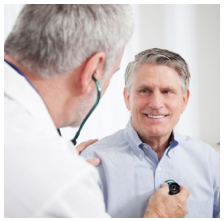
European Federation of Pharmaceutical Industries and Associations

CMC Strategy Forum Europe 2021

Agile (aka Autonomous & Portable) manufacturing with specific focus on Aseptic Modular Chamber

Karoline Bechtold-Peters on behalf of the MQEG Agile Manufacturing Workstream,
18th Oct 2021






EFPIA MQEG Biomanufacturing Satellite Session

PERSPECTIVE

BIOTECHNOLOGY and BIOENGINEERING

Modular

Disposable Bioprocessing: The Future Has Arrived

standardized

Govind Rao,[1] Antonio Moreira,[1] Kurt Brorson[2]
[1]Center for Advanced Sensor Technology, Department of Chemical and Biochemical Engineering, TRC, UMBC, Baltimore, Maryland 21250;
telephone: 410-455-3415; fax: 410-455-1049; e-mail: grao@umbc.edu
[2]Division of Monoclonal Antibodies, Office of Biotech Products, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Silver Spring, Maryland 20903

Portable

VIEWPOINT

BIOTECHNOLOGY and BIOENGINEERING

The Future of Industrial Bioprocessing: Batch or Continuous?

Croughan et al.: The Future of Industrial Bioprocessing
Biotechnology and Bioengineering

People • Science • Regulation
PDA Letter
Volume LIII • Issue 3 www.pda.org/pdaletter March 2017

intensification

configurable

GEN Genetic Engineering & Biotechnology News

Aseptic Filling Adjusting to New Paradigm

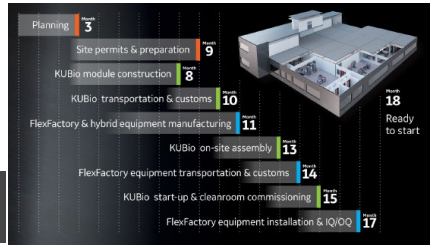
Complex and Sensitive Drugs Necessitate High-Tech Manufacturing Operations

reduced foot print

DAILY NEWS
No. 49,725 THE BEST SELLING NEWSPAPER IN THE WORLD Today's Edition
National - World - Business - Lifestyle - Travel - Technology - Sport - Weather

"globally distributed markets are adding more uncertainty to the existing clinical, regulatory and demand risks"

KUBio



low cost

Rapid tech transfer

Can biomanufacturing be inspired by technological advances and be transformed?

Courtesy Nitin Rathore

Autonomous & Portable Manufacturing

- Technologies are evolving at a rapid pace, and innovative pharmaceutical companies invest significantly in the modernisation of their manufacturing and supply operations towards more agile processes and methods that includes 'Autonomous & Portable' solutions.
- These provide unique opportunities to enhance consistency, in relation to traditional scale up, especially when moving from clinical to initial commercial supply or subsequent transfer/addition of manufacturing sites due to the consistency of equipment, procedures and Quality systems. Higher production volumes can more easily be reached through *scale-out*, in comparison to a traditional *scale-up* approach, and can overall enable more rapid response to patients' demands.
- This reflection paper serves to initiate a dialogue with Regulators to introduce the concept in a way that ensures regulatory standards continue to be met, and products' Quality preserved, as these remain the innovative industry driving manufacturing principles….
- Published on EFPIA website March 2021 *https://www.efpia.eu/media/602579/mqeg-rp-mobile-manufacturing_final23mar2021.pdf*

efpia
European Federation of Pharmaceutical Industries and Associations

Draft ☐ Final ☒

Autonomous & Portable Manufacturing

Author: EFPIA ✱ Date: 23 March 2021 ✱ Version: 1

Reflection Paper

Executive Summary

✱ Technologies are evolving at a rapid pace, and innovative pharmaceutical companies invest significantly in the modernisation of their manufacturing and supply operations towards more agile processes and methods that includes 'Autonomous & Portable' solutions.

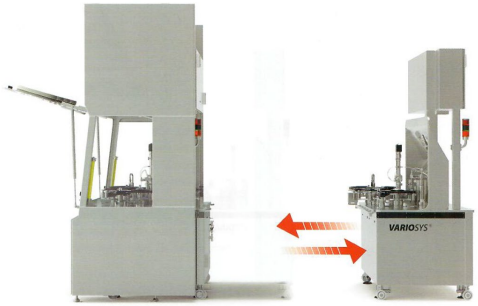
✱ These provide unique opportunities to enhance consistency, in relation to traditional scale up, especially when moving from clinical to initial commercial supply or subsequent transfer/addition of manufacturing sites due to the consistency of equipment, procedures and Quality systems. Higher production volumes can more easily be reached through scale-out, in comparison to a traditional scale-up approach, and can overall enable more rapid response to patients' demands.

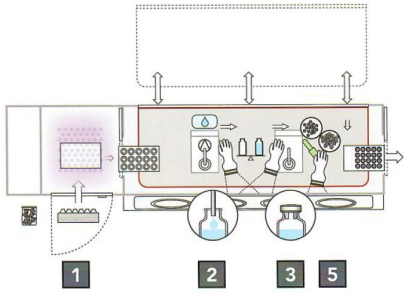
✱ This reflection paper will serve to initiate a dialogue with Regulators to introduce the concept in a way that ensures regulatory standards continue to be met, and products' Quality preserved, as these remain the innovative industry driving manufacturing principles. In Europe, such considerations are especially timely to address the EU Pharmaceuticals Strategy that will consider the "*impact of emerging new manufacturing methods such as decentralised or continuous manufacturing. These methods create new manufacturing models, with a shift from industrial to 'bedside' manufacturing. While speeding up production times, they create new challenges in terms of appropriate quality, inspection and oversight*", and building on the EFPIA initiated dialogue with the EMA Quality office to engage in discussions on emerging technologies.

Innovations 2010 – 2020 in „Agile“ Aseptic Manufacturing of Steriles

(the pictures/machines given here are not exhaustive, only examples)

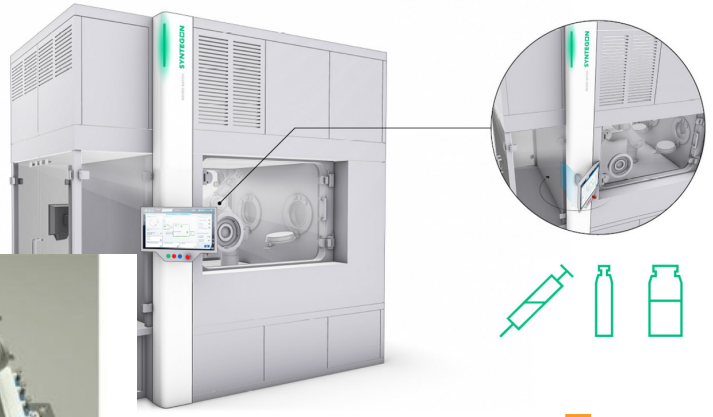
Innovation 1.0: Highly Modular



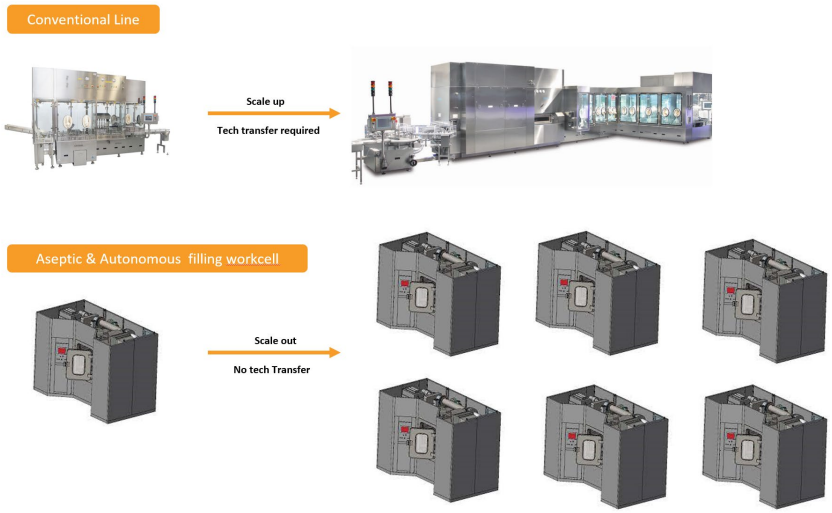


Innovation 2.0 NOW: Gloveless, fully automated and autonomous

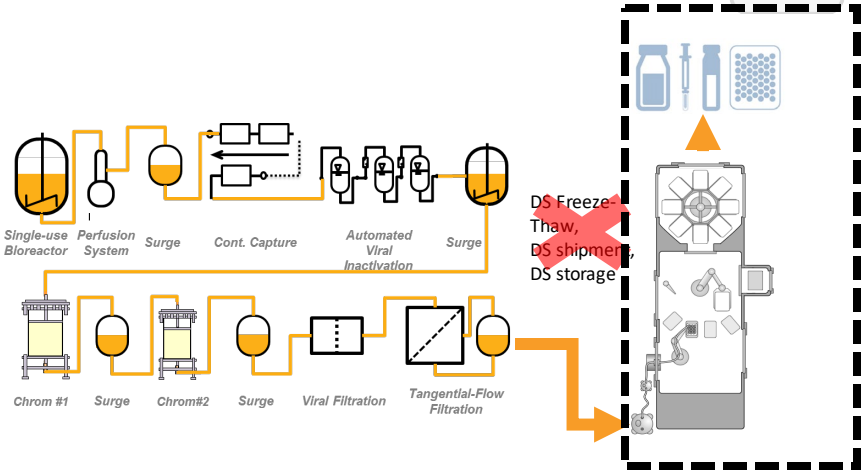
Just plug in!



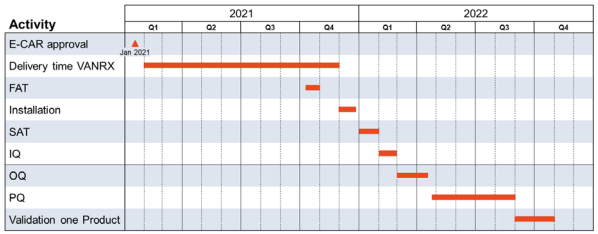
Advantages of „Agile“ Aseptic Manufacturing of Steriles using Autonomous Aseptic Workcell Concepts



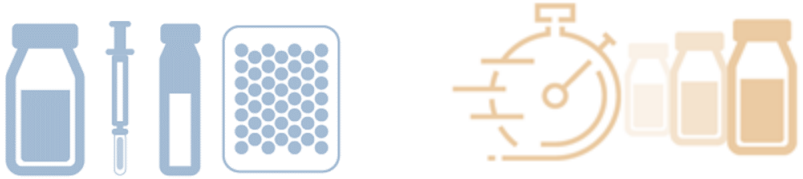
Increasing the throughput by scaling out



Potential for Connectivity DS-DP



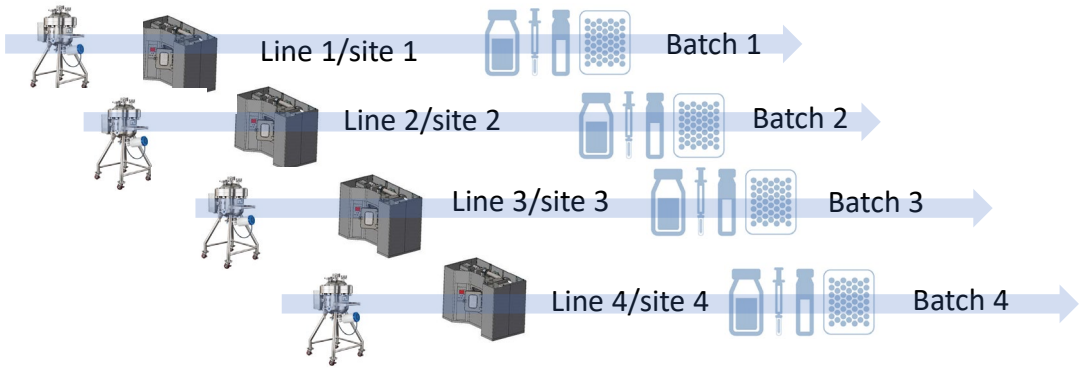
Agility in adding new lines



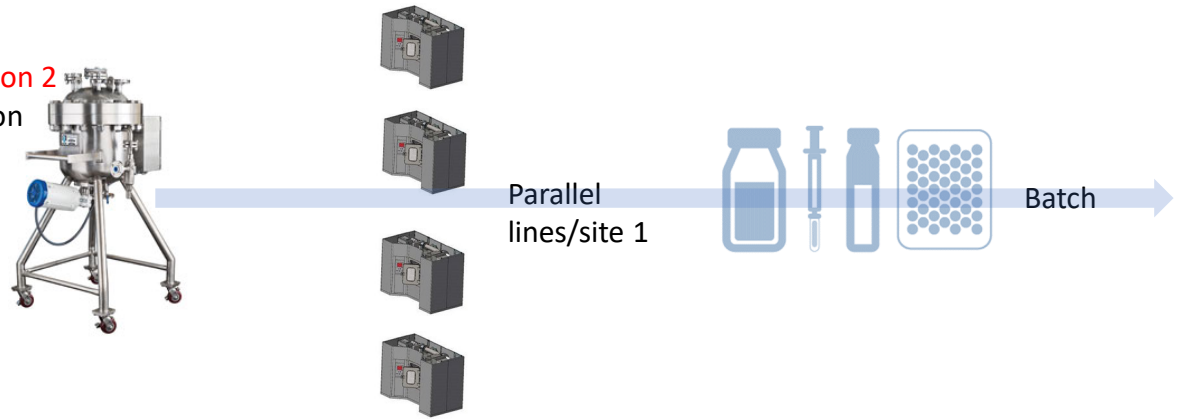
Flexibility in Dosage Forms and Fast Changeover (hours instead of days)

Scale-out definitions

Scale out Option 1
= matrixing and bracketing



Scale out Option 2
= parallelization



General remark: also Scale Down is easier compared to fast running machines (in case product needs go down)

In order to really end up at «Agile» Aseptic Manufacturing more than the technical equipment needs to be provided...here some guiding questions

Let us assume a multitude = "fleet" of those "agile work chambers" at a company

- **Can some elements of the qualification/validation be transferred and only a confirmation run be performed if machines identical?**
  - Examples:
    - VHP cycle (one machine as a pilot, the other machines just make a confirmation run)
    - Alarm testing (first machine full testing, further machines only critical tests)
    - VHP residual amounts or CIP/SIP or...(one machine as a pilot, the other machines just make a confirmation run)
    - FAT/OQ (full program for first machine, further machines only check parts of the circuit diagram and of the P & I scheme)
    - Matrix of media fills across sites
- **To accelerate acceptance, do all fleet machines need to be specified at the time of registration or is the term "or equivalent" acceptable?**
- **Multi-product facility – does the design allow for more flexibility as regards a multi-product manufacturing compared to conventional lines because of the increased closure and reduced likelihood of spills?**
- **Microbial monitoring**
  - How can we make best use of upcoming technologies of rapid testing?
  - What can we omit/not do with an acceptable rationale? E.g. settle plates
- **Value of data in case of non-conformity to guidelines not addressing the specifity of such autonomous work chambers? Can angencies be „convinced" by data?**
  - Non-conformity may comprise
    - Air flow
    - Kind and positioning of robot
    - Environment of w ork chamber
    - Monitoring concept

Current Sub-Team on *Agile manufacturing with specific focus on Aseptic Modular Chamber*

Andrea Kurz, Roche

Karoline Bechtold-Peters, Novartis

Michel Eppink, Byondis

Nitin Rathore, Amgen

Yemi Babatola, Amgen

Arnab Ganguly, Amgen

Lucy Chang, MSD

Ana-Silva Nita, MSD

Joerg Zimmermann, Vetter

Dieter Bachmann, J&J

NN from Novo

NN from Bayer