ICAR-NATIONAL RESEARCH CENTRE ON EQUINES
SIRSA ROAD, HISAR-125 001 (HARYANA)

F. No. 21-434/S&P/VTC/21-22 Dated: 11.08.2021

EXPRESSION OF INTEREST

On behalf of Secretary, ICAR, the Director, NRCE, Hisar invites sealed **Expression of Interest (EoI)** from eligible firms/CROs for a multicenter, randomized controlled phase-II study to assess the safety and efficacy of emetine in the management of mild to moderate COVID-19 patients. Interested firms may download complete document of EoI from the NRCE website http://nrce.gov.in. The last date for submission of the EoI is 1th September, 2021 at 02.00 PM and EOI will open on 02.09.2021 at 2.30 PM.

S/d
ASSISTANT ADMINISTRATIVE OFFICER (P)

ICAR-National Research Centre on Equines
Ministry of Agriculture and Farmers Welfare, Government of India
HISAR, Haryana-125001

F. No.21-434/S&P/VTC/21-22 **Dated: 11.08.2021**

Subject: Inviting an Expression of Interest (EoI) for a multicenter, randomized controlled phase-II study to assess the safety and efficacy of emetine in the management of mild to moderate COVID-19 patients

Objective and scope of the requirement:

We have identified **"emetine"** as one of the candidate drug against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of COVID-19 (Kumar et al., 2021, Antiviral Research; 189:105056). Emetine is a FDA-approved drug which is used to treat amebiasis (a parasitic disease) since 1970's. However, before being used, it needs clinical trials in COVID-19 patients. We are looking for a Clinical Research Organization (CRO) to assist us in conducting the clinical trial. An EoI from institutions, hospitals and other organization interested with the facilities and capacity available to participate in the above-mentioned clinical trial is invited in a two stage bidding process.

Eligibility criteria:

1. The participating CROs/research organization must have past experience in conducting clinical trials. The proof of at least 20 clinical trials conducting in the past must be submitted in EoI.
2. The CRO must be authorized by the Drugs Controller General of India (DCGI), the regulatory authority for clinical trials in India.
3. The CRO is also expected to identify suitable manufacturer who can provide GMP drug (emetine; Tablets/Injection). The price for the same may be separately quoted in the price bid.
4. Once the formulation is complete, in vitro antiviral bridging study, shall be run to prove the efficacy of the product by ICAR and once the results are favourable, we shall advance to the next level of assessment.
5. In consultation of NRCE, the CRO is also expected to seek permission from the (DCGI), approval from respective Ethics Committee where the study is proposed to be carried out and registering for the clinical trial at Indian Council of Medical Research (ICMR) portal.

Terms and conditions

1. On receipt of the EoI following first stage of the bidding, technical discussion/presentation may be held with the shortlisted CROs which are prima facie considered technically and financially capable of performing the task.
2. In the second stage of the bidding process, we shall invite bids from all those bidders whose bids at the first stage were not rejected, to present final bid with bid prices.
3. Any bidder, invited to bid but not in a position to supply the subject matter of procurement due to modification in the specifications or terms and conditions, may withdraw from the bidding proceedings without forfeiting any bid security that he may have been required to provide or being penalised in any way, by declaring his intention to withdraw from the procurement proceedings with adequate justification.
4. The Bidder is expected to examine all instructions, forms, terms, and specifications in the bidding documents. Failure to furnish all information required by the bidding documents or submission of a bid not substantially responsive to the bidding documents in every respect will be at the Bidder's risk and may result in rejection of its bid.
5. The trial will be initiated only after obtaining requisite regulatory and ethical approvals. A brief synopsis of the study plan is attached herewith.
6. Institutions/Clinical research Organization (CROs) which are interested to collaborate with NRCE, Hisar on undertaking this trial, may express their interest by providing the details through the following link: http://nrce.gov.in. Please send your response on or before 10 August 2021, 05:30 PM.

   For further details, please contact:

   Dr. Naveen Kumar
   Principal Scientist (Veterinary Virology)
   National Center for Veterinary Type Cultures
   ICAR-NRC on Equines

Sirsa Road, Hisar, Haryana-125001 (India)
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	Synopsis of the study
Title	A multicenter, randomized controlled phase-II study to assess the safety and efficacy of emetine in the management of mild to moderate COVID-19 patients
Clinical Study Phase	II
Objective	• Primary objective is to compare the efficacy of emetine on the risk of progression to moderate/ severe respiratory disease • To compare the safety of emetine-treated to control, up to Day 21 of follow-up • To compare the rate of hospitalisations due to COVID-19 in emetine-treated versus control • To compare the time to hospitalisation due to COVID-19 in emetine-treated versus control • To compare the rate of hospitalisations for other reason than COVID-19 in emetine-treated control • To compare the disease-free rate in emetine-treated versus control • To compare the death rate in emetine-treated versus control • To compare time to worsening of SpO2 < 93in each study arm versus control • To compare the capacity to prevent severe progression between emetine-treated and controls
Investigational Products	1. Emetine Tablets (oral) 2. Emetine intravenous injection
Study Duration	Patient participation will be for 22 days.
Indication	Mild to moderate COVID-19
Major Inclusion and Exclusion Criteria	***Inclusion Criteria*** • Male or female patients with mild to moderate COVID-19 and having pre-defined risk factors • COVID-19 confirmed by molecular biology or validated antigenic test available in India for SARS-Cov2 according to national guidelines, based on result within 24 hours prior to screening and maximum 48 hours after sampling. • Viral syndrome with or without uncomplicated pneumonia, defined as blood oxygen saturation level (SpO2) > 94%. • Signed written consent from the patient ***Exclusion Criteria*** • Abnormal physical examination findings (respiratory rate >25 per minute, blood pressure < 90/60 mmHg or > 160/100 mmHg) • End-organ compromise requiring admission to a resuscitation or continuous care unit or short-term life-threatening comorbidity with life expectancy < 3 months. • On-going treatment at screening with (chronic systemic glucocorticosteroid > 40 mg daily, immunosuppressive treatment) • Known pulmonary arterial hypertension or fibrosis.

Study Design	Multicentre, randomised
Number of Patients	Between 400 and 500 patients will be included
Primary Endpoint	The primary endpoint is SpO2 ≤ 93% within 21 days after randomisation to treatment, including death for any reason
Secondary Endpoints	• Mean number and incidence rate of serious adverse events • Number of hospitalisations due to severe progression • Time to hospitalisation • Disease-free status: disease-free based on normalisation of pre-existing symptoms and SpO2 > 94% at Day 21 and no hospitalisation for COVID-19 • Time to worsening of SpO2 < 93% within 21 days • Occurrence of SpO2 < 93% or death or hospitalisation due to COVID-19
Statistical Analyses	***Statistical analyses include*** Intent-to-treat (ITT): all patients who received at least one dose of IP, including Per protocol (PP): all patients in the ITT population who were free from major protocol violations that could lead to bias Safety: all patients who received at least one intake of IP ***Efficacy Analyses*** Interim analyses when emetine is declared either effective, ineffective or is dropped for futility will be based on the ITT population. The primary analysis will be a Bayesian comparison of the proportions experiencing progression to severe disease with the treatment versus control, with adjustments for site and temporal effects.

Cost of Bidding

- The Bidder shall bear all costs associated with the preparation and submission of its bid, and "the Purchaser", will in no case be responsible or liable for these costs, regardless of the conduct or outcome of the bidding process.

Technical bid (Annexure)

- Bidder Information Form: Annexure-I
- Manufacturing Authorization form: Annexure-II
- Integrity Pact - Annexure-III

Code of Integrity

- The bidders/suppliers should sign a declaration about abiding by the Code of Integrity for Public Procurement in bid documents. In case of any transgression of this code, the bidder is not only liable to be removed from the list of registered suppliers, but it would be liable for other punitive actions such as cancellation of contracts, banning and blacklisting or action in Competition Commission of India, and so on.
- **Code of integrity for Public Procurement**: The Purchaser as well as bidders, suppliers, contractors and consultants should observe the highest standard of ethics and should not indulge in the following prohibited practices, either directly or indirectly, at any stage during the procurement process or during execution of resultant contract.

- "**corrupt practice":** making offers, solicitation or acceptance of bribe, rewards or gifts or any material benefit, in exchange for an unfair advantage in the procurement process or to otherwise influence the procurement process or contract execution;
- "**Fraudulent practice**": any omission or misrepresentation that may mislead or attempt to mislead so that financial or other benefits may be obtained or an obligation avoided. This includes making false declaration or providing false information for participation in a tender process or to secure a contract or in execution of the contract;
- "**anti-competitive practice**": any collusion, bid rigging or anti-competitive arrangement, or any other practice coming under the purview of the Competition Act, 2002, between two or more bidders, with or without the knowledge of the purchaser, that may impair the transparency, fairness and the progress of the procurement process or to establish bid prices at artificial, non-competitive levels;
- "**coercive practice**": harming or threatening to harm, persons or their property to influence their participation in the procurement process or affect the execution of a contract;
- "**conflict of interest**": participation by a bidding firm or any of its affiliates that are either involved in the consultancy contract to which this procurement is linked; or if they are part of more than one bid in the procurement; or if the bidding firm or their personnel have relationships or financial or business transactions with any official of purchaser who are directly or indirectly related to tender or execution process of contract; or improper use of information obtained by the (prospective) bidder from the purchaser with an intent to gain unfair advantage in the procurement process or for personal gain; and
- **Obstructive practice**": materially impede the purchaser's investigation into allegations of one or more of the above mentioned prohibited practices either by deliberately destroying, falsifying, altering; or by concealing of evidence material to the investigation; or by making false statements to investigators and/or by threatening, harassing or intimidating any party to prevent it from disclosing its knowledge of matters relevant to the investigation or from pursuing the investigation; or by impeding the purchaser's Entity's rights of audit or access to information;

Annexure-I

Bidder Information Form

a. The Bidder shall fill in this Form in accordance with the instructions indicated below. Noalterations to its format shall be permitted and no substitutions shall be accepted. This shouldbe done of the letter head of the firm]

Date: *[insert date (as day, month and year) of Bid Submission*]

Tender No.: *[insert number from Invitation for bids]*

1.	Bidder's Legal Name *[insert Bidder's legal name]*
2.	In case of JV, legal name of each party: *[insert legal name of each party in JV]*
3.	Bidder's actual or intended Country of Registration: *[insert actual or intended Country of Registration]*
4.	Bidder's Year of Registration: *[insert Bidder's year of registration]*
5.	Bidder's Legal Address in Country of Registration: *[insert Bidder's legal address in country of registration]*
6.	Bidder's Authorized Representative Information Name: *[insert Authorized Representative's name]* Address: *[insert Authorized Representative's Address]* Telephone/Fax numbers: *[insert Authorized Representative's telephone/fax numbers]* Email Address: *[insert Authorized Representative's email address]*
7.	Attached are copies of original documents of: *[check the box(es) of the attached original documents]* Articles of Incorporation or Registration of firm named in 1, above.

Signature of Bidder _____

Name _____

Business Address _____

Annexure-II

MANUFACTURERS' AUTHORIZATION FORM

(**The Bidder shall require the Manufacturer to fill in this Form in accordance with the instructions indicated. This letter of authorization should be on the letterhead of the Manufacturer and should be signed by a person with the proper authority to sign documents that are binding on the Manufacturer and be enclosed with the technical bid**)

Date: *[insert date (as day, month and year) of Bid Submission]*

TenderNo.: *[insert number from Invitation for Bids]*

To: *[insert complete name and address of Purchaser]*

WHEREAS

We *[insert complete name of Manufacturer]*, who are official manufacturers of *[insert type of goods manufactured]*, having factories at [insert full address of Manufacturer's factories], do hereby authorize *[insert complete name of Bidder]* to submit a bid the purpose of which is to provide the following Goods, manufactured by us *[insert name and or brief description of the Goods]*, and to subsequently negotiate and sign the Contract.

Signed: *[insert signature(s) of authorized representative(s) of the Manufacturer]*

Name: *[insert complete name(s) of authorized representative(s) of the Manufacturer]*

Title: *[insert title]*

Duly authorized to sign this Authorization on behalf of: *[insert complete name of Bidder]*

Dated on_____day of_____,_____*[insert date of signing]*

Annexure-III

Format of Integrity Pact

Between

ICAR-Nation Research centre on Equines Ministry of Agriculture and Farmers Welfare, Government of India HISAR, Haryana-125001represented by_____hereinafter referred to as "The Principal".

And.....herein referred to as "The Bidder/ Contractor."

Preamble

The Principal intends to award, under laid down organizational procedures, contract/s for

……The Principal values full compliance with all relevant laws of the land, rules, regulations, and economic use of resources and of fairness / transparency in its relations with its Bidder and/or Contractor.

Section 1 – Commitments of the Principal

(1) The Principal commits itself to take all measures necessary to prevent corruption and to observe the following principles:

(a) No employee of the Principal, personally or through family members, will in connection with the tender for, or the execution of a contract, demand, take a promise for or accept, for self or third person, any material or immaterial benefit which the person is not legally entitled to.

(b) The Principal will, during the tender process treat all Bidder(s) with equity and reason. The Principal will in particular, before and during the tender process, provide to all Bidder(s) the same information and will not provide to any Bidder(s) confidential/additional information through which the Bidder(s) could obtain an advantage in relation to the tender process or the contract execution.

(c) The Principal will exclude from the process all known prejudiced persons.

(2) If the Principal obtains information on the conduct of any of its employees which is a criminal offence under the IPC/PC Act, or if there be a substantive suspicion in this regard, the Principal will inform the Chief Vigilance Officer and in addition can initiate disciplinary action.

Section 2 – Commitments of the Bidder(s)/Contractor(s)

(1) The Bidder(s)/Contractor(s) commit himself to take all measures necessary to prevent corruption. He commits himself to observe the following principles during his participation in the tender process and during the contract execution.

(a) The Bidder(s)/Contractor(s) will not, directly or through any other Person or firm, offer, promise orgive to any of the Principal's employees involved in the tender process or the execution of the contract or to any third person any material or other benefit which he/she is not legally entitled to, in order to obtain in exchange any advantage of any kind whatsoever during the tender process or during the execution of the contract.

(b) The Bidder(s)/Contractor(s) will not enter with other Bidders into any undisclosed agreement or understanding, whether formal or informal. This applies in particular to prices, specifications,

Certifications, subsidiary contracts, submission or non-submission of bids or any other actions to restrict competitiveness or to introduce cartelization in the bidding process.

(c) The Bidder(s)/Contractor(s) will not commit any offence under the relevant IPC/PC Act; further the Bidder(s)/Contractor(s) will not use improperly, for purposes of competition or personal gain, or pass on to others, any information or document provided by the Principal as part of the business relationship, regarding plans, technical proposals and business details, including information contained or transmitted electronically.

(d) The Bidder(s)/Contractor(s) will not instigate third persons to commit offences outlined above or be an accessory to such offences.

Section 3 – Previous transgression

(a) The Bidder declares that no previous transgressions occurred in the last 3 Years with any other Company in any country conforming to the anti-corruption approach or with any other Public Sector Enterprise in India that could justify his exclusion from the tender process.

(b) If the Bidder makes incorrect statement on this subject, he can be disqualified from the tender process or action can be taken as per the procedure mentioned in "Guidelines on Banning of business dealings."

(For & On behalf of the Principal) (Office Seal)	For & On behalf of Bidder/Contractor) (Office Seal)
Place	Place
Date	Date
Witness 1:(Name & Address")	
Witness 2:(Name & Address	