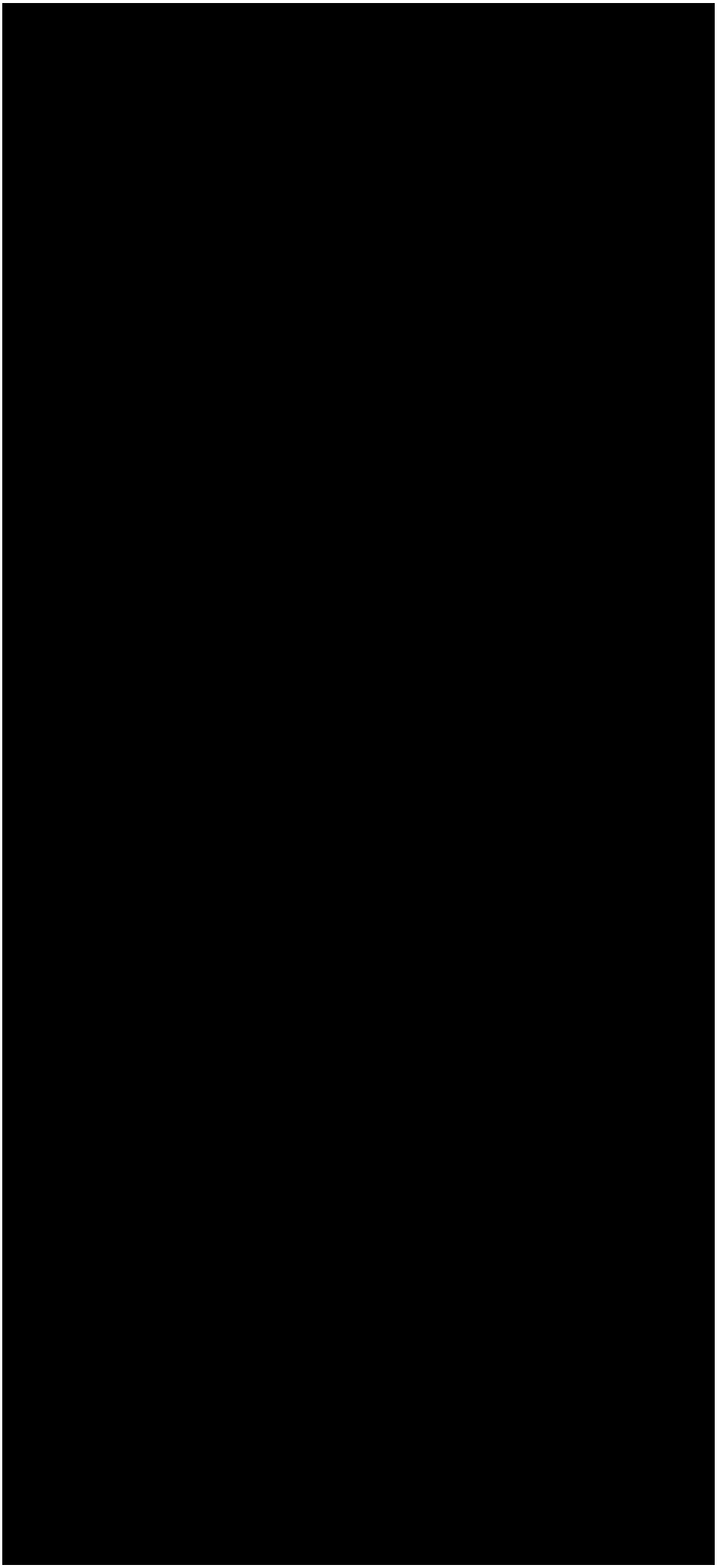

3/31/2023

IRBm23-082
[redacted]
Division of Diagnostic Oncology
[redacted]

NETHERLANDS CANCER INSTITUTE
ANTONI VAN LEEUWENHOEK

Amsterdam, 31/03/2023

[redacted]

Your application, entitled: CONCRETE â€“ pilot study , for the use of human material and or data is registered under number IRBm23-082 .

Your application has been reviewed and approved by the NKI-AVL Institutional Review Board (IRB). The NKI IRB is a board for tailor-made reviewing of non-WMO research with human material and data. The purpose of the IRB is to assure that appropriate steps are taken to protect the rights and welfare of humans participating as subjects in a research study and to safeguard ethical conduct of research concerning, amongst others, the Dutch norm for information security NEN7510 and the GDPR.

The decision is based on all the documents registered on 31/03/2023 in IRB ART (IRBm23-082) which can be viewed on this page

This application reviewed by the IRB does not meet the WMO criteria and can be considered as a non-WMO statement.

For the record, this approval letter only applies to the study as far as it is carried out in the NKI-AVL. If the study will also be carried out in other centers, you are advised to check per center whether there is a local testing procedure there.

Sincerely

[redacted]

[redacted]
Committee Secretary IRB
On behalf of Institutional Review Board (IRB)
The Netherlands Cancer Institute, Amsterdam

[redacted]

DocuSign

Certificaat betreffende voltooiing

Envelop-id: 518CA7EB5E39416AA5A5C924806AC709 Status: Voltooid

Onderwerp: Vul aan met DocuSign: 15034_IRBm23-082_Material Transfer Agreement for Patient Samples_NKI-AVL_...

Bronenvelop:

Documentpagina's: 15 Handtekeningen: 2 Opdrachtgever van envelop:

Certificaatpagina's: 2 Paraaf: 0 [redacted]

Begeleide ondertekening: Ingeschakeld

Stempel met envelop-id plaatsen: Ingeschakeld

Tijdzone: (UTC+01:00) Amsterdam, Berlijn, Bern, Rome, Stockholm, Wenen

Records bijhouden

Status: Original Houder: [redacted] Locatie: DocuSign

22-9-2023 09:39:15 [redacted]

Ondertekenaargebeurtenissen	Handtekening	Tijdstempel
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Elektronische document- en handtekeninginformatie:
Niet aangeboden via DocuSign

[redacted] Head of Knowledge Transfer & Contracting Stichting Het Nederlands Kanker Instituut - [redacted] [redacted] Beveiligingsniveau: E-mailadres, Accountverificatie (geen)	[redacted] geselecteerde stijl IP-adres gebruiken: 109.36.148.33 Aangemeld via mobiel	Verzonden: 22-9-2023 09:43:33 Bekeken: 22-9-2023 09:44:02 Ondertekend: 22-9-2023 09:44:05

Elektronische document- en handtekeninginformatie:
Niet aangeboden via DocuSign

Gebeurtenissen voor persoonlijke ondertekenaar	Handtekening	Tijdstempel

Verzendingsgebeurtenissen voor bewerker	Status	Tijdstempel

Verzendingsgebeurtenissen voor vertegenwoordiger	Status	Tijdstempel

Verzendingsgebeurtenissen voor tussenpersoon	Status	Tijdstempel

Gecertificeerde verzendingsgebeurtenissen	Status	Tijdstempel

Carbon copy-gebeurtenissen	Status	Tijdstempel

Getuige evenementen	Handtekening	Tijdstempel

Notarisgebeurtenissen	Handtekening	Tijdstempel

Gebeurtenissen voor envelopsamenvatting	Status	Tijdstempels
Envelop verzonden	Gehasht/gecodeerd	22-9-2023 09:43:34
Gecertificeerd verzonden	Beveiliging gecontroleerd	22-9-2023 09:44:02
Ondertekening voltooid	Beveiliging gecontroleerd	22-9-2023 09:44:05
Voltooid	Beveiliging gecontroleerd	22-9-2023 10:02:36

Betalingsgebeurtenissen	Status	Tijdstempels