HLL Biotech Limited
Ticel Biopark Campus (Module # 013-015)
CSIR Road, Taramani
Chennai - 600113

Sub: Invitation of Expression of Interest (EOI) from Contract Research and Manufacturing Organizations having cGMP compliant Pilot facility, process development labs, process equipments, experienced manpower for development and production of Bacterial and Cell culture based Human Vaccines

I. INTRODUCTION

HLL Biotech Limited a 100% subsidiary of HLL Lifecare Ltd. (a Govt. of India Enterprises) is in the process of setting up of an Integrated Vaccines Complex for manufacturing of the vaccines**.** The facility will manufacture various vaccines required for immunization program of Government of India at affordable cost.

It has been decided to invite Expression of Interest (EOI) from Contract Research & Manufacturing Organizations having cGMP compliant biopharmaceutical manufacturing facility, validated utilities, Process equipment's, consumables, chemicals and reagents for the production of vaccines for pre-clinical and clinical trial batches.

The facility is required for development and production of following vaccines:

Vaccine Products

- Rabies (Vero cell based)
- Hepatitis B (yeast cell based)
- Haemophilus influenza type b (Polysaccharide – Protein Conjugate) .
- Measles (cell culture based)
- Japanese Encephalitis (cell culture based)
- Formulation of Pentavalent vaccine (DPT+ Hep. B+ Hib)

The development is to complete the Pre-clinical trials (Product development & process standardization), Phase I & II human clinical trials for the above vaccines in these outsourced facilities, before our production facility is commissioned.

II. SCOPE OF SERVICES & INFRASTRUCTURE:

The scope of services of the project is divided in to two parts ; Part A and Part B

1. **Part A**

The process technology and expertise is available with HLL Biotech Limited and the facility and manpower of the contract research and manufacturing organization will be utilized for the test run batches for replication of the process and establishment of the production process parameters as per the technology know how.

The activities for Part A (GLP facility) of the Project are mentioned below:

- Pre cell bank preparation and primary characterization
- Analytical method verification for Bulk Drug Substance (Analytical methods will be transferred by HLL Biotech Ltd)
- Test run batches production – Up stream and downstream process parameters establishment
- In vitro and In-vivo tests
- Preclinical trial batches – production
- Pre-clinical trial studies

  - GLP lab and infrastructure (up-stream & down-stream process labs, and QC testing labs including animal house) for the development of yeast cell based recombinant vaccine, poly saccharide conjugate bacterial vaccines, formulation and filling of vaccines, cell culture based viral vaccines.

  - Lab scale fermenter, Biosafety cabinets, Yeast cell DNA lysis systems, purification systems, chromatography systems etc

  - Chromatography equipment for viral vaccine purification

2. **Part B**

The activities for Part B (GMP facility) of the Project are mentioned below:

- Master/Working cell bank preparation
- Analytical method verification for Final Drug Product (Analytical methods will be transferred by HLL Biotech Ltd) – In vitro & In vivo

- Scale up batches production – Upstream & Downstream
- Formulation of batches

- GMP compliant facility, classified clean rooms, validated utilities, WFI, Central CIP and SIP stations, Pilot scale GMP compliant bioreactors (50 L and 100 L)
- Tissue homogenizer, Dyno mill/Homogenizer, Chromatography – HPLC, ELISA systems, other downstream purification systems like microfiltration and ultrafiltration systems
- Cell culture facility for viral vaccine production and inactivation
- Chromatography equipment for viral vaccine purification
- Formulation unit for vaccines
- Filling station
- In process testing of vaccines- facility
- Approved experimental animal house
- Qualified and experienced man power : vaccine production, down stream processes, QC testing, animal experiments

III. FACILITY REQUIREMENT – PHASES WISE

PHASES	INFRASTRUCTURE & EQUIPMENTS REQUIRED
Part A	GLP Facility: Product development, Equipments for lab scale production and down-stream processes, process standardization of Hepatitis B and Hib vaccines, process development for cell culture based viral vaccines.
Part - B	GMP Facility : • Fermentation based production • upstream production equipment's like : - Shake Flasks - Shaker Incubator - 2/5, 50 and 100 L WV fermentors - Homogenizer/ other cell disruption

	system • Downstream purification process equipments) like -Continuous and Batch centrifuge - Depth filtration - Tangential flow filtration (UF/DF) skids - Chromatography systems • Cell culture based viral vaccine and infrastructure for roller bottle culture and cell factory based production • Process equipments : Incubators, water bath, roller bottle apparatus, Deep freezers (- 20 and -80 degree), Biosafety cabinets(B-2), Low pressure chromatography systems (affinity /gel filtration), TFF systems, Ultrafiltration system, Centrifuges etc. • Consumables for vaccines production and testing • Chemicals and reagents for vaccine production

IV. MINIMUM ELIGIBILITY CRITERIA:

1. The firm should have the experience of contract research & manufacturing of biological/vaccines like Hepatitis B, Hib and viral vaccines for the **last three** years.

2. Should have proven and demonstrable experience in development and production of vaccines for Phase I & II trials for any vaccine manufacturing organizations in India.

3. The firm shall have attained a turnover of not less than **INR 1.0 Crore** in anyone of the past three years.

4. The firm should have the facilities/infrastructure/expertise to carry out and complete the activities for at least one vaccine product for the Part A and Part B phases.

Personnel Qualification:

a) At least three senior bioprocess scientists having the experience in production of biological/vaccines by fermentation method, capsular polysaccharide separation and conjugation with proteins, cell culture methods for virus propagation and purification, QC testing methods for vaccines, In vivo testing of vaccines in experimental animals.

b) At least two of the senior bio process engineers of the organization shall have more than 5 years of experience in operation and maintenance of biopharmaceutical process equipment's and facility.

c) Firms should have the capabilities to understand the process and develop the process-focused support.

d) CV's of at least six research scientists/research associates having minimum 5 years' experience in the relevant field shall be attached.

V. SELECTION PROCESS

The organization shall be short listed based the evaluation of EOI document and at later stage bids will be invited from only the short listed organizations.

Technical Evaluation

The Technical Evaluation Committee (TEC) appointed by HBL will screen the EOI document based on the Minimum Eligibility Criteria and the details of availability of infrastructure and services offered by the organizations. The organizations will be invited for a detailed presentation for the evaluation of infrastructure and services offered by them.

Invitation of bids

Bids will be invited only from short listed organizations after the evaluation of EOI.

Format for submitting eligibility criteria

1	1.1 Years of Experience **(In contract manufacturing)**	
	1.2. Should have proven and demonstrable experience in development and production and formulation of Biologicals/Vaccines- Bacterial vaccines and Cell culture based viral vaccines for Pre-clinical Phase I/II trials projects for any biopharmaceuticals/vaccine manufacturing organizations in India. Project Implemented: (a) Name of the Project(s) (b) Duration	**Details of each project to be attached by the Bidder**
2.	**Turnover** The organization should have a turnover of **at least Rs 1.0 Crore** in anyone of the last three years	**Audited annual Reports for the last three years**
3	**Qualification and experience of the key personnel** At least 6 CVs spread across in the fields of biopharmaceuticals/Vaccine Projects.	**CV's to be attached by the Bidder**

4	**Availability of infrastructure and equipments**	**Detail on :** • **Availability GMP facility: space of minimum 10,000 sq.feet** • **List of process and utility equipments available** • **Commitment to procure the specific equipments for each product** • **GLP facility- Product development (Upstream, Down stream) : List of equipments, consumables and infrastructure** • **Cell banking and storage facility** • **Analytical testing facility and equipment details** • **Biological testing – list of equipments** • **In vivo testing – Details of experimental animals and facility either in-house or out sourced.** • **Fill-finish, lyophilization stations**

Documents to be submitted with EOI:

- Profile of the Organization (emphasis to implemented Human Vaccine Projects)
- Organization Structure
- Memorandum of Association/Articles of Association.
- Authenticated copy of the certificates of incorporation/registration of the organization
- Authenticated copy of annual accounts for the last three years
- Details of the team which is proposed to handle the assignment with their CVs, in brief, mentioning their experience in similar projects done earlier.
- List of process equipments (GLP and GMP)
- Cell culture lab infrastructure and equipments list
- Testing facility and equipments
- Commitment to procure the specific equipments
- Details of experimental animals house

VI. MODE OF SUBMISSION OF EXPRESSION OF INTEREST/BID

Documents in electronic form will not be accepted. The documents to prove the eligibility criteria should be submitted in a separate sealed envelope marked ***'ELIGIBILITY CRITERIA'*** in the format provided with all relevant documents to prove the eligibility.

The EOI envelope should be super-scribed as **"EOI for Qualifying the Contract Research and Manufacturing Organizations having cGMP facility and process equipment for development and production of Bacterial and Cell culture based Viral vaccines"** and should be delivered at the following address before the stipulated closing time.

E.A. Subramanian
Chief Executive Officer
HLL Biotech Limited
Ticel Biopark Campus (Module # 013-015)
CSIR Road, Taramani
Chennai - 600113

VIII. PRE-BID CONFERENCE

A pre-bid conference for the prospective organization will be conducted on 11th December 2012 at HBL office, Ticel Biopark Campus (Module # 013-015), CSIR Road, Taramani, Chennai – 600113.

IX. CLOSING TIME FOR RECEIPT OF EOI

The closing time for submission of EOI is 27-12-2012-upto **–3-PM.**

The EOI documents shall be opened on the same day , 27-12-2012 at 3.30 PM.

The date of Technical presentation will be informed to the organizations after the preliminary evaluation of EOI.

X. RIGHTS OF HLL

(i) HBL reserves the right to accept / reject the EOI received without assigning any reasons whatsoever, or may call for any additional information / clarification if so required.

(ii) HBL reserves the right to limit or delete any part of the scope of work and extend the last date of submission of the EOI and bid.

XI. COURT JURISDICTION

This shall be subject to the exclusive jurisdiction of courts at Thiruvananthapuram.

XII. MISCELLANEOUS

In case any further clarification or information is required, the following officer may be contacted:

E.A. Subramanian
Chief Executive Officer
HLL Biotech Limited
Ticel Biopark Campus (Module # 013-015)
CSIR Road, Taramani
Chennai – 600113
eas@lifecarehll.com