COLLABORATION AGREEMENT

between

University of Oslo, [971 035 854] - "UiO" c/o School of Pharmacy

with headquarters and address for tax purposes at: Boks 1072 Blindern, 0316 Oslo, Norway, Tax and VAT N. 971 035 854, represented by Henrik Schultz acting in his capacity of Head of School of Pharmacy, in accordance with the delegated authority.

and

Università degli Studi di Milano-Bicocca – "UniMiB"
with headquarters and address for tax purposes at Piazza dell'Ateneo Nuovo, 1 in Milan, Tax and VAT No. 12621570154, represented by Prof. Mario Mezzanzanica, acting in his capacity of Director of Department of Statistics and Quantitative Methods, in accordance to the proxy of the Rector dated 02/10/2018 DR Prot. n°70008/18

(UiO and UniMiB are jointly referred to as "the Parties")

WHEREAS

- UniMiB, through its Department of Statistics and Quantitative Methods and the Healthcare Research & Pharmacoepidemiology Center, acts as a scientific reference body for institutions, operators and researchers who, for various reasons, and at various levels of institutional responsibility, are interested in starting innovative projects on use, appropriateness, effectiveness and efficiency and equality of medical care in current clinical practice through the study, development and dissemination of scientifically valid methods and with particular regard to the generation of evidence in the areas of its competence;
- UiO, carries out research activities related to drug safety and effectiveness in pregnancy and lactation and is interested in carrying out scientific collaborations in the field of perinatal pharmacoepidemiology;
- The parties intend to cooperate in order to advance the evidence-based knowledge on drug safety and efficacy in pregnancy.

In consideration of the promises and mutual covenants contained herein, and intending to be legally bound hereby, the Parties hereto agree as follows:

1. Introduction

This Collaboration Agreement (the "Agreement") regulates the rights and obligations of the Parties in a project: The pharmacoepidemiology field with special reference to pharmacoepidemiology and drug safety in pregnancy – hereafter referred to as the" Project".

The following attached documents shall be part of the Agreement:
Appendix 1: Project description
Appendix 2: Relevant Background brought to the Project by UiO and UniMiB.

2. Definitions

Background	Material contributions or intellectual property rights or know-how that a party brings to the Project. The background provided by the individual participant in the project is specified in Appendix 2.
Commercial Utilisation	Direct or indirect use of project results in the development and marketing of products/services or processes based on the project results, or the transfer and/or licensing of use of project results to third parties, with the exception of publication in accordance with section 5.3.
Intellectual Property	All rights to technical solutions, methods, processes and procedures, regardless of whether or not these are or may be patented, as well as all copyrights and rights to trademarks, design, plant species, databases, integrated circuit designs, drawings, specifications, prototypes, trade secrets and the like.
Project Results	Research results produced or achieved in the Project, including Intellectual Property, regardless of whether the results are or may be protected by law.
Project Period	The time span during which the Project is to be performed, as specified in Appendix 1.

3. Obligations

3.1 Execution of the Project

The Parties are required to perform the tasks set down in the Project description. Project activities shall be carried out in accordance with accepted research practice. The Partner is required to comply with all applicable legislation and regulations, as well as all rules and guidelines of relevance to the implementation of the Project, including rules and guidelines relating to ethical considerations as well as recognised quality standards and norms.

3.2 Funding

There is no funding between the parties. The parties will themselves carry their own costs.
The Parties may together seek funding for the project(s), where they find it most appropriate.

4. Background

No rights to any intellectual property rights owned or controlled by either of the parties at the date of this Agreement or developed independently of this Agreement are granted under this Agreement. Background that is considered relevant upon entry into the Agreement is specified in Appendix 2. The ownership of Background will be maintained by the Party that brought it into the Project. Any Project Results from the Project that do not comprise Background pursuant to Appendix 2 and are not approved as Background by the Parties will automatically be assigned the status of Project Result.

For the duration of the Project Period, the Parties shall have access at no charge to the Background that is necessary for the implementation of their own work in the Project.
Commercial Utilisation of Background owned by the other Party can be negotiated between the Parties and regulated by written agreement.

5. Project Results

5.1 Ownership

The Parties shall communicate in writing within 1 month after a Project Result has been identified. Each Party will have exclusive ownership rights to the Project Results produced by that Party and its employees independently.

The Parties shall have joint ownership to the Project Result produced in collaboration, in the ratio of 50/50. If requested by a Party, a joint ownership agreement must be entered into between the parties. The joint ownership agreement shall as a minimum include a definition of relevant Project Result having joint ownership, and a detailed description of how the jointly owned Project Result shall be protected, defended, managed, funded and used. The Parties will consider whether protect intellectual property of Project Results that may be of commercial value, to the degree that is deemed appropriate.

If ownership rights are shared between both parties, the Parties can put in place appropriate protection measures, at the owners' expense. Should one party not wish to protect a Project Result, then that party must allow the other party to establish protection at its' own expense.

5.2 Access rights

For the duration of the Project, the Parties shall have access at no charge to Project Results that are necessary for implementation their own work in the Project.

The Parties shall have access at no charge to Project Results that is to be used for teaching and research purposes.

Any access not covered by the provisions above shall be subject to terms and conditions agreed between the owning and the receiving party.

5.3 Publication

Project Results shall be published as soon as possible, normally through publication in scientific journals, professional meetings and conferences, or in other agreed ways.

The Parties shall submit to each other plans for publication of Project Results. The Parties have a deadline of 14 working days from the date on which the publication notification was issued to request postponement of publication in order to implement the necessary measures to protect the Project Results. The relevant authors shall within 14 working days attempt to find acceptable adjustments to the planned publication, or alternatively request for postponement of up to 3 months from the date on which notification from the Party that has produced the Project Results was received. The Parties will not grant permanent postponement of publication.

Project Results will be jointly published where there have been direct collaborations between the Parties. In such case, joint authorship will be based on the amount of individual intellectual contributions, according to the Vancouver protocol (http://www.icmje.org/).

6. Confidentiality

The Parties are under obligation to refrain from disclosure of any confidential information, received in the Project;

- which is provided in writing or in another form and marked "confidential", or
- which was provided orally and stated to be confidential and which is written down within 14 days and marked confidential by the party that provided the information.

Confidential information shall not be revealed to others or published without prior written consent from the rightholder.

The provision does not apply to information;

- which at the time information is provided is generally known, or later becomes generally known without the recipient of the information being responsible for this,
- which in a lawful manner has become to the knowledge of the recipient, directly or indirectly through others who are not subject to a corresponding confidentiality requirement,
- which was known to the recipient before the information was provided,
- which disclosure is demanded by the authorities and/or the courts pursuant to the law.

7. Changes

The Parties shall have the right to make a written claim for modifications or changes in the Project as long as these changes are within the framework of the Project as defined in Appendix 1 both Parties agree.

8. Liability

Each party shall indemnify the other party against any loss, damage or injury to their own and any possible subcontractor's property or personnel, unless the loss, damage or injury is due to deliberate action or gross negligence by the other party.

Scientific contact persons

UiO's contact person: Dr. Angela Lupattelli, School of Pharmacy

UniMiB's contact person: Prof. Giovanni Corrao, full Professor at Department of Statistics and Quantitative Methods and Director of Healthcare Research & Pharmacoepidemiology Center.

9. Administrative contact persons

UiO's contact person: Henrik Schultz, Head of School of Pharmacy –
E-mail: henrik.schultz@farmasi.uio.no

UniMiB's contact person: Gianpiero Latino, Capo Ufficio Supporto alla Ricerca –
E-mail: ricerca.eco-stat@unimib.it

10. Duration and jurisdiction

The Agreement will have effect from the date of signatures from both Parties, and until the Project Period is completed. The first part of the project will be completed in April 2019 and the subsequent parts will be completed by December 2023, according to plans. The Agreement terminates therefore at the latest on December 31, 2023.

The Agreement may be terminated by each Party with three (3) months written notice. The provisions in Sections 4, 5, 6 and 8 will continue to apply between the Parties after the expiration of the Agreement.

The Agreement is subject to Norwegian law. Attempts shall be made to resolve any disputes by negotiation. In the event such attempts do not succeed, the dispute may be brought before the Oslo district court as the legal venue.

11. Insurance

The University UniMiB ensures insurance coverage for the permanent staff involved in the research activities covered by the agreement. The insurance coverage relates to accidents occurring at work. The University UniMiB can employ temporary staff (e.g. PhD students, postdoc). In the case the temporary staff lacks adequate insurance coverage, this has to be obtained before starting any research activity.

The Department of Pharmacy-UiO confirms that all employees are automatically covered by the State in all insurance issues.

12. Occupational Health and Safety

In accordance with the Italian law on occupational health and safety, articles 2 and 26 of Legislative Decree No. 81/08, it is agreed that:

- before the commencement of any activities covered by this agreement the Scientific Head or the Contact Person for this agreement will communicate to the corresponding human resources department the following details: the staff's personal details, start date of work, and other details on the research activities performed;

-the responsible persons within the Human Resources department will then evaluate the risk level of the activities, and eventually complete other documents/take further preventive measures.

-If deemed necessary, the staff working under these risky conditions must undergo regular medical check-ups by the hosting institution.

The hosting institution must ensure the following:

- provide training on the applicable emergency procedures;
- provide information to the guest researcher/visitor about specific risky areas that they may be visiting;
- provide specific devices for health protection in the relevant areas;
- guarantee appropriate supervision for the health and safety of the workers and students during the conduct of any research activity in these areas of risk.

13. Processing of Personal Data

The Parties ensure that the handling, dissemination and communication of personal data in relation to this agreement, are in accordance with the European Directive 2016/679 on GDPR and any stricter national legislation in Italy or Norway.

14. Signatures

The Agreement has been signed in two (2) originals. Each of the Parties will keep one original.

For UiO;	For UniMiB
Signature:	Signature: .....
Name: Henrik Schultz	Name: Prof. Mario Mezzanzanica
Title: Head of Department of Pharmacy	Title: Director of Department of Statistics and Quantitative Methods
Date:	Date: 21 FEB. 2019 .....

Appendix 1: Project description

PROPOSED RESEARCH PROJECT

Title: **Utilization, effectivness and reproductive safety of medications during pregnancy**

Short description of targets/methods

Up-to-date drug utilization studies in pregnant women are constantly needed to monitor changes in prescribing patterns, and to address priorities for pregnancy safety studies. Psychotropic drugs are used by 3-10% of pregnant women for treatment of important mental illnesses. Yet, it remains unclear how effective these medications are in lowering the risk of maternal relapse of the mental disorder during pregnancy, or after childbirth. Until now, most drug in pregnancy studies have explored adverse immediate perinatal outcomes, and this has been recently paralled by a growing interest in longer-term developmental outcomes in children prenatally exposed to psychotropic drugs. Yet, the effect of timing of antideressant exposure on specific adverse outcomes remains to date unresolved.

This umbrella project aims to address these specific research gaps in drug in pregnancy research. The specific aims are:

1) Examine drug utilization and purpose avoidance of prescribed drugs in pregnant women in Italy;
2) Quantify psychotropic drug effectiveness in pregnancy and/or postpartum;
3) Explore whether discontinuation in late pregnancy of antidepressants, with or without other important comedications (opioids, benzodiazepines), can reduce the risk of withdrawal symptoms in the newborn, compared to pharmacotherapy continuation.

To address aim 1, the parties will use data from the Multinational Medication Use in Pregnancy Study, which collected anonymous data on drug use in pregnancy in 916 women in Italy. To address aims 2-3, the parties will utilize Health Registry data from the region Lombardy, which include:(i) the archive of beneficiaries of the Regional Health Service (RHS), i.e., the entire resident population, reporting demographic and administrative data (e.g., municipality, date of birth and date of start and end of being RHS beneficiary), (ii) the database on diagnosis at discharge from public or private hospitals of Italy (diagnoses classified according to the International Code of Disease, 9th Revision, ICD-9); and (iii) the database reporting Certificates of Delivery Assistance (CeDAP) including information self-reported by the mother relating to her socioeconomic traits in the period recent to her current pregnancy, other than medical information relating to pregnancy, childbirth, and child presentation at delivery.

Time period of survey: The Multinational Medication Use in Pregnancy Study was conducted between October 2011 and February 2013. Data from the health registry in region Lombardy provide data from 2005 to 2010.

Appendix 2: Relevant Background brought to the Project by UiO and the UniMiB.

UiO and UniMiB will both materially contribute with the data sources necessary for the project, depending on the aims (UiO=data for aim 1; UniMiB=data for aims 2-3). Both parties will scientifically and intellectually contribute to the study design and planning, data analysis, and interpretation of the findings. UiO will write-up the scientific publications resulting from this project, but UniMiB may also contribute to this task depending on resources and scientific interest. UniMiB will intellectually and scientifically contribute to the entire project with its expertise in the field of biostatistics and big data analysis. UiO will contribute with its expertise in the field of pharmacology and pharmacoepidemiology, specifically in the field of drug in pregnancy research.