EOI No. ICMR / EOI / ELISA / 2020 Dated 25th May 2020

Indian Council of Medical Research, New Delhi

Invites

Expression of Interest (EOI)

For

Transfer of Technology for Development of anti-SARS CoV-2-IgG antibody detection ELISA for screening human serum samples

CONTENTS

1. Letter of Invitation

INVITATION OF EXPRESSION OF INTEREST

Indian Council of Medical Research, New Delhi, invites Expression of Interest (EOI) through email from experienced Indian agencies for undertaking ***Transfer of Technology for Development of anti-SARS CoV-2-IgG antibody detection ELISA for screening human serum samples.***

The EOI Document containing the details of qualification criteria, submission details, brief objective & Scope of work and evaluation criteria etc. can be downloaded from the ICMR website

Schedule for the Proponents is as under:

EOI Document Number	ICMR / EOI / ELISA / 2020 dated 25th May 2020
Date of Publication	25th May 2020
Last date/Time of submission	28th May 2020 : 1300 hrs

Note: Due to the current COVID-19 situation, the EOI may be submitted through email to icmrnew.sm@icmr.gov.in Shortlisted manufacturing companies shall only be contacted for the further process of Technology Transfer. ICMR reserves the right to cancel this request for EOI and/ or invite afresh with or without amendments, without liability or any obligation for such request for EOI and without assigning any reason. Information provided at this stage is indicative and ICMR reserves the right to amend/add further details in the EOI.

2. Background

The Indian Council of Medical Research (ICMR), New Delhi, the apex body in India for the formulation, coordination and promotion of biomedical research, is one of the oldest medical research bodies in the world. The ICMR has always attempted to address itself to the growing demands of scientific advances in biomedical research on the one hand and to the need of finding practical

solutions to the health problems of the country, on the other. The ICMR has come a long way from the days when it was known as the IRFA, but the Council is conscious of the fact that it still has miles to go in pursuit of scientific achievements as well as health targets.

3. Objective

National Institute of Virology (NIV), Pune one of the constituent Institutes of the Indian Council of Medical Research (ICMR), New Delhi, has developed a new and useful TECHNOLOGY, (Technology as indicated in **Schedule-A**) and is the owner of said TECHNOLOGY including any underlying Intellectual Property(ies) and Commercialization rights. By virtue of financial support and research endeavour provided by ICMR, they legally possess the rights and authority to retain full or part of the 'TECHNOLOGY' by itself or to assign at its discretion full or part of the TECHNOLOGY including any patent(s) or intellectual property rights(s) on the invention(s) arising out of such endeavours, and/or ICMR is lawfully entitled to enter into any form of non-exclusive license agreements with selected manufacturer / manufacturers including transfer of the TECHNOLOGY through suitable agreement to any other interested manufacturers.

4. Broad Scope of Work

Subject to the terms and conditions of an Agreement, ICMR shall grant a non-exclusive License to the manufacturer (s), a royalty bearing right and license to use and practice the Technology and PROCESSES ("Licensed Technology") to manufacture, sell and commercialise the Product (Technologies as indicated in Schedule-A) in the designated Territory, including without limitation the right to use, copy, modify, distribute, make derivative works of and otherwise exploit the Licensed Technology including a non-exclusive right to manufacture, sell and market Products worldwide and the right to use Licensed Technology for manufacturing Products worldwide; during the Term of this Agreement ("License"). The agreement is proposed to be executed on "Non-Exclusive"

basis with multiple manufacturers, due to the large quantity demand of CODID-19 ELISA test kits that is being envisaged.

Manufacturers may quote Royalty not less than 5 % (five percentage) on Net Sales of the PRODUCT on half yearly basis as entered in the books of account maintained by LICENSEE, up to 31st March and up to 30th September respectively every year regularly and punctually and in any event not later than the first day of May and first day of November immediately following in every such year provided that the liability of the LICENSEE to pay royalty under and in terms of this sub-clause (A) shall accrue upon the commencement of the commercial sale of the Product ("**Royalty**") manufactured at the plant and shall continue till the Term from such commencement and after the Term the Licensed Technology will be royalty free. In the event of default in payment of royalty as above, interest @ 2% (two percentage) per annum on the Royalty due shall be charged for the first six months. If default persists for more than six months interest at similar rate will be charged on the accrued interest also from the due dates of payments till realisation/recovery of such amounts by the LICENSOR. Taxes and levies, as made applicable by the Government, shall be charged at the time of payments made to LICENSOR over and above the payments mentioned in this Agreement.

This LICENCE shall be valid from the EFFECTIVE DATE and subject to covenants and conditions herein contained and shall remain in force for a period of twenty (20) years commencing from the accrual of LICENSEE's obligation to pay Royalty to LICENSOR, after the commercialization of the Product (the "Term"). After the period of 20 years the LICENSE will be royalty free.

"**NET SALES**", means, with respect to a given calendar quarter, the gross amount invoiced, less the deductions calculated in accordance with the Indian Accounting Standards.

5. Instructions to Proponents

5.1 Documents to furnish

Proponents are requested to go through all pre-qualification requirements, scope of work for execution & requirements w.r.t technical / financial capabilities for acceptance and submission of documents for verification by ICMR.

Documents to be furnished are:

a. Authorization Letter (Format – 1)
b. Declaration - Expression of Interest (Format – 2)
c. Undertaking with regard to Blacklisting (Format-3)
d. Undertaking with regard to Non-Litigation (Format – 4)
e. Production Capacity Undertaking (Format-5)
f. Royalty Offer (Format-6)
g. EOI document with each page duly stamped and signed by the Authorized signatory.
h. Supporting documents, as mentioned in Format-2
i. MSME Certificate (if applicable)
j. Any other information which proponent may like to provide.

ICMR reserves the right to call for any clarifications confined in the broad scope, wherever such a clarification become necessary for proper judgment in evaluation.

5.2 Rejection Criteria

The application is liable to be rejected if:

a. The proposal is not submitted as per the requirements indicated in the EOI.
b. Not in the prescribed format.
c. Not properly stamped and signed as per requirements.
d. Received after the expiry of due date and time.

e. All relevant supporting documents are not furnished with the PQC.
f. The proposal shall be substantially responsive without any material deviation, failing which the proposal shall be summarily rejected.

5.3 Disclaimer

a. ICMR shall not be responsible for any late receipt of applications for any reasons whatsoever.
b. ICMR reserves the right to reject all applications without assigning any reasons thereof.
c. ICMR may relax or waive any of the conditions stipulated in this document as deemed necessary in the best interest of the ICMR without assigning any reasons thereof.
d. To include any other item in the Scope of work at any time after consultation with proponents or otherwise.

6. Evaluation Methodology

Screening of EOIs shall be carried out as per Pre-Qualification criteria mentioned in the EOI document and based on verification of documents submitted.

Shortlisted proponents shall be sent the Memorandum of Understanding (MoU), Material Transfer Agreement (MTA) and other required documentations.

7. Pre-Qualification Criteria (PQC)

The following will be the minimum Pre-Qualification Criteria (PQC). Responses not meeting the minimum PQC will be summarily rejected and will not be evaluated further:

Sl. No.	Pre-Qualification Criteria	Supporting copy of documents required ***(All documents must be self-attested by the authorised person of the proponent).***
1	The proponent shall be a legal entity, registered as a Company/LLP/Society/ partnership firm/ proprietorship firm under respective acts in India.	Company Incorporation Certificate from ROC/Partnership deed etc.
2	The proponent must be registered in India with taxation and other administrative authorities.	GST Registration or GST exemption certificate/ PAN Card
3	The proponent should have manufactured ELISA products for any other disease, atleast in three (3) immediate preceding years (2017-18 to 2019-20).	Pamphlet / brochure of the product
4	The proponent has to be profitable and should not have incurred loss atleast in three (3) immediate preceding years (2017-18 to 2019-20).	Certificate from the Chartered Accountant of the Organization/ Audited Balance sheets for last three financial years or Income Tax return.
5	The proponent should not have been black-listed by any Central /State Government / Public Sector Undertaking, Govt. of India, atleast	Undertaking on the Letter Head of the Proponent duly signed & Stamped by Authorized Signatory (As per format – 3).

	in three (3) immediate preceding years (2017-18 to 2019-20).	
6	The proponent should have a registered office and a manufacturing Unit in India	Registration copies of both
7	The proponent should not be involved in any major litigation that may have an impact of affecting or compromising the conditions required under this EOI and in the MoU.	Undertaking on Proponent's Letter Head, duly signed and stamped by the Authorized Signatory (As per format – 4)
8	GMP and ISO Certification	Registration copies of both
9	DCGI License, can be obtained parallely	Licence copy
10	Capacity to produce atleast one lakh ELISA test kits per week	Undertaking (As per format – 5)
11	Royalty offer	(As per format – 6)

In case of any clarification required, please contact:

<u>For scientific issues</u>

Dr. Gajanan Sapkal, Scientist-E, ICMR-NIV, Pune - 9766846024

<u>For Administrative issues</u>

Dr. R. Lakshminarayanan, ADG (A), ICMR, New Delhi - 9422517998

Format-1

Authorization Letter

(To be submitted on Agency's Letter Head)

To,

The Director General,

Indian Council of Medical Research,

Ansari Nagar, New Delhi.

Subject: Letter for Authorized Signatory

Ref. No. Ref: EOI No. ICMR / EOI / ELISA / 2020 dated 25th May 2020

Sir,

This has reference to your above mentioned Expression of Interest (EOI) for Transfer of Technology for Development of anti-SARS CoV-2-IgG antibody detection ELISA for screening human serum samples.

Mr./Miss/Mrs/Dr _____ is hereby authorized to submit the EOI documents and participate in the processing on behalf of M/s_____ (Agency Name).

The specimen signature is attested below:

Name: _____

(Specimen Signature of Representative)

_____

Yours faithfully,

(Signature of the Authorised signatory)

Name:

Designation:

Seal:

Date:

Place:

Format-2

Expression of Interest

(To be submitted on Agency's Letter Head)

To

The Director General

Indian Council of Medical Research,

Ansari Nagar, New Delhi.

Subject: Submission of Expression of Interest (EOI) for Transfer of Technology for Development of anti-SARS CoV-2-IgG antibody detection ELISA for screening human serum samples

Ref: EOI No. ICMR / EOI / ELISA / 2020 dated 25th May 2020

Sir,

The undersigned having read and examined in detail all the EOI documents pertaining to your transfer of technology, do hereby express the interest to undertake the manufacture of the product as mentioned in the EOI document. The details of the Company and contact person are given below:

1	Name of the Proponent	
2	Address	
3	Name, designation & address of the person to whom all references shall be made	
4	Telephone No. (with STD code)	
5	Mobile No. of the contact person	
6	Email ID of the contact person	

The following documents are enclosed:

Sl. No.	Documents required	Type of document attached	Page No.
1	Company Incorporation Certificate from ROC/Partnership deed etc.		
2	GST Registration or GST exemption certificate/ PAN Card.		
3	Pamphlet or Brochure		
4	Certificate from the Chartered Accountant of the Organization/Audited Balance sheets for last three financial years, Income Tax return.		
6	Proof of a registered office and a manufacturing Unit in India.		
8	GMP and ISO Certification. Registration copies of both		
9	DCGI License		
10	Authorization Letter	As per format – 1	
11	Expression of Interest	As per format – 2	
12	Undertaking on the Letter Head of the Proponent duly signed	As per format – 3	

	& Stamped by Authorized Signatory (As per format – 3).		
13	Undertaking on Proponent's Letter Head, duly signed and stamped by the Authorized Signatory	As per format – 4	
14	Undertaking to produce atleast one lakh test kit per week	As per format – 5	
15	Royalty Offer	As per format – 6	
16	MSME Certificate (if applicable)		

I/we hereby declare that my/our EOI is made in good faith and the information contained is true and correct to the best of my/our knowledge and belief.

Thanking you,

Yours faithfully,

(Signature of the Authorised signatory)

Name:

Designation:

Seal:

Date:

Place:

Format-3

Undertaking with regard to blacklisting

(To be submitted on Agency's Letter Head)

To,

The Director General,

Indian Council of Medical Research,

Ansari Nagar, New Delhi.

Subject: Undertaking regarding Blacklisting / Non-Debarment

Ref. No. Ref: EOI No. ICMR / EOI / ELISA / 2020 dated 25th May 2020

Sir,

It is hereby confirmed and declared that M/s _____ is not blacklisted/debarred by any Government Department/Public Sector Undertaking/ Private Sector/or any other agency for which works/assignments/services have been executed / undertaken.

Yours faithfully,

(Signature of the Authorised signatory)

Name:

Designation:

Seal:

Date:

Place:

Format-4

Undertaking with regard to Non-Litigation

(To be submitted on Agency's Letter Head)

To,

The Director General,

Indian Council of Medical Research,

Ansari Nagar, New Delhi.

Subject: Undertaking regarding Litigation

Ref. No. Ref: EOI No. ICMR / EOI / ELISA / 2020 dated 25th May 2020

Sir,

It is hereby confirmed and declared that M/s ----------, does not have any litigation / arbitration history with any Government department/ Public Sector Undertaking/ / or any other public authority with which any MoU was / has been executed / undertaken.

Yours faithfully,

(Signature of the Authorised signatory)

Name:

Designation:

Seal:

Date:

Place:

Format-5

Undertaking with regard to production capacity

(To be submitted on Agency's Letter Head)

To,

The Director General,

Indian Council of Medical Research,

Ansari Nagar, New Delhi.

Subject: Undertaking regarding Production Capacity

Ref. No. Ref: EOI No. ICMR / EOI / ELISA / 2020 dated 25th May 2020

Sir,

It is hereby confirmed and declared that M/s ----------, does have the capacity (including fund, material, staff etc) to produce and market atleast 01 (one) lakh test kits per week of anti-SARS CoV-2-IgG antibody detection ELISA for screening human serum samples.

Yours faithfully,

(Signature of the Authorised signatory)

Name:

Designation:

Seal:

Date:

Place:

Format-5

Undertaking for Royalty

(To be submitted on Agency's Letter Head)

To,

The Director General,

Indian Council of Medical Research,

Ansari Nagar, New Delhi.

Subject: Undertaking for Royalty

Ref. No. Ref: EOI No. ICMR / EOI / ELISA / 2020 dated 25th May 2020

Sir,

It is hereby confirmed that M/s ----------, agrees to pay a Royalty of ---- % (in words----) on Net Sales to the ICMR, as per the terms for the Transfer of Technology of anti-SARS CoV-2-IgG antibody detection ELISA for screening human serum samples.

Yours faithfully,

(Signature of the Authorised signatory)

Name:

Designation:

Seal:

Date:

Place:

SCHEDULE – A

TECHNOLOGY

Development of anti-SARS CoV-2 human IgG ELISA for COVID-19

ICMR's invention/Collaborated Inventions: It is developed by ICMR- National Institute of Virology (ICMR-NIV), Pune, India a premiere institute of ICMR.

Inventors: Dr. G N Sapkal*& Dr. Pragya Yadav*

Co-Inventors: Dr. Anita Shete, Dr. Rajlakshmi Jain, Dr. Gururaj Deshpande, Mr. Prasad Sarkale, Rajen Lakra, Deepak Mali, and BipinTilekar

Coordinators: Dr. Priya Abraham, Director, Scientist G,ICMR-NIV, Pune

Dr. Nivedita Gupta, Scientist F, ICMR, New Delhi

Need of Technology: A new coronavirus, SARS-CoV-2, has recently emerged to cause a human pandemic. Whereas molecular diagnostic tests were rapidly developed, serologic assays are still lacking, yet urgently needed. Validated serologic assays are important for sero-surveillance and sero-epidemiological studies.

Technology details:

Virus propagation and titration: SARS-CoV-2 strain (NIV2020-770) was propagated in the ICMR-NIV, Pune. The virus propagation and titration was performed in Vero CCL81 cells. Virus titer ($TCID_{50}$/ml) was calculated by the Reed and Muench method and found to be $10^{6.5}$ $TCID_{50}$/ml.

*Gamma inactivation of the virus:*Gamma irradiation of the virus stock was performed using Co-60 source (24Kgy) of GC- 5000 Gamma chamber. This irradiated stock was again innoculated in Vero CCL81 to confirm that the virus has been inactivated as per standard protocal.

Concentration of gamma inactivated antigen: Gamma irradiated SARS-CoV-2 infected tissue culture fluid (TCF)as well as control cell TCF were concentrated using Millipore 100 kDa filters and further passed through 0.2um filters, aliquoted and stored at -80^0C.

Serum/plasma panel generation

*Positive panel:*Real-time RT-PCR is currently the only approved method for confirmation of COVID-19 infection, which detects viral RNA present in different specimens (nasal/throat/oropharyngial) of patients in early phase of infection. For panel generation Serum/plasma of COVID-19 positive patients were collected on different post infection days (POD).

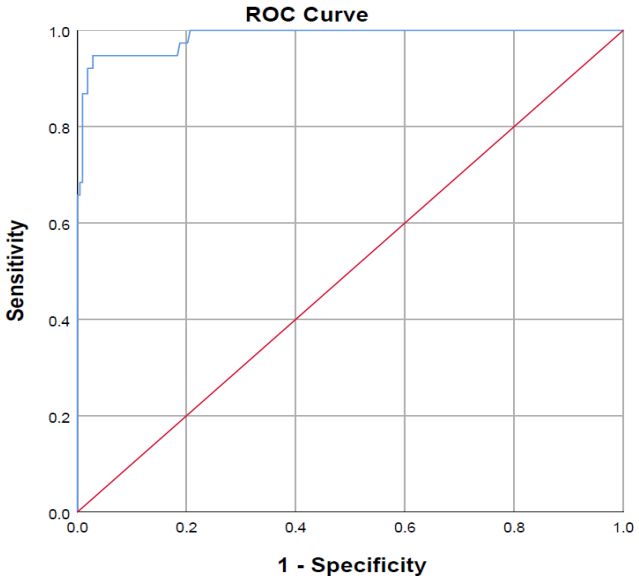
Negative panel: Blood/plasma sample collection from healthy, asymptomatic individuals negative for COVID-19 by real-time RT-PCR was collected.

Cross reactivity panel: The serum samples of influenza A, influenza B, respiratory syncytial virus, parainfluenza, NCoV-43, hepatitis C virus, hepatitis B virus were tested for analyzing cross reactivity. No cross reactivity was observed.

Usingvirus neutralization test as the gold standard,sensitivity and specificity of **Anti-SARS CoV-2 human** IgG ELISA was determined.

Optimization of Anti SARS-CoV-2 humanIgG ELISAwas performed using different coating, post-coating and conjugate buffers were used for finalization of assay.

- The performance and definition of cut-off of the assay was performed by Receiver Operator Characteristics (ROC) curve.
- A total of 251 samples were considered for the analysis (NT positives =38).
- The analysis was supported by the micro-neutralization assay results for the samples
- After the ROC analysis, the AUC was found to be 0.986
- The cut-off threshold for the assay, which gives a sensitivity of 92.1% and specificity of 97.7%.



Diagnostic Performance Parameters and Assay Performance

- Negative Predictive rate = 98.14%
- Positive Predictive rate = 94.44%
- Yoden's Index = 0.898
- Likelihood ratio = 95.29
- Diagnostic Odds ratio = 896.8
- Pearson's Correlation (r) = 0.7584 (95% CI 0.7004 – 0.8065)
- Cohen's Kappa (k) = 0.905 (95% CI 0.830 - 0.980).

Application areas/Applicability: Anti SARS CoV-2 IgG ELISA developed for detecting IgG antibody for purposes of sero- surveillance and identifying exposure in a “hot-spot” area with COVID-19 cases.

Unique points:

- The ELISA uses inactivated whole virusSARS CoV-2 antigen and hence can be performed at a BSL-2 laboratory setting
- This is the first indigenous, anti-SARS CoV-2 IgG antibody detection ELISA and is cost-effective for an Indian setting. This will be useful for screening for IgG in contacts of SARS-CoV-2 positive patients as well as studying the timing and duration of the antibody response.
- The test developed is rapid, cost-effective, user friendly and can detect anti-SARSCoV-2 IgG in serum/plasma in several samples simultaneously.

Up scaling Status

- The technology has been developed up to a large scale. The tissue culture grown SARS CoV-2 antigen will be prepared by infecting Vero CCL81 cells, which will be followed by inactivation using gamma irradiation.
- ELISA plates have been coated with the SARS CoV-2 antigen and uninfected VeroCCL-81 cells. The reactivity of the antigen will be checked against known positive and negative serum/plasma panel (controls).
- Individual kit lots will be tested for QA/Qc and only then dispatched as per need.

Validation (3rd party): External validation would be taken up soon

Patent profile: Not applicable

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