Inter-Sustain Evaluation Committee,
Novo Nordisk Foundation,
Copenhagen

9th February 2026

Dear Colleagues,

RE: Letter of commitment; the Fenland Study for the grant by Daniel Witte et al entitled "Metabolic Signatures: Coupling incretin and glucagon pathways with metabolic traits in cardiometabolic disease progression"

As Chief PI of the Fenland Study I write to provide confirmation that we gladly support this application to the Inter-SUSTAIN Part 2: Research Projects call.

Confirmation of Suitability, Feasibility, and Appropriateness of the Fenland Study Data
I confirm that the data requested in the proposal from the Fenland Study (listed at the end of this letter) are available, suitable, feasible to access and appropriate for the scientific aims of the project. We also confirm that these data align with the needs of the proposed analytical framework ie. to investigate causal inference, longitudinal trajectories, mediation, clustering, and prediction models. No new participant-level data will be collected and all work will comply with existing ethical approvals.

Commitment to No-Payment Access
If the project is funded under the Inter-SUSTAIN Part 2 call, we commit to providing no-payment access to the above-listed data types, in accordance with our governance and data-sharing policies. I can confirm the feasibility of data access within standard timelines. These limitations are standard for the cohort and do not affect the ability to carry out the analyses proposed.

Added value to the Fenland Study
I can confirm that the proposed study will provide added value to the Fenland study, most notably through the use of reproducible methods for causal inference models including pathway-specific mediation and machine-learning-based prediction models. The work will enable harmonization between the Fenland study, ADDITION-PRO, and UK Biobank and all workflow code (including data processing, analysis, and validation) will be published on GitHub for sharing reproducible workflow. These outputs will enrich the utility of the Fenland data and contribute to future precision-prevention research by creating data on metabolic trait clusters, giving improved characterisation of metabolic heterogeneity across indivduals in

the Fenland study. The study will also enable the identification of causal genotypes, metabolites, and phenotypes that influence cardiometabolic disease risk.

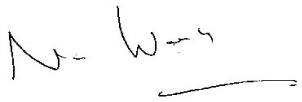
Status of Applicant and Collaborators as Users of the Database

The Principal Investigator Daniel R. Witte and his collaborating Danish partners are new users of the Fenland Study and we are delighted that they see the value in working with this detailed metabolic quantitative trait study.

Statement of Support

I am, therefore, pleased, as the Fenland Study PI to confirm our full support for this project and its ambitious scientific aims.

Yours sincerely,



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Requested available and accessible data types in the Fenland Study

Category	Requested Data
OGTT hormonal & metabolic measurements	Glucose, Insulin, GLP 1, GIP, Glucagon (0, 120 min)
Clinical phenotyping and biomarkers	Anthropometrics Blood pressure Lipids (fasting) Liver markers ALT, AST, GGT, ALP, glucagon–alanine index Inflammation markers IL 6, hsCRP, adiponectin
Imaging and body composition data	DEXA body composition (visceral & subcutaneous fat) Liver ultrasound imaging
Metabolomics	Targeted metabolomics (175 acylcarnitines, amines, sphingolipids, phospholipids)
Genetic data	Genome wide genotyping
Long term follow up outcomes	Incident type 2 diabetes Mortality Repeated phenotypic data from Phase 2 & Phase 3 Planned collection of outcomes in 2026 Macrovascular events (IHD, heart failure) Microvascular complications (CKD)