EoI No. VU/31/2024/ECD dated 4th February 2025

Invitation for Expression of Interest (EoI)
For
Joint collaboration in R&D for development of human vaccine candidate against Highly Pathogenic Avian Influenza (HPAI) H5N1, and manufacturing/commercialization

By ICMR-Hqrs

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

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Letter of Invitation

1. Invitation for Expression of Interest

Indian Council of Medical Research ((ICMR), New Delhi invites Expression of Interest (EoI) from the eligible organizations, companies, manufacturers for **Joint collaboration in R&D for development of human vaccine candidate against Highly Pathogenic Avian Influenza (HPAI) H5N1, and manufacturing /commercialization.**

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	**EoI No. VU/31/2024/ECD**
Date of Publication	**4th February 2025**
Last date of submission	**5th March 2025**

Note:
Interested applicants may please send their proposals in a sealed envelope to the following address:

Dr. Jitendra Narayan
Scientist D
Communicable Disease Division
Indian Council of Medical Research,
V. Ramalingaswami Bhawan,
P.O. Box No. 4911,
Ansari Nagar, New Delhi - 110029, India

EoI Document No **VU/31/2024/ECD** along with the title of the EOI as "**EoI for Joint Development of Human Vaccine Candidate against H5N1**" in **Bold** and complete address as above must be clearly mentioned on the sealed envelope.

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 ICMR and duly notified on its website.

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 the growing demands of scientific advances in biomedical research on the one hand and the need of finding practical solutions to the health problems of the country, on the other.

Avian Influenza H5N1, a highly pathogenic strain of bird flu, continues to pose a significant threat to animal and human health in India. Recent outbreaks in 2021, 2023 and 2024 have been reported in several states, primarily affecting poultry and wild birds. These outbreaks have caused significant economic losses in the poultry industry and raised public health concerns due to the virus's zoonotic potential. The Avian Influenza H5N1 virus poses a grave public health risk because of its high mortality rate and its potential to cause a global pandemic if it mutates to allow sustained human-to-human transmission. While human cases remain sporadic globally, they highlight the virus's ability to infect humans with severe consequences.

H5N1 infection in humans has a high case fatality rate, exceeding 50%. Although human cases are rare and typically result from direct contact with infected birds, the severity of the illness underscores the need for vigilance. Symptoms in infected individuals range from fever and respiratory distress to multi-organ failure. In India, no significant human cases have been reported in recent years, but the risk persists due to frequent human-animal interactions in poultry farming and live bird markets. Despite primarily affecting birds, sporadic human infections with severe outcomes have occurred globally, emphasizing the need for preparedness.

India's preparedness for H5N1 includes active surveillance and the availability of medical countermeasures such as vaccines and medicines. Developing a vaccine for human use is crucial to mitigate the risk of outbreaks, protect vulnerable populations, and ensure readiness in the event of a pandemic. Such a vaccine would serve as a critical tool in controlling the spread of the virus, reducing morbidity and mortality, and alleviating the socio-economic impacts of potential outbreaks. The Indian Council of Medical Research has initiated efforts to develop an indigenous vaccine using mRNA or traditional platforms to strengthen India's pandemic preparedness. A targeted vaccine, combined with public awareness campaigns and strengthened health infrastructure, will lead to better outcomes in managing future H5N1 outbreaks. Efforts to develop and deploy effective vaccines, along with robust surveillance and response mechanisms, will ensure that India remains prepared to tackle the challenges posed by Avian Influenza H5N1, safeguarding the human health.

The ICMR-National Institute of Virology (ICMR-NIV), Pune, one of the constituent institutes of the Indian Council of Medical Research, is actively working on Highly Pathogenic Avian Influenza (HPAI) and low-pathogenic avian influenza viruses. Well-characterized strains of HPAI H5N1 are available at the laboratory. The ICMR-NIV team possesses expertise in outbreak investigations, avian influenza surveillance, virological and

molecular characterization, vaccine candidate development through virus inactivation and molecular methods, and conducting preclinical trials using BALB/c mice. The institute also specializes in laboratory testing to evaluate antibody responses to vaccines during phases II, III, and IV clinical trials.

In addition, the ICMR-National Animal Resource Facility for Biomedical Research (ICMR-NARFBR), located in Genome Valley, Hyderabad, is another critical institute under ICMR. It provides essential resources for preclinical research on drugs, vaccines, and medical devices. This facility houses a diverse range of laboratory animals, including mice, rats, guinea pigs, hamsters, rabbits, pigs, goats, dogs (Beagle dogs), horses, and non-human primates (Rhesus macaques). These laboratories support both regulatory and non-regulatory research, including preclinical trials for drugs and vaccines against infectious diseases in humans. Furthermore, ICMR-NARFBR is developing specialized Animal Biosafety Level-3 (ABSL-3) facilities for large animals (Indian Rhesus macaques, pigs, etc.), which are expected to be operational by the end of this year. These facilities will enable critical research on highly infectious pathogens, including challenge studies on Risk Group-III agents.

The infrastructure and resources available at ICMR institutes, as indicated above at ICMR-NIV and ICMR-NARFBR, will be leveraged for joint R&D and preclinical studies.

The virus isolates and the technical-know-how available with ICMR-NIV and ICMR-NARFBR collectively (hereinafter) referred to as **"Technology".**

ICMR is lawfully entitled to enter into any form of **non-exclusive agreements** with eligible manufacturing companies hereinafter referred to as the **"Company"** through a defined **agreement** for Licensing for R&D/Manufacturing/ Commercialization of **human vaccine candidate against Highly Pathogenic Avian Influenza (H5N1)**, hereinafter referred to as the **'Product',** which shall be governed by ICMR IP Policy, as revised and approved by the Competent Authority.

3. Objective

To collaborate with eligible companies for the joint development of **human vaccine candidate against Highly Pathogenic Avian Influenza (H5N1)** and commercialization.

4. Scope of Work

i. ICMR is willing to collaborate with eligible organizations, companies, and manufacturers for **'Joint collaboration in R&D for development of human vaccine candidate against Highly Pathogenic Avian Influenza (H5N1)'**

ii. The Company would be granted rights to undertake further development, manufacture, sell, and commercialize the Technology/Product '**human vaccine candidate against Highly**

Pathogenic Avian Influenza (H5N1)' or undertake further R&D and commercialize the end product(s)/technology.

iii. An Agreement (in case of joint development or licensing) following EoI is proposed to be executed on a "Exclusive/Non-Exclusive" basis with single/multiple companies to enable wider outreach of the **human vaccine candidate against Highly Pathogenic Avian Influenza (H5N1)** (Technology/Product) for societal benefit and public health use. All the related issues shall be governed by ICMR IP Policy, as revised and approved by the Competent Authority.

iv. ICMR-NIV and ICMR-NARFBR have expertise in various techniques, methods and information relating to aforesaid technology which could be used in **R&D for development of human vaccine candidate against Highly Pathogenic Avian Influenza (H5N1).**

Role of ICMR:

i. **ICMR and its Institutes** will provide expert guidance & technical support in **R&D for development of human vaccine candidate against Highly Pathogenic Avian Influenza (H5N1)**, in all phases. Such technical oversight by **Scientist of ICMR** would accelerate the development of the Product and its commercialization.

ii. ICMR would provide technical support through its team of experienced scientists in study planning, product development, development of study protocol, results/data analysis, outcome assessment, safety & efficacy assessment, product improvement, etc., if deemed fit upon the mutual understanding between ICMR and collaborative company.

iii. ICMR through its Institutes would provide support and facilitation to conduct the R&D/clinical study of new technology/ product in India through its Affiliates/ Institutes, in collaboration with the company/institutions in a professional and mutually agreed-upon manner and timelines, which will be decided later under the Agreement.

iv. ICMR would provide technical support in development of technology/ product and will also facilitate the validation, if required, as per the terms & conditions of the Agreement.

v. ICMR shall have no financial implications unless otherwise specified.

Role of Company

i. The Company shall have valid provisions to provide all necessary infrastructure/ material/ manpower required for product development/ validation/ scale-up either directly or otherwise.

ii. The Company shall have provisions to undertake the scale-up as required, manufacturing and commercialization of the **human vaccine candidate against Highly Pathogenic Avian Influenza (H5N1),** in a set milestone.

iii. The Company agrees to share the technical data with ICMR and participate in all discussions in a professional and mutually agreed-upon manner.

iv. The Company agrees to allow authorized personnel/scientist/team of ICMR to visit the designated lab/ production facility as and when required, as envisaged under this EoI and subsequent Agreement.

v. The Company shall be responsible for obtaining all the regulatory approvals required for commercialization or starting from R&D for product development to its commercialization

5. Intellectual Property Rights

It is submitted that in case of transfer of Technology, ICMR is the sole owner of the said Technology, including any underlying Intellectual Property(ies) and commercialization rights.

Intellectual Property (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.

ICMR 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) or the invention(s), and/or ICMR is lawfully entitled to enter into any form of non-exclusive License Agreements with selected companies including transfer of the Technology through suitable Agreement(s).

In case of collaboration between ICMR and the Company for the Joint development of the Technology/ Product, Background Intellectual Property ("BGIP") shall always remain the sole and exclusive property of the Party generating the BGIP. Any IP, if generated during the course of collaboration, including any improvement thereof, shall be jointly owned by ICMR and the Company. All such provisions related to intellectual property rights shall be governed by ICMR IP Policy, as revised and approved by the Competent Authority.

6. Process involved in Partnership/Collaboration/Technology Transfer

Interested companies/manufacturers are invited to join hands with ICMR for co-development/ further development & commercialization of the Technology/ Product(s). Under this EoI, the manufacturers/companies who are responsive and fulfilling all the technical need will be shortlisted based on their R&D plan, facilities and capabilities. Qualified companies/manufacturers will only be contacted for execution of MoA/MoU/Agreement for partnership/collaboration/technology transfer, etc. Subsequent to the execution of the Agreement such companies/manufacturers shall be responsible to pay

the Royalty @ 1% or 2% on Net sales, as applicable, according to the ICMR Guidelines for Technology Development Collaboration.

7. Publication

i. In case of Co-development, the Parties shall have equal rights on the manuscripts/scientific publications (joint publication/acknowledgment /other credits as applicable) and in accordance with guidelines of International Committee of Medical Journal Editors (ICMJE.org).
ii. Support of ICMR must be duly acknowledged in all publications by the Company.
iii. ICMR Scientists can be given due to advantage of authorships in the publications arising out of Licensing/co-development.

8. Data Rights

i. Data Rights will be exclusively with ICMR, if ICMR provide 100% funding.
ii. Data rights shall be jointly owned by ICMR and Licensee/Co-developer, in case of joint funding.
iii. Data rights in cases where Artificial Intelligence is involved shall be dealt separately.
iv. Licensee/ Company to ensure that data is anonymized, kept confidential and strictly abide by the provisions of Information Technology Act, 2000 while dealing with such data

9. 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 capabilities for submission of interest, subject for verification by ICMR.
Documents to be furnished are as follows:

i. Declaration - Expression of Interest (Format – 1)
ii. Authorization Letter (Format – 2)
iii. Undertaking with regard to Blacklisting (Format-3)
iv. Undertaking with regard to Non-Conviction (Format – 4)
v. EoI document with each page duly stamped and signed by the Authorized signatory.
vi. Undertaking with regard to laboratory facility (Format – 5)
vii. Production Capacity Undertaking (Format-6)
viii. Supporting documents, as mentioned in Format-1
ix. MSME Certificate (if applicable)
x. Concept note on business plan- A brief concept note on R&D, clinical studies, planning & execution, production, marketing etc. with timeline (not more than 5 pages)
xi. Any other information which proponent may wish to provide to support the EoI.

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

10. Rejection Criteria

The application is liable to be rejected if:

i. The proposal is not submitted as per the requirements indicated in the EoI.
ii. Not in the prescribed format.
iii. Not properly stamped and signed.
iv. Received after the expiry of due date and time.
v. All relevant supporting documents are not furnished with the Pre-Qualification Criteria (PQC).
vi. The proposal shall be substantially responsive without any material deviation, failing which the proposal shall be summarily rejected.
vii. Applications not fulfilling the terms of the document will be summarily rejected.
viii. Any other non-compliance.

11. 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.

12. 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 (General)**	**Supporting copy of documents required** (All documents must be self- attested by the authorized person of the proponent)
General Criteria		
1	The proponent shall be a legal entity, registered as Institution/Company/ LLP/ Society/ partnership firm/ proprietorship firm under respective acts in India and shall have more than 51% of Company stakes by promoters from India.	Registration of firm/ organization/Company Incorporation Certificate from Registrar of Companies (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 proven prior experience of manufacturing and/or R&D with manufacturing during the last three years, either in-house or through agreed collaboration and must have marketed same/similar products in the past with a good track record.	Research paper/Pamphlet / brochure of the product/DCGI License for existing product. Supporting documents for collaboration, if any.
4	The proponent has to be profitable and should not have incurred overall loss in past three (03) 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 currently not black-listed/ barred by any Central / State Government/ Public Sector Undertaking, Govt. of India, (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 manufacturing unit in India.	Registration copies/ factory license/ DSIR certificate, if have any.
7	The proponent and its promoters should not have been convicted for any offence in India by any competent court or judicial body during the past 3 years.	Undertaking on Proponent's Letter Head, duly signed and stamped by the Authorized Signatory (As per format – 4)
8	GMP/ quality certification (ISO or approved Indian certification) of manufacturing facility and GLP/necessary certifications for R & D	Copies of Certificates
Specific Criteria (Based on the nature of the Proposal)		
9.	The proponent should have functional laboratory to carryout R&D for the product development	Undertaking on Proponent's Letter Head, duly signed and stamped by the Authorized Signatory (As per format – 5)
10.	Capacity to produce at least 1 lakhs doses per week	Undertaking (As per format – 6)

NOTE- For MSMEs and Start-ups, Start-Up-India, Make-in-India and other relevant guidelines of Government of India shall be applicable

13. Disclaimer

i. ICMR shall not be responsible for any late receipt of applications for any reasons whatsoever.
ii. ICMR reserves the right to cancel the call for EoI without assigning any reasons thereof.
iii. 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.
iv. To include any other item in the Scope of work at any time after consultation with

proponents or otherwise.

v. For International Clients, please note that EoI and other necessary correspondences shall be submitted in English only.

14. Arbitration

That any dispute and/ or any part of the dispute which couldn't be resolved through mutual consultation, the same shall be referred to the sole arbitrator as per the Arbitration & Conciliation Act, 1996 and any amendment thereafter. The Venue and Seat of the arbitration proceedings shall be New Delhi and the courts at New Delhi will have exclusive jurisdiction.

15. Contacts

In case of any clarification required, please contact:

For scientific issues-

Dr. Shailesh D. Pawar
Scientist 'F' & Officer-in-charge
Dept/Div/Lab: Poliovirus group,
ICMR-NIV, Pune; and ICMR-NIV Mumbai Unit
d. Telephone No.: 020-65906848, 9421018275
e. E-mail: pawar.sd@gov.in

Format-1

Expression of Interest

(To be submitted on Company's Letter Head)

To,

The Director General,
Indian Council of Medical Research, Ansari Nagar, New Delhi.

Subject: Submission of Expression of Interest (EoI) for joint collaboration in **R&D for development of human vaccine candidate against Highly Pathogenic Avian Influenza (H5N1)**.

Ref: VU/31/2024/ECD dated 4th Feb 2025

Sir,

The undersigned having read and examined in detail all the EoI documents pertaining to your transfer of technology, and do hereby express the interest to undertake the research & development/manufacture/ sale /commercialization 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. Including DSIR certificate		

6	GMP / GLC and ISO Certification. Registration copies of both		
7	Authorization Letter	As per format – 2	
8	Undertaking on the Letter Head of the Proponent duly signed & Stamped by Authorized Signatory	As per format – 3	
9	Undertaking on Proponent's Letter Head, duly signed and stamped by the Authorized Signatory	As per format – 4	
10	MSME Certificate (if have any)		
11	Business Plan	A brief concept note on planning & execution, production, marketing etc. (not more than 5 pages)	

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-2

Authorization Letter

(To be submitted on Company's Letter Head)

To,

The Director General,
Indian Council of Medical Research,
Ansari Nagar, New Delhi.

Subject: Letter for Authorized Signatory
Ref: EoI No. **VU/31/2024/ECD** dated 4th Feb 2025

Sir,

This has reference to your above-mentioned Expression of Interest (EoI) for joint collaboration in **R&D for development of human vaccine candidate against Highly Pathogenic Avian Influenza (H5N1)**.

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

(Specimen Signature of Representative)

Date:
Place:

Yours faithfully,

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

Format-3

Undertaking with regard to blacklisting

(To be submitted on Company's Letter Head)

To,

The Director General,
Indian Council of Medical Research,
Ansari Nagar, New Delhi.

Subject: Undertaking regarding Blacklisting / Non-Debarment.
Ref: VU/31/2024/ECD dated 4th Feb 2025

Sir,

It is hereby confirmed and declared that M/s ..... (Company Name) currently has not been blacklisted / debarred by any Government Department / Public Sector Undertaking / or any other company 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-Conviction

(To be submitted on Company's Letter Head)

To,

The Director General,
Indian Council of Medical Research,
Ansari Nagar, New Delhi.

Subject: Undertaking regarding Non-Conviction.
Ref: VU/31/2024/ECD dated 4th Feb 2025

Sir,

It is hereby confirmed and declared that M/s….....(Company Name) and owner of the firm / board of directors, have not been convicted for any offence in India by any competent court or judicial body during the past 3 years.

Yours faithfully,

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

Format-5

Undertaking with regard to laboratory facility

(To be submitted on Company's Letter Head)

To,

The Director General,
Indian Council of Medical Research,
Ansari Nagar, New Delhi.

Subject: Undertaking regarding laboratory infrastructure.
Ref: VU/31/2024/ECD dated 4th Feb 2025

Sir,

It is hereby confirmed and declared that M/s.....(Company Name) do have

i. Adequate laboratory infrastructure (equipped laboratory facility). Please tick BSL-2/BSL-3/ABSL-3/GMP/GLP/ Other* (if other please specify) and

ii. Adequate no. of experienced staff/skilled manpower to undertake R&D/ pre-clinical & clinical studies/manufacturing/commercialization of **human vaccine candidate against Highly Pathogenic Avian Influenza (H5N1)**.

Yours faithfully,

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

*The Laboratory/ facility requirement will depend on the technology/ product

Format-6

Undertaking with regard to production capacity

(To be submitted on Company's Letter Head)

To,

The Director General,
Indian Council of Medical Research,
Ansari Nagar, New Delhi.

Subject: Undertaking with regard to production capacity.
Ref: VU/31/2024/ECD dated 4th Feb 2025

Sir,

It is hereby confirmed and declared that M/s ..... does have the capacity in all mean (including infrastructure, fund, material, staff etc.) for manufacturing of **human vaccine candidate against Highly Pathogenic Avian Influenza (H5N1)**, minimum ……(mention the quantity per week).

Yours faithfully,

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

SCHEDULE-A

TECHNOLOGY DETAILS

i. **About the Technology/Product/Process:**

The Highly Pathogenic Avian Influenza (HPAI) H5N1 viruses have significant zoonotic and public health implications with pandemic potential. The HPAI H5N1 viruses belonging to the clade 2.3.4.4b are causing unprecedented mortality in avian and mammalian species globally. Unprecedented infections have been reported in seals, penguins, cows, and other mammals; human infections have also been reported. The first outbreak of HPAI H5N1 virus in India was reported in the year 2006. Since then, more than 350 outbreaks have been reported in wild birds and poultry, with majority of the outbreaks in winter season. So far, total ten clades of HPAI H5N1 viruses have been reported in the country. The first human infection of HPAI H5N1 from India was reported in 2021. This virus belonged to the clade 2.3.2.1a. Recently, in June 2024, outbreaks of HPAI H5N1 viruses belonging to the clade 2.3.4.4b were reported in wild birds and domestic poultry in Kerala.

The World Health Organization recommends candidate vaccine virus (CVV) strains for the circulating clades of H5N1 viruses. The HPAI H5N1 virus belonging to clade 2.2 isolated from India by the ICMR-NIV in the year 2006, has been recommended as a CVV by the WHO (https://www.who.int/publications/m/item/a(h7n9)---northern-hemisphere-2022-2023). In view of the emergence and global spread of clade 2.3.4.4b HPAI H5Nx viruses, there is an urgent need to develop HPAI H5N1 CVVs belonging to this clade.

The objective is to develop CVV against HPAI H5N1 virus using various platforms for example, generation of Virus Like Particle based vaccine; m-RNA Vaccine; Recombinant Vaccine and Reverse Genetics-based vaccine candidates, which can be scaled up for vaccine production by the vaccine manufacturers.

ii. **Need and utility of the Technology from Public health perspective:**

Avian Influenza H5N1, a highly pathogenic strain of bird flu, continues to pose a significant threat to animal and human health in India. Recent outbreaks in 2021, 2023 and 2024 have been reported in several states, primarily affecting poultry and wild birds. These outbreaks have caused significant economic losses in the poultry industry and raised public health concerns due to the virus's zoonotic potential. The Avian Influenza H5N1 virus poses a grave public health risk because of its high mortality rate and its potential to cause a global

pandemic if it mutates to allow sustained human-to-human transmission. While human cases remain sporadic globally, they highlight the virus's ability to infect humans with severe consequences.

H5N1 infection in humans has a high case fatality rate, exceeding 50%. Although human cases are rare and typically result from direct contact with infected birds, the severity of the illness underscores the need for vigilance. Symptoms in infected individuals range from fever and respiratory distress to multi-organ failure. In India, no significant human cases have been reported in recent years, but the risk persists due to frequent human-animal interactions in poultry farming and live bird markets. Despite primarily affecting birds, sporadic human infections with severe outcomes have occurred globally, emphasizing the need for preparedness.

iii. **Technology Readiness level (TRL)**

TL-02/05

iv. **Work done so far-**

ICMR-NIV has recently reported the molecular and virological characterization of the clade 2.3.4.4b HPAI H5N1 viruses from outbreaks in Kerala. HPAI H5N1 virus was isolated using 10-day-old embryonated chicken eggs. The virus was also propagated in MDCK cell line. The virus showed high virus titers in embryonated chicken eggs and MDCK cell line. The H5N1 viruses showed avian type receptor specificity and cross-reactivity with the H5N1 clade 2.3.4 antiserum, and partial reactivity with H5N1 clade 2.2 antiserum, in the hemagglutination inhibition assay. There was no cross-reactivity observed with H5N1 clade 2.3.2.1a antiserum Full genome sequencing revealed several markers associated with high pathogenicity and mammalian adaptation. Phylogenetic analysis revealed that all the isolates belonged to clade 2.3.4.4b. All the viruses showed a single genotype with multiple assortments. The HA, NA and NS genes were of clade 2.3.4.4b origin, PB2 genes were Low Pathogenic Avian Influenza (LPAI) H7N7-like, PB1 genes were similar to LPAI H3N8 viruses reported from the Netherlands; while the PA, NP and M genes had the LPAI H3N8 virus reported from Kerala as the possible progenitor.

The virus was inactivated using beta propiolactone. The virus inactivation was confirmed by two passages in 10-day-old embryonated chicken eggs. Safety and immunogenicity experiments in rabbit and chicken are in progress. The inactivated virus of which virological and molecular characterization has been completed is available with ICMR-NIV.

The ICMR-NIV, Pune is working on HPAI and low pathogenic avian influenza viruses, Well-characterized strains for HPAI H5N1 are available at the laboratory. The team has expertise to work on outbreak investigations, AI surveillance, virological, molecular characterization, vaccine candidate development using virus inactivation and molecular methods, preclinical trials using BALB/c mice, and laboratory testing for evaluation of antibody response to vaccines during phase II, III and IV clinical trials. The team has contributed significantly in the above aspects in India.

v. **IP Filing Status/Publications: Following publications have been published in reputed journals.**

- Tare DS, Keng SS, Walimbe AM, Pawar SD*. Phylogeography and gene pool analysis of highly pathogenic avian influenza H5N1 viruses reported in India from 2006 to 2021. Arch Virol. 2024 Apr 25;169(5):111. doi: 10.1007/s00705-024-06032-4. PMID: 38664271.
- Tare DS, Kode SS, Hurt AC, Pawar SD*. Assessing the susceptibility of highly pathogenic avian influenza H5N1 viruses to oseltamivir using embryonated chicken eggs. Indian J Med Res. 2019 Nov;150(5):486-491. doi: 10.4103/ijmr.IJMR_845_18. PMID: 31939392; PMCID: PMC6977371.
- Pawar SD*, Murtadak VB, Kale SD, Shinde PV, Parkhi SS. Evaluation of different inactivation methods for high and low pathogenic avian influenza viruses in egg-fluids for antigen preparation. J Virol Methods. 2015 Sep 15;222:28-33. doi: 10.1016/j.jviromet.2015.05.004. Epub 2015 May 18. PMID: 25997377.

vi. **Capacity and Infrastructure**

The following key capacities are available;

1. Well-equipped, state-of-the-art biosafety levels 2 and 3 laboratories for carrying out work on HPAI viruses.
2. NABL laboratory accreditation as per ISO/IEC 17025:2017 standard.
3. Molecular techniques such as molecular cloning, real time PCR and full genome sequencing.
4. Virus isolation using in vitro (MDCK cell line) and in ovo (embryonated chicken eggs) methods.
5. Virus titration using hemagglutination assay, 50% tissue culture infectious dose and 50% egg infectious dose.
6. Virus inactivation protocols using beta propiolactone for development of inactivated antigens and vaccine candidates.
7. Serological assays: hemagglutination inhibition and microneutralization assays.
8. Preliminary studies of safety and immunogenicity in embryonated chicken eggs, white leghorn chickens and BALB/c mice.
9. Capacity to test serum and respiratory samples during phase I, II, II and IV clinical

trials of influenza vaccines.

In addition to the above, the ICMR-National Animal Resource Facility for Biomedical Research (ICMR-NARFBR) is an ICMR institute located in Genome Valley, Hyderabad. It has critical resources for preclinical research on drugs, vaccines, and medical devices. This facility houses a diverse range of laboratory animals, including mice, rats, guinea pigs, hamsters, rabbits, pigs, goats, dogs (Beagle dogs), horses, and non-human primates (Rhesus macaques). All animals are bred and maintained under specific pathogen-free (SPF) conditions, with rigorous health and genetic monitoring programs in place. The institute is registered with the Committee for Control and Supervision of Experiments on Animals (CCSEA) and has well-equipped laboratories for toxicology, pathology, microbiology, virology, haematology, biochemistry, molecular biology, and parasitology. These laboratories support both regulatory and non-regulatory research, including preclinical trials for drugs and vaccines against infectious diseases in humans. Furthermore, NARFBR is developing specialised Animal Biosafety Level-3 (ABSL3) facilities for large animals (Indian Rhesus macaques, pigs, etc.), which is expected to be operational by the end of this year. These facilities will enable critical research on highly infectious pathogens, including challenge studies on Risk Group-III agents. The Ferrets facilities are also likely to be functional this year. The institute also maintains a valuable repository of transgenic mouse models, which serve as indispensable tools for investigating the genetic and immunological mechanisms underlying infectious diseases.

The ICMR-NARFBR facility can also be used for animal studies for under this joint collaboration

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