PARTICLE MEASURING SYSTEMS
a spectris company

Decentralized Manufacturing: Compliance in the Future of Production

As new products are brought to market there is an opportunity to look at the production and manufacturing schedule of how and where these products are defined. Traditionally a central facility is required for all production activities, centralized production has many advantages associated with the management of process and product quality, personnel skills, form factor for packaging, storage and release to market. But as the products become more personalized a distributed model allows for manufacturing to be maintained at pilot scale and replicated at multiple locations to gain advantage of increased overall production volumes.

Distributed manufacturing allows for production to be divided into regional, geographic locations, with potential for international expansion. The core, traditionally centralized manufacturing model, is dissected at opportune delineation points allowing for remote performance of those activities. There are significant advantages to be gained from such a model by geographically assigning supply, personnel to locally required tasks, such as cell collection, harvesting and preparation, these can then be complemented using a centralized production facility for core active components to be distributed to the local facilities; and then formulated at the decentralized location to meet local demands for delivery and volume deadlines.

There are however challenges associated with this distributed model, specifically as discussed here associated with the environmental monitoring and control of the remote production facilities and the automated controls required to ensure a centralized Contamination Control Strategy (CCS) can be implemented at multiple locations. These controls are essential as the product itself becomes the validated target and not the facility or location of process.

The advance of distributed control systems such as **PHARMACEUTICAL-NET PRO** and **PHARMACEUTICAL-INTEGRITY** software platforms allows use of interconnected computers, virtual systems which can allow for visualization, data management, tolerance deviation identification and criticality, reporting of controls throughout the entire process of a production batch form a single portal.

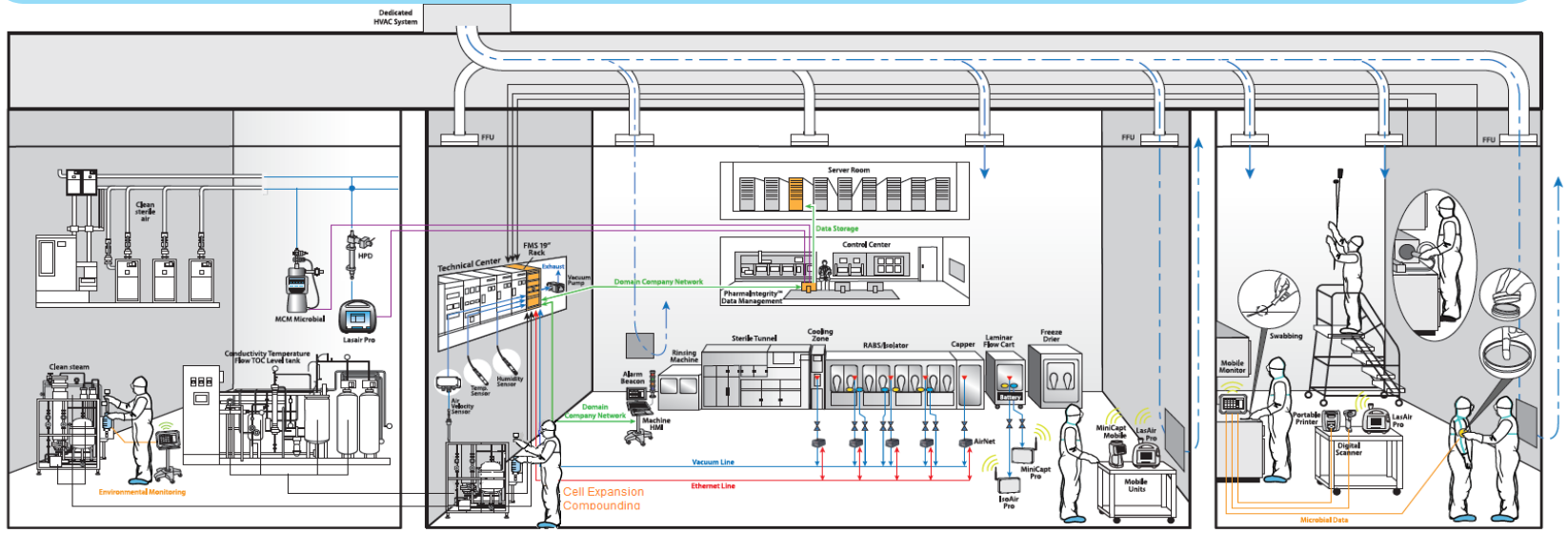
The combined technologies allow for a common Contamination Control Strategy (CCS) to be defined and automatically alert both regional facilities of any local alarms, associated with high particle counts within critical areas, or excessive bioburden taken from incubated samples via a quality control microbiology facility, which again can be a distributed, local provider. Advances in IoT will allow for local systems adapting to regional variances and tolerance thresholds can adopt to appropriate control limits as required. The central system will manage the overall control for release of batch to distribution, and these connections will traverse via the installed systems. The regional facilities will in essence replicate the central facility and maintain manufacturing quality across the network of sites.

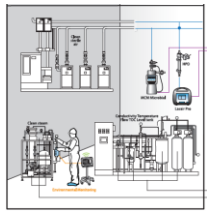
The validation of distributed systems can be managed via a central team that is used as a mobile technical support squad to ensure that any regional facility can be deployed with the least disruption to current activities. Personnel can be sourced local to the production facilities, alleviating the demands on a single central location for qualified staff.

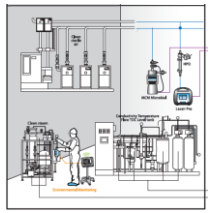
Centralized Production

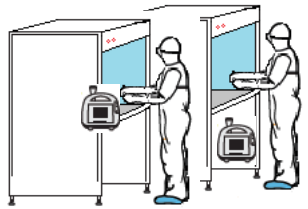
Traditional centralized pharmaceutical production has all functions associated with a product or range of products available under a single roof, or at least available at a single geographic location. It may be that raw materials are harvested and prepared in a separate building, but this building is immediately available to the production environment. Also, the final quality control verification, packaging and storage facilities may also be adjacent, within the site to the core manufacturing facility, and from a production visibility perspective everything is "under-one-roof". This allows for the environmental monitoring program to be controlled and executed using a single multidisciplinary team with access to central instrumentation and download opportunities for data, records and reporting of field information.

The environmental data can be collected at the source location and easily compared to the batch release of a product, from collection at incoming quality controls, through formulation and the fill and finish process. Point of use sensors can collect data and feed directly back into a central monitoring system for local alarm annunciation and registration of any out of tolerance conditions can be identified as cause for either intervention or a CAPA.









De-centralized – sample collection preparation and raw material

– Sample collection from patients is performed at a local facility, hospital or healthcare center and sent to a regional decentralized center for sample preparation. This facility will employ a series of particle counters, microbial samplers and either a terminal node for data entry connected via a network to a central server, or a local instance of a connected system for data automation.

The formulation and harvesting of cells and the additional of active components is performed locally under regional guidance of regulatory compliance, any additional environmental concerns and measurements can be added to the CCS as a function of a specific facility.

The facilities will be monitored for air, surface and water quality, and providing these meet the assigned limits for regional production, no alert or action procedures will be required, and production continue unabated, within the quality control envelope defined by the CCS. If any parameter should be determined as statistically out of control and a potential threat to product quality, then local arms will annunciate the condition, and an alarm will also be transferred to the central site where overall validation of product for release is reported. Any time zone challenges can be overcome with additional remote connectivity to critical quality personnel.

De-centralized Packaging, Distribution and Patient Delivery

– Once a product has been harvested and combined with any active elements required, it can either be centralized for fill and finish, depending on application type, or filled locally in the regional facility. It is this fill finish component that aligns best with traditional GMP requirements, as any lyophilization for transport or long-term storage can be performed at the central facility, as urgent patient turn around and response becomes a lower priority.

Packaging and distribution costs are reduced and alignment with regional requirements for packaging can be made, for suitable quantities determined by the scale of manufacturing. Again, the facilities will be monitored for air, surface and water quality, and providing these meet the assigned limits for regional production, no alert or action procedures will be required, and production continue unabated, within the quality control envelope defined by the CCS.

The final form for delivered product and timings can be added to the batch master file and these transferred via network to the central repository for archive and analysis.