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* | |  |  |

|  |  |  |  |
| --- | --- | --- | --- |
| 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 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 | | |

|  |  |  |  |
| --- | --- | --- | --- |
| 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 |