FORM C3

APPLICATION TO RCGM TO CONDUCT PRECLINICAL AND/OR SAFETY STUDIES OF rDNA PRODUCTS DEVELOPED USING GENETICALLY MODIFIED ORGANISMS (GMOs)/ LIVING MODIFIED ORGANISMS (LMOs) FOR HEALTHCARE, INDUSTRIAL OR ANY OTHER USE

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1. **Name of the Applicant:**

   Designation:

   Address:

   Telephone No.:

   Fax No.:

   e-mail:

2. **DBT Office Memorandum No.:**

3. **Application for :**

   3.1 Purpose (not more than 100 words)

   3.2 New Yes ◯ No ◯

   3.3 Ongoing Project Yes ◯ No ◯

If yes, No. & Date of permission letter issued and also briefly state the purpose for which permission was granted.

3.4 Category (Biosafety level) of experiments as per the Guidelines of DBT

4. Objectives of the proposal:

5. Background about the nature of the product with appropriate references:
(may include in about 100 words, the process of development, mode of action, therapeutic indication, therapeutic dose if available, whether product is already in use elsewhere, if yes, any known side effects, animal toxicology data, similarity / dissimilarity between the molecule / compound under consideration)

6. Molecular biology details of the GMOs/LMOs employed:

6.1 Origin of gene

6.2 Sequence

6.3 Vector/promoter/terminator

6.4 Transformation process

6.5 Host organism characteristics

6.6 Safety of the organism

6.7 Copy number of the plasmid

6.8 Stability data of the plasmid

6.9 Expression level in the host

6.10 Containment levels and biosafety

7. Standardization of fermentation/production procedures:

7.1 Basic transformation and laboratory work to assess the expression of the target gene

7.2 Five batches of reproducible fermentation data (Batch size adequate to give after purification enough purified product to generate preclinical data) with detail kinetics of one single batch.

7.3 Fermentation kinetics data from one representative batch indicating cell growth, product formation, pH, temperature, dissolved oxygen, major nutrient consumption pattern, RPM for agitation

7.4 Concentration of product/L, yield and volumetric productivity.
(Provide details to show that the specific protein yield (amount of protein per unit cell mass) remains more or less constant at different cell concentration during fermentation).

8. Downstream process for purification:

8.1 Steps involved in purification of the product

8.2 Batch size for protein purification

8.3 Description of each unit operation step during purification and recovery of protein

8.4 Quality of the product and recovery efficiency

8.5 Overall recovery of the product in each batch operation

8.6 Consistency of recovery in 5 consecutive batches of purification

9. Product/protein characterization:

9.1 Molecular weight / western blot/SDS-PAGE/ mass spec

9.2 Amino acid sequence (10 N terminal AA)

9.3 Peptic digest

9.4 Secondary structure by CD (near and far UV)

9.5 Fluorescence spectra

9.6 Disulfide bond presence if any

9.7 Carbohydrate content and details of components (for glycoproteins)

9.8 Presence of aggregates

9.9 Host cell protein/contaminants

9.10 Residual DNA and LPS/endotoxin

9.11 Pyrogen content

10. Formulation and stability studies:

10.1 Extended stability

10.2 Use of stabilizer(s) and its concentration

10.3 Product quality in formulated condition

10.4 Bioactivity/immunogenicity of the formulated product

11. Effica cy of the product: Information on:

11.1 Receptor binding assay if any

11.2 Cellular proliferation assay

11.3 Signal transduction pathways

11.4 Tissue specific a ctivity

11.5 In vivo studies in animal models

11.6 Pharmacokinetics and Pharmacodynamics studies

12. Immunogenicity studies:

12.1 Sequence specific

12.2 Non-Specific to other proteins

12.3 Immunogenicity with adjuvants

13. Acceptability criteria of the bulk and the formulated material wherever ready for preclinical or safety studies:

14. Proposed work plan for preclinical or other safety studies:

14.1 List of the studies to be done

14.2 Information about the route of administration, dose, vehicle, mode of administration in each study

14.3 Basis of dose calculation for each animal used (indicate the guidelines followed such as Schedule-Y, ICH, FDA or justify deviations if any).

14.4 Toxicity and allergenicity protocols
(Provide complete study design including test species, age, body weight, control groups such as vehicle control, comparator group, recovery groups, details of biochemical, histopathological and other parameters to be measured, organs to be weight, monitoring schedule etc.)

14.5 Address and accreditation status of the labs where studies proposed to be conducted.

14.6 Status of Institutional Animal Ethics Committee.s Approval (Please specify the studie and products to be tested in each lab).

15. Proposed containment facility as well as measures:

16. Decontamination and disposal mechanisms:

17. Risk management (Emergency plan):

18. Any other relevant information:

19. Declaration :

I declare that the information provided in the above format is correct and accurate to the best of my knowledge. The "Safety Guidelines" brought out by the Department of Biotechnology, Ministry of Science & Technology, Govt. of India will be and is being strictly followed. In case any untoward incident occurs, the Chairman of the IBSC and the Member-Secretary of the RCGM will be informed immediately.

Date: **Signature of the Applicant**

Forwarded:

The proposal set out above has been considered and approved by the "Institutional Biosafety Committee" in its meeting held on and is forwarded to RCGM for further necessary action.

Date: **Signature and name of the Chairman, IBSC**

Note:

1. Please submit 23 copies of the application along with the enclosures to the Member Secretary, RCGM, Department of Biotechnology for consideration by RCGM.
2. Enclosed: (Kindly tick the enclosures):
   - Sequence map of the gene
   - Vector Map
   - Copy of the import/receive permits, or any other approval letters issued earlier
   - Copy of the minutes of IBSC meeting in which the proposal was approved