Material Transfer Agreement (MTA)
for Biological Material and Research Data

UNIVERSITÄTSKLINIKUM HEIDELBERG (UKHD), the Coordinator

and

INSTITUTO NACIONAL DE ENFERMEDADES NEOPLASICAS (INEN), the Research Partner,

enter into the following agreement, which complements and specifies the Consortium Agreement, whereby UKHD will transfer the funding for the implementation of the project **EULATE Eradicate GBC** to the INEN, conditionally to the transfer of the biological material and research data from the INEN to the UKHD. The transfer of the funding shall be conditioned on the following terms:

INEN agrees to recruit the following patients per year during a complete recruitment period of four consecutive years:

- at the INEN in Lima, Peru: 120 GBC patients
- at the Instituto Regional de Enfermedades Neoplásicas (IREN) Sur in Arequipa, Peru: 600 patients with gallstones and 40 GBC patients
- at the IREN Norte in Trujillo, Peru: 60 patients with gallstones and 60 GBC patients

Data will be continuously transferred from the recruitment centers to UKHD through an automated data collection system or, exceptionally, as printed patient interviews, case report forms, information on the biological material and food frequency questionnaires. Biological samples will be shipped 3, 6, 12, 18, 24, 30, 36, 42 and 48 months after the start date of recruitment.

An initial budget covering the estimated recruitment costs for the first 6 months will be transferred to INEN's bank account (Instituto Nacional de Enfermedades Neoplásicas, Banco de la Nación, account number 00000862304, interbanking account number 018-000-000000862304-03, swift code BANCPEPL) to enable the start of the project. Subsequent payments will be made at months 6, 12, 18, 24, 30, 36 and 42 based on the actual number of recruited patients, and material and data transferred to UKHD (**Figure 1**).

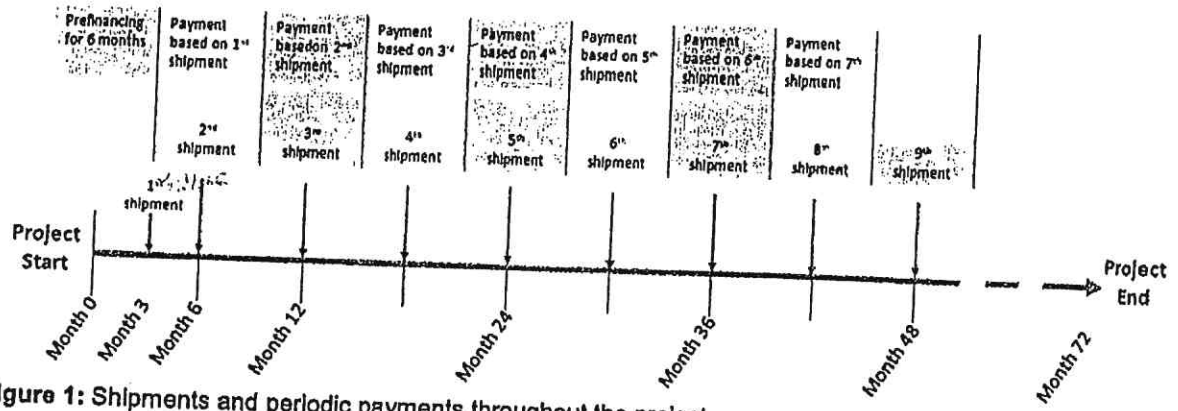

Figure 1: Shipments and periodic payments throughout the project

For the patient recruitment during the first six months, INEN will receive the following payments:

a. Salary of personnel at the INEN	
Administrative support	500 Eur
Study nurse	50 Eur/patient x 60 patients = 3000 Eur
Salary of study nurse at the IREN Sur	791 Eur/month x 6 months = 4746 Eur
Salary of personnel at IREN Norte	
Study nurse	50 Eur/patient x 30 patients = 1500 Eur
b. Equipment and consumables	4250 Eur
c. Sample shipments	1333 Eur
d. Data retrieval	1000 Eur
Total for 6 months	**16329 Eur**

According to the following anticipated distribution:

Payment in kind: Equipment and consumables, sample shipments (5583 Eur)
Payment in cash: Personnel salaries and data retrieval (10746 Eur)

In addition to the periodic payments associated to the patient recruitment, UKHD will transfer the following budget to the INEN in order to financially support a PhD student during the first year of research at **EULAT Eradicate GBC:**

Salary of PhD student	791 Eur/month x 12 months = 9492 Eur

1. **Material.** The material covered by this agreement includes human blood and its derivatives, saliva, urine and feces appropriately collected by and stored at INEN as part of the **EULAT Eradicate GBC** project. A detailed description of the material is attached hereto as **ANNEX 1**, including the type and amount of material considered in this agreement.

2. **Purpose for Transfer.** UKHD and INEN will use the material only for academic research purposes and will not use the material for any commercial purpose. In particular, UKHD and INEN will not use the material in any research that is subject to consulting or licensing obligations to any for-profit organizations. Furthermore, it will not conduct contract-research to screen compound libraries, to produce or manufacture products for general sale, or to conduct research activities that result in any sale, lease, license, or transfer of the material to a for-profit organization.

3. **Use of the Material.** The material shall be transferred to UKHD as part of the EU-funded action **EULAT Eradicate GBC** to fulfill the aims of the project as outlined in the Grant Agreement. The samples shipped to UKHD may be used, under the direction of or in collaboration with Dr. Lorenzo Bermejo at the UKHD, including the transfer, in pseudonymized form, to other academic or non-profit institutions as part of collaborative non-profit research. Proposals on the use of samples stored at the INEN should be made to the Executive Board of **EULAT Eradicate GBC**, which will review them and decide on approval/disapproval. All material will be used under suitable containment conditions and will not be used in any manner in or on human subjects, in clinical trials, or for diagnostic purposes involving human subjects. The UKHD and the INEN agree to use the material in compliance with all applicable statutes and regulations, such as, for example, those relating to research involving the use of animals or recombinant DNA and including General Data Protection Regulation (GDPR) by the EU, Guideline for Good Clinical Practice (GCP) of the International Conference on Harmonisation (ICH) of Technical Requirements for the Registration of Pharmaceuticals for Human Use and other generally accepted applicable Guidelines of the ICH or the European Community and in compliance

with the respective study protocols and the informed consents of the patients. Further, the material will be used solely in accordance with the approval letter of the ethic commissions responsible for INEN.

4. **Data.** The data covered by this agreement is data associated with the study designated in paragraph no. 1 (Material) above. The conditions of transfer and the conditions of use relating to the material as per paragraphs no. 2. and 3. above shall apply likewise to the data. As data, in contrast to material, does not need to be materially divided and allocated, INEN will transfer to UKHD all relevant data including patient interviews, case report forms, information on the biological material and food frequency questionnaires.

5. **Publication.** Dr. Lorenzo Bermejo will coordinate the scientific publication of results within the EU-funded action **EULATE Eradicate GBC** as part of a research collaboration among the participating researchers and include the appropriate INEN authors and attribution, where applicable applying the guidelines of good scientific research (e.g. ICMJE) and consistent with the Publication Policy outlined in the Consortium Agreement. Statistical methods research may not require collaboration or co-authorship, but the researchers providing the material and data shall be informed if their provided data will be sought for that purpose. In any publication proper acknowledgment shall be made for the contributions of each party and the source of the material and data. The scientific publications within the EU-funded action **EULATE Eradicate GBC** will be coordinated by means of a Manuscript tracking list (see **ANNEX 2**). Manuscript proposals should be made to the Executive Board, which will review them and decide on approval/disapproval. The applicants of approved proposals will be granted a 18-month period for manuscript publication. After this period, the approved manuscript proposal will be opened to all the Consortium participants.

6. **No Warranty.** The material/data is understood to be experimental in nature and the material may have hazardous properties. INEN commits to collect the material and data according to the Standardized Operating Procedures (SOPs) of the EU-funded action **EULATE Eradicate GBC.** INEN makes no warranties of the material/data as to fitness for any particular purpose, and makes no warranty/representations that the material/data, or use thereof, does not infringe patent or other intellectual property rights of others.

7. **Hold Harmless.** To the extent permitted by applicable law, UKHD will hold INEN harmless from and be responsible for any liability for, and will defend INEN from any claims or damages, including attorneys' fees, resulting from, arising out of or in any way relating to UKHD's use of the Material, except to the extent permitted by law when caused by the gross negligence or willful misconduct of the INEN.

8. **Applicable Law.** This agreement and its performance shall be governed under the laws of Germany. The parties shall endeavour to settle their disputes amicably. If, and to the extent that, any such dispute, controversy or claim has not been settled pursuant to the mediation within 60 calendar days of the commencement of the mediation, the courts of Heidelberg shall have exclusive jurisdiction.

The parties to this agreement, UKHD and INEN, hereby indicate their agreement to the terms by affixing the signature below of an appropriate representative or officer who is specifically authorized to execute documents of this type.

UNIVERSITÄTSKLINIKUM HEIDELBERG (UKHD)

Signature:
Name: Prof. Hendrik Dienes
Title: Scientific Director
Date: 12.3.20

Signature:
Name: Dipl.-Kfm. Hartmut Masanek
Title: Acting Business Director
Date: 10.03.20

Universitätsklinikum Heidelberg
vertreten durch den Kommissarischen Kaufmännischen Direktor
Dipl.-Kfm. Hartmut Masanek
im Neuenheimer Feld 672
69120 Heidelberg
der Ruprecht-Karls-Universität Heidelberg, Medizinische Fakultät

Signature:
Name: Prof. Dr. Justo Lorenzo Bermejo
Title: UKHD-Scientist
Date: 13.3.20

INSTITUTO NACIONAL DE ENFERMEDADES NEOPLASICAS (INEN)

Signature:
Name: Dr. EDUARDO PAYET MEZA
Title: Jefe Institucional
Date: INSTITUTO NACIONAL DE ENFERMEDADES NEOPLÁSICAS

ANNEX 1 Biological material subject to this Agreement

Material	Collection tube	Number x size	Total volume	Sample type	Min. volume	Shipped samples	Samples stored recruitment center	Storage
Blood[1]	Red tube	1 x 10 ml	10 ml	Serum	4.5 ml	3 x 1ml	1 x 1.5ml[2]	-80°C
	Violet tube	1 x 4 ml	4 ml	Whole Blood	4 ml	2 x 1ml	1 x 1.5ml[2]	-80°C
		2 x 6 ml	12 ml	Plasma	5 ml	3 x 1 ml	1 x 2 ml	-80°C
				Buffy Coat	500 ul	1 x 0.5 ml[2]		-80°C
Urine	Urine Cup	1 x 60 ml	60 ml	Urine	20 ml	3 x 2 ml	3 x 2 ml	-80°C
Faeces	Stool Container	1 x 60 ml	60 ml	Faeces	2.5 gr	2 x 500 mg	2 x 500 mg	-80°C
Saliva	Saliva Kit	1 x 2 ml	4 ml (buffer 2 ml)	Saliva	4 ml			Room temperature
				TOTAL		**14 aliquots**	**8 aliquots**	

(1) A lower volume of blood (~ 3 ml in red tube) and saliva will be collected from patients with a poor health status

(2) The largest possible amount

ANNEX 2 Manuscript tracking list

Pub.No	WP	Manuscript title/topic	Status	Recruitment sites	Timeline / last Update	First author	Last author
1	1	EULAT Eradicate GBC – Study Design Paper		All		Barahona	Lorenzo Bermejo
2	2	Identification and validation of the association between GBC risk and dietary factors, lifestyle factors, metabolites and gut barrier function.		Depends on dietary data		PhD student	Scherer
3	2	Sex/gender and ethnic differences in the associations between GBC risk and dietary factors, lifestyle factors, metabolites and gut barrier function.		Depends on dietary data			Scherer
4	2	Assessment of confounding effects of ethnicity, sex/gender and other established GBC risk factors (e.g. BMI) on metabolites and gut barrier function				Scherer	Scalbert/Jenab
5	3	Assessment of confounding effects of ethnicity, sex/gender and other established GBC risk factors (e.g. BMI) on sncRNA expression and DNA methylation					Rounge
6	3	Functional characterization of the identified and validated GBC biomarkers on gallbladder organoids and GBC cell lines		none			Roa
7	4	Identification of actionable targeted mutations in GBC					Marcelain
8	4	Evaluation of the synthetic lethal effect of ARID1A in GBC cell lines					Marcelain
9	5	Lifestyle and environmental factors, and their interaction with sncRNAs in GBC risk prediction				PhD student	Lorenzo Bermejo
10	5	Lifestyle and environmental factors, and their interaction with DNA-methylation in GBC risk prediction				PhD student	Lorenzo Bermejo
11	5	Establishment of a multifactorial GBC risk score				PhD student	Lorenzo Bermejo
12	5	Epidemiology of GBC in Latin American immigrants to Sweden and native Swedes				PhD student	Lorenzo Bermejo
13	5	Integrative analysis of multi-omics GBC biomarker data using novel network methods				PhD student	Lorenzo Bermejo
14	5	Causal mechanisms of GBC development - A Mendelian randomization study				PhD student	Lorenzo Bermejo

DECLARATION OF HONOUR

(To be filled out by the applicant and signed by its legal representative)

I, the undersigned:

☐ for natural persons: in my own name

or

☒ for legal persons or 'legal entities without legal personality'[1]: representing the following legal person/entity without legal personality:

INSTITUTO NACIONAL DE ENFERMEDADES NEOPLASICAS-INEN

AV ANGAMOS ESTE 2520 URB LA CALERA DE LA MERCED

LIMA

Peru

VAT number PE20514964778

hereby certify

that (subject to the additional declarations below):

1 — the information provided in the Participant Portal for the grant agreement preparation is correct and complete;

2 — the information concerning the legal status given in the Beneficiary Register is correct;

3 — my organisation commits to comply[2] with all the eligibility criteria, as defined in the work programme and the call for proposals;

4 — my organisation:

- is committed to participate in the action;
- has stable and sufficient sources of funding to maintain its activity throughout its participation in the action and to provide any counterpart funding necessary, and
- has or will have the necessary resources as and when needed to carry out its involvement in the abovementioned action;

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[1] See Article 131(2) of the Regulation (EU, Euratom) No 966/2012 of the European Parliament and of the Council of 25 October 2012 on the financial rules applicable to the general budget of the Union and repealing Council Regulation (EC, Euratom) No 1605/2002 (OJ L298, 26.10.2012, p.1) and Article 198 of the Commission Delegated Regulation (EU) No 1268/2042 of 29 October 2012 on the rules of application of Regulation (EU, Euratom) No 966/2012 of the European Parliament and of the Council on the financial rules applicable to the general budget of the Union (OJ L 362, 31.12.2012, p. 1).

[2] 'commits to comply' means that I comply now and will comply for the duration of the grant agreement concluded with the *Commission* should a grant be awarded.

5 — my organisation is not in one of the situations which would exclude it from receiving EU grants[3], i.e. it:

- is not bankrupt or being wound up, is not having its affairs administered by the courts, has not entered into an arrangement with creditors, has not suspended business activities, is not the subject of proceedings concerning those matters, or is not in any analogous situation arising from a similar procedure provided for in national legislation or regulations;
- it (or persons having powers of representation, decision making or control over it) have not been convicted of an offence concerning their professional conduct by a judgment of a competent authority of a Member State which has the force of res judicata;
- has not been guilty of grave professional misconduct proven by any means which the *Commission* can justify including by decisions of the EIB and international organisations;
- is in compliance with its obligations relating to the payment of social security contributions and the payment of taxes, in accordance with the legal provisions of the country in which it is established and with those of the country of the authorising officer responsible and those of the country where the action is to be performed;
- it (or persons having powers of representation, decision making or control over it) have not been the subject of a judgment which has the force of res judicata for fraud, corruption, involvement in a criminal organisation or any other illegal activity, where such illegal activity is detrimental to the EU's financial interests;
- is not currently subject to an administrative penalty under Article 131(5) of Regulation (EC, Euratom) No 966/2012;
- is not subject to a conflict of interest in connection with the grant;
- will inform the *Commission*, without delay, of any situation considered a conflict of interests or which could give rise to a conflict of interests;
- has not granted and will not grant, has not sought and will not seek, has not attempted and will not attempt to obtain, and has not accepted and will not accept any advantage, financial or in kind, to or from any party whatsoever, where such advantage constitutes an illegal practice or involves corruption, either directly or indirectly, inasmuch as it is an incentive or reward relating to the award of the grant;
- has not made false declarations in supplying the information required by the *Commission* as a condition of participation in the grant award procedure or does not fail to supply this information.

6 — I will inform the *Commission* of any other grant applications or grants from the EU or Euratom budget related to this action.

7 — my organisation is aware that the *Commission* may impose administrative or financial penalties[4] on legal entities which:

[3] See Article 131(5) of Regulation (EU, Euratom) No 966/2012.
[4] See Article 131(5) of Regulation (EU, Euratom) No 966/2012.

- are guilty of misrepresentation in supplying the information required by the Commission as a condition of participation in the grant award procedure or fail to supply this information;

- have been declared to be in serious breach of their obligations under any contract/grant agreement covered by the budget of the Commission.

Such penalties will be proportionate to the importance of the contract/grant agreement and the seriousness of the misconduct, and may consist in their exclusion from contracts/grants financed by the EU or Euratom budget and payment of financial penalties.

and acknowledge

that:

1 — Grants will be signed and managed electronically, through the Commission's electronic exchange system (in the 'My Area' section[5] of the Participant Portal).

2 — Access and use of the electronic exchange system is subject to the Terms and conditions of use[6] of the Participant Portal).

3 — Personal data submitted or otherwise collected by the *Commission* will be subject to the privacy statement[7].

4 — Any sensitive information or material that qualifies as 'EU classified information' under Decision 2001/844/EC[8] must comply with specific rules (i.e. it must be indicated in the technical annex of the proposal: a Security Aspect Letter (SAL) will be annexed to the grant agreement; an amendment is necessary if (more or new) sensitive information or material becomes relevant only later on).

SIGNATURE

For the applicant

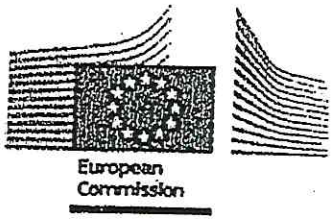
Dr. EDUARDO PAYET MEZA
Jefe Institucional
INSTITUTO NACIONAL DE ENFERMEDADES NEOPLÁSICAS

[5] Available at http://ec.europa.eu/research/participants/portal/

[6] Available at http://ec.europa.eu/research/participants/data/ref/h2020/grants_manual/lev/h2020-lev-terms-of-use_en.pdf

[7] Available at http://ec.europa.eu/geninfo/legal_notices_en.htm

[8] See Commission Decision 2001/844/EC, ECSC, Euratom amending the Commission's internal Rules of Procedure (OJ L 317, 3.12.2001). Available at http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:02001D0844-20130701&rid=1



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