

REQUEST FOR PROPOSALS SPECIFIC AND TECHNICAL CONDITIONS FOR THE CONTRACTING OF A SUPPLIER TO ANALYSIS OF DNA METHYLATION IN THE BLOOD OF PARTICIPANTS IN THE GCAT COHORT.

(EXPEDIENTE N.º33-2024)

I. Objective

The purpose of this Request for Proposals is to invite suppliers to submit proposals for the contracting of a laboratory the contracting of a supplier for the analysis of DNA methylation in the blood of participants in the GCAT cohort.

All the technical specifications contained in this document are considered to be part of the minimum requirements and do not exclude any other needs for compliance with the purpose of the service contracted.

II. Scope

Background

Alterations in circadian rhythm linked to the activities of a modern 24-hour society, such as working at night, eating late or reducing sleep, can increase the risk of cardiometabolic diseases such as obesity, diabetes and cardiovascular disease. Nevertheless, many aspects of circadian behaviours, particularly those related to diet “chrono-nutrition”, need to be considered in a holistic manner to better understand their impact on health. There is a lack of studies to better understand the molecular mechanisms that explain these associations. One possible hypothesis is that alterations in circadian rhythms have an effect on epigenetics, i.e. on how genes are expressed, in particular in a mechanism that can control gene expression without affecting genetic information, known as DNA methylation. The CUPID project will investigate how this relates to cardiovascular health: if the circadian epigenetic markers modified by chrono-nutritional behaviours are related to differences in the risk of cardiometabolic diseases, this would indicate a possible mediating effect of methylation in the role of nutritional circadian misalignment in these diseases.

Objective of the procurement

ISGlobal is seeking a laboratory/supplier with the capacity to DNA methylation in the blood in at least N=365 blood samples using state-of-the-art methods in a period of 6 months.

The purpose is to contract the services of a company specialized in high-throughput genomics for the discovery of methylation patterns using Illumina technology, specifically the "Methylation Epic V2.0 BeadChip Kit," for the research project CUPID "Understanding the link between chrono-nutrition and cardiometabolic disorders: an epigenetic perspective." The goal is to carry out an Epigenome-wide association study (EWAS) between chrono-nutritional patterns and methylated CpG marks of the genome, to subsequently define the relationship

with the risk of cardiovascular events.

III. Contract Responsible

ISGlobal will appoint a person responsible for relations with the supplier (the "Contract Responsible"), who will coordinate with the entity's staff and who will channel communications between the two parties.

IV. Management of work and quality control

ISGlobal and the laboratory will establish by common agreement a calendar of communications that will consist of bi-weekly or monthly progress calls.

Regardless of these scheduled calls, the Contract Responsible and the project management team may meet at any time if any of the two parties considers it appropriate, depending on the progress of the work hired. At any meeting the responsible person may choose to bring additional participants from ISGlobal if considered convenient. Bimonthly (every two months) reports will be provided by the awarded supplier.

V. Required qualifications

The selected laboratory should meet these requirements:

- Specific experience in working with high-performance epigenomics platforms such as the "Methylation Epic V2.0 BeadChip Kit" (approximately 935K sites), with minimum sample volumes and high sensitivity.
- Date of delivery of results
- Sample quality control

Proposals will be evaluated on the basis of the following criteria:

Description	Máximo points
Specific experience in working with high-performance epigenomics platforms such as the "Methylation Epic V2.0 BeadChip Kit" (approximately 935K sites), with minimum sample volumes and high sensitivity.	5
Date of delivery of results	5
Sample quality control	20

Notice: The points for each criteria are described in Annex 1.

VI. Period of execution and delivery of reports

The execution of the work will be carried out over a period of 6 months.

VII. Essential contractual obligations

The following will be considered as essential obligations of the awarded supplier:

- Initial meeting at the beginning of the project and communication at the end of each stage: assay design, sample reception, quality control, sample preparation for the assay (aliquoting), result control, final results, and on-demand at any time during the project.
- Conducting cross-quality controls with previously analyzed GCAT samples.

- Ensure feedback from project partners is taken into account for the development of the solution
- Ensure all data is kept safe and with accomplishment with legal regulations
- Report any problems encountered during the development of the digital solution
- Bimonthly report on progress of the work
- Delivery of final results

VIII. Duration and start date

The duration of the contract will be 6 months.

The estimated start date of the contract is the first week of July 2024.

IX. Estimated value

The contract budget is set to **67,500 euros** (EUR), excluding taxes. The amount will not exceed this budget in any case. Consequently, for non-exempt suppliers, the final price of the contract will be the budget amount plus the corresponding Value Added Tax (VAT).

X. Method of payment

The laboratory will periodically provide reports on the state of development of the sample analyses. Payment will always be made upon invoice, within 30 days of invoice date, by bank transfer:

- First payment: 30%
- Second payment (month 3): 30%
- Final payment upon completion of analyses in all samples and delivery of results: 40%

This is a proposed timeline, which is subject to change based on negotiated scope of work.

XI. Advertising

The present Request for Proposals document will be published in the Suppliers section of the contracting entity's website: <https://www.isglobal.org/en/contrataciones>.

XII. Procurement procedure:

The selection procedure will be made complying with the internal procurement regulations of the contracting entity, as provided in sections VIII and IX of the Procurement Manual.

XIII. Nature of the contract

This contract is considered a private contract and is subject to private law, governed by the contract and attached documentation, and by the applicable civil and commercial legislation.

XIV. Submission of proposals

Interested applicants are invited to submit a comprehensive proposal, addressing the needs described in the Request for Proposals document, to the following e-mail address: contrataciones@isglobal.org.

Proposals must be sent in one single consolidated document in PDF format.

The deadline for the submission of proposals is set on **July 1st, 2024, at 18:00 h.**

Barcelona, June 17th 2024.

**REQUIRED QUALIFICATIONS
(EXPEDIENTE N.º33-2024)**

1) TECHNICAL BIDS WHOSE EVALUATION DEPENDS ON VALUE

JUDGEMENTS VALUE Máximo 30 points

The selected laboratory should meet these requirements:

Specific experience in working with high-performance epigenomics platforms such as the "Methylation Epic V2.0 BeadChip Kit" (approximately 935K sites), with minimum sample volumes and high sensitivity..... **Máximo 5 points**

The service should include:

Quality control of the samples **Máximo 20 points**

An accurate measurement of DNA concentration reduces the possibility of technical bias in methylation measurements. Among the techniques used, those based on spectrophotometric methods are the most common, but other methods based on the integration of fluorochromes into DNA, such as Picogreen, offer a more precise and less variable measurement of DNA, allowing for a reliable assessment of the sample.

Timely delivery of results and reports..... **Máximo 5 points**

The proposals shall be evaluated on the basis of the following criteria:

Specific experience in working with high-performance epigenomics platforms such as the "Methylation Epic V2.0 BeadChip Kit" (approximately 935K sites), with minimum sample volumes and high sensitivity.....Máximo 5 points

5 points: Over 4 years of experience.

3 points: 3 years of experience.

2 points: 2 years of experience.

1 points: 1 year of experience.

0 points: No experience.

Quality control..... Máximo 20 points

20 points: Nanodrop quantification or other spectrometry methods

10 points: Picogreen quantification

0 point: No quality control offered

Delay in providing the results and reports after sending the samples..... Máximo 5 points

5 points: 2 weeks less than the term asked

2.5 points: 1 week less than the term asked

0 points: No reduction of the delay

2) ECONOMIC PROPOSAL Máximo 70 points

The economic proposal (total amount) will be evaluated from 0 to 70 points, according to the following formula:

$$\text{Points} = \left(1 - \frac{\text{Offer price} - \text{Lowest offer}}{\text{Lowest offer}} \right) \times \text{Máximo points}$$