EU GMP ANNEX 1 AND ITS IMPACT ON MANUFACTURING AND PROCESSING OF PRIMARY PACKAGING COMPONENTS

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What is Annex 1?

Annex 1 is a guideline most recently updated in 2022 covering the manufacture of sterile products, with a primary emphasis on medicinal products. Most recent updates include active substances, sterile excipients, primary packaging material, and finished dosage form.

Annex 1 was published with cooperation from global health organizations.

When was Annex 1 published?

1971 First publication

2008 Last revision

2022 Major revision since original publication

Why is Annex 1 important?

Prevent microbial, particulate, and endotoxin/pyrogen contamination in the final product

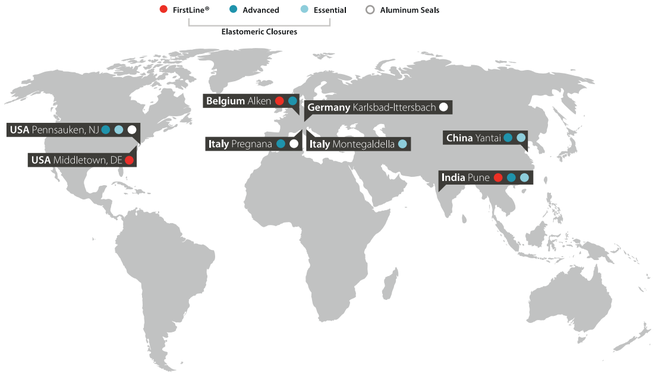
Who should comply with Annex 1?

Pharmaceutical companies must demonstrate compliance during regulatory inspections
Primary packaging manufacturers should enable this demonstration of compliance.

How is Annex 1 compliance demonstrated?

Use principles of Quality Risk Management and (new) through the implementation of Contamination Control Strategy (CCS).

Our Global Manufacturing Footprint



Contamination Control Strategy

A key addition to the new Annex 1 is the focus on a Contamination Control Strategy (CCS), with the ultimate goal of preventing contamination risks. A spotlight is cast on the quality of primary packaging components with importance placed on their design, manufacture, and selection.

Datwyler's support for Pharmaceutical Companies' CCS

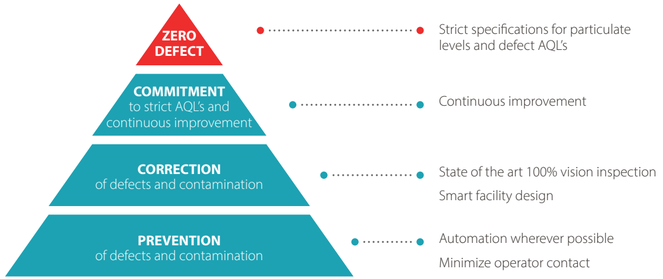
Through compliance with specific primary packaging requirements in Annex 1, Datwyler can make a significant contribution in the CCS of drug manufacturers.

The overarching goal is that products are adequately controlled to ensure that the level of bioburden and endotoxin/pyrogen are suitable for use

Datwyler Manufacturing Standards

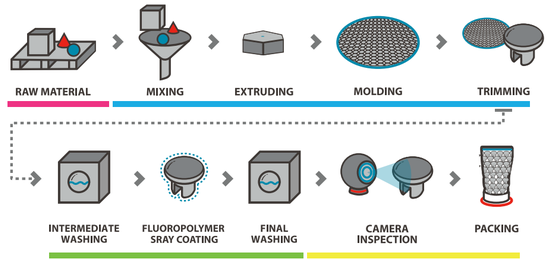
Datwyler's Advanced manufacturing standard is the proven and reliable solution for applications which require quality and production flexibility. It is the foundation upon which our **FirstLine®** manufacturing standard is built.

Datwyler's state of the art manufacturing standard, **FirstLine®**, is especially designed to address contamination risks by the manufacture of rubber parenteral packaging components with ultra-modern cleanroom technology, automation,, vision inspection, validated washing processes and in-house RTU-Steam process.



Datwyler FirstLine® Manufacturing Flow

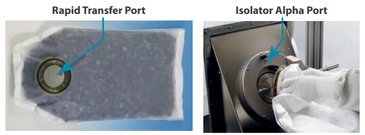
Datwyler **FirstLine®** manufacturing standard incorporates separate process flows for material, personnel, and waste. As a product moves through the manufacturing process, tighter environmental controls are in place to minimize contamination risks.



Zone 4	Controlled
Zone 3	ISO CLass 8
Zone 2	ISO Class 7
Zone 1	ISO Class7 & ISO Class 8

Elastomer Packaging

Datwyler offers Ready-for-Sterilization (RfS) and Ready-to-Use (RTU) packaging configurations that support compliance with essential Annex 1 guidance. Most critically, Rapid Transfer Port (RTP) bags are offered to address contamination risks during component transfer by enabling direct connection to isolator alpha ports.



Sterilization Validation

Annex 1 highlights the importance of sterility assurance. Datwyler operates in accordance with ISO requirements to ensure sterilization processes are validated and all RTU processes are validated according to ISO standards for sterilization (gamma, 11137 and steam, 17665).

Sterilization Validation Document Package in Accordance with Annex 1	
Ready to Use Gamma Sterilized	Ready to Use Steam Sterilized
Establishment of minimum sterilization dose	Product Validation
Establishment of maximum acceptable dose	Process Validation: Physical Qualification
Process Validation	Process Validation: Biological Qualification
Packaging Qualification	Packaging Qualification: Bag Qualification, Box Qualification