

**SPECIFIC AND TECHNICAL CONDITIONS FOR
FDA PRE-IND MEETING REQUEST PACKAGE AND MEETING SUPPORT**

(File 14/2019)

I. OBJECT OF THE SUBJECT

The present document (the "Pliego") is intended to contract a consultant for preparation of an FDA Pre-IND Meeting Package, and Support through the meeting related to the use of ivermectin for Malaria, specifically for the use of high-dose ivermectin to reduce malaria transmission.

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. CONTENT OF THE WORK

Ivermectin as a complementary tool to reduce malaria transmission, Pre-IND meeting application through FDA's 505(b)(2) using an experimental high dose.

Scope of work

ISGlobal – Barcelona Institute for Global Health is a research centre in international health whose ultimate goal is to help close the gaps in health disparities between and within different regions of the world. For this, we leverage on knowledge generation (research), transmission (training) and application (policy and global development). ISGlobal is a WHO Collaborative Center for Malaria Elimination and Eradication.

One of ISGlobal's research lines is the potential use of drugs (particularly ivermectin) that administered to humans and/or livestock reduce the live span of mosquitoes feeding on treated individuals, potentially contributing to reduce malaria transmission if distributed at community level at the appropriate time. For this, ivermectin would be used at a dose/regimen that is higher than currently approved.

ISGlobal is looking for an experienced consultant to prepare a FDA Pre-IND Meeting Package, and Support through the meeting including attendance for the regulatory repurposing of ivermectin. We are particularly interested in pursuing the FDA 505(b)(2) pathway.

The key deliverables are:

1. Prepare and Submit Pre-IND Meeting Request Letter

2. Prepare Pre-IND Meeting Package
3. Perform Quality Control (QC) and Substantive Quality Assurance (QA) Review of Pre-IND Meeting Package
4. Submit Pre-IND Meeting Package to FDA
5. Pre-IND Meeting Attendance (or Address FDA Written Responses)

III. PERSON RESPONSIBLE FOR THE CONTRACT

ISGlobal will appoint a person responsible for relations with the consultant group (The "Contract Responsible"), who will be assure the necessary coordination with the staff of the entity and that will channel communications.

IV. MANAGEMENT OF WORK AND QUALITY CONTROL

ISGlobal and the consultant will establish by common agreement a calendar of communications that will consist of at least fortnightly progress calls. Regardless of these scheduled calls, the Responsible for the Contract and the consultants may meet at any time if any of the two parties considers it appropriate, depending on the development of the works hired.

At any meeting the responsible person may choose to bring additional participants from ISGlobal if considered convenient.

V. REQUIRED QUALIFICATIONS

- Proven track record of successfully conducted INDs preparations using the FDA 505(b)(2) pathway. Candidates with more than 10 successful INDs will be given preference.
- Experience with international projects
- Track of regular interaction with FDA

VI. PERIOD OF EXECUTION AND DELIVERY OF THE REPORT

The execution of the works will be carried out in a maximum period of 6 months.

VII. ESSENTIAL CONTRACTUAL OBLIGATIONS

They will be considered as essential obligations of the successful bidder, the following:

- a) Guarantee absolute confidentiality of the documentation received, taking the due diligence not to disclose it, or use it in any way other than the purpose of this contract. Failure to comply with this obligation will automatically imply termination of the contract and will result in a claim by ISGlobal for damages that may have been

inflicted.

b) Guarantee and take responsibility for the technical quality of the works and services that develops and the consequences that may occur, by ISGlobal or for third parties, as a consequence of omissions, errors, inadequate methods or incorrect conclusions in the execution of the contract.

c) To carry out a strict follow-up in carrying out the work of the report audit.

d) Deliver the works and reports hired in the manner and terms provided in the Bidding Document.

VIII. CONTRACT PERIOD

The duration of the contract will be 6 months

The estimated start date of the contract is May 6, 2019.

IX. BUDGET, PRICE AND ESTIMATED VALUE OF THE CONTRACT

The contract budget amounts to the maximum amount of

USD 139.500 exempt bidders
(EUR 97.950,52) (excluding VAT) for non-exempt bidders

The award amount will not exceed this budget in any case. The price of the contract, consequently, will be that to which it rises plus the corresponding Value Added Tax, in the case of non-exempt bidders, which must be included in the separate item.

The estimated value of the contract for the purpose of determining the procedure awarding, advertising and competition of the contracting authority, is:

USD 139.500,00 exempt bidders
(EUR 97.950,52) (excluding VAT) for non-exempt bidders

X. CIVIL LIABILITY POLICY

The company that is awarded the contract commits to have throughout the validity of the contract of a liability policy with coverage minimum of € 500,000.- per claim

XI. ADVERTISING

The present contract will be published by announcement in the Contracting Profile of the entity on the website: www.isglobal.org

XII. PLACE AND DATE OF SUBMISSION OF PROPOSALS

The economic proposals must be submitted by email to the address

licitaciones@isglobal.org

The deadline for submitting proposals will end on 3 May, at 12:00.

XIII. LEGAL SYSTEM OF THE CONTRACT

The contract is considered a private contract and is subject to private law, ruling by this Schedule, by the contract and documentation attached, and in everything not provided by the applicable civil and commercial legislation.

XIV EXPENDIENT OF RECRUITMENT, AWARD PROCEDURE OF THE CONTRACT AND DOCUMENTATION TO BE PROVIDED TENDERS

The contracting of the reference services will be awarded by the procedure envisaged in Section IX of the Internal Contracting Instructions of the entity. From the day of publication of the tender notice, interested companies can be obtained through the contractor's profile on the website www.isglobal.org the necessary documentation to prepare your proposals.

XV. PAYMENT METHOD

Payment will always be made under invoice and 30 days invoice date by bank transfer:

Upon Sponsor signing this Service Agreement 30%

Upon delivery of the draft Pre-IND Meeting Request Letter 20%

Upon delivery of the final Pre-IND Meeting Request Letter 15%

Upon delivery of the draft Pre-IND Meeting Package 12.5%

Upon delivery of the final Pre-IND Meeting Package 12.5%

Upon attendance at pre-ind meeting or assessment and recommendations to fda written responses 10%

Barcelona, April 24, 2019

ANNEX 1 TECHNICAL REPPORT

1. Project Background

ISGlobal is developing an experimental ivermectin, intended for use in the prevention of malaria in mass drug administration.

The ivermectin-treated individual receives no immediate benefit in terms of malaria), but biting mosquitoes die, the anticipated result of which is a potential reduction in malaria transmission at community level. This is expected to result in a potential 'delayed' benefit for the individual. Additional direct benefits include treatment of head lice, scabies and some intestinal helminths.

There is a precedent for which the FDA Center for Biological Evaluation and Research (CBER) has evaluated a malaria transmission-blocking vaccine with only a delayed benefit to the individual, similar to the Sponsor's proposed dose. If the Center for Drug Evaluation and Research (CDER) views the Sponsor's product as having a delayed benefit, it is anticipated that CDER will evaluate the Sponsor's product as a drug.

ISGlobal requests that the consultant assess the dose's regulatory viability of approval under the 505(b)(2) pathway; and conducts an analysis of the clinical, clinical pharmacology, and nonclinical components required for the product development and 505(b)(2) approval that may be missing or incomplete/inadequate in ISGlobal's intended development program.

2. Tasks

1.- Prepare and Submit Pre-IND Meeting Request Letter.

- Write the Pre-IND Meeting Request Letter according to current guidance, including statement of the purpose and objectives of the meeting; product information and proposed indication; proposed agenda; and specific questions for FDA to answer.
- Address all technical disciplines (nonclinical, CMC, clinical) that may require resolution for submission and activation of an Investigational New Drug Application (IND) for this product.
- Submit Meeting Request Letter to FDA.

2.- Prepare Pre-IND Meeting Package.

Consultor will write and assemble the Pre-IND meeting package, which will include:

- Product name and application number.
- Chemical name and structure.
- Proposed Indication.
- Dosage form, route of administration, and dosing regimen.
- An updated list of Sponsor or applicant attendees, affiliations and titles.

- Background, including a brief history of the development program and current status.
- Supporting data, grouped by discipline and question, including:
 - Proposed clinical and nonclinical development plan.
 - Proposed study design.
 - Summaries of nonclinical, Pharmacokinetics (PK), clinical, and CMC information.

3.- Perform Quality Control (QC) and Substantive Quality Assurance (QA) Review of Pre-IND Meeting Package

conduct QC and QA review of documents submitted to FDA.

4.- Submit Pre-IND Meeting Package to FDA.

- Submit an electronic copy through the Electronic Submissions Gateway (ESG).
- Submit required number of desk copies as outlined in the Meeting Grant Letter received from FDA, or other communications and requirements from FDA.

5.- Pre-IND Meeting Attendance.

The goal of this meeting is to obtain FDA agreement on the plan for product development, in anticipation of NDA submission.

If the FDA meeting is a face-to-face meeting or a teleconference, the consultant will:

- Review regulatory communications and draft FDA Preliminary Comments before meeting.
- Attend the FDA meeting with Sponsor; provide regulatory and scientific input related to the meeting discussion; and provide detailed notetaking.
- If appropriate, submit Sponsor's meeting minutes based on the FDA Preliminary comments and meeting discussion.
- Review and interpret final meeting minutes after meeting is held.

If FDA provides Written Responses Only (no meeting) the consultant will:

- Review the Written Responses to the Meeting Questions.
- Develop a summary of the responses.
- Interpret the responses.
- Identify any clarifying questions that may be required.
- Develop the strategy for obtaining clarifying information, write the clarifying questions, and send the clarifying questions to FDA through the mechanism agreed upon with the FDA Project Manager (email, official submission to the Pre-IND, etc.).
- Follow FDA's responses on the clarifying questions. This Service Agreement covers up to receipt and interpretation of one set of clarifying questions after Written Responses Only are received, provided that the clarifying questions are sent to FDA within 3 weeks of Sponsor receipt of Written Responses Only.

ANNEX 2
ECONOMIC PROPOSAL FOR THE CONTRACTING OF THE SERVICE
OF GAP ANALYSIS/PRE-IND MEETING REQUESTER LETTER, MEETING PACKAGE AND
FDA MEETING SUPPORT AND ATTENDANCE

Mr. [..], With address at [..] Street [..] Núm. [..], Aware of the announcement published in the Profile of the Contractor of the Private Foundation Institute of Global Health Barcelona and the conditions and requirements that are required for the award of the service of strategic assessment / gap analysis, undertakes, on behalf of the company it represents, to perform them strictly subject to the aforementioned requirements and conditions, for the amount of [insert economic offer clearly in letters and numbers, with VAT excluded], by which the bidder commits to the execution of the services, plus the amount of [insert amount corresponding to VAT, in letters and in numbers] euros our USD for VAT, if applicable.

CONCEPT	BUDGET CONCEPT OFFERED (VAT excluded)	VALUES MAXIMUM ESTIMATED RECRUITMENT (VAT excluded)
Pre-IND Meeting Request Letter, Meeting Package, and FDA Meeting Support and Attendance		USD 139,500 exempt bidders (EUR 97.950,52) (excluding VAT) for non-exempt bidders

Billing and payment will always be done under invoice and 30 days from invoice date by bank transfer.