

## **Generic Questionnaire for Biopharmaceutical Production Candidates Involving Recombinant Virus Vectors**

**Principal Investigator:**

**Institution:**

1. What amount(s) of delivered product(s) is desired?
  - A. Non-GMP (laboratory grade for additional pre-clinical development)
  - B. cGMP (clinical grade)
2. Please provide details of your molecular construct including starting materials (e.g. plasmids, relevant vector maps, detailed vector construction scheme, etc.)
3. If your construct contains an antibiotic-resistance gene or other selectable marker, please indicate which one. Are alternative methods of selection available?
4. Is your vector replication competent or replication defective? (For replication-selective vectors, please describe the molecular basis of the selectivity and the conditions under which the vector would replicate.)
5. Does your vector have an altered cell tropism? Please describe.
6. Have you sequenced your construct and if so, is the sequence available in an electronic format?
7. Do you have data evaluating the genetic stability of the recombinant vector? Have you established mutation rates and/or rates of reversion to either wild type or alternate viral genomes?
8. Do you have data evaluating the potential for genetic recombination with other organisms in the patient or in the environment? Please describe.
9. Is the organism currently being grown in a qualified cGMP cell line? If not, is there a qualified cell line available for propagation of this vector? Was the cell line genetically modified to support this vector? If so, please describe the details of its construction and any information you have regarding the stability of the genetic alteration in the cell line.
10. Do you have a cGMP qualified Virus Seed Bank?
11. Please provide details of your production method.
12. Has this material ever been produced for laboratory or clinical studies using this production system?
13. Has this material ever been produced in a related or other production system? If so,

please provide the details.

14. Please provide details of your purification methods.
15. What is the average yield of your production system before and after purification? What is the largest amount of material that you have produced in your laboratory in a single production batch? Please provide average ratios obtained by this production method for virus particle/infectious unit and infectious units/cell.
16. Do you have any material to supply as a reference standard?
17. Do you have any material to supply as bulk biological substance for preliminary pharmacology and toxicology studies? If so, how much is available for these studies?
18. Do you have reproducible assays for your product? Please describe the following assays for evaluating your material, if available:
  - Identity:
  - Purity:
  - Potency:
19. Do you have a proposed list of release criteria for your product? If so, please provide the information.
20. In what form (lyophilized, formulated product, etc.) and fill size do you want the final product? What is the desired final product formulation?
21. Are there issues of formulation that must be resolved?
22. What is known about the stability of your product with respect to physical integrity and activity?
23. Do you have any information regarding the estimated costs associated with this project?
24. Have you identified any possible sources of production with any commercial firms? Please provide any details that you have.
25. Are there any safety issues connected with the production, purification, and/or handling of your product?
26. What is the status of your product(s) regarding intellectual property issues?
27. Sometimes, proposed projects are an improvement or modification of an existing approach. In these cases, this information may significantly affect our analysis of feasibility, cost, and other production issues. Of course, this information may also be important in consideration of intellectual property issues. To the extent that you are

aware, please provide a brief summary of the nature of any such antecedents or other approaches that may appear closely related to the project you propose.

28. Have you had or are you preparing to have any meeting with Regulatory Agencies, such as a pre-IND meeting with the US FDA or a presentation to the NIH RAC? If so, please indicate the type of meeting, the regulatory agency, and the date or proposed date.
29. If you have had a pre-IND or RAC meeting, were any issues concerning manufacturing, safety, or stability raised by the FDA that will have an impact on producing your product?
30. Who will sponsor the IND for the proposed study?
31. Has a source of funding been identified for performing the clinical trial with this product?
32. Please describe any other aspects of your project that have not been addressed in this questionnaire.