Integration of Single Use Systems in Formulation and Filling Process Step

SCC – 16.04.2018

Philippe Sturchler

Continuously Improving Bioprocesses

Agenda

- Definition of Formulation and Filling area
- Implementing SU Systems in Cleanroom
- Quality by Design (QbD)
- Documentation/Control
- Summary

Definition of F&F Area

Formulation

Bioburden Filtration

Bulk Filling / Storage

Freezing & Storage

Thawing

Sterile Filtration

Final Filling

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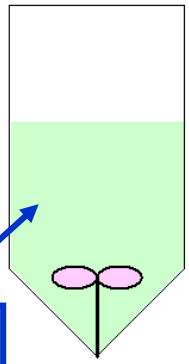
Technical Solutions Formulation

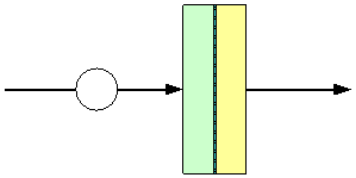
Mixing & formulation prior to bulk or final filling

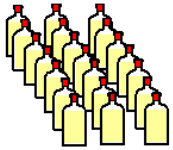
Formulation

Sterile Filtration

Final Filling







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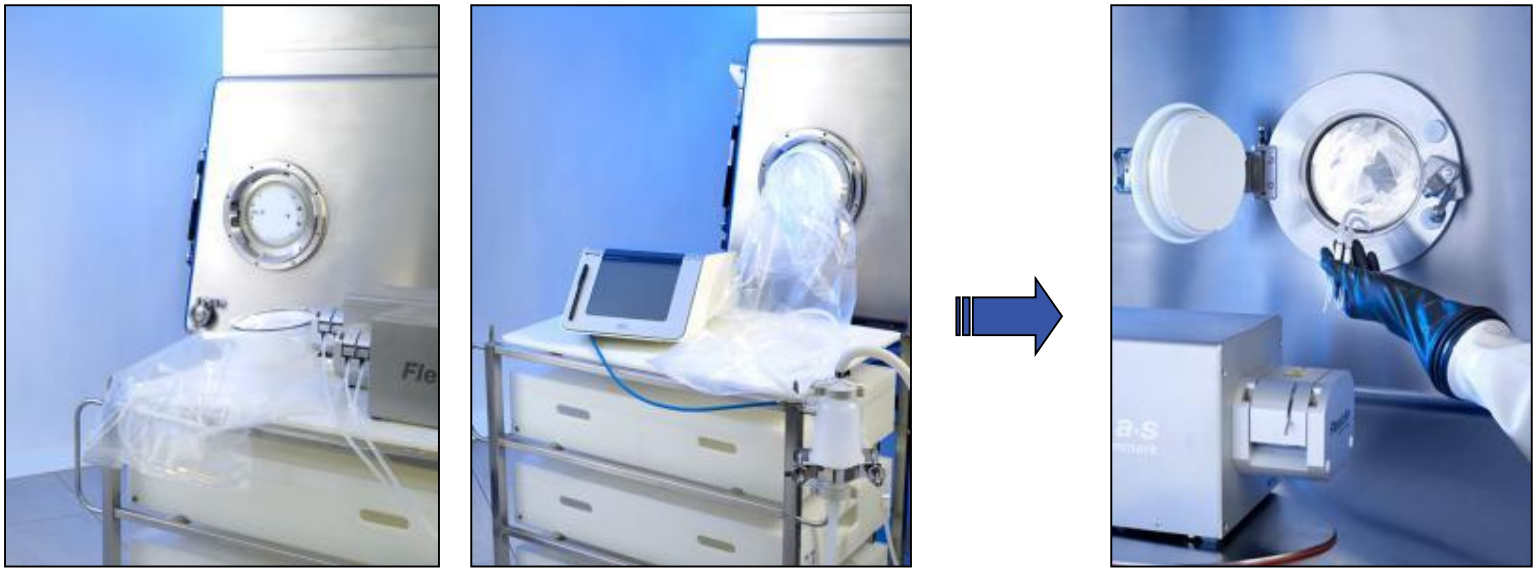
Implementing SU Systems in Cleanroom

- Packaging

- Cleaning

Implementing SU Systems in Cleanroom

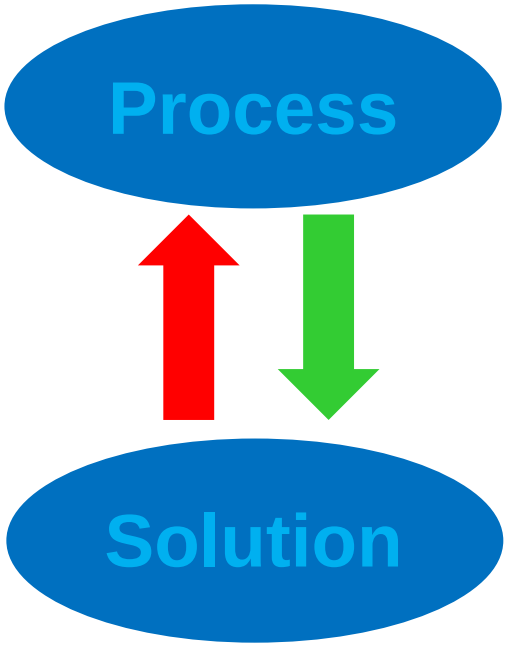
- RTP Port



Grade C/D zone

Grade A zone (isolator)

Quality by Design (QbD)

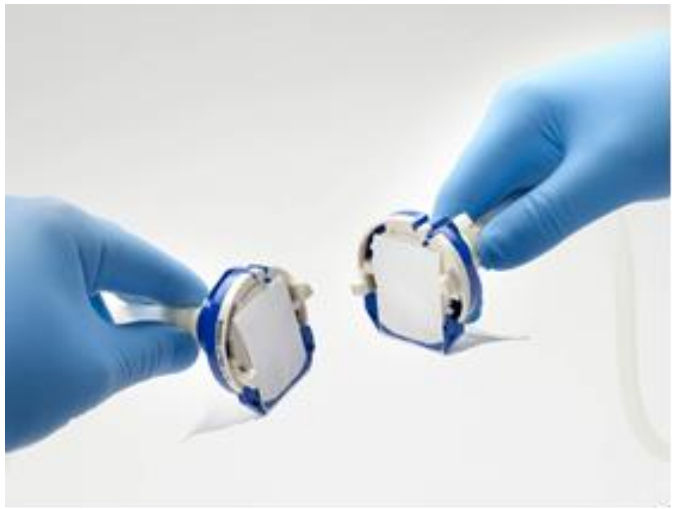


- Adapt material/system to process (not the contrary!)

Quality by Design (QbD)

- Sterile Connectors
  - Gendered VS Genderless

Kleenpak Sterile Connector



Presto Sterile Connector

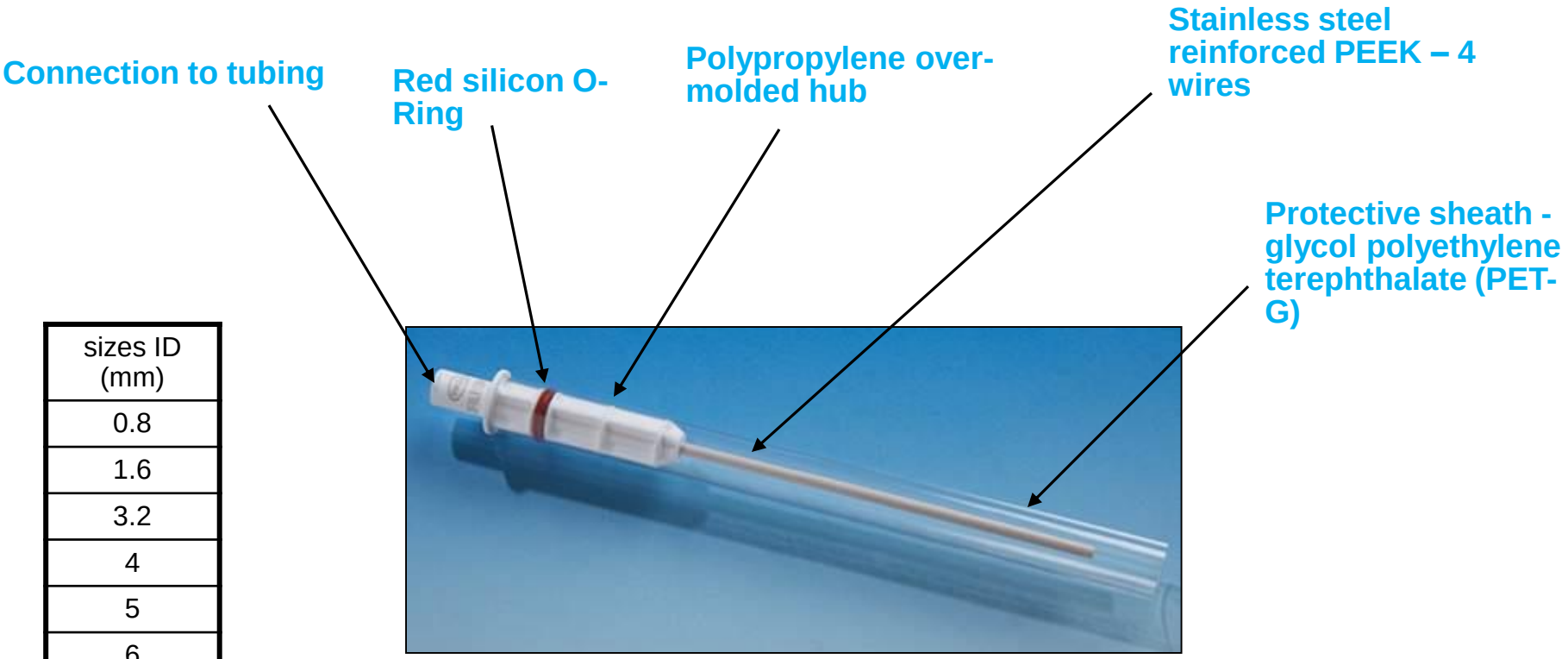
Quality by Design (QbD)

- Tubings and Fittments

Tubing			Connectors
Platinum Cured Silicon	Braided PCS	C-Flex	'T's, 'Y's, elbows reducers etc
			
Connectors			
Quick Connect	Steam-Thru	Sanitary Hose Barb	BarbLock™
			

Quality by Design (QbD)

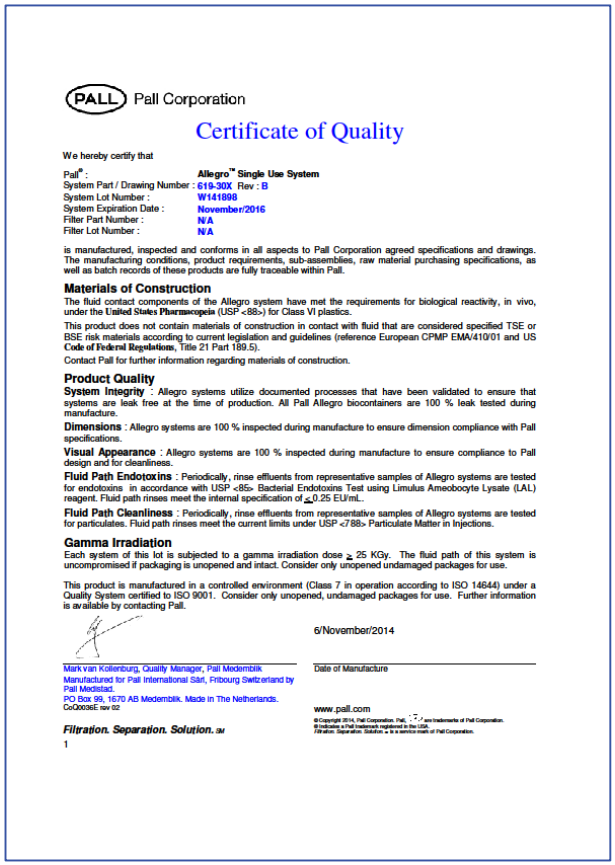
- Needles



sizes ID (mm)
0.8
1.6
3.2
4
5
6

PEEK = Poly Ether Ether Keton

Documentation / Control



Pall Corporation

Certificate of Quality

We hereby certify that

Pall® :	**Allegro™ Single Use System**
System Part / Drawing Number :	**619-30X** Rev : **B**
System Lot Number :	**W141898**
System Expiration Date :	**November/2016**
Filter Part Number :	**N/A**
Filter Lot Number :	**N/A**

is manufactured, inspected and conforms in all aspects to Pall Corporation agreed specifications and drawings. The manufacturing conditions, product requirements, sub-assemblies, raw material purchasing specifications, as well as batch records of these products are fully traceable within Pall.

Materials of Construction

The fluid contact components of the Allegro system have met the requirements for biological reactivity, in vivo, under the **United States Pharmacopeia** (USP <88>) for Class VI plastics.

This product does not contain materials of construction in contact with fluid that are considered specified TSE or BSE risk materials according to current legislation and guidelines (reference European CPMP EMA/410/01 and US **Code of Federal Regulations**, Title 21 Part 189.5).

Contact Pall for further information regarding materials of construction.

Product Quality

System Integrity : Allegro systems utilize documented processes that have been validated to ensure that systems are leak free at the time of production. All Pall Allegro biocontainers are 100 % leak tested during manufacture.

Dimensions : Allegro systems are 100 % inspected during manufacture to ensure dimension compliance with Pall specifications.

Visual Appearance : Allegro systems are 100 % inspected during manufacture to ensure compliance to Pall design and for cleanliness.

Fluid Path Endotoxins : Periodically, rinse effluents from representative samples of Allegro systems are tested for endotoxins in accordance with USP <85> Bacterial Endotoxins Test using Limulus Ameobocyte Lysate (LAL) reagent. Fluid path rinses meet the internal specification of ≤ 0.25 EU/mL.

Fluid Path Cleanliness : Periodically, rinse effluents from representative samples of Allegro systems are tested for particulates. Fluid path rinses meet the current limits under USP <788> Particulate Matter in Injections.

Gamma Irradiation

Each system of this lot is subjected to a gamma irradiation dose ≥ 25 KGy. The fluid path of this system is uncompromised if packaging is unopened and intact. Consider only unopened undamaged packages for use.

This product is manufactured in a controlled environment (Class 7 in operation according to ISO 14644) under a Quality System certified to ISO 9001. Consider only unopened, undamaged packages for use. Further information is available by contacting Pall.

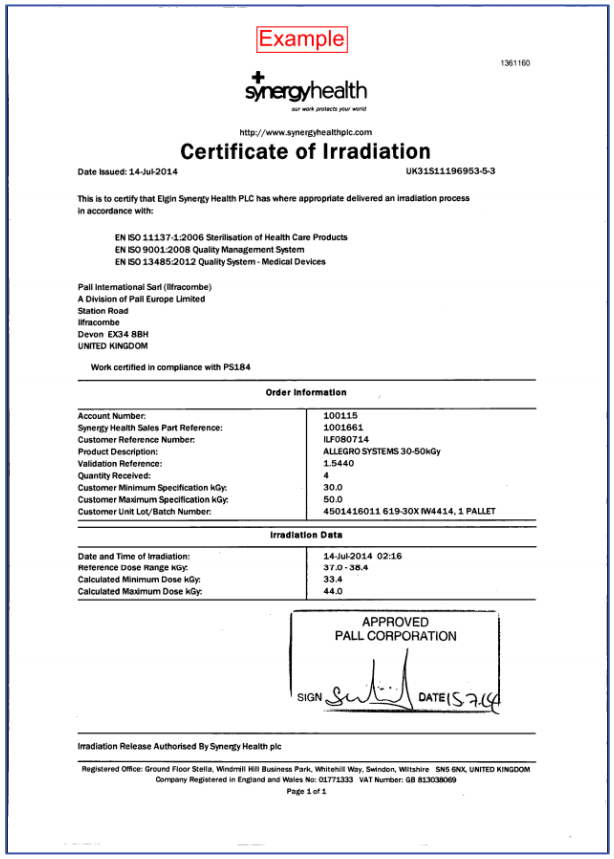
6/November/2014

Mark van Kollenburg, Quality Manager, Pall Medemblik.
Manufactured for Pall International Sàrl, Fribourg Switzerland by Pall Medistad.
PO Box 99, 1670 AB Medemblik. Made in The Netherlands.
CoQ0036E rev 02

Date of Manufacture

www.pall.com

Filtration. Separation. Solution. *sm*



Example

1361160

synergyhealth
our work protects your world

http://www.synergyhealthplc.com

Certificate of Irradiation

Date Issued: 14-Jul-2014 **UK31511196953-5-3**

This is to certify that Elgin Synergy Health PLC has where appropriate delivered an irradiation process in accordance with:

EN ISO 11137-1:2006 Sterilisation of Health Care Products
EN ISO 9001:2008 Quality Management System
EN ISO 13485:2012 Quality System - Medical Devices

Pall International Sarl (Ilfracombe)
A Division of Pall Europe Limited
Station Road
Ilfracombe
Devon EX34 8BH
UNITED KINGDOM

Work certified in compliance with PS184

Order Information

Account Number:	100115
Synergy Health Sales Part Reference:	1001661
Customer Reference Number:	ILF080714
Product Description:	ALLEGRO SYSTEMS 30-50kGy
Validation Reference:	1.5440
Quantity Received:	4
Customer Minimum Specification kGy:	30.0
Customer Maximum Specification kGy:	50.0
Customer Unit Lot/Batch Number:	4501416011 619-30X IW4414, 1 PALLET

Irradiation Data

Date and Time of Irradiation:	14-Jul-2014 02:16
Reference Dose Range KGy:	37.0 - 38.4
Calculated Minimum Dose kGy:	33.4
Calculated Maximum Dose kGy:	44.0

APPROVED
PALL CORPORATION
SIGN [signature] DATE 15.7.14

Irradiation Release Authorised By Synergy Health plc

Registered Office: Ground Floor Stella, Windmill Hill Business Park, Whitehill Way, Swindon, Wiltshire SN5 6NX, UNITED KINGDOM
Company Registered in England and Wales No: 01771333 VAT Number: GB 813038069
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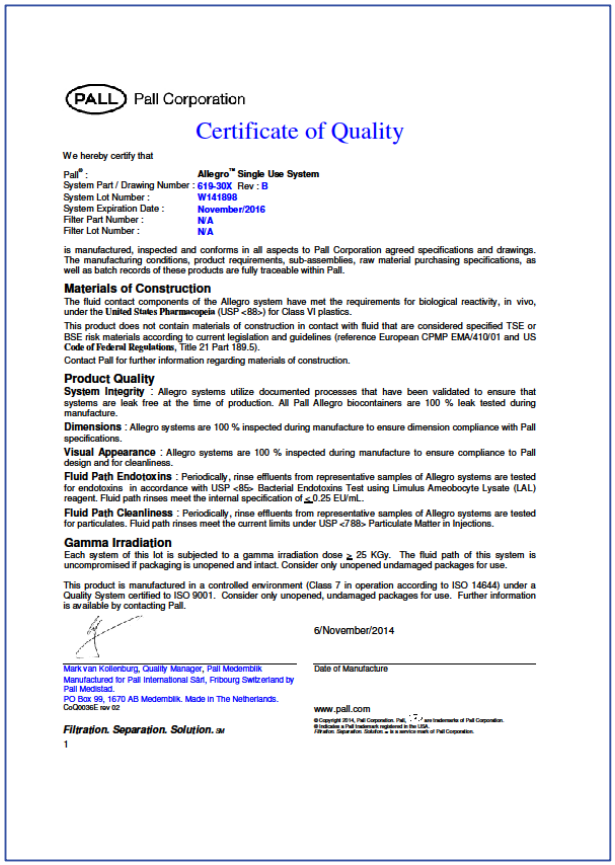
- Sterile Claim if needed

PALL Biotech

Documentation / Control



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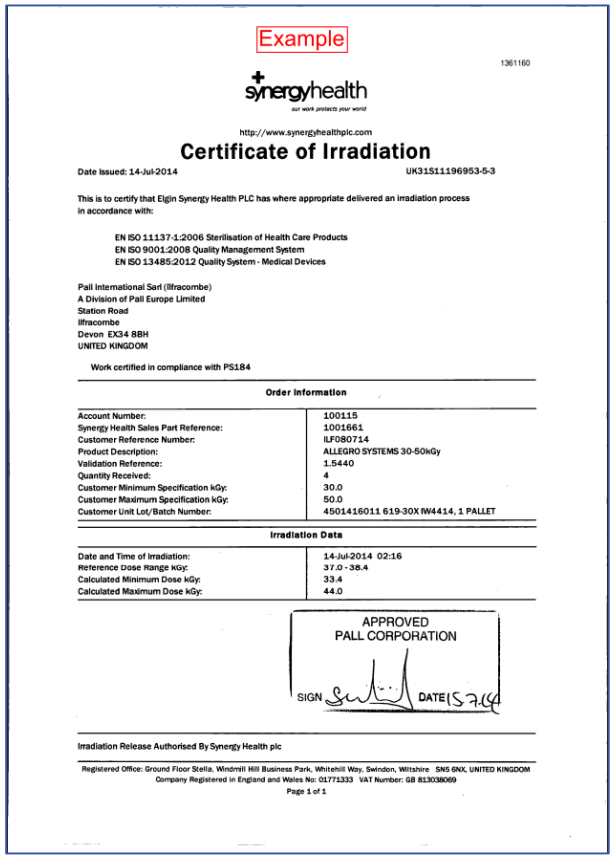
CoQ00ISE rev 02

www.pall.com

Filtration. Separation. Solution. SM



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Documentation / Control

- Point of Use leak test – Flowstar LGR

Summary

- Formulation and filling is a key area
  - Must provide the high level of quality and validation required to facilitate SUS implementation
  - Fits very well with flexible business model of complex solutions, including multiple SU technologies

Summary

- Key points for integration of SUS in Cleanrooms

  - Quality by Design is essential
  - Packaging
  - Implementation and handling
  - Documentation/Control

Discussion

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