



No.ICMR-VCRC/ST/Tender/*Wolbachia*/2019-20/

Date: 10.09.2019

NOTICE INVITING TENDER UNDER TWO BID SYSTEM

TENDER DOCUMENT TO ASSESS THE RISK ASSOCIATED WITH THE FIELD RELEASE OF *Aedes aegypti* MOSQUITOES CARRYING *Wolbachia* IN INDIA

Tenders are invited under two bid system to undertake the above task by the Director, ICMR-Vector Control Research Centre, Puducherry–605 006.

Background

Dengue control continues to be a priority for public health authorities across the globe. The viral disease is transmitted primarily by the mosquito *Aedes aegypti*, which also transmits a number of other viruses, including Chikungunya, Zika and Yellow fever viruses. An estimated 390 million dengue infections occur annually as the virus spreads into new geographic regions and affects both urban and rural settings. *Wolbachia* is an endosymbiotic bacterium, naturally occurs in 60% of insects. The *Wolbachia* trans-infected *Ae. aegypti* strains are shown to inhibit the replication and transmission of dengue virus. *Ae. aegypti*, carrying *Wolbachia* are released and tested in different countries for their potency to establish in nature and control dengue.

An alternate strategy for dengue control in India

The Indian Council of Medical Research–Vector Control Research Centre (ICMR–VCRC), Puducherry has planned to explore/ undertake the alternate strategy for dengue control, through releasing *Ae. aegypti* carrying *Wolbachia* in the field.

Bio-safety aspects

The bio-safety of the proposed release needs to be assessed and is considered a key element for obtaining permission from the Regulatory Body. Thus, all elements of risk associated with the release of *Ae. aegypti* containing *Wolbachia* into naturally occurring populations need to be identified and assessed to ensure that the field release would “cause no more harm” than that posed by natural *Ae. aegypti* populations. The novelty of the project is to state that there exists only a few empirical data-set and subsequently high levels of uncertainty surrounding the potential for negative impacts. Since the historical data relevant to assessing risk are lacking in India, expert knowledge from related disciplines may be elicited as appropriate proxy for empirical data to address uncertainties in knowledge assumptions and limited data-sets. Keeping in view of the novelty of the system, and potentially wide-ranging effects on individuals and communities in release areas, non-technical community experts must also be involved in the elicitation of risk estimates as well as technical experts to ensure transparency in the process.

Call for Risk Assessment

The proposed risk analysis is to determine the likelihood of an event occurring and the consequences of the event if it does occur. The level of risk is to be calculated from the product of the likelihood and consequence. To assess the risk associated with the proposed release, two risk end points (undesirable states of a system) may be considered, as under:

- i) that release would not occur within a set time frame due to logistical, regulatory, political, epidemiological, and community concerns, referred to as “Don’t Achieve Release” (DAR)

and

- ii) that the release of *Ae. aegypti* mosquitoes carrying *Wolbachia* would result in more harm through impacts on the economy, social wellbeing and community health, future mosquito control effort, and/or adverse changes to the biology of the vector, *Wolbachia* or dengue viruses, in the release locations when compared with the current situation within a 30-year timeframe, known as “Cause More Harm” (CMH).

Also, the risk assessment needs measures to incorporate feedback opportunities to improve predictions and reduce uncertainty.

Objective

The main objective of this assessment is to identify any potential hazards in considering the use of *Wolbachia*-transfected *Aedes aegypti* population in India, and to evaluate the possible ecological and public health risks associated with such hazards.

Methods / Techniques desired to be adopted, but not limited to the following:

The hazard identification process may involve (i) a thorough / critical review of literature, (ii) consultations with experts at the local, national and international level and (iii) stakeholders such as academic / researchers, medical and healthcare professionals, government agencies and non-governmental organisations by conducting interactive meetings / discussions / workshops, and through e-mail.

The assessment should essentially be focused to answer the following questions:

1. What are the potential hazards associated with the release of *Aedes aegypti* mosquitoes carrying *Wolbachia* into the environment?
2. What are the possible consequences?
3. How severe are/could be the potential hazards?
4. How likely are the potential hazards?
5. What are the levels of associated risk?

If the risks are high or severe, what additional measure(s) are or can be undertaken to reduce the levels of risk?

Analysis

It is desired to

- (i) describe problem formulation
- (ii) draw hazard chart / map
- (iii) perform fault tree analysis and
- (iv) use Bayesian belief network model to capture expert opinion of the likelihood and consequence of the potential hazards.

Expected Deliverables

The overall end product [deliverables] (report) should comprise of the results of the risk analysis, providing the details of specific hazard domains identified, the model (preferably Bayesian) networks constructed to explore the hierarchical structure and relationship of the hazards, and the final expert-derived estimates of risk associated with the release of *Ae. aegypti* carrying *Wolbachia* in India.

Terms of Reference (TOR):

- The broad principles and specific procedures are to be adopted for carrying out the assignment.
- The expertise needed / professional requirements for each of the issues identified / outlined are to be drawn from respective disciplines / Institutes, across the country.

- Analysis of data / information, and report writing and submission are to be strictly in confirmation with the requirements, stipulated.
- **The cost for carrying out this risk assessment to be furnished in detail, indicating all aspects (to meet the objectives) with justification thereof.**
- The Schedule of activities and outcome are to be updated at every stage, with the Director, ICMR-VCRC or the designated Official of ICMR–VCRC.
- The date of submission of the Final Report is to be adhered to, strictly.
- All the data, including the basic (raw) and analyzed ones are to be handed over to the Director, ICMR-VCRC or the designated Official of ICMR-VCRC, along with the Final Report.
- The report either in full or in part should not be shared with anyone other than the Director, ICMR-VCRC or the designated Official of ICMR-VCRC.

Note: The Director, ICMR-VCRC reserves the right to cancel this tender and / or invite afresh with or without amendments to this tender, without liability or any obligation for such request for application and without assigning any reason. Information provided at this stage is indicative and the ICMR – VCRC reserves the right to amend / add further details in the document.

TERMS & CONDITIONS

1. Tender is invited in sealed cover in two bid system from the Agencies / Organizations having valid essential registrations along with PAN Card, up to date - VAT clearance certificate/ GST Registration certificate for taking up Risk Assessment in ICMR-VCRC, Puducherry.
2. A Demand Draft for ₹ 1000/- (Rupees one thousand only) towards the cost of the tender document to be drawn in favour of **“The Director, ICMR-VCRC, Puducherry-605 006”**, payable at Puducherry and shall be enclosed along with the tender.
3. The tender should be accompanied with an Earnest Money Deposit @ 5% of the cost quoted, drawn in favour of **“The Director, ICMR-VCRC, Puducherry-605 006”**, payable at Puducherry – 605 006. Agencies registered with MSME, NSIC and govt. public undertakings, which are exempted from payment of EMD may be allowed exemption on production of relevant certificate.
4. The tender should be submitted in two sealed covers and for technical details, refer to **Annexure VI**.
 - a) One sealed cover should be superscripted as **“Technical Bid”** in r/o. Tender **“TO ASSESS THE RISK ASSOCIATED WITH THE FIELD RELEASE OF Aedes Aegypti MOSQUITOES CARRYING WOLBACHIA IN INDIA”** and should contain the following documents:
 - i. The duly filled in Proforma (as in **Annexures – I to III & V**).
 - ii. **Profile showing evidence/ proof for similar assignments carried out in the past and cost of such assignments, along with the contact details of the agencies for whom the assignment was carried out (for verification purpose).**
 - iii. Demand Draft towards the cost of tender document for ₹1000/-.
 - iv. Demand Draft towards the EMD.
 - v. All other required documents such as IT, Service Tax Registrations/GST Registration etc.
 - vi. Average annual turnover of the Agency / Organization.
 - vii. A certificate in the Agency / Organization letter head certifying that the firm has not been black-listed so far.

- b) The other sealed cover should be superscripted as “**Financial Bid**” in r/o. Tender “TO ASSESS THE RISK ASSOCIATED WITH THE FIELD RELEASE OF *Aedes Aegypti* MOSQUITOES CARRYING *WOLBACHIA* IN INDIA” and should contain duly filled in Proforma (Annexure IV). Both the Sealed covers should be addressed to **The Director, ICMR-VCRC, Puducherry-605 006**.
5. **Duration of the contract from the date of acceptance of tender shall be 02 months.**
 6. **The Consultancy Evaluation Committee constituted by ICMR-VCRC will assess the ability of the tenderer participating in the bid to render the requisite services based on their profile, compliance with regard to our technical requirement, methods used for risk analysis, evidences for past experience of similar nature of assignment and on such other criteria as it may fix.**
 7. The Agencies / Organizations are required to submit the cost of the tender document by way of a D.D drawn in favour of the Director, ICMR-VCRC, Puducherry-605 006 along with the attested copies of valid Registration Certificate, Pan-card and Up-to date Service Tax Clearance /GST Registration certificate along with the bid documents, failing which the tenderer shall be declared as non-responsive and the bid will be summarily rejected.
 8. The Agencies / Organizations also should submit a self-undertaking accepting all the terms and conditions of ICMR-VCRC along with their tender document without which the tender will be summarily rejected.
 9. If any of the tender are rejected for any reasons the cost of the tender document will be forfeited in favour of ICMR-VCRC. No claim in this regard will be entertained at any point of time.
 10. The Agencies / Organizations, while submitting the tender, shall furnish an undertaking along with the tender about the authenticity of the tender document. Conditional tender will not be accepted under any circumstances.
 11. The Demand Draft produced along with the tender should be drawn from any Nationalized Bank in favour of ‘**The Director, ICMR-VCRC, Puducherry-605 006**’, payable at Puducherry.
 12. Other details can be obtained from the tender document given below.
 13. Tender received after the due date and time will not be considered under any circumstances. Incomplete and conditional tender shall not be accepted. In case the date of opening of tender is declared a holiday for unexpected reasons, the tender will be opened in the afternoon of the next working day.
 14. **The Tender is liable to be rejected inter-alia:**
 - a. If it is not in conformity with the instructions mentioned in the tender document.
 - b. If it is not properly signed by the Tenderer.
 - c. If it is received by email / fax.
 - d. If it is received after the closing date and time.
 - e. If the cost of the tender Document and the Earnest Money Deposit are not enclosed with the tender by way of D.D.
 - f. If it is not accompanied with proper documents.
 - g. If the self-undertaking accepting the terms and conditions of the tender is not submitted along with the tender document.

15. The Director, ICMR-VCRC reserves the right to:

- a. Reject any or all tenders in full or part without assigning any reason there to.
- b. Revise the requirement at any time prior to or at the time of placing the order.
- c. Change the conditions of the tender according to the circumstances as deemed fit.

Last date & time for receipt of tender document under two bid system.	Dt: 30.09.2019	Time: 05.30 p.m.
Date & time of opening of Technical Bid by Consultancy Evaluation Committee (CEC).	Dt: 03.10.2019	Time: 10.00 a.m.
Date & time of opening of Financial Bid by Consultancy Evaluation Committee (CEC) in respect of technically qualified bidders	Dt: 04.10.2019	Time: 10.00 a.m.

Payment terms:

- (i) 1st Instalment of 25% payment will be released after acceptance of the award of contract and signing of the MoU between ICMR-VCRC and the tenderer.
- (ii) 2nd Instalment of 50% payment will be released after evaluation of interim Report (mid-term evaluation)/ after one month from the date of award of the contract and
- (iii) 3rd instalment (final) of 25% payment will be released on submission and acceptance of the final report by the committee constituted for the purpose after 2 months from the date of award of the contract.

Penalty Clause:

Compensation for delay of work will be charged @ 1.5% of tendered cost of work, per month of delay, computed on per day basis.

DIRECTOR

Suggested references for more details on technical aspects of risk assessment:

- Popovici J, Moreira LA, Poinignon A, Iturbe-Ormaetxe I, McNaughton D, O'Neill SL. Assessing key safety concerns of a Wolbachia-based strategy to control dengue transmission by Aedes mosquitoes. Memórias do Instituto Oswaldo Cruz. 2010 Dec;105(8):957-64. URL: <http://www.scielo.br/pdf/mioc/v105n8/02.pdf>
- Murray JV, Jansen CC, De Barro P. Risk associated with the release of Wolbachia-infected Aedes aegypti mosquitoes into the environment in an effort to control dengue. Frontiers in public health. 2016 Mar 22;4:43. URL: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4802996/pdf/fpubh-04-00043.pdf>
- Murphy B, Jansen C, Murray J, De Barro P. Risk analysis on the Australian release of Aedes aegypti (L.) (Diptera: Culicidae) containing Wolbachia. Austrália: CSIRO Entomology. 2010 Mar. URL: http://www.eliminatedengue.com/library/publication/document/csiro_report_australia_2010.pdf
- Hoc TQ, UyenNinh T, Tuat NV, Hung NV, Cuong ND. Risk assessment of the pilot release of Aedes aegypti mosquitoes containing Wolbachia. URL: http://www.eliminatedengue.com/library/publication/document/july_2011_ra_report_eng.pdf
- Iturbe-Ormaetxe I, O'Neill SL. Use and release of mosquitoes for the control of dengue transmission: a world-first trial in Australia. In Biosafety and the Environmental Uses of Micro-Organisms: Conference Proceedings 2015 (pp. 159-174). URL: <https://www.oecd-ilibrary.org/docserver/9789264213562-15-en.pdf?expires=1567659253&id=id&accname=guest&checksum=E07160870CCAFF3F2347BE1090B39D5>

CHECK LIST

(To be filled by the Agency / Organization compulsorily)

Tender should be enclosed with the documents as given in the Check-List

NAME OF THE WORK: **TO ASSESS THE RISK ASSOCIATED WITH THE FIELD RELEASE OF Aedes Aegypti MOSQUITOES CARRYING WOLBACHIA IN INDIA** DUE ON:

Sl.No.	Description	Tenderer should give appropriate remarks against each item i.e. Yes/No/Agreed/Not agreed/Enclosed/Not Enclosed etc.
01	Acceptance of General terms & conditions	
02	EMD D/D No. dt: on	
03	Tender cost D/D No. dt: on	
04	Catalogues/Brochure and technical details	
05	Validity of the offer _____	
06	Under two bid system-sealed and superscripted envelope is submitted as per the terms & conditions (The Original Tender document i.e., Technical Bid & Financial Bid with terms & conditions and the annexures signed by the tenderer at the bottom of each page with his Office seal duly affixed)	
07	Attested photocopy of latest GST issued by the department of Trades and Taxes/Sales Tax etc., as the case may be.	
08	Attested documents of Annual turnover for last three years (i.e.,) 2016-17, 2017-18 & 2018-19	
09	Proof of filing Income Tax return (Photocopy attested) for the Financial Years 2016-17, 2017-18 & 2018-19	
10	Copy of partnership deed in case of partnership firm with undertaking and authorization for signing the tender document?	
11	Evidence/proof of similar assignment(s) carried out in the past with contact details of the agencies (Refer to 4. a) ii under 'Terms & Conditions')	

[Please note that failure to submit any one of the above certificates/documents shall render the tender invalid]

N.B: 1. All the photocopies are to be self-attested.

2. Valid up-to-date means the certificate should be valid on or beyond the date of opening of tender.

Signature of Tenderer with seal
Name of the Tenderer
Address of the Tenderer

To

The Director,
ICMR-Vector Control Research Centre,
Department of Health Research,
Government of India,
Indira Nagar, Medical Complex,
PUDUCHERRY 605006.

Sub:-Assessment of Risk associated with the Field release of *Aedes aegypti* mosquitoes carrying *Wolbachia* in India.

Sir,

..... for and on behalf of Messrs.....
..... submit the bid for participation in the tender invited by the
Director, ICMR-VCRC for the above said assignment and to state as under.

1. It is certified that offered work is as per the prescribed specifications. The literature /pamphlet/brochure containing details of the requirement of the work along with user list are attached herewith for perusal and ready reference for the purpose of evaluation.
2. It is certified that all the terms and conditions are acceptable to us and agreed to abide by all the said terms and conditions.
3. It is certified that we agree to keep this offer valid for a period up to _____ .
4. It is certified that the amount of EMD remitted by Demand draft/Banker's cheque/Bank guarantee bearing No..... dated..... drawn on (Name of the bank)..... In favour of **the Director, ICMR-VCRC, payable at Puducherry** and Tender cost ₹ 1000/- for this assignment is remitted by Demand draft bearing No..... dated..... drawn on (Name of the Bank) In favour of **the Director, ICMR-VCRC, payable at Puducherry** are put together in a envelope sealed and marked on the cover "**Assessment of Risk associated with the Field release of *Aedes aegypti* mosquitoes carrying *Wolbachia* in India**", Due onfor consideration.
5. Charges have been indicated correctly in the tender and have not offered lesser than the present total cost quoted to any other government organization in India.

Encl: as above

Date:

Name:

Signature of the Tenderer

Place:

Seal:

STATUS OF THE AGENCY / ORGANIZATION

- 01 Name of the Agency / Organization (in full)

- 02 Whether a proprietary firm/partnership firm/Pvt. Company Ltd./Public Company Ltd./Trust or other

- 03 Registration No.

- 04 Income Tax PAN No. (enclose a copy)

- 05 GST No. (enclose a copy)

- 06 Authorities with whom registered

- 07 Name & Address of the Proprietor/Partners/Directors/Authorized Attorneys with full address, Telephone No. & E-mail ID

- 08 Previous working experience (in brief)

- 09 Resourcefulness / Financial status

- 10 Name of the Bankers & Address with Telephone Number

- 11 Infrastructure Facility available with the Tenderer

- 12 Notice of time required to attend short falls, if any, identified by the Consultancy Evaluation Committee

Signature & Name with Designation
of Tenderer with seal

COMMERCIAL OFFER / FINANCIAL BID (FORMAT)

(To be submitted in duplicate in letter head)

SCHEDULE OF WORK

Name and address of the Indenter: THE DIRECTOR
ICMR-VECTOR CONTROL RESEARCH CENTRE
Department of Health Research,
Indira Nagar,
PUDUCHERRY 605 006, INDIA

Tender document to Assess the Risk Associated with the Field Release of *Aedes aegypti* mosquitoes carrying *Wolbachia* in India

Due on:

Sl. No.	Description of item	Charges for the work (in Rs. both figures & words)
01	<p>Assessment of Risk associated with the Field release of <i>Aedes aegypti</i> mosquitoes carrying <i>Wolbachia</i> in India</p> <p>Cost of the Risk Assessment work (Please give item-wise details with justification thereof)</p> <p>GST</p> <p>Any other charges not covered above</p>	

1. Prices given above are firm with all duties and taxes as shown above separately.
2. Submission of report – As mentioned in the Technical Bid.
3. We are bound by tender terms and conditions.
4. Any of the above work can be modified/deleted/reduced from the above schedule at the sole discretion of the Director, ICMR- VCRC, Puducherry.
5. The above quoted prices are valid for 60 days.

Signature of the Tenderer
Name & Address of the Tenderer with seal.

DECLARATION

I/We have read the above terms and conditions carefully and taken note of them for compliance and I/We hereby accept/agree to abide by all these terms and conditions.

I/We also declare that I/we have not been black-listed by any organization (Govt./ Private) and that if evidence to the contrary is found then I/ we are liable for any action deemed fit by the Director, ICMR-VCRC.

Date:

Signature of the Tenderer

Name & Address of the Tenderer and Seal
(Phone/Fax No./E-mail ID may also be stated for easy communication)

ICMR-Vector Control Research Centre
Puducherry

Brief Note on

***Wolbachia*-based control of dengue/chikungunya transmitted by *Aedes aegypti*.**

Wolbachia pipientis, a bacterium, first discovered in 1924 by Marshall Hertig and Burt Wolbach in the ovaries of *Culex pipiens* was estimated to be naturally found in about 40% of Arthropods and about 60% of insects. Several mosquito species namely *Cx. pipiens*, *Cx. quinquefasciatus*, *Cx. tritaeniorhynchus*, *Aedes albopictus* that transmit viral diseases in humans are naturally infected with *Wolbachia*. *Ae. albopictus* is naturally infected with two types of *Wolbachia*, *wAlbA* and *wAlbB*, but *Ae. aegypti* is not naturally infected with *Wolbachia*. Except for one strain of *Anopheles gambiae* so far, no other species of *Anopheles* have been found with *Wolbachia*.

There were reports that natural *Wolbachia* infections in *Drosophila* provide protection against a broad range of RNA viruses. Therefore, *Wolbachia* was isolated from *Drosophila* and transferred to eggs of *Ae. aegypti*, which did not have natural infection of *Wolbachia*, at The University of Queensland, Australia. Adults emerged from these *Wolbachia* infected eggs have been maintained in colony as *wMel Ae. aegypti* strain.

Wolbachia in *Ae. aegypti* have been shown to reduce the replication and transmission of dengue, chikungunya and Zika virus. *Wolbachia* are maternally transmitted i.e., *wMel Ae. aegypti* transmits *Wolbachia* to its progeny. In crosses between *wMel Ae. aegypti* females and wild type *Ae. aegypti* males (which do not have natural *Wolbachia*), the progeny inherits *Wolbachia* and also the property of not allowing the replication of the viruses. In the reciprocal cross no progeny are produced i.e., the cross is sterile. This property is referred to as cytoplasmic incompatibility. When the *Ae. aegypti* mosquitoes carrying *Wolbachia* are released into an area, the maternal inheritance acts as drive mechanism to spread *Wolbachia*, and cytoplasmic incompatibility helps in the reduction of wild *Ae. aegypti* population.

Before testing the release of the *Ae. aegypti* mosquitoes carrying *Wolbachia* in field, experiments were done to see whether it is harmful to humans, environment and animals that prey on mosquitoes. Experiments conducted using fish, spiders, geckos and predatory mosquitoes found no evidence that organisms that prey on *Ae. aegypti* acquired the *Wolbachia* infection from eating *Wolbachia*-infected mosquitoes. The analysis of soil and plant samples, earthworms, spiders and millipedes collected in enclosed cages where *Wolbachia*-infected mosquitoes were bred for several months at James Cook University showed no presence of *Wolbachia*. *Wolbachia* cannot survive in the environment outside live mosquitoes. Mosquitoes carrying *Wolbachia* do not transmit the bacteria to the humans or any other vertebrates they bite. *Wolbachia* commonly live in association with insects, as they are present in a number of insects that bite humans such as the pest mosquito species *Cx. quinquefasciatus* and *Ae. albopictus*. No *Wolbachia* or antibodies against *Wolbachia* were found in the blood of researchers who have voluntarily blood-fed thousands of *Wolbachia*-infected mosquitoes by letting them bite their arms and legs. *Wolbachia* are obligate symbionts that can only live inside other cells, and cannot be grown in free culture.

In 2011, the first releases of *Ae. aegypti* mosquitoes carrying the artificially transinfected endosymbiotic bacterium, *Wolbachia pipientis*, began in field trials in Northern Australia as part of the Eliminate Dengue Program. *wMel Ae. aegypti* strain has been released in small-scale field trials in Australia, Brazil, Columbia,

Indonesia and Vietnam. In the field trials that were carried out earlier and that are ongoing in Australia, Brazil, Colombia, Indonesia and Vietnam with *wMel Ae. aegypti* releases, *Wolbachia* has been successfully established in the local *Ae. aegypti* populations. And after more than 2 years of initial releases, *Wolbachia* infection was found stable in the field, and the infection was found exhibiting complete cytoplasmic incompatibility. Now, large scale city-wide field trials are under way in Yogyakarta city, Indonesia, Rio de Janeiro, Brazil, and Medellín, Colombia. It has been observed in earlier trials that there was no indigenous transmission of dengue in the released sites; and in the large-scale city-wide field trials, dengue cases are monitored. Furthermore, the project is now operational in Mexico, Vanuatu, Fiji, New Caledonia, Kiribati, India and Sri Lanka in addition to the above mentioned five countries. Field release are ongoing in all these countries except in India and Sri Lanka. The *Wolbachia-Ae. aegypti* strains are being tested in these countries for their potential to establish in nature and control of dengue.

In addition to *wMel Ae. aegypti*, the strains of *Ae. aegypti* and other mosquito species that have been developed are: *wMelPop-CLA Ae. aegypti*, *wAlbBAe. aegypti*, *wSiAe. aegypti*, *wAlbBAn. stephensi*, *wMelwAlbBAe. albopictus*

WHO Vector Control Advisory Group (2016 & 2018) has recommended *Wolbachia* based control of *Aedes* borne diseases as one of the biological control methods and its deployment under operational conditions should be accompanied by rigorous monitoring and evaluation.