



Collaboration Agreement

concerning

scientific collaboration under the title

International Working Group on Neurotransmitter Related Disorders (iNTD)

**This collaboration agreement is made
between**

1. Agia Sofia Hospital, Thivon and Ievadias, 11527 Athens, Greece, Legal representative: Emmanuel Papasabas, Project leader: Roser Pons
2. AOU Città della Salute e della Scienza di Torino, represented in law by its General Director Dr. Silvio Falco, corso Bramante, 88 - 10126 Torino, executing department: Department of Pediatrics, Medical Director Dr. Marco Spada, Principal investigator Dr. Francesco Porta, on behalf of AOU Città della Salute e della Scienza di Torino, University of Torino
3. Aristotle University, Thessaloniki, Greece, represented in law by its sub-Dean of Research, Eustratios Stylianidis, Research Committee, 3rd of September St., Campus, 54636 Thessaloniki, Greece executing Department: 1st Department of Pediatrics, "Hippokratis" General Hospital, Project Leader Prof. Dimitrios Zafeiriou, MD, PhD, on behalf of the Aristotle University of Thessaloniki
4. BC Children's Hospital and Vancouver General Hospital, Vancouver, BC, Principal Investigator: Gabriella Horvath
5. Children's Hospital San Diego, Rady Children's Institute for Genomic Medicine, 8001 Frost St. San Diego, CA 92123, USA. legal representative: Catherine Galton, Project leader: Jennifer Friedman, MD
6. Clinic of Neurology and Psychiatry for Children and Youth, Dr. Subotica 6a str., 11000 Belgrade, Serbia, represented in law by VD Prof. Dr. Jasna Jancic, Scientific representative: Dr. Galina Stevanovic
7. Çukurova University Hospital, Faculty of Medicine, Department of Pediatrics, Division of Pediatric Metabolism and Nutrition, Balcalı Kampüsü 01330 Sarıçam/ Adana,

Turkey. Legal Representative: Prof.Dr.Nejat Narlı, iNTD representative(s); Project Leader:Prof.Dr. Neslihan Önenli Mungan, Sebile Kılavuz, MD

8. Department of Pediatrics, University of Alberta Edmonton Clinic Health Academy (ECHA), 11405-87 Avenue Edmonton, AB T6G 1C9, Canada, Legal representative(s) of your institution: Dr. Sarah Forgie Department Chair, iNTD representative: Dr. Helly Goez
9. Department of Pediatrics and Pediatric Health Care Center, Faculty of Medicine, University of Szeged, Koranyi fasor 14-15, H-6720, Szeged, Hungary, Legal Representative of the Institution: Dr. Csaba Bereczki, Project leader Dr. Gabor Racz
10. Fundación para la Investigación Biomédica de Córdoba (FIBICO), Legal representative of the institution: Álvaro Granados del Río, Project leader: Project leader Dr. Eduardo Lopez
11. Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla, Legal representative of the institution: D. José Cañón Campos , Project leader: Dr. Pablo Mir Rivera.
12. General University Hospital in Prague with registered offices at U Nemocnice 499/2, 128 08, Prague 2, Czech Republic, represented by its Director for research prof. Pavel Michalek, MD, PhD, DESA, M.Sc executing department: Department of Pediatrics and Adolescent Medicine, Head prof. Tomas Honzik, MD, PhD, project leader prof. Tomas Honzik, MD, PhD, co-investigator/collaborator Jan Kulhanek, MD
13. Hacettepe University Faculty of Medicine, Department of Pediatrics, Section of Metabolism, 06100, Ankara, Turkey, Head of the Department of Pediatrics: Prof. N. Elif Özmert, project leader: Prof. Dr. H. Serap Sivri
14. Hospital Sant Joan de Déu, Passeig Sant Joan de Déu 2, 08950 Esplugues de, Spain. Legal representative: Dr. Manuel del Castillo. Project leader: Dr. Àngeles García Cazorla
15. Institute for Children and Youth Health Care of Vojvodina, 10th Hajduk Veljkova St., 21000 Novi Sad, Serbia, executing department Service for Medical Genetics, Manager of Institute for Children and Youth Health Care of Vojvodina: Assistant Professor Jelena Antic; Manager of Pediatric Clinic: Associate Professor Vesna Stojanovic; principal investigator of INTD (scientific representative): Associate Professor Ivana Kavecán.
16. Institute of Mother and Child, 93 Burebista str, Chisinau, MD-2062, Republic of Moldova. Director Dr. Sergiu Gladun, Project Leader - Dr. Natalia Usurelu
17. Istanbul University, Istanbul Faculty of Medicine, Istanbul University, Istanbul Faculty of Medicine
Department of Child Neurology, Millet Cad. Floor: 3,5, 34093, Capa-Fatih, Istanbul, Turkiye, iNTD representative: Prof. Dr. Zuhâl Yapıcı
18. Katholisches Klinikum Bochum gGmbH, Klinik für Kinder- und Jugendmedizin der Ruhr Universität Bochum, St. Josef Hospital, Alexandrinenstrasse 5, 44791 Bochum, iNTD and legal representative: Prof. Dr. med. T. Lücke
19. Klinikum Dritter Orden, Department of Pediatrics, Menzinger Strasse 44, 80638 Munich, Germany, legal representative: Markus Morell, Sprecher der

Geschäftsführung, iNTD representative: Prof. Dr. Jochen Peters, Chairman of Pediatrics

20. KTP-National University Children's Medical Institute, National University Health System, 5 Lower Kent Ridge Road, Singapore 119074.
21. Lawson Health Research Institute, a joint venture of London Health Sciences Centre Research Inc. and Lawson Research Institute having a business address of 750 Base Line Road, Suite 300, London, Ontario N6C 2R5, Canada, iNTD representative: Dr. Chitra Prasad, with a business address at London Health Sciences Centre, 800 Commissioners Road E, B5-134, London, ON N6A 5W9, Canada
22. Medical University of Innsbruck, represented by Dean Univ.-Prof. Dr. Wolfgang Fleischhacker, Anichstrasse 35, 6020 Innsbruck, executing department: Clinic for Pediatrics I, Inherited Metabolic Disorders, Medical Director Prof. Dr. Thomas Müller, Project leader PD Dr. Sabine Scholl-Bürgi
23. "Petru Poni" Institute of Macromolecular Chemistry, Aleea Grigore Ghica Voda 41-A, RO-700487 Iasi, Romania. Director Dr. Valeria Harabagiu, NMR manager Dr. Calin Deleanu, Project Leader Dr. Alina Nicolescu
24. Radboud University Medical Center, Nijmegen, The Netherlands, represented in law by its Dean (Prof dr J. Smit). Amalia Children's Hospital, Department of Pediatric Neurology, Geert Grooteplein Zuid 10, 6525 GA, Nijmegen, The Netherlands. PI: prof dr Michèl A. Willemsen.
25. Showa University School of Medicine, represented in law by its Dean of the Graduate School of Medicine, Dr. Akatsuki Kokaze, 1-5-8 Hatanodai, Shinagawa-ku, Tokyo 142-8666: Department of Pediatrics, iNTD representative: Prof. Dr. Mitsuhiro Kato
26. Sydney Children's hospital, High Street, Randwick, NSW, Australia, 2031, Legal representative: The Sydney Children's Hospitals Network (Randwick and Westmead) (incorporating The Royal Alexandra Hospital for Children), a body corporate established pursuant to the Health Services Act 1997 (NSW), ABN: 53 188 579 090 of Hawkesbury Rd and Hainsworth St, Westmead, NSW, 2145 (the "SCHN"); iNTD representative: Rani Sachdev
27. The Children's hospital at Westmead, Locked Bag 4001, Westmead, NSW. Australia 2145, Legal representative: The Sydney Children's Hospitals Network (Randwick and Westmead) (incorporating The Royal Alexandra Hospital for Children), a body corporate established pursuant to the Health Services Act 1997 (NSW), ABN: 53 188 579 090 of Hawkesbury Rd and Hainsworth St, Westmead, NSW, 2145 (the "SCHN"); iNTD representative: Shekeeb S Mohammad
28. The Hospital for Sick Children, 555 University Avenue, Toronto, Ontario, Canada M5G 1X8, Legal Services, potential Legal Counsel Sisi Jia, Principal Investigator Saadet Andrews
29. The Institute of Mother and Child, represented in laws by its Director Tomasz Maciejewski, MD, PhD, Kasprzaka 17A, 01-211 Warsaw, Poland and principal investigator Jolanta Sykut-Cegielska, MD, PhD, Ass Prof
30. The Sheba Fund for Health Services and Research, Katzir Road 2, Sheba Medical Center, Ramat Gan, Israel, represented by legal Signatories: Prof. Dror Harats, Chair the Division of R&D & Mr. Moshe Barak (CEO), iNTD representative: Prof. Yair Anikster,

- 31.** The Washington University, One Brookings Drive, Campus Box 1054, St. Louis, MO 63130, USA, Legal representative: Megan White (Director, Research Contracts)
PI: Dr. Toni Pearson, Department of Neurology, Washington University School of Medicine
- 32.** University of Rome "La Sapienza", Department of Human Neuroscience - Unit of Child Neurology and Psychiatry, Via dei Sabelli 108, 00185 Rome, Italy. Legal representative: prof. Alfredo Berardelli. Project leader: prof. Vincenzo Leuzzi
- 33.** UCL Great Ormond Street Institute of Child Health (more broadly, University College London), United Kingdom, Legal representative: Diran Solanke, Assistant Director - Research Contracts, iNTD representative: Prof Manju Kurian
- 34.** University Hospital Heidelberg, represented in law by its Commercial Managing Director Ms Katrin Erk , Im Neuenheimer Feld 672, 69120 Heidelberg, executing department: Pediatric Clinical Center, Medical Director Prof. Dr. Georg F. Hoffmann, Project leader Prof. Dr. Thomas Opladen, on behalf of the Ruprecht Karls University Heidelberg, Faculty of Medicine.
- 35.** University Hospital of Nantes, having its registered office at 5 allée de l'île Gloriette 44093 Nantes Cedex 1, represented by its interim General Director, Mrs Laëtitia Micaelli-Flender, On behalf of the pediatric and neonatal reanimation department, with Dr. Alice Kuster
- 36.** Universitätsklinik für Pädiatrie I, Tirol Kliniken GmbH, Anichstr. 35, 6020 Innsbruck, Austria, legal representative: Univ.-Prof. Dr. Thomas Müller, iNTD repräsentative: PD Dr. med. Dipl. oec. troph. Sabine Scholl-Bürgi
- 37.** UZ Brussels, laarbeeklaan 101, 1090 Jette (Brussels), Belgium., legal representative: Prof Dr Marc Noppen, project leader:Dr Luc Régal

Preliminaries

The International Working Group on Neurotransmitter Related Disorders (iNTD) has been founded on January, 1st 2015, with the aim to promote health for individuals affected with inborn defects of the neurotransmitter, pterin and folate metabolism.

iNTD has established a patient-based registry [REDACTED] including comprehensive basic and follow-up data of more than 400 patients with neurotransmitter related disorders, has developed and published evidence based clinical care guidelines for several diseases, has established a website as major instrument for dissemination, among other activities. All iNTD members contribute their activities on a voluntary basis.

This Collaboration Agreement aims to build the legal framework for sustaining the iNTD network, its instruments and activities of its members.

The overall aims of iNTD are

- Promotion of health for individuals affected with neurotransmitter related disorders.
- Research on diagnostics, treatment, care and outcome, including guideline development.
- Dissemination of knowledge about diagnostics, treatment, care and outcome.
- Sustaining and extending iNTD by grant applications in the area for neurotransmitter related disorders and collaborations with scientific consortia, patients' organisations, healthcare providers, policy makers and industry.
- Coordination of relations between science, medicine and industry.
- Development and implementation of new instruments.

Definitions of terms

Data: Any pseudonymized data included in the iNTD Registry as specified in the Protocol.

Data Access Rights: Rights to use the data entered into the iNTD registry under the terms and conditions set out in this agreement.

Pre-existing Intellectual Property: Any data, know-how and/or information whatever their form or nature, tangible or intangible, including any rights such as intellectual property rights which are held by the Parties prior to the execution of this agreement and which is necessary for the performance of a Research Project.

Work results: Any tangible or intangible output of a Research Project, such as data, knowledge, inventions and information whatever their form or nature, whether or not they can be protected, which are generated directly out of the Research Project as well as any attached rights, including intellectual property rights.

Access Rights: Rights to use the pre-existing Intellectual Property or work results under the terms and conditions set out in this Agreement

iNTD PARTNERS: the legal entities participating to the iNTD Registry (e.g. University, Hospital, Institute)

iNTD MEMBERS: the scientific representatives affiliated with or appointed by each iNTD PARTNER pursuant to section 4.1.1.

Project Initiator: Any entity submitting a project to the Steering and Scientific Board for approval in order to obtain Data access.

Protocol: The iNTD scientific document submitted to the locally responsible ethics commission or Institutional Review Board (IRB)

Research Project: Any research project approved by the iNTD steering and Scientific Board. (including industry collaboration)

1. Instruments and products of iNTD

1.1 Instruments of iNTD

- 1.1.1. The core facility of iNTD is a web-based registry for systematic long-term follow-up data of patients with inborn defects of the neurotransmitter, pterin and folate metabolism.
- 1.1.2. Guideline development groups for establishment and regular revision of evidence based guidelines for inborn defects of the neurotransmitter, pterin and folate metabolism.
- 1.1.3. The iNTD Website [REDACTED] is a major dissemination instrument.
- 1.1.4. New instruments can be developed and implemented on demand after approval of the MEMBERS Board.

1.2. Products of iNTD

iNTD provides systematic data describing diagnostic procedures and results and long-term follow-up of patients with neurotransmitter related disorders. The data allows addressing specific research questions in cooperation with various stakeholders:

- 1.2.1. Other research consortia, networks (e.g. compared and combined data analysis, publication, guidelines)
- 1.2.2. Policy makers (e.g. providing epidemiologic information, evaluation of national newborn screening programs)
- 1.2.3. Professional societies (e.g. teaching courses)
- 1.2.4. Industry (e.g. post marketing surveillance of orphan drugs, feasibility analysis of clinical studies)
- 1.2.5. Patient organisations (e.g. information brochures)

2. Subject matter of the contract

The purpose of this Collaboration Agreement is to specify the relationship and the respective rights and obligations among and between the collaborating iNTD PARTNERS and MEMBERS, to fix the governance structure of the iNTD, the election procedures and intellectual property rules.

3. Responsibilities of the iNTD PARTNERS

3.1. General principles

- 3.1.1.** Each Party undertakes to take part in the efficient implementation of the iNTD, and to cooperate, perform and fulfil, promptly, on time, and in good faith all of its obligations under this agreement.
- 3.1.2.** Each Party undertakes to notify promptly, in accordance with the governance structure of iNTD, any significant information, fact, problem or delay or any other risk likely to affect iNTD.
- 3.1.3.** Each Party shall promptly provide all information reasonably required by an iNTD Body to carry out its tasks as foreseen in this agreement.
- 3.1.4.** Each Party undertakes to provide all information necessary pursuant to any requirement imposed by the MEMBERS Board.
- 3.1.5.** Each Party shall take reasonable measures to ensure the accuracy of any information or materials it supplies to the other Parties.
- 3.1.6.** Each Party shall contribute to network activities such as systematic collection of follow-up data for the patient registry, development and revision of evidence-based clinical care guidelines, preparation of information materials to be used for dissemination, development and update of website contents, organization of and participation at meetings, and development of new instruments (if applicable)
- 3.1.7** The Parties, as applicable shall conduct the Research Project in accordance with:
 - a. the Protocol and the Research Project participant informed consent form, as approved by the REB;
 - b. any terms and conditions imposed by the REB;
 - e. any terms and conditions imposed by the regulatory authority;
 - f. Applicable law; especially the General Data Protection Regulation (GDPR) and national data protection law.
 - g. the terms and conditions of this Agreement.

3.2. Ethics committee approval, regulatory authorizations and patient consent

- 3.2.1.** Each iNTD PARTNER is responsible for obtaining and maintaining the required ethics committee approval and regulatory authorization(s) for its participation to the iNTD registry in compliance with the Protocol.
- 3.2.2.** University Hospital Heidelberg is responsible for obtaining and maintaining the required ethics committee approvals and regulatory authorizations for the management and supervision of the iNTD central registry held in Heidelberg in compliance with the Protocol.
- 3.2.3.** iNTD PARTNERS are responsible for applying the national guidelines and directives concerning patient consent.

3.2.4. Access to the patient registry under the terms and conditions set out in this agreement will not be provided to iNTD PARTNERS until written ethical authorization is given by the local ethics committee / IRB.

4. Governance structure of iNTD network

4.1 The iNTD Steering + Scientific board = EXECUTIVE BOARD

4.1.1. The EXECUTIVE Board is the operating Board of the iNTD and is composed of up to ten members elected by the MEMBERS Board. One of the MEMBERS is elected as a chairperson by the MEMBERS Board. The chairperson holds the casting vote in case of equal votes, invites to and moderates the annual EXECUTIVE and MEMBERS board meetings.

4.1.2. EXECUTIVE Board members are elected by the MEMBERS Board for a legislation period of three years. At least three months before the end of the legislation period, the EXECUTIVE Board requests self-nomination of candidates among the MEMBERS Board for the next legislation period. In principle, membership of individual members can be sustained for more than one legislation period if they are elected for another period.

4.1.3. The EXECUTIVE Board shall be responsible for

- (a) Seeking for new funding opportunities
- (b) Being the main contact partner for stakeholders
- (c) Coordinating external collaborations (MetabERN, UIMD etc.)
- (d) Reporting to the MEMBERS Board about all their activities
- (e) Dissemination of (newsletter/webpage...)
- (f) Organization of annual MEMBERS Board meetings
- (g) Providing draft concepts for new publication projects, grant applications and collaborations with stakeholders such as industry and patient organizations.
- (h) Advising, monitoring and supporting the activities of the working groups defined below.

4.1.4. The EXECUTIVE Board shall meet at least half-yearly and shall also convene meetings in the case of an emergency situation. Meetings can also be held via teleconference or videoconference or through circulation of written documents among the members.

4.1.5. The main tasks of the chairperson of the EXECUTIVE Board are:

- (a) Organization of meetings of the EXECUTIVE Board
- (b) Giving annual reports to the MEMBERS Board

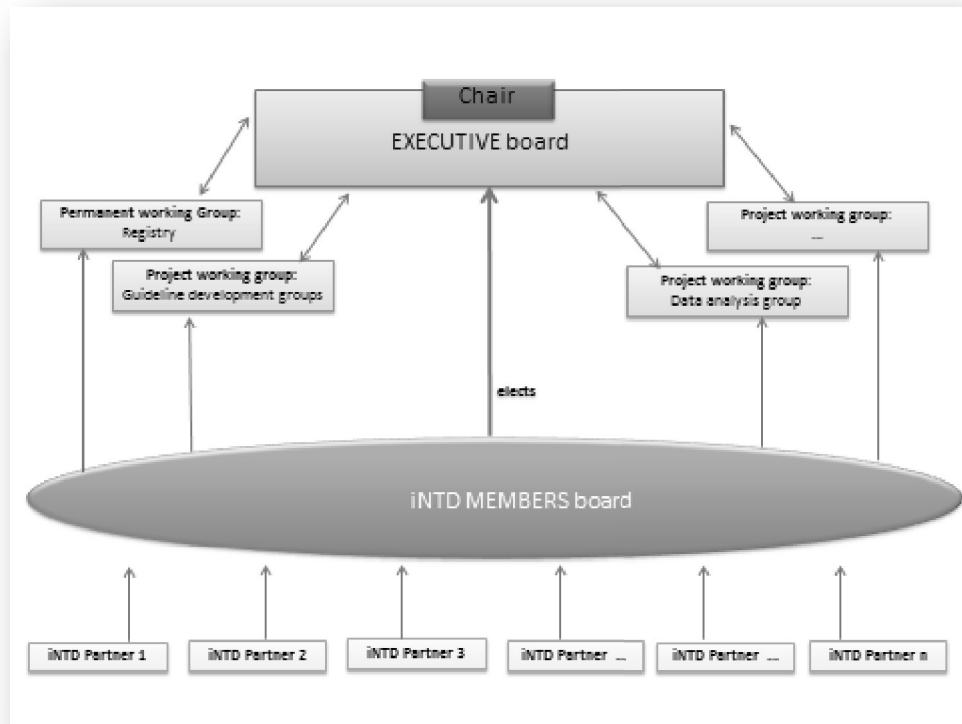


Figure1. Bodies of iNTD

4.2 The MEMBERS Board

4.2.1 The MEMBERS Board shall be responsible for:

(a) the election of the members of the EXECUTIVE board (legislation period: 3 years).

4.2.2. There will be held one annual assembly of all Board MEMBERS. During its first meeting the MEMBERS Board will elect the members of the Steering and scientific board.

4.2.3. However, any decision required or permitted to be taken by the MEMBERS Board such as votes on selected projects may be taken as follows:

- (a) In meetings including meetings held via teleconference or videoconference; or
- (b) Without a meeting, through circulation of a written document among the Board members setting forth the decision to be made which must be returned within fifteen (15) calendar days to the EXECUTIVE Board duly signed and with their recommendations indicated in relation thereof. In such a case, the Executive Board shall formalize in writing the decisions taken, taking into account the documents returned and shall dispatch them to the representatives within fifteen (15) calendar days of the expiration date of the above fifteen (15) days. Each PARTNER will have one vote at MEMBERS Board meetings. The MEMBERS Board shall make decisions by simple majority of all voting rights. In case of equality of votes the Chairman of the EXECUTIVE Board holds the casting vote. MEMBERS Board decision will not be validly decided unless and until at least

50% of its representatives are present or represented, or have expressed their votes in a written form.

- (c) In the event the MEMBERS Board identify a breach by a Party of its obligations under this Collaboration agreement, or one of the following misconducts especially such as violation of good scientific, violation of clinical practice, or inactivity or disregard of MEMBER responsibilities for two years or more the EXECUTIVE Board will give written notice to such Party requiring that such breach be remedied within thirty (30) calendar days. If such breach is not remedied within that period or is not capable of remedy, the MEMBERS Board can decide by absolute majority the exclusion of the PARTNER of the iNTD.

4.2.4. All voting under this agreement shall be secret following a secret ballot.

4.3. iNTD Working groups

Additionally to the above defined Boards the work of the iNTD will be completed by Permanent and Project Working Groups

4.3.1. Permanent working Group

4.4.1.1. Registry

4.3.2. Project Working Groups (working within a specified time period on defined subjects and questions)

4.4.2.1. Data analysis group

4.4.2.1. Guideline development groups

4.4.2.1 Further project working groups may be established

5. Data entry, data access, intellectual property rights, and access rights

5.1. Data entry

5.1.1. Two modes of data entry are available to network members: (1) members have their own access to the database and enter their own data to a central database held in Heidelberg, Germany; (2) members send pseudonymised data in a paper format to the lead data manager in Heidelberg, Germany, who enters the data on their behalf.

5.1.2. Only pseudonymised or anonymized data is entered into the database.

5.1.3. "Pseudonymisation" means the processing of personal data in such a way that the personal data can no longer be assigned to a specific person without additional information ("key"). This additional information shall be kept separately and shall be subject to technical and organisational measures to ensure that the personal data are not assigned to an identified or identifiable natural person.

"Anonymisation" is the change of personal data in such a way that the person concerned can no longer be identified or only with a disproportionately large cost or time.

5.2. Data access

- 5.2.1.** Data access may be granted only for the research purposes described in the Protocol and subject to the prior approval of the Research Project by the steering and scientific board in compliance with Section 5.2.4. of this agreement.
- 5.2.2.** Access to raw data relevant for a project will only be given to iNTD members. Other Project Initiators will only get access to aggregated data calculated from individual data (e.g. frequencies, measures of central tendency or dispersion by age, sex, country or deficiency).
- 5.2.3.** The entity requiring Data access (“Project Initiator”) is responsible for obtaining the regulatory authorizations required for the performance of the Research Project (if any). The project initiator is also responsible for ensuring that the patient consents already obtained by the iNTD PARTNERS are consistent with the scope of its Research Project.
- 5.2.4.** iNTD PARTNERS may submit a Project Proposal for approval to the steering and scientific board in order to obtain Data Access for research purposes. The steps of processing project proposals are outlined in Figure 2.
- 5.2.5.** The steering and scientific board performs an assessment of the Research Project based on its scientific interest for the iNTD consortium.
- 5.2.6.** Each iNTD PARTNER is free to accept or to refuse to participate in a Research Project. Refusal to participate will be based on an active opt-out scheme.
- 5.2.7.** Members are able to access their own data on a free basis for internal research purposes.

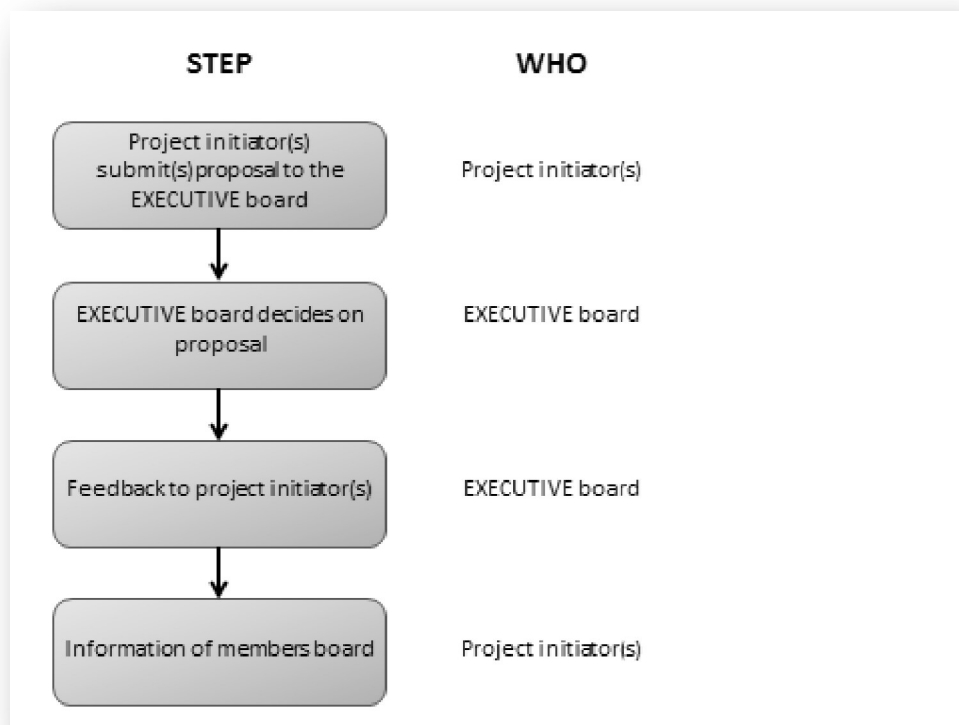


Figure 2. Steps of processing project proposals

5.3. Ownership of data

Each INTD PARTNER is and shall remain the owner of all data entered by him in the INTD Registry.

5.4. Intellectual Property Rights (IPR) concerning research results

5.4.1. Pre-existing intellectual property

Each PARTNER is and shall remain the owner of any protected or unprotected intellectual property rights existing at the time of contract closure.

Subject to third party rights, each PARTNER shall grant the non-exclusive right of use free of charge for any such pre-existing intellectual property rights to another PARTNER to the extent these are required for the completion of the research project adopted by the steering and scientific board and to the extent there are no conflicting third party rights. Any commercial use of the pre-existing intellectual property rights is governed by article 5.5.1.2.

5.4.2. Work results generated in the course of a research project approved by the steering and scientific board

Work results such as data, knowledge and information whatever their form or nature, whether or not they can be protected, which are generated in the research project as well as any attached rights including intellectual property rights shall be owned by the PARTNER who carried out the project generating this results. These results are to the free and unrestricted disposal of the generating iNTD PARTNER.

5.4.3. Jointly generated work results

If, in the course of carrying out a project, work results are generated and two or more PARTNER contributed to it, and if the contributions to or features of such work results form an indivisible part thereof, such that under applicable law it is not possible to separate them for the purpose of applying for, obtaining and/or maintaining and/or owning the relevant patent protection or any other IPR protecting or available to protect such work results, the Contributors agree that, subject as expressly provided to the contrary in this 5.4., all patents and other registered IPRs issued thereon, and any other IPRs protecting such work results, shall be jointly owned by the Contributors. The iNTD PARTNERS concerned may jointly apply for the relevant patent or other property rights. The arrangements for applying for and maintaining such patent or other property rights shall be agreed between the iNTD PARTNERS concerned on a case-by-case basis. Subject to any other agreement between the iNTD PARTNERS concerned, and so long as any such patent or other property rights is in force, the iNTD PARTNERS concerned shall be entitled to use and to license such patent or other property right without any financial compensation to or the consent of the other iNTD PARTNERS concerned.

5.4.4. Assigning ownership of work results

5.4.3.1. Each Party may assign ownership of its own work results (including without limitation its share in work results that it owns jointly with another Party or Parties, and all rights and obligations attaching to it) to any of its Affiliates, to any assignee of the assignor's relevant business or a substantial part thereof without prior notification to the other PARTNERS.

However:

- (a) any such assignment shall be made subject to the Access Rights, the rights to obtain Access Rights and the right to disseminate work results that are granted to the other Parties and their Affiliates in this agreement. Therefore, each assignor shall ensure that such assignment does not prejudice such rights of the other Parties or their Affiliates. This may be done, for example, (i) by effecting such assignment subject to a licence back to the assigning Party that is sufficient for the assigning Party to grant to the other Parties and their Affiliates such Access Rights, or (ii) by the assigning Party obtaining from the assignee of the work result legally binding undertakings (that can be enforced by the other Parties and their

Affiliates) to grant such Access Rights; and

- (b) the assignor shall pass on its obligations regarding the assigned work results to the assignee, including the obligation to pass them on to any subsequent assignee; and
- (c) if the assignment is made to a third party or an Affiliate, the assigning Party shall, either before or within a reasonable period following assignment of any rights in any work result, notify the other Parties of the assignment, including details of the work result assigned and the identity and contact details of the assignee.

5.4.3.2. Each Party hereby waives any right to object to any assignment that is made in compliance with this Section 5.4.

5.4.5. Employees' rights

Each Party shall, to the fullest extent it can lawfully do so, ensure that it can grant Access Rights and fulfil the obligations under this agreement notwithstanding any rights of its employees or Subcontractors in the work result they create. This is regulated on an individual basis in accordance to national law.

5.5. Access Rights

5.5.1. General principles relating to Access Rights

5.5.1.1. All Access Rights needed for the execution of a Research Project are granted on a non-exclusive, non-transferable basis.

5.5.1.2. Other than in exceptional circumstances, no transfer costs shall be charged for the granting of Access Rights necessary for the execution of non-commercial Research Projects. Acting in good faith, when a Project Initiator believes that for carrying out a Research Project:

- (a) he might require Access Rights to another Party's pre-existing intellectual property or work results, or
- (b) another PARTNER might need Access Rights to that PARTNERS' pre-existing intellectual property or work results,

he will promptly notify such other PARTNERS of the pre-existing intellectual property or work results needed. The PARTNER/s owning the pre-existing intellectual property or work results shall make its best effort to provide access on a free basis to it to the Project Initiator for the purpose of the Research Project.

Any commercial use of the pre-existing intellectual property or work results shall be subject to a written agreement between the PARTNER/s owning the pre-existing intellectual property or work results and the PARTNER entity requesting such commercial use, specifying the conditions for the use of the pre-existing intellectual property or work results.

5.5.2. Access Rights to third parties

Subject to obligations in relation to Confidential Information each PARTNER may enter into a collaboration or licensing agreement with a third party in respect of its own work results even if there are minor amounts of work results owned by another PARTNER, or even of pre-existing intellectual property, unavoidably incorporated into or amalgamated with such own work results. In such circumstances, and upon request of the PARTNER entering the collaboration or licensing agreement, the other PARTNER shall grant non-exclusive rights to permit such collaboration or licensing agreement against terms and conditions to be agreed, provided such grant does not adversely affect a commercial interest of the other PARTNER.

6. Publications: authorship and acknowledgements

- 6.1.** The Project Initiator should discuss the publication plan and proposed authorship issues frankly early in the course of their work.
- 6.2.** Authorship credit should be based on 1) substantial contributions to conception and design, acquisition, analysis and interpretation of data (honorary or guest authorship is not acceptable); 2) drafting the article or revising it critically for important intellectual content. Acquisition of funding and provision of technical services and patients are not in themselves sufficient contributions to justify authorship.
- 6.3.** Order of authors: the authors should decide the order of the authorship together. The lead author who takes primary responsibility for the work as a whole should give his/her advice. It is proposed that the lead author should be the first or the last author and those others should be listed alphabetically unless one or two authors have made contributions that are agreed to be sufficient to justify first or first and second authorship. If journals allow to list a limited number of authors, all authors will make a decision on who is mentioned by name, whereas all others are mentioned by the expression "...for the iNTD consortium".
- 6.4.** Other contributors who were not directly involved, and others contributing to the project, but not sufficiently to justify authorship, should be listed, with their permission, in the Acknowledgements.
- 6.5.** Any problems about authorship should be resolved by the steering and scientific board. If the problem cannot be solved, the EXECUTIVE Board acts as arbitration body.
- 6.6.** The final (revised) version of all manuscripts must be reviewed and approved by all authors before (re-)submission to a journal.

7. Confidentiality

- 7.1. The parties hereto undertake to maintain secrecy and confidentiality with respect to all business secrets and to information, documents and experience of the other party or of any Project Initiator which they acquire knowledge of in connection with this agreement and which are marked as confidential or which are to be treated as confidential on the basis of the circumstances, and shall only disclose such information to third parties to the extent absolutely required for the performance of this agreement, this obligation surviving the term of the agreement for a period of five years.
- 7.2. The duty to maintain secrecy shall not apply if it can be demonstrated that this information was known to the recipient party prior to notification, if the party obtained this information independently or acquired it by lawful means, or if this information is part of the current state of technology.
- 7.3. The parties hereto may depart from the duty to maintain secrecy by mutual written agreement. However, if knowledge will likely be revealed that by nature constitutes an invention (level of invention and innovation), the patent departments of the parties hereto are to be informed hereof in due time (usually two months) in advance.

8. Liability

8.1. Liability towards each other

In respect of information or materials supplied by one Party to another under this agreement, the supplying Party shall be under no obligation or liability and no warranty condition or representation of any kind is made by, given by or to be implied against the supplying Party as to the sufficiency, accuracy or fitness for purpose of such information or materials, or, subject to the obligations expressly stated in this agreement, the absence of any infringement of any proprietary right (including, without limitation, IPRs, trade secret rights and right over confidential information) of third parties by the use of such information and materials, and the recipient Party shall in any case bear the entire risk of any consequences that may arise from the use to which it, or to which any person that it directly or indirectly permits or allows to use such information or materials, puts such information and materials.

No Party shall have any liability in respect of the infringement of any patent or other right of any third party resulting from any other Party exercising any of the Access Rights granted under this agreement.

No Party makes any representation or warranty, express or implied, other than as expressly stated in this agreement.

8.2. Liability towards third parties

Subject to such other undertakings and warranties as are provided for in this agreement, each Party shall be solely liable for any loss, damage or injury to third parties resulting from the carrying out by it or on its behalf of its parts of the Project and/or from its Use of work results and/or pre-existing intellectual property.

8.3 Liability for Subcontractors

- (a) Each Party shall be fully liable for the performance of any part of its share of the Project, in respect of which it enters into any contract with a Subcontractor.
- (b) Each Party engaging any Subcontractor shall be solely responsible for all obligations incurred in relation to that Subcontractor. The other Parties shall have no obligation whatsoever to any such Subcontractor, save to the extent that they separately agree any such obligation in writing.

8.4. Excluded liabilities

To the extent permissible under applicable law and except as otherwise provided specifically below in this Section 5.2, in no event shall any Party be liable in connection with this agreement for any of the following, however caused or arising, on any theory of liability, and even if such Party was informed or aware of the possibility thereof:

- (a) loss of profits, revenue, income, interest, savings, shelf-space, production and business opportunities;
- (b) lost contracts, goodwill, and anticipated savings;
- (c) loss of or damage to reputation or to data;
- (d) costs of recall of products; or
- (e) any type of indirect, incidental, punitive, special or consequential loss or damage.

9. Financial Provisions

The PARTNERS will get no economic compensation from this collaboration agreement.

10. Duration of the agreement, termination and withdrawal of a INTD MEMBER

10.1. Duration of the contract and termination

This agreement shall come into force upon conclusion of the Contract/on July, 1st, 2020. It shall expire after 10 years. The agreement will be extended for another period of ten years if after the expiration of the ten year duration the PARTNERS decide about the continuation of the agreement in writing. If not otherwise decided in writing by the partners the agreement will be extended for additional periods of ten years as long as the partners want to cooperate under this agreement with the possibility to terminate it every ten years in writing.

The provisions relating to Access Rights, Confidentiality, Liability, Applicable law and Settlement of disputes shall survive the expiration or termination of this INTD Collaboration agreement.

10.2. Withdrawal of the participation of an iNTD MEMBER

The Parties agree that if a Party wishes to withdraw from the iNTD, it will be considered as a request for termination (and be subject to the unanimous agreement of the MEMBERS Board).

Such Withdrawing Party gives written notice to the steering and scientific board as soon as reasonably practicable after it has become apparent and such Withdrawing Party completes all of its obligations under this agreement.

Voluntary withdrawal of a Party shall not affect and will be without prejudice to any rights of a Party accrued at the date of termination or withdrawal or any of the obligations of a Party leaving the iNTD incurred prior to such date, unless otherwise agreed between the MEMBERS Board and the leaving Party. This includes the obligation to provide all input, deliverables and documents for the period of its participation. Entered patient data of a Withdrawing Party will remain in the registry and used for future analyses if not explicitly stated otherwise by the Withdrawal Party.

11. Settlement of disputes and applicable law

- 11.1. Any Party shall have the right to have recourse to the pre-arbitral referee procedure of the International Chamber of Commerce in accordance with its Rules for a Pre-Arbitral Referee Procedure.
- 11.2. All disputes arising out of or in connection with this Collaboration Agreement, which cannot be solved amicably, shall be finally settled by the courts of the defendant party.
- 11.3. Nothing in this Collaboration Agreement shall limit the Parties' right to enforce an arbitration award in any applicable competent court of law.

This contract shall be subject to, and be construed with, in accordance with, German law.

The German collisions of law provisions do not apply

12. Written form

Changes and amendments to this Contract must be made in writing to be effective. Collateral agreements have not been made; in the event that such agreements are made, they must also be made in writing.

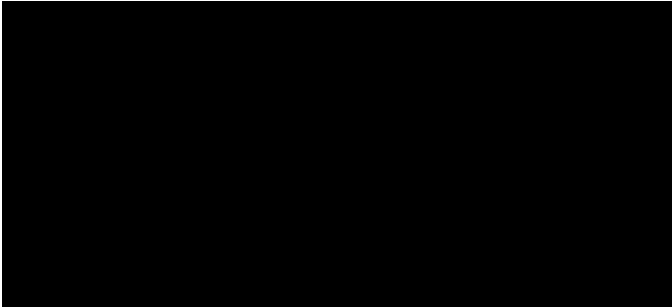
12. Severability

In the event that individual provisions of this Contract are ineffective, this shall not affect the validity of the remaining provisions. Any such invalid provision shall be replaced by a provision which best reflects what the parties hereto intended or would have intended if they had been aware of the invalidity of the provision. The same shall hold for any omissions in the Contract.

13. Signatures

For Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla

Sevilla, SPAIN

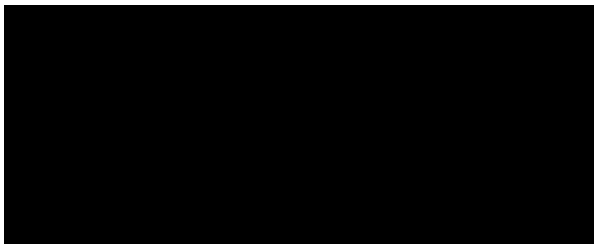


D. José Cañón Campos

Seville
Place

20/04/2022
Date

Legal Representative



Dr. Pablo Mir Rivera

Seville
Place

20/04/2022
Date

Scientific Representative