**Biomarkers4Pediatrics data use agreement**

Between:

Please insert institution*,* Please insert address, *email:* Please insert email address*.*

- Hereinafter the "**Data Provider**" -

and

**Leibniz-Institut für Präventionsforschung und Epidemiologie - BIPS GmbH** (in English: Leibniz Institute for Prevention Research and Epidemiology - BIPS GmbH), Achterstr. 30, 28359 Bremen, Germany, coordinator of the Biomarkers4Pediatrics collaboration, email: NN@leibniz-bips.de

- Hereinafter the "**Data Recipient"** -

 - Hereinafter Data Provider and/or Data Recipient also "**Parties**" or "**Party**" -

1. Purpose of this Biomarkers4Pediatrics data use agreement:
	1. The purpose of this Biomarkers4Pediatrics data use agreement (hereinafter the "Agreement") is to provide the Data Recipient with access to Please insert study namedata files for the use in the project (see Collaboration proposal, **Appendix I**):

 *"International Multicohort Pediatric Biomarkers Collaboration - Biomarkers4Pediatrics"*

* 1. The Agreement shall enter into force upon signature by the Parties and shall end on 31-12-2030, unless the Parties agree to extend the Agreement’s duration prior to its termination.
1. Responsibilities of the Data Provider:
	1. The Data Provider will prepare data files containing the variables described in **Appendix II** (data request).
	2. The data files will be pseudonymized, meaning that the data file does not contain any names and/or personal identifiers.
2. Responsibilities of the Data Recipient:
	1. The Data Recipient keep the list up-to-date with the persons who have direct access to the Please insert study namedata (see **Appendix III**). The persons on this list must sign for “read” of the Agreement.
	2. The persons in **Appendix III** will only use Please insert study namedata for research purposes as described above, unless a new contract is signed between the Data Recipient and the Data Provider.
	3. The persons in **Appendix III** will not pass any data to third parties, unless additional permissions for further data use and sharing are granted by the Data Provider. In addition, the Data Recipient will take all necessary measures to ensure that no third parties gain access to any part of the data file. This includes that all data may only be stored and analyzed on a secured server. If this does not seem possible, a solution will be sought in consultation with the Data Provider of the Please insert study namestudy before the data are stored by the Data Recipient.
	4. The Data Recipient shall delete all original data obtained from the Please insert study namestudy, as well as all data derived from the original data set at the end date of the Agreement.
	5. Before the Data Recipient delete the data, the processed data files must be forwarded to the Please insert study name study for archiving (first ask for instructions). After the destruction of all data, the Data Recipient must be sent a written confirmation to the Data Provider of Please insert study namestudy.
3. Publication of findings from data:
	1. All reports, publications and presentations resulting from this collaboration will be produced and published according to the publication policy outlined in **Appendix I**.
4. Termination of the Agreement:
	1. The Data Recipient and Data Provider may terminate the Agreement at any time by notifying the other Party by a written notice. The Data Recipient will then delete all data within 30 days as described under section 3d.
	2. In the event of the Data Recipient did not keep his obligations according to section 3 and 4, the Data Provider can demand the immediate deletion of all data described in section 3d.
	3. All disagreements arising from the Agreement will be resolved by mutual agreement between the Parties.
	4. If either the Data Provider or the Data Recipient would like to change the terms of the Agreement in any way, this shall be valid only if the change is made in writing and approved and signed by mutual agreement between authorized representatives of the Parties hereto.
5. This Agreement shall be governed by, subject to and construed in accordance with the laws of Germany except its choice of law rules. For any and all proceedings arising hereunder the Parties agree to the exclusive jurisdiction of the competent courts of Bremen.

Agreed and drawn up in duplicate and signed:

|  |  |
| --- | --- |
| ***NN*** | **Leibniz-Institut für Präventionsforschung und Epidemiologie - BIPS GmbH** |
| - Data Provider - | - Data Recipient - |
| Place: |  | Place:  | Bremen |
| Date:  |  | Date:  |  |
| Signature:  | \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ | Signature: | \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ |
|  | *Title, First name, Surname* |  | Prof. Dr. rer. nat. Iris Pigeot-Kübler |
|  | *Function* |  | Executive Director and Institute Director |
| Signature:  | \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ | Signature: | \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ |
|  | *Title, First name, Surname* |  | Dr. rer. nat. Norman Wirsik |
|  | *Function* |  | Executive Director |

**Appendix I: Collaboration Proposal**

**Aims**

*Initial, project-specific:*

* To pool, harmonize and analyze globally available data from pediatric populations to provide age-, sex- and ethnic-specific reference curves for metabolic biomarkers to facilitate the diagnosis of metabolic syndrome in early life in clinical practice and public health.

*Long-term:*

* To create a collaborative framework and data infrastructure that facilitates individual participant based meta-analyses and studies with a specific focus on biomarkers in pediatric populations to answer clinically relevant questions in the field.

**Inclusion criteria**

* Population-based epidemiological studies (longitudinal, cross-sectional data)
* 0-18 years of age (optional: ages up to 24 years, if available)
* At least one of the following variables: waist circumference, blood pressure, HDL-cholesterol, triglycerides, fasting blood glucose measurements.
	+ plus, weight and height measurements, socio-demographics (e.g. age, sex, parental education level).

**Rationale and Background**

Health monitoring and clinical decision making in pediatric care largely depend on the availability of reference values for clinical parameters. Hence, the diagnosis of highly prevalent conditions in children and adolescents such as metabolic dysfunction has been hampered by the lack of a worldwide consensus on diagnostic criteria, as definitions and cut-offs being used in the pediatric population are frequently derived from the adult population. Providing globally applicable reference curves for the metabolic syndrome and its components, in early life - from birth to adolescence - represents a big step towards the ultimate goal: developing cut-offs for clinically relevant biomarkers for pediatric practice. By making use of the increasing availability of research data worldwide, we aim to establish a global pooling initiative building on a previously published special issue of the International Journal of Obesity "Filling the gap: international reference values for health care in children" (edited by Ahrens W, Moreno LA, Pigeot I), and further taking advantage of increased statistical power and variations across age groups, geographical regions and socio-cultural backgrounds. Thus, biomarker data for the metabolic syndrome are being collected, harmonized, pooled and analyzed to provide age-, sex- and ethnic-specific reference curves for metabolic biomarkers to facilitate the diagnosis of metabolic syndrome in early life globally.

**Methods**

*Harmonization and Pooling*

Established IT infrastructure is used for secure data storage at BIPS institute. Harmonizing data across different studies involves standardizing variables, data formats, and measurement techniques based on common protocols. This process will be developed to ensure compatibility and comparability of data, facilitating seamless integration and reducing potential biases or confounding factors. We further recognize the importance of accommodating different data pooling preferences. Study collaborators in our initiative are free to choose either traditional pooling methods or the federated analysis approach in which individual research teams retain control of their respective datasets while sharing aggregated results. For the latter we will use the open-source DataSHIELD software.

*Statistical analyses*

For the estimation of sex-specific percentile curves, generalised additive models for location, scale and shape (GAMLSS) will be used. To find an appropriate model for each biomarker a forward-backwards algorithm will be used for the normal, the Box-Cox-Cole and Green (BCCG), the Box-Cox-t- (BCT) and the Box-Cox power exponential (BCPE) distribution to find a respective model with lowest Bayesian Information Criterion (BIC). Here, the distribution parameters are modelled as constant or depending on age (as penalized splines or linear function). The overall goodness of fit for each primary outcome will be assessed by the Bayesian Information Criterion (BIC), worm plots and percentages of data below the percentile curves to choose a final model. Covariates will be used for sensitivity analyses or/and as variables for subsample-depending worm plots.

**Steering Committee**

The Steering Committee (SC) consists of all data holders of the participating studies.

The tasks of the Steering Committee will be:

* To safeguard the quality and methodological feasibility of project proposals.
* To review and actively accept or decline participation for subprojects.
* Review and approve manuscripts that should be sent at least 3 weeks before any submission.

**Publication Policy**

**Authorships**

Authors should participate in the writing of the paper in accordance with the International Committee of Medical Journal Editors guidelines (ICMJE, 2024, see below).

The first author together with the senior author will invite all Principle Investigators (PI) (in case of multicenter studies, each individual study center PI) to a working group for the project. The project working group will be eligible for more prominent authorships, and in return are expected to be easily approachable for questions and discussion by the first and senior author, and contribute to analyses and writing of the manuscript in an early phase of the project. Based on total workload and addition of original data; the first and senior author will set the authorship order.

Each PI has the right to propose additional co-authors to any project embedded in, or manuscript resulting from, the Biomarkers4Pediatrics collaboration. Based on their contributions to study organization and data collection the PI will decide on addition of the proposed individual as a co-author. To attain co-authorship, the proposed individual should be included in the manuscript reviewing (depending on stage of entering the project).

**Review and approval of abstracts and manuscripts**

Manuscripts must be submitted to the Steering Committee a minimum of 4 weeks prior to any deadline to allow time for review and possible revision. Abstracts should be submitted a minimum of 2 weeks prior to the abstract deadline.

Abstracts/manuscripts must be approved by the Steering Committee prior to submission to a meeting or a journal.

**International Committee of Medical Journal Editors key authorship criteria (ICMJE, 2024)**

1. **Substantial contributions to the conception or design of the work, or the acquisition, analysis, or interpretation of data:** Authors must have actively contributed to the intellectual content or methodology of the research, ensuring they play a significant role in its development or execution.
2. **Drafting the work or revising it critically for important intellectual content: Authors should be involved in the drafting or substantial revision of the manuscript, ensuring its accuracy, clarity, and intellectual coherence.**
3. **Final approval of the version to be published: Authors must agree to the final version of the manuscript, acknowledging their responsibility for its content and ensuring its readiness for publication.**
4. **Agreement to be accountable for all aspects of the work: Authors should be willing to take responsibility for the integrity and accuracy of the research, ensuring that any questions related to the work can be appropriately addressed.**
5. **Ensuring that all appropriate authors are included on the manuscript: Authors should ensure that all individuals who have made substantial contributions to the work are included as authors, while also ensuring that all authors meet the criteria for authorship and that no individuals who do not meet these criteria are included.**

These criteria aim to ensure that authorship is attributed appropriately, acknowledging the contributions of individuals who have played a significant role in the research process while maintaining transparency and integrity in scientific publishing.

**Appendix II: Data-request**

Name dataset Variable name Description

**Appendix III: List of Data Recipient’s persons[[1]](#footnote-1) who have access to Please insert study name data:**

|  |  |  |  |
| --- | --- | --- | --- |
| Name person | Function of the person | Date | Signature to confirm that the contract has been read |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |

1. In the event that these persons are visiting scientists or students associated with the Data Recipient who are not employees of the Data Recipient, the Data Recipient will ensure that these persons are subject to the same data protection regulations and restrictions as the other persons who have access to Please insert study name data. [↑](#footnote-ref-1)