EOI No. ICMR/EOI/Dengue/Vaccine Trial/2022, dated 3rd March 2022

Expression of Interest (EOI)

Indian Council of Medical Research, New Delhi

Invites EoI for

Collaboration for conducting Phase-III clinical trial of vaccine candidates developed against Dengue Virus Disease

Indian Council of Medical Research
(Department of Health Research, GoI)
V. Ramalingaswami Bhawan,
P.O. Box No. 4911, Ansari Nagar,
New Delhi - 110029, India

CONTENTS

Letter of Invitation

1. INVITATION OF EXPRESSION OF INTEREST

Indian Council of Medical Research, New Delhi, invites Expression of Interest (EOI) through email from vaccine manufacturer/ pharma companies etc., who have developed potential vaccine candidate against Dengue virus disease and have successfully completed its phase I and phase II clinical trials. Under this EoI, ICMR offers institutional infrastructure for undertaking further R&D activities and vaccine clinical trial for evaluation of efficacy alongwith safety and immunogenicity as per regulatory requirement.

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 (https://www.icmr.gov.in)

Schedule for the Proponents is as under:

EOI Document Number	ICMR/EOI/ Dengue/Vaccine Trial/2022 dated 3rd March 2022
Date of Publication	3rd March 2022
Last date/Time of submission	11th March 2022

Note: Due to the current COVID-19 pandemic situation, the EOI may be submitted through email to jitendra.narayan@gov.in. Shortlisted firm(s)/organization(s) shall only be contacted for the further process of finalization of Agreement.

ICMR reserves the right to cancel this EOI and/ or invite afresh with or without amendments, without liability or any obligation for such EOI and without assigning any reason. Information provided at this stage is indicative and ICMR reserves the right to amend/add any further details in the EOI, as may be desired by the competent authority at ICMR and duly notified on its website

2. Background

Dengue virus disease causes significant morbidity and mortality across the globe. The global incidence of dengue has grown dramatically with about half of the world's population now at risk. Although an estimated 100-400 million infections occur each year, over 80% are generally mild and asymptomatic. Hence, the World Health Organization has identified Dengue to be one among the top ten global health threats in 2019. As of now, there is no specific treatment for dengue/severe dengue. Therefore, there is an urgent need to develop effective vaccines against Dengue viral disease.

The ICMR has been mandated to address the growing demands of scientific advances in biomedical research and find practical solutions to the health problems of the country. Efforts are being undertaken with a view to reduce the total burden of disease and to promote health and well-being of the population. ICMR, over the years, developed procedures, protocols and systems to support clinical trials. ICMR is the key agency for formulation of ethical guidelines for conduct of biomedical research in India. Several reforms concerning ethical and regulatory reviews have taken place in the country as applicable to clinical trials.

ICMR's institutional infrastructure spans across a network of national repute across all parts of the country. ICMR Institutes have made enormous contribution in tackling regional health problems. ICMR with its institutes has proven the strength in evaluation of new drugs, insecticides, vaccines, devices, diagnostic kits & other interventions for all diseases of national health priority along with neglected and regional priorities. The strength & potential of scientific team of ICMR and its institutional infrastructure can be utilized to conduct clinical trial for evaluation of safety and efficacy of vaccines.

In view of this, ICMR invites expression of interest from the Indian manufactures who have developed potential tetravalent vaccine candidate/or have non-exclusive license of the tetravalent vaccine candidates and intend to conduct field study as Phase-III clinical trial after completion of Phase-I and Phase-II trial for successful development of a Dengue vaccine.

3. Objective

To offer institutional infrastructure for undertaking R&D activities and Phase -III clinical trial for evaluation of efficacy along with safety and immunogenicity of tetravalent dengue vaccine candidate developed by Indian manufacturers or having license for the same.

4. Broad Scope of Work

i. ICMR is willing to collaborate/facilitate the Phase-III clinical trial of tetravalent dengue vaccine candidates 'developed by the Indian manufacturer/or having license to use' who have successfully completed Phase I and Phase II clinical trials in India or aboard.

ii. The collaboration with Indian vaccine manufacturer will be on **Royalty** (as per ICMR Guidelines) basis for a fixed term contract condition for conducting phase-III clinical trial.

iii. ICMR would provide technical support through team of experienced scientists in study planning, development of clinical trial protocol, implementation of Phase III Clinical trial of tetravalent Dengue vaccine, generating results/data analysis, outcome assessment, safety, immunogenicity & efficacy assessment, product improvement, and funding essential activities or others, if deemed fit upon the mutual understanding between ICMR and the collaborating company.

iv. ICMR through its institutes would provide support and facilitate the conduct of the clinical trial of developed vaccine candidate in India through one or more of its Affiliates/ Institutes, in collaboration with company/institutions in a professional and mutually agreed-upon manner and timelines, which will be decided later under a specific agreement.

v. The process developed by firm(s)/organization(s) during the course of development of the Product encompassing IP, shall be owned jointly by ICMR and firm(s)/organization(s). IP shall mean patents, rights to inventions, copyright and related rights, moral rights, rights in designs, rights in trademarks, rights to preserve the confidentiality of information (including know-how and trade secrets) and any other intellectual property rights, in each case whether registered or unregistered and including all applications (or rights to apply for and be granted), divisional, continuations, continuations-in-part, reissues, renewals or extensions of, and rights to claim priority from, such rights and all similar or equivalent rights or forms of protection which subsist or will subsist now or in the future in any part of the world regarding subject matter disclosed in Licensed patents; and shall include without limitation, the Technology, Licensed Patents and Licensed Trademarks, developed/ created pursuant to this EoI through ICMR support;

5. Revenue upon the product (vaccine)

Indian Manufacturer/Companies who have developed/having license of tetravalent Dengue vaccine candidate can collaborate with ICMR for undertaking Phase III clinical trial on **Royalty** basis. The manufacturers/companies interested in this collaboration may offer **Royalty 5% or**

above (in percent) on **Net Sales** of the **ENDPRODUCT** on half yearly basis as entered in the books of account maintained by Company/Manufacturer, up to 31st March and up to 30th September respectively every year regularly and punctually and in any event not later than the last day of April and last day of October immediately following in every such year provided that the liability of the Company/Manufacturer to pay royalty shall accrue upon the commencement of the commercial sale of the Product **("Royalty")** manufactured at the plant, as per the terms of ICMR-Technology Transfer and Revenue Sharing Guidelines 2021 and as per the amendments approved by the competent authority from time to time.

In the event of default in payment of royalty as above, interest @ 12% (twelve 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 realization/recovery of such amounts by the ICMR. Taxes and levies, as made applicable by the Government, shall be charged at the time of payments made to ICMR over and above the payments that shall be applicable as per terms of specified license Agreement to be executed with selected companies.

"NET SALES" shall mean gross sales made by company/its sub-licensee/marketing partner/affiliates based on ex-factory sale price of the product excluding sales Tax & Excise Duty or any other tax, as applicable at the given point of time, on invoice price which is realized from the party as defined by the Indian Accounting Standards and duly certified by the Chartered Accountant.

6. Validity of contract:

i. An Agreement shall be executed with Company/Manufacturer to decide conditions for execution of this collaborative activity. The Agreement shall have a defined timeline, which will be decided mutually by both the parties, considering the projected time to be taken in phase-III clinical trial.

ii. The Agreement shall be valid from the EFFECTIVE DATE and subject to covenants and conditions herein contained and shall remain in force for a specific period which shall not be less the twenty (20) years or shall be decided mutually with the approval of competent authority, commencing from the accrual of Company's obligation to pay **Royalty** to ICMR, after the commercialization of the Product (the "Term").

7. Details of documents to be furnished

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

Documents to be furnished are:

i. Authorization Letter (Format – 1)
ii. Declaration - Expression of Interest (Format – 2)
iii. Undertaking with regard to Blacklisting (Format-3)
iv. Undertaking with regard to Non-Litigation (Format – 4)
v. Undertaking with regard to ownership of vaccine candidate or license (Format – 5)
vi. Undertaking with regard to completion of Phase-I and Phase-II clinical trial (Format – 6)
vii. Production Capacity Undertaking (Format-7)
viii. Royalty Offer (Format-8)
ix. EOI document with each page duly stamped and signed by the Authorized signatory.
x. Supporting documents, as mentioned in Format-2
xi. MSME Certificate (if applicable)
xii. 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.

8. Rejection Criteria

The application is liable to be rejected if:

- The proposal is not submitted as per the requirements indicated in the EOI.
- Not in the prescribed format.
- Not properly stamped and signed as per requirements.
- Received after the expiry of due date and time.
- All relevant supporting documents are not furnished with the PQC.
- The proposal shall be substantially responsive without any material deviation, failing which the proposal shall be summarily rejected.

9. 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 proponent shall be sent the License agreement, approved by the competent authority, ICMR for execution.

10. 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 authorized person of the proponent)
1	The proponent shall be a legal entity, registered as Institution/Company/LLP/Society/ partnership firm/ proprietorship firm under respective Acts in India.	Registration of firm/ organization/ Company Incorporation Certificate from ROC/ Partnership deed etc. whichever is applicable
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 prior experience in R&D and manufacturing of vaccine/drug/pharma product for any infectious disease and must have marketed such products in three (3) immediate preceding years.	Research paper/Pamphlet / brochure of the product/DCGI License for existing product
4	The proponent has to be profitable and should not have incurred overall loss in past three (3) years. (applicable on commercial firms/organizations only)	Certificate from the Chartered Accountant of the Organization/ Audited Balance sheets for last three financial years or Income Tax return.
5	The proponent should have good track record and not black-listed by any Central /State Government / Public Sector Undertaking, Govt. of India, at least in three (3) immediate preceding Years. (applicable on commercial firms/organizations only)	Undertaking on the Letter Head of the Proponent duly signed & Stamped by Authorized Signatory (As per format – 3).
6	The proponent should have a registered office, 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	The proponent should have ownership rights of vaccine candidate or have owned license for using it to vaccine development and production.	Undertaking on Proponent's Letter Head, duly signed and stamped by the Authorized Signatory (As per format – 5)
	The proponent should have completed Phase-I and Phase-II clinical trial using the vaccine candidate.	Undertaking on Proponent's Letter Head, duly signed and stamped by the Authorized Signatory (As per format – 6) and should submit the outcome report.
9	GMP and ISO Certification (applicable on commercial firms/organizations only)	Registration copies of both
10	Capacity to produce at least one lakh doses per week	Undertaking (As per format – 7)
11	Royalty offer	(As per format – 8)
12	Business Plan	A brief concept consisting of the following details to be enclosed: Key Milestones such as Technical/ Regulatory/ IP/ Business Development/ Commercialization etc with measurable parameters & timelines for each component

11. Disclaimer

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

12. Contact details for enquiry

In case of any clarification required, please contact:

For scientific issues-

Dr. Leyanna Susan George, Scientist-E, ICMR-HQ, Delhi, Email: george.leyanna@icmr.org.in

For Administrative issues

Dr. R. Lakshminarayanan, DDG (Admin), ICMR HQ, New Delhi

Email: -lakshminarayanan.r@icmr.gov.in

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: EOI No. ICMR/EOI/ Dengue/Vaccine Trial/2022dated ……..

Sir,

This has reference to your above-mentioned Expression of Interest (EOI) for collaboration for conducting Phase-III clinical trial of tetravalent vaccine candidates developed against Dengue virus disease.

Mr./Ms./Mrs./Dr……..is here by authorized to submit the EOI documents and participate in the processing on behalf of M/s……. (Agency Name)……., who's signature is below.

(Specimen Signature of Representative)

Date:

Place:

Yours faithfully,

(Signature of the Authorized signatory)

Name:……..

Designation:……..

Seal:……..

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) collaboration for conducting Phase-III clinical trial of tetravalent vaccine candidates developed against Dengue virus disease.

Ref: ICMR/EOI/ Dengue/Vaccine Trial/2022dated ……..

Sir,

The undersigned having read and examined in detail all the EOI documents pertaining to conduct of Phase-III clinical trial of tetravalent vaccine candidates developed against Dengue virus disease do hereby express the interest to undertake the research & development/ commercialization /manufacture/ sale of the product as mentioned in the EOI document. The details of the Company and contact person are given below:

Name of the Proponent	
Address	
Name, designation & address of the person (to whom all communications shall be made)	
Telephone No. (with STD code)	
Mobile No. of the contact person	
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	DCGI/CDSCO license for the existing products available in the market		
4	Certificate from the Chartered Accountant of the Organization/Audited Balance		

	sheets for las three financial years, Income Tax return.		
5	Proof of a registered office and a manufacturing Unit in India.		
6	GMP and ISO Certification. Registration copies of both		
7	Authorization Letter	As per format – 1	
8	Undertaking with regard to blacklisting, on the Letter Head of the Proponent duly signed& Stamped by Authorized Signatory	As per format – 3	
9	Undertaking with regard to Non-Litigation, on Proponent's Letter Head, duly signed and stamped by the Authorized Signatory	As per format – 4	
10	Undertaking with regard to ownership of vaccine candidate or license, on Proponent's Letter Head, duly signed and stamped by the Authorized Signatory. Copy of ownership rights (IPR) or rights under specific license must be enclosed.	As per format – 5	
11	Undertaking with regard to completion of Phase-I and Phase-II clinical trial, on Proponent's Letter Head, duly signed and stamped by the Authorized Signatory along with outcome report.	As per format – 6 Supporting documents to be enclosed.	
12	Undertaking for declaring capacity to produce at least one lakh doses per week	As per format – 7	
13	Royalty Offer	As per format – 8	
14	MSME Certificate (if have any)		

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 Authorized signatory)
Name:
Designation:
Seal:
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: EOI No. ICMR/EOI/ Dengue/Vaccine Trial/2022dated ……..

Sir,

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

Yours faithfully,

(Signature of the Authorized signatory)
Name:
Designation:
Seal:
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: EOI No. ICMR/EOI/ Dengue/Vaccine Trial/2022 dated ……..

Sir,

It is hereby confirmed and declared that M/s…..... and owner of the firm/board of directors, do not have any litigation / arbitration pending/under trial in court.

Yours faithfully,

(Signature of the Authorized signatory)
Name:
Designation:
Seal:
Place:

Format-5

Undertaking with regard to ownership of vaccine candidate or rights under license

(To be submitted on Agency's Letter Head)

To,

The Director General,

Indian Council of Medical Research,

Ansari Nagar, New Delhi.

Subject: Undertaking regarding ownership of vaccine candidate or rights under specific license.

Ref: EOI No. ICMR/EOI/ Dengue/Vaccine Trial/2022 dated ……..

Sir,

It is hereby confirmed and declared that M/s…..... do have ownership rights /have granted non-exclusive license w.r.t. tetravalent vaccine candidate developed against the Dengue virus disease.

2. The company has all the rights to collaborate or grant further license to perform **Clinical Trials**.

3. The company has all the rights to collaborate or grant further license to perform R&D.

4. The company has all the rights to collaborate or grant further license to commercialize final product.

5. The company has all the rights to offer/share revenue/royalty arising out of Net Sales of the finished product.

Encl: as above as applicable

Yours faithfully,

(Signature of the Authorized signatory)
Name:
Designation:
Seal:

Place:

Format-6

Undertaking with regard to completion of Phase-I and Phase-II Clinical Trials

(To be submitted on Agency's Letter Head)

To,

The Director General,

Indian Council of Medical Research,

Ansari Nagar, New Delhi.

Subject: Undertaking regarding completion of Phase-I and Phase-II Trials w.r.t. tetravalent vaccine candidate against Dengue virus disease.

Ref: EOI No. ICMR/EOI/ Dengue/Vaccine Trial/2022 dated ……..

Sir,

It is hereby confirmed and declared that M/s…..... has completed/jointly completed necessary R&D, preclinical studies and Phase-I and Phase-II clinical trials.

2. The company has the rights/license to collaborate for Phase-III clinical trial.

Encl: Outcome report of Phase-I and Phase-II clinical Trials

Yours faithfully,

(Signature of the Authorized signatory)
Name:
Designation:
Seal:

Place:

Format-7

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 with regard to production capacity.
Ref: EOI No. ICMR/EOI/ Dengue/Vaccine Trial/2022 dated ……..

Sir,

It is hereby confirmed and declared that M/s…… has full capacity (including infrastructure, fund, material, staff etc.) for manufacturing the required vaccine doses min. 01 (one) lakh unit per week.

Yours faithfully,

(Signature of the Authorized signatory)
Name:
Designation:
Seal:
Place:

Format-8

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: EOI No. ICMR/EOI/ Dengue/Vaccine Trial/2022 dated ……...

Sir,

It is hereby confirmed that M/s ……, agrees to pay a Royalty of **……. % (……. Percent)** to the ICMR to be calculated against the **Net Sales** done with respect to the product developed under this collaboration.

(As per the terms of ICMR-Technology Transfer and Revenue Sharing Conditions, the **"NET SALES"** shall mean gross sales made by company/its sub-licensee/marketing partner/affiliates based on ex-factory sale price of the product excluding sales Tax & Excise Duty or any other tax, as applicable at the given point of time, on invoice price which is realized from the party as defined by the Indian Accounting Standards and duly certified by the Chartered Accountant)

Yours faithfully,

(Signature of the Authorized signatory)
Name:
Designation:
Seal:
Place:

SCHEDULE – (A)

Joint collaboration for development of vaccine against Dengue

I. Dengue Problem statement:

The Dengue virus is a mosquito-borne viral disease that is transmitted by the bite of the female mosquitoes mainly of the species *Aedes aegypti* and, to a lesser extent, *Ae. albopictus*. It belongs to the Genus Flavivirus and consists of four serotypes (DENV-1, DENV-2, DENV-3 and DENV-4). Recovery from infection by one of the serotypes provides lifelong immunity against that particular serotype. However, cross-immunity to the other serotypes after recovery is only partial and temporary. Subsequent infections by other serotypes increase the risk of developing severe dengue. The clinical manifestations of dengue range from asymptomatic cases to flu-like illnesses to severe dengue occurring as a result of plasma leakage resulting in fluid accumulation, respiratory distress, severe bleeding, or even organ impairment.

The actual numbers of dengue cases are underreported and many cases are misclassified. However, the incidence of dengue has grown dramatically around the world in recent decades with extension of the disease to pediatric population. A recent estimate indicates an occurrence of 390 million dengue infections per year (95% credible interval 284–528 million), of which 96 million (67–136 million) manifest clinically (with any severity of disease). Hence, the World Health Organization has identified Dengue to be one among the top ten Global Health threats in 2019. In India, the Dengue sero-prevalence survey conducted from June 2017 to April 2018, revealed that the overall seroprevalence of DENV infection in India was 48·7% (95% CI 43·5–54·0), increasing from 28·3% (21·5–36·2) among children aged 5–8 years to 41·0% (32·4–50·1) among children aged 9–17 years and 56·2% (49·0–63·1) among individuals aged between 18–45 years. The seroprevalence was found to be higher in the southern (76·9% [69·1–83·2]), western (62·3% [55·3–68·8]), and northern (60·3% [49·3–70·5]) regions of India.

II. Need and utility of invention:

Dengue, has emerged as a major public health problem in India with an increase in the number of cases. However, there is no specific treatment for Dengue and its management is purely symptomatic. The prevention and control strategy currently available is mainly focused on vector control practices. Hence, there is an urgent need to develop effective vaccines against Dengue viral disease.

III. Scope for collaboration:

This collaboration will open up scope for development of a new dengue vaccine. It will enable

the conduct of Phase III Clinical trial of Dengue tetravalent vaccine across different sites in India.

IV. Role of ICMR

a. ICMR would provide technical support through team of experienced scientists in study planning, development of clinical trial protocol, implementation of Phase III Clinical trial of Dengue tetravalent vaccine, results/data analysis, assessment, of efficacy along with safety & immunogenicity, product improvement, and funding required activities or other requirements, if deemed fit upon the mutual understanding between ICMR and collaborative company.

b. ICMR through its institutes would provide support and facilitate the conduct of the clinical trial of developed dengue vaccine candidate in India through one or more of its Affiliates/ Institutes, in collaboration with company/institutions in a professional and mutually agreed-upon manner and timelines, which will be decided later under the MoA/MoU.

c. ICMR shall operationalise the phase III clinical trial of dengue vaccine candidates that have successfully completed its phase I and phase II clinical trials.

V. Role of company

a. The Company will collaborate with ICMR in conducting the Phase III clinical trials by conducting specific activities like development, manufacturing and commercialization of COVID-19 vaccine.

b. The partnering company should provide necessary infrastructure and depute experienced/skilled manpower.

c. The company will share the technical data with ICMR and participate in all discussions in a professional and mutually agreed-upon manner.

d. The company will allow authorized personnel/scientist/team of ICMR to participate in R&D activities and to carry out specific project activities as envisaged under this EoI and subsequent MoA.

e. The company shall be responsible for obtaining all the regulatory approvals and supporting other mutually agreed upon activities required starting from R&D for product development to its commercialization.

VI. Envisaged outcome:

Development of a safe and efficacious Dengue tetravalent vaccine that would elicit a strong, durable, and broad immune responses for robust clinical protection against all four strains of the Dengue virus.

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