Understanding Hypoglycaemia:

The underlying mechanisms and addressing clinical determinants as well as consequences for people with diabetes by combining databases from clinical trials

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Need for public-private collaboration

- **Unique scientific opportunity to address hypoglycaemia**
  - Industry partners have generated large clinical trial datasets around hypoglycaemia which can be pooled
  - Academic partners have the scientific insights and tools to probe/analyse pooled datasets
  - Hypotheses and correlations that arise from probing the dataset can be applied further:
    - To test data from glucose monitoring device companies
    - To test in pre-clinical settings
    - To understand social and economic impacts of hypoglycaemia
- **Opportunity to bring together patient groups to influence and assess the hypoglycaemia researc**h

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The objective is to reduce the risk and burden of hypoglycaemia through a series of integrated activities

Scope

- Research into the **mechanisms of counter-regulation and hypo unawareness** to identify new targets for intervention
- Establishment of **pooled data bases** of i)hypoglycaemia captured in clinical trials across glucose lowering drug development programs and ii)CGM clinical trials with glucose monitoring devices
- Probing the data bases to **characterize clinically relevant hypoglycaemia** and to determine the causes and consequences of such events
- Evaluating **glucose measuring techniques** to define standard detection guidelines
- Developing **best practice for clinical trials** regarding the collection of clinical and lab data
- Shaping **health economic outcomes** research to determine the value of reducing hypoglycaemia risk
- Identifying **patient-driven research** and conducting a related meta-analysis of the data
- Opening a **dialogue with regulatory agencies** to define clinically meaningful endpoints/methods to reduce these with pharmacologic intervention

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Pre-competitive nature: Non-profit organizations join industry partners

- **EFPIA companies** bring anonymized clinical trial data
  - Eli Lilly
  - Sanofi
  - Novo Nordisk
  - Abbott
  - Dexcom
  - Medtronic
- **Non-profit** Associated Partners
  - JDRF
  - Helmsley
  - T1D Exchange
  - IDF

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Expected impact

- **A better understanding of the causes and impacts of hypoglycaemia will provide:**
  - important guidance to patients, healthcare professionals and regulatory authorities
  - the development of therapeutic approaches that will help to:
    - reduce the risk of hypoglycaemia;
    - improve glycaemic control;
    - reduce the risk of short and long-term diabetes related complications.
- **Creating a standard guideline on how to measure hypoglycaemia episodes will allow for:**
  - choice of therapy that provides optimal glycaemic control within the context of individualised therapy;
  - lowering the risk of hypoglycaemia through the use of newly developed devices, e.g. those with predictive alarms/guidelines;
  - better comparison of blood glucose lowering drugs with respect to hypoglycaemic episodes and severities.
- **Agreement on a standardised approach for the collection of clinical and laboratory data in clinical trials will provide:**
  - a better understanding of factors and clinical consequences related to the development of hypoglycaemia;
  - the basis for regulatory authorities to recommend standardised approaches of measurement to be included in clinical trials.

Expected impact…. cont'd

- **The establishment of clear, robust and consistent definitions of hypoglycaemia will allow:**
  - Development of consistent approaches to the management of hypoglycaemia;
  - Improved design of diabetes trials for glucose lowering therapies;
  - Development of drugs and treatment paradigms with improved hypoglycaemia benefits;
  - Enhanced interpretation of clinical trial outcomes;
  - Clearer understanding of regulatory (licensing) requirements for existing and novel glucose lowering therapies
- **Improvement in overall diabetes therapy:**
  - Better patient outcomes, including physical, mental, social and economic benefits
  - Reduce the direct and indirect costs of hypoglycaemia treatment
  - better comparison of blood glucose lowering drugs with respect to hypoglycaemic episodes and severities.
- **Outcome of 360 ° assessment of the burden of diabetes for patient and society:**
  - Enrich the understanding of the importance of hypoglycaemia in affecting daily life
  - Consequences of the fear of hypoglycaemia from the patient perspective
  - Alleviation of the burden of disease through intervention and prevention of hypoglycaemia

Suggested architecture of the project

Project Duration 48 months

Future project expansion 24-36 months

- Apply learnings to **real world data**
- Open up to specific **new partners** e.g. with access to real world data and specific patient populations of interest, in particular to test non-clinical findings in clinical trials
- New **clinical studies** implementing the standardized methodologies, guidelines, patient reported outcome instruments etc. that have been developed in the project
- It will be critical to **ensure continuity** from the original project by maintaining the established databases and applying the original findings and knowledge into the expansion period

Work Package structure

2 Preclinical

3 Databases

4 Clinical data analysis

5 Glucose measurements

6 HEOR

7 Patient role

8 Regulatory

* WP1 Project Management

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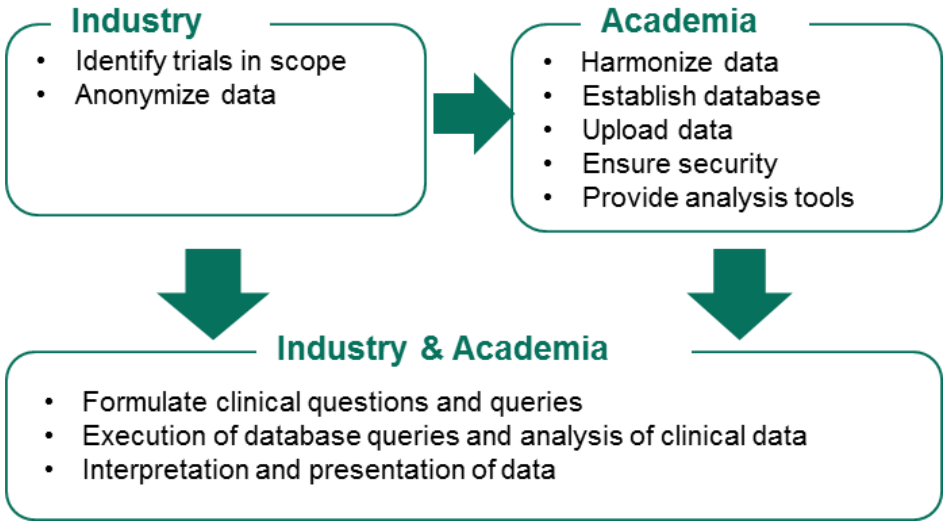
Expected contributions of the applicants

- Propose projects to address non-clinical topics which can be carried out by joint post-doctoral fellows/students
- Establish combined database (harmonize)
- Formulate clinical questions and queries
- Execute database analysis
- Interpretation and presentation of data



- Provide additional novel clinical cohort datasets (special populations of interest)
- Standardization of definitions of hypoglycaemia based on clinical analysis
- Evaluate glucose monitoring technologies
- Assess the experienced based impact and burden related to hypoglycaemia (patient-driven research, including PRO instrument development)
- Determine economic consequences of hypos and value of hypoglycaemia prevention and patient impact
- Establish a process for engagement with regulatory authorities

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Expected (in kind) contributions of industry consortium

- Sponsorship of post-doctoral fellows/students to conduct non-clinical research projects
- Provide access to in-house animal models and molecular/cellular tools for non-clinical studies
- Identify clinical trials that are in scope for combined database
- Anonymize clinical trial data
- Provide data in standardized format
- Contribute to the formulation of clinical questions and queries
- Participate in the data interpretation
- Participation in all work package groups

What's in it for you?

- Academic researchers:
  - Access to unique, extensive clinical trial datasets established by pooling data from industry partners
  - Collaboration with clinical and non-clinical industrial research groups on projects of common interest in the area of hypoglycaemia
- Patients' and non-profit organisations
  - Opportunity to contribute to the ground-breaking research to understand hypoglycaemia and subsequently improve the treatment of diabetes and the lives of people with diabetes

Key deliverables of the full project

- Establishment of a unique clinical trial database with anonymised, standardised and harmonised data from patients with T1DM and/or T2DM on glucose lowering treatment regimens. This database will subsequently become available for other interested researchers to access;
- Agreement amongst all stakeholders on the applicability of the definitions of clinically meaningful hypoglycaemia through examination of the combined clinical trial data set, clinical data and CGM;
- Enhanced understanding and agreement of standard approaches for how best to design trials to assess hypoglycaemia and how to analyse the data;
- Generation of information relating to existing and novel aspects of hypoglycaemia and hypoglycaemia risk leading to a better understanding of hypoglycaemia mechanisms, and novel targets for prevention and/or intervention;
- Exploration of the relationship between clinical trial database findings and real-time glucose measurement datasets from continuous glucose monitoring;.

Key deliverables of the full project….cont'd

- Stronger evidence on the utility of non-laboratory glucose measurement and data analysis technologies;
- A 360° assessment of the burden of hypoglycaemia for patients and society that will enrich our understanding of hypoglycaemia, complement our understanding derived from clinical studies and add perspective to related clinical recommendations;
- Generation of evidence-based data to support discussions with regulatory authorities on acceptable definitions of hypoglycaemia

Questions?

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