

Table 28: Scaling Out: What Is It? What Are the Requirements

Facilitators –

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Scope:

This table will discuss opportunities and challenges associated with scaling out for small/large molecules, high/low volume production and product development stage. The traditional manufacturing promoted starting with small scale and scaling up to accommodate larger production demand. However, with globalization and numerous individualized therapies, will traditional manufacturing concept continue or would trends shift towards scaling out. The participants will discuss opportunities for scaling out or scaling up, enabling factors for scaling out, scenarios unfriendly for scaling out and regulatory and validation considerations.


Questions for Discussion:

1. Decision of scaling up vs. scaling out
 - a. Challenges
 - b. Opportunities, e.g. Individualized therapies
2. Impact of automation and adoption of SU: Enable scaling out?
3. Benefits of scaling out on other activities
 - a. Does it enable automation of supply chain?
 - b. Provide flexibility with global production, decentralized facilities, manage demand volatility
 - c. Enable multi-product facilities, multiple modalities
 - d. Easier regulatory path for facility extension, commissioning, change management, family approach for validation
4. Scenarios where scale out is not feasible or cost effective

Discussion Notes:

January 26 and 28, February 1 and 3, *combined* –

- Decision of scaling up vs. scaling out
 - Definition of scaling out
 - To increase the volume of production via replicating a similar process at a given volume
 - Replicate the equipment and process stream and make more of the same product or a new product
 - Different from scaling up as this introduces large volume equipment, etc. leading to revalidation runs, more time and more unknowns
 - Opportunities
 - It can be leveraged for transferring to a CMO, or multiple sites
 - A similar approach could be used if the equivalency and comparability is shown with the process and equipment
 - Challenges
 - If there are minor changes in equipment, what would it be compared to? What will be the baseline comparability equipment/state. The comparison will be with the last equipment qualified. However, comparison should be maintained with baseline equipment if used as basis for family approach
 - Molecules with process challenges. Multiple process trains can result in variability or higher probability of process issues. Scale-up is a better option to reduce variability.
- Single use systems have enabled flexible production at smaller scale enabling scale-out especially in unpredictable markets.
- Benefits
 - Individual therapies or small doses (one patient → one lot)
 - Makes automation easier of smaller scale processes
 - Provide flexibility for global production, decentralized facilities, manage volatility better

- Easier regulatory pathway for facility extension, change management. Use of same equipment at same scale for early and late phase/commercial can simplify comparability and tech transfers.
 - Potentially apply family approach for validation if
 - Equipment is like for like
 - Same analytical testing organization
 - Same raw materials, vendors
 - Change Management can be simplified since same change will be applied. Testing can be performed on one equipment and leverage data for other pieces of equipment
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- Prior data, x scale justification, verification  call it good with scaling out
 - Have to show equivalence, comparability by writing a protocol and gathering data to show you have understanding of your process, product and equipment
 - For example for 2nd source suppliers, choose a CMO with similar equipment, process, etc. as your primary source to use scaling out
 - Have to start thinking about this from inception of the product or need to add this to your policies as this can be a time, money saver when the need arise
 - Example included when adding on to your facilities, ensure gray space is available for scaling out purposes but ensure facilities/utilities and etc. are built to handle the replicates as needed
 - If replicates are needed, everything is already completed and only the same modular equipment/skids are needed to be added to already qualified space
 - Ballroom Facility discussed including how equipment is considered the barrier against product/personnel in closed equipment and processes
 - Need rigorous layers of protection including for leaks, process, engineering, and safety
 - Scenarios where scale out is not feasible or cost effective
 - Large volume production, blockbuster products