



# If only we thought about the future when developing a process at small scale

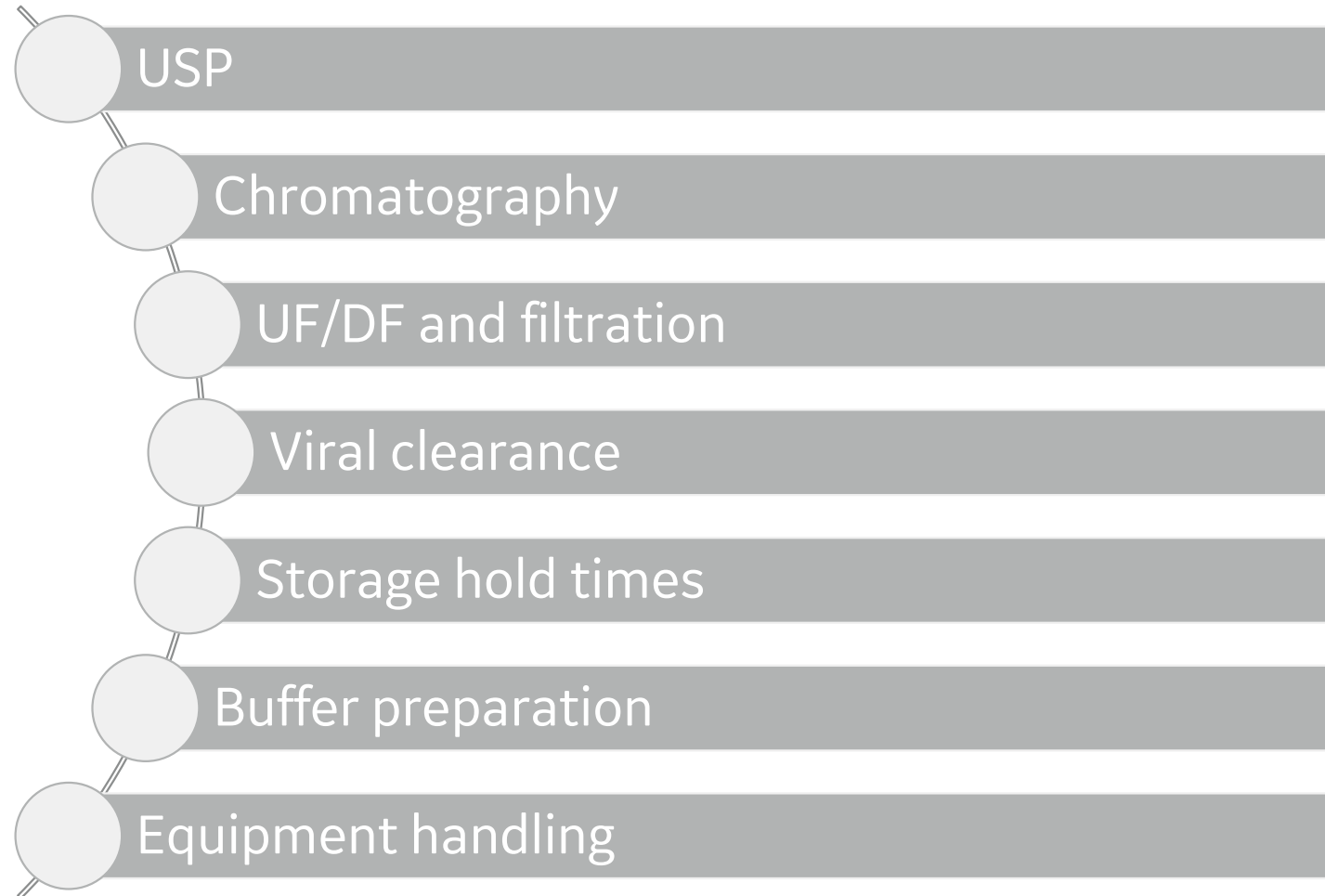
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# Key factors to consider for a successful scale-up



# Many points to consider



# General considerations

- Think of the final manufacturing scale during lab scale process development
- Keep the number of process steps to a minimum
- Avoid difficult operations
- Define parameters, their ranges, and how to control them
- Know the product limits
- Use linear scaleable disposables



# Key points to consider in USP<sup>1</sup> scale-up

- **Maximize production and quality**
  - Spend time selecting a good clone
  - Develop an appropriate cell culture
- **Develop scalable USP**
  - Bioreactor anatomy has an impact in cell growth - find out final manufacturing scale
  - Critical parameters - dissolved oxygen, pH, temperature, and metabolite concentrations
- **Confirm scale-up in several steps**
  - 10L and/ or 50L before going to >200L



<sup>1</sup>USP: Dowsntream Processing



# Key points to consider in DSP<sup>1</sup> scale-up

- **Running parameters**
  - Keep residence time constant
- **Hardware**
  - Maintain bed height, increase column diameter
  - Build pressure/flow curves
  - Consider resin packability and wall effect
- **Process economy**
  - Operate at 70% DBC<sup>1</sup>
  - Spend time to optimize resin cleaning conditions - maximize resin utilization



<sup>1</sup>DSP: Downstream Processing

<sup>2</sup>DBC: Dynamic Binding Capacity



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