Cyto-Mine®: Single cell analysis and monoclonality assurance system for Cell Line Development

Corporate:

Sphere Fluidics Ltd, an established Life Sciences company based near Cambridge (UK), develops unique product for use in single cell analysis and characterisation and provides collaborative R&D services. The Company has 59 patents (13 patent families with 34 patents being granted) and over 200 international customers. To enable a step-change in the way the biopharmaceutical industry finds and isolates rare cells producing biologics of interest, Sphere Fluidics is currently developing Cyto-Mine®, the single cell analysis and monoclonality assurance system.

Key Application Areas:

- **Biopharmaceutical Discovery**:
  Isolation, assaying, sorting and dispensing of individual B-cells or hybridomas based on antigen-specificity.
- **Bioprocessing:**
  Analysis of heterogeneous cell populations for identification and cloning of the highest secreting single cells.
- **Quality Assurance:**
  Allow ongoing analysis of working cell lines to detect early onset of potential genetic drift of bulk cultures.

Technology Enabling Efficient Screening and Isolation of High-Producing Clones:

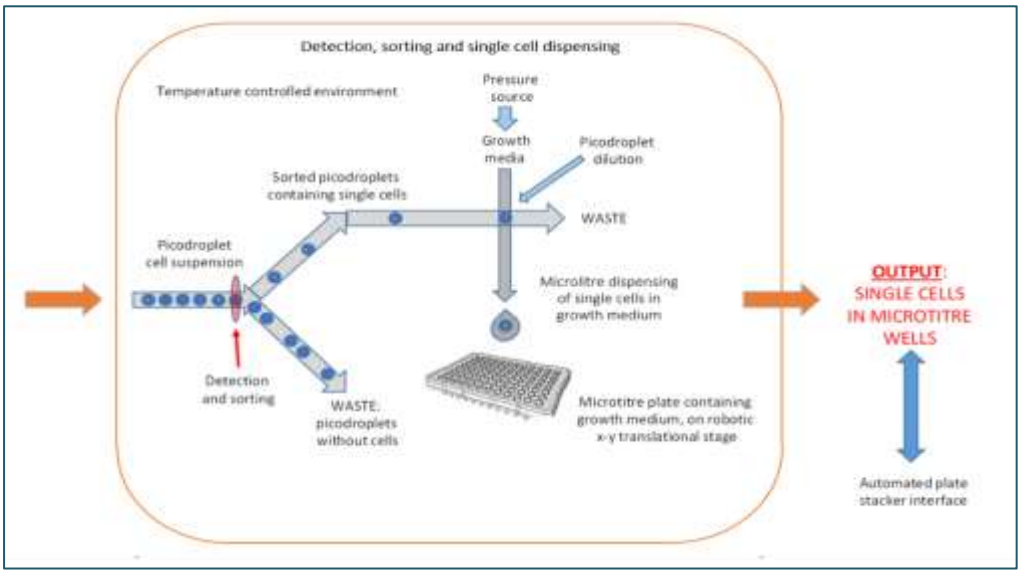
Sphere Fluidics has developed ground-breaking technology for rapidly screening tens of thousands of cells for single cell protein production and then isolating each of the highest producers with assured monoclonality. The proprietary patented technology incorporates novel microfluidics to compartmentalize each cell into its own aqueous picodroplet 'bioreaction chamber'. Each picodroplet is analysed and only those containing a single cell secreting a high level of the target biomolecule are collected and dispensed into individual wells of microplates. The platform utilises sterile "Animal Origin Free" Cyto-Cartridges™ to keep sterility and minimize turnaround time.

Picodroplets during incubation

System Features:

- Processes a heterogeneous population of tens of thousands of cells in less than half a day.
- Directly measures secretion rate of each individual cell in a culture medium environment.
- Isolates the highest-producing single cells into wells with high viability.
- Ensures conformance with FDA requirements that the Ab is derived from a single progenitor cell.
- Single-use, disposable flow pathway ensures sterility and minimal turnaround time.
- All system interfaces and consumables are validated as "Animal Origin Free".
- Benchtop system compatible for use in Class II biosafety cabinet.

Single Cell Analysis and Monoclonality Assurance Process:



Technology Comparison: Current Technologies **Technology Comparison: Cyto-Mine®**

Parameter	Technology Comparison / Approach			
	Manual / Limiting Dilution	**Automation / Clone Pickers**	**Flow Cytometry / FACS**	**Picodroplets / Cyto-Mine®**
Throughput/Run	1,000	10,000	> 1 billion	Up to 1 million
Time Per Run (days)	90	21	1	< 1
Monoclonality Efficiency (%)	8 - 40	95.6	98 to > 99	≥ 99.9
Single Cell Compartmentalisation	No	No	No	Yes
In-Line Assays	No	No	No	Yes
Single-use Disposable Flow Path	Yes	No	Yes/No	Yes
Cell-cell Interaction Studies	No	No	No	Yes
Optical analysis and Verification	No	Yes/No	Yes	Yes
Low Shear Forces	Yes	Yes	No	Yes
Detects Low-abundance, Cell-Surface Proteins on a Single Cell (using enzyme amplification)	No	No	No	Yes
High Accuracy	No	Yes/No	Yes	Yes
Small Footprint/Size	Yes	No	No	Yes
Sample Environment Sterility	n/a	Yes	Yes/No	Yes
Enables Single Molecule Assays	No	No	No	Yes

Cyto-Mine® Additional Benefits:

- Compact design.
- Uses animal-origin free components.
- Dispenses “hit” single cells to individual wells of 96- or 384-well microtitre plates.
- Proprietary.
- Compatible, easy to use consumables.
- Full technical support.

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