COMPREHENSIVE CELL MANUFACTURING SYSTEM BASED ON FLEXIBLE MODULAR PLATFORM

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In cell manufacturing, as it is known that the serial processes influence the quality of the cells, the processes in appropriate cell processing facility (CPF) is expected not only to maintain an aseptic environment but also to lead to stable processing. “Design for manufacturability (DFM)” is known to be the general engineering art of designing products in such a way that they are easy to manufacture. This concept exists in almost all engineering disciplines, but the implementation differs widely depending on the manufacturing technology. DFM for cell production will lead to facilitation of the consistency and robustness for process as well as reduction cost for the cell manufacturing. As shown in Fig. 1, the system consists of input and output for the process. There are several fluctuations derived from extrinsic noises (environmental errors) against the system, input quality such as starter cells and materials (medium, reagents, vessel and pipet etc.), and intrinsic disorders (in-process errors). Especially, intrinsic disorders cause the difficulty to make consistency and robust process for stable quality because the cells have uncertainty accompanied by time-dependent and time-delay properties. Therefore, environmental, material, and operational standardizations are required to realize consistent process. A novel design of manufacturing facility has been proposed based on the isolator technology (Fig.2). Our proposal system is the flexible modular platform (fMP) which realize that the individual aseptic modules can connect and disconnect between modules (or pods) flexibly with keeping the aseptic environment in each module (or pods), leading to the compactness of aseptic processing area and quick change-over for multi-purposes and patients. To effectively implement this fMP technology, an interface that can be aseptically detached and attached from one module to another is required, responding to diversified requirements for cell processing. A common tool utilized in isolator based manufacturing of sterile pharmaceuticals is a transfer pod of rapid transfer ports (RTP). However, its interface limited to a circular configuration, and a more versatile aseptic transfer mechanism is sought for handling the connection between modules (or pods). Therefore, the interface of double door system is developed for the flexible connections between modules with shorten of the decontamination process. Furthermore, the standardization of the configuration suggests that the companies, who have novel modules with advanced technologies, lead to taking part in planning for further development of cell processing easily, compared to that in case of monopoly business by a certain company.
Thus, our attempts are concluded to build an advanced culture system employing isolator technology, and the adaptation of the fMP in CPF will lead to easy installation of the new modules for production line addition and/or revision through the clinical phases as well as commercial production, which contributes to the reduction of production costs.

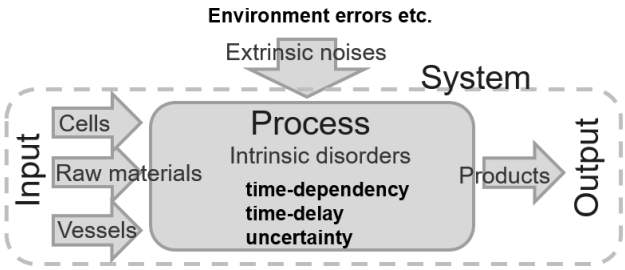

Fig. 1 Cell manufacturability

Fig. 2 Cell manufacturing system based on fMP