Upstream BioProcessing Questionnaire

Please answer the following questions as completely as possible.

|  |
| --- |
| **I. Customer Information**  |
| Contact Person  |   |
| Designation  |   |
| Department  |   |
| Company Name  |   |
| Contact Number  |   |
| Email Address  |   |

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| **II. General Details**  |  |  |
| 1.  | Target Product  | □  | Secreted Protein  |
|  |  | □  | Non-secreted protein  |
|  |  | □  | Cell bank  |
|  |  | □  | mAbs  |
|  |  | □  | Virus production  o Human  o Veterinary  |
|  |  | □  | Cell therapy (Please answer Cell Therapy Questionnaire)  |
|  |  | □  | Others:  |
| 2.  | Cell Type  | □  | Adherent cell (Proceed to Adherent Cell Questionnaire)  |
|  |  | □  | Suspension cell (Proceed to Suspension Cell Questionnaire)  |

# Adherent Cells Questionnaire

|  |  |
| --- | --- |
| **I. Experiment Details**  |  |
| *a. General Details*  |  |
| 1.  | Cell Line  | □  | CHO  |
|  |  | □  | MDCK  |
|  |  | □  | Vero  |
|  |  | □  | HEK 293  |
|  |  | □  | Hybridoma  |
|  |  | □  | Sf 9  |
|  |  | □  | Others:  |
| 2.  | Any special features or peculiarities of the cell line or methods  |      |  |
| 3.  | Intended Use  | □  | Human Use  |
|  |  | □  | Animal Use  |
| 4.  | Product  | □  | Secreted Protein  |
|  |  | □  | Non-Secreted Protein  |
|  |  | □  | Cell Banking  |
|  |  | □  | mAbs  |
|  |  | □  | Virus Production  |
|  |  | □  | Cell Therapy  |
|  |  | □  | Others:  |
| 5.  | Current Culture System  | □  | T-flask  |
|  |  | □  | Roller bottle  |
|  |  | □  | Spinner flask  |
|  |  | □  | Cell factory  |
|  |  | □  | Cell stack  |
|  |  | □  | Hyper flask  |
|  |  | □  | Stirred Tank Bioreactor with Carriers  |
|  |  | □  Indicate  | Others: Capacity in liters (L):  |
| 6.  | If carriers are used, please specify type and amount of carrier.  | □ Microbeads, Specify: □ Fibers, Specify: □ Others, Specify: Amount of carrier:  |
| 7.  | Current Media in milliliters (mL)  |   |  |
| 8.  | Medium change frequency for current system  | □ □  | 1. day
2. days
 |
|  |  | □  | 3 days  |
|  |  | □ Other : \_\_\_\_\_ days Media volume per change: \_\_\_\_\_ ml  |

|  |  |  |  |
| --- | --- | --- | --- |
| 9.  | Culture condition for cell growth  | □ □  |  Media: Serum:  |
|  |  | □  | Temp.:  |
| 10.  | Currently using serum-free culture medium?  | □ □  | Yes No  |
| 11.  | Concentration of additives  | □  | Sodium bicarbonate:  |
|  |  | □  | Hepes buffer:  |
|  |  | □  | Others:  |
| 12.  | Cell Harvesting Required  | □  | Yes  |
|  |  | □  | No  |
| 13.  | Glucose concentration in initial culture medium  |   |  |
| 14.  | Use of trypsin during cell harvest  | □ □  | Yes No  |
|  |  | □  | Use others. Please specify:  |
| 15.  | Cell Quantification  | □  |  Manual counting  |
|  |  | □  | Auto-counter  |
|  |  | □  | Nuclei counting  |
|  |  | □  | Others:  |
| 16.  | Access to a bio-analyzer for measuring glucose, lactate, glutamine, etc.  | □ □   | Yes No  |
| 17.  | System preference  | □  | Single-Use Preference  |
|  |  | □  | Multiple-Use Preference  |
|  |  | □  | No Preference  |
| 18.  | Scale-up plan  |   |  |
| 19.  | Expected Scale  | □  | 50L  |
|  |  | □  | 100L  |
|  |  | □  | 500L  |
|  |  | □  | Others:  |
| 20.  | For virus production, annual manufactured dose  |      |  |
|   |  |  |
| *b. Protein Production*  |  |  |
| 1.  | Culture period prior to harvesting  | □ □  |  3 days 5 days  |
|  |  | □  | 7 days  |
|  |  | □  | Other (Please Specify): \_\_\_\_\_ days  |
| 2.  | Protein extraction method  | □  | By cell harvest  |
|  |  | □  | By medium harvest  |
|  |  | □  | Freeze/Thaw method  |
|  |  | □  | Others:  |
|   |  |  |
| *c. Virus Production*  |  |  |

|  |  |  |
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| 3.  | Virus Type/Strain  |  □ Secreted Virus  □ Non-secreted Virus Virus Strain:  |
| 4.  | Please describe the Virus Strain? (ds, ssDNA, ds,+/- ssRNA, enveloped, nonenveloped, temperature sensitivity, etc.)  |   |  |
| 5.  | Cell density prior to infection in current culture system  |   |  |
| 6.  | Multiplicity of Infection (MOI)  |   |  |
| 7.  | Period of time for cell lysis to occur after infection in current culture system  |   |  |
| 8.  | Culture condition post infection  | □ □  |  Media: Serum:  |
|  |  | □  | Temperature:  |
| 9.  | Best phase for infection  | □  |  Right after seeding  |
|  |  | □  | Exponential phase  |
|  |  | □  | Plateau phase  |
| 10.  | Is the virus stable during post infection?  |   |  |
| 11.  | Virus titer in current culture system (dose/ml)  |   |  |
| 12.  | Best time to harvest the virus  |   |  |
| 13.  | Is there CPE (cytopathic effect) after infection? When?  | □ □  | Yes \_\_\_\_\_ hours / days later No  |
| 14.  | What kind of CPE is formed (e.g. syncytium, destruction, etc.)  | □  |   |
| 15.  | Cell lysis post infection  | □  | Yes \_\_\_\_\_ hours / days later  |
|  |  | □  | No  |
| 16.  | Number of harvests that could be done during post-infection period  | □ □ □  | Single Harvest Multi-harvest for \_\_\_\_\_ times Continuous Harvest for \_\_\_\_\_ days  |
| 17.  | Do cells keep propagation after virus infection?  | □ □   | No Yes, Indicate fold increase post infection:  |
|   |
| *d. CelCradle™ System*  |
| 1.  | Will seeding of 1 x 108 cells be difficult?  |  □ Yes  □ No If yes, how many cells do you plan to seed?  |
| 2.  | Will the CO2 incubator be exclusively used for the CelCradle™ system?  |  □ Yes □ No  Can you adjust the percentage of $CO\_{2}$ concentration?  □ Yes  |
|  |  |  □ | No  |
| 3.  | Expected maximum cell density (total cell harvest per bottle)  | □ □ □  | Total Harvest Volume: Cell Density (cells/ml): Expected culture period:  |

# Fermentation/Suspension Cells

|  |  |
| --- | --- |
| **I. Experimental Details**  |  |
| *a. General Details*  |  |
| 1.  | Application  | □  | Microbial Culture  |
|  |  | □  | Suspension Cell Culture  |
|  |  | □  | Adherent Cell Culture  |
| 2.  | Cells Culture  | □  | Bacteria  |
|  |  | □  | Yeast  |
|  |  | □  | Fungi  |
|  |  | □  | Cell Line:  |
|  |  | □  | Other:  |
| 3.  | a. For adherent cells, specify type and amount of carrier used  | □ □ □  | Microbeads, Specify: Fibers, Specify: Others, Specify:  |
|   | b. Amount of carrier  |   |  |
| 4.  | Product  | □  | Secreted Protein  |
|  |  | □  | Non-Secreted Protein  |
|  |  | □  | Fermentation  |
|  |  | □  | Cell Banking  |
|  |  | □  | Secreted Virus  |
|  |  | □  | Non-Secreted Virus  |
|  |  | □  | Others:  |
| 5.  | a. Current Culture System  | □  | Spinner Flask  |
|  |  | □  | Stirred Tank Bioreactor  |
|  |  | □   | Other:  |
|   | b. Current Culture Scale in liters (L):  |   |  |
| 6.  | Current Process Mode  | □  | Batch  |
|  |  | □  | Fed-Batch  |
|  |  | □  | Continuous  |
|  |  | □  | Other:  |
| 7.  | Culture condition for cell growth  | □ □  | Media: Serum:  |
|  |  | □  | Temp.:  |
| 8.  | Currently using serum-free culture medium?  | □ □  | Yes No  |
| 9.  | Concentration of additives  | □  | Sodium bicarbonate:  |
|  |  | □  | Hepes buffer:  |
|  |  | □  | Others:  |
| 10.  | Cooling system required?  | □  | Yes  |
|  |  | □  | No  |
| 11.  | Temperature sensitive?  | □  | Yes  |
|  |  | □  | No  |

|  |  |  |
| --- | --- | --- |
| 12.  | pH Sensitive?  | □ Yes □ No  |
| 13.  | a. Shear Stress Tolerance  | □ High Sensitivity □ Medium Sensitivity □ High tolerance to shear stress  |
|   | b. Preferred Impeller Type  |   |
|   |
| *b. Process Control*  |
| 1.  | Reactor Size  | Minimum working volume: Maximum working volume:  |
| 2.  | Agitation Speed  | Range: \_\_\_\_ rpm to \_\_\_\_ rpm  |
| 3.  | Measurements Required  | □  | Temperature  | \_\_\_\_ oC to \_\_\_\_ oC  |
| □  | pH  | \_\_\_\_ to \_\_\_\_  |
| □  | DO  | \_\_\_\_ % to \_\_\_\_ %  |
| □  | Redox  | \_\_\_\_ mV to \_\_\_\_ mV  |
| □ Turbidity  |
| □ Foaming  |
| □ Level  |
| □ pCO2  |
| □ O2/CO2 in Exhaust Gas  |
| □ Others  |
| 4.  | Temperature Control  | □ Double wall vessel □ Heating Jacket □ Heating Pad □ Heating/Cooling Pad □ Other:  |
| 5.  | pH Control  | □ Addition of Base □ Addition of Acid □ Addition of CO2 □ Others:  |
| 6.  | Dissolved Oxygen Control  | □ Impeller Speed □ Addition of O2 □ Gas Flow Rate □ Others:  |
| 7.  | Foaming  | □ High □ Low □ Not yet determined  |

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| 8.  | Applied Gases for Aeration  | □ Air □ Air + O2 □ Air + O2 + N2 □ Air + O2 + N2 + CO2 □ Others Mixing System: □ Yes □ No  |
| 9.  | Airflow  | Range: \_\_\_\_ vvm to \_\_\_ vvm Control: □ Regulator (manual)  |
|  |  | □  | Mass Flow Controller  |
|  |  | □  | Others:  |
| 10.  | Aeration Delivery  | □  | Overlay  |
|  |  | □  | Sparger, Type: o Ring Sparger o Microsparger o Others:  |
|  |  | □  | Both  |
| 11.  | Pressure Control Requirements  |       |  |
| 12.  | Other Special Requirements  |       |  |
|   |  |
| *c. Reactor Requirements*  |  |
| 1.  | Vessel Material  | □  | Borosilicate Glass  |
|  |  | □  | SS 316L  |
|  |  | □  | Others:  |
| 2.  | Seeding  | □  | Needleless Seeding Port  |
|  |  | □  | Needle Injection Inoculation Port  |
|  |  | □  | Others:  |
| 3.  | Pressure Control System  | □  | Manual Control  |
|  |  | □  | Automatic Control  |
| 4.  | Sterilization  | Temperature: \_\_\_\_ oC to \_\_\_\_ oC Period:  |
| 5.  | Fluid Addition  | Volume: Number of Ports: □ 0  |
|  |  | □  | 1  |
|  |  | □  | 2  |
|  |  | □  | 3  |
|  |  | □  | 4  |
|  |  | □  | Others:  |
| 6.  | Number of Sampling Port  | □  | 0  |
|  |  | □  | 1  |
|  |  | □  | Others:  |
| 7.  | Air Filter Housing  | Filter Size: □ 0.2µm □ Others: Integrity Test Port: □ Yes □ No  |
| 8.  | Exhaust Filter Housing  | Filter Size: □ 0.2µm □ Others: Integrity Test Port: □ Yes □ No  |

# Cell Therapy

|  |  |  |
| --- | --- | --- |
| **I. Experiment Details**  |  |  |
| *a. General*  |  |  |
| 1.  | Target  | □  | Autologous Cell Therapy  |
|  |  | □  | Allogeneic Cell Therapy  |
|  |  | □  | Research  |
|  |  | □  | Others:  |
| 2.  | Cell Source  | □  | Bone Marrow  |
|  |  | □  | Adipose-derived  |
|  |  | □  | iPS  |
|  |  | □  | Embryo  |
|  |  | □  | Placenta  |
|  |  | □  | Umbilical  |
|  |  | □  | Dermal fibroblast  |
|  |  | □  | Others:  |
|   |  |  |
| *b. Previous Culture*  |  |  |
| 1.  | System Used  | □  | T-flask  |
|  |  | □  | Petri dish  |
|  |  | □  | Roller bottle  |
|  |  | □  | Cell Factory  |
|  |  | □  | Cell Stack  |
|  |  | □  | HyperStack  |
|  |  | □  | HyperFlask  |
|  |  | □  | Microcarrier (Spinner Flask)  |
|  |  | □  | CellCube  |
|  |  | □  | Hollow Fiber  |
|  |  | □  | Others:  |
| 2.  | Scale in millliters (mL)  |   |  |
| 3.  | Total number of cells per cell culture device  |   |  |
|  |  |  |  |
| 4.  | Cell Harvest  | □  | Trypsin  |
|  |  | □  | Collagenase  |
|  |  | □  | Others:  |
| 5.  | Number of culture device used per batch  |   |  |
|   |  |  |
| *c. Process Plan*  |  |  |
| 1.  | System  | □  | Autoclavable  |
|  |  | □  | Single-Use  |
|  |  | □  | Hybrid (both autoclavable and single-use components in 1 system)  |
| 2.  | Process  | □  | Batch  |
|  |  | □  | Fed-batch  |
|  |  | □  | Perfusion  |

|  |  |  |  |
| --- | --- | --- | --- |
| 3.  | Culture Medium  | □  | Serum-containing  |
|  |  | □  | Serum-free  |
|  |  | □  | Xeno-free  |
|  |  | □  | Protein-free  |
|  |  | □  | Animal component-free  |
|   |  |  |
| *d. Scale-up*  |  |  |
| 1.  | Plan for scale-up  | □  | Yes  |
|  |  | □  | No  |
| 2.  | Scale in terms of number of cells  | □ □  | 109 1010  |
|  |  | □  | 1011  |
|  |  | □  | 1012  |
|  |  | □  | >1013  |