

Basics in Single-Use Bioprocessing → Single-Use Bags

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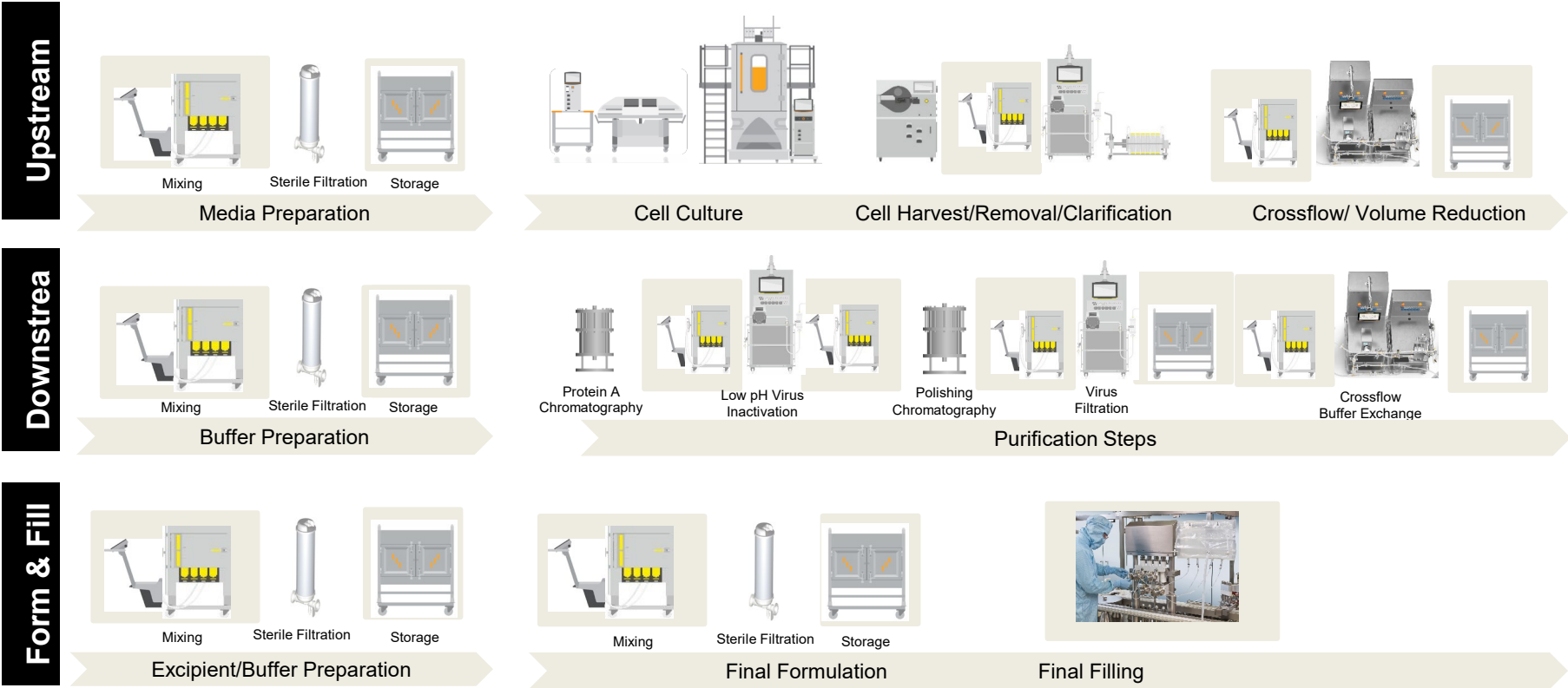
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Drug Manufacturing Process

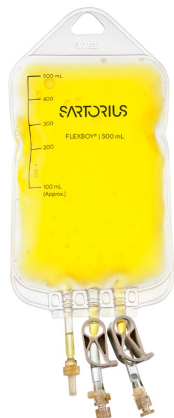


Stainless Steel vs. Single Use



picture: stainless steel

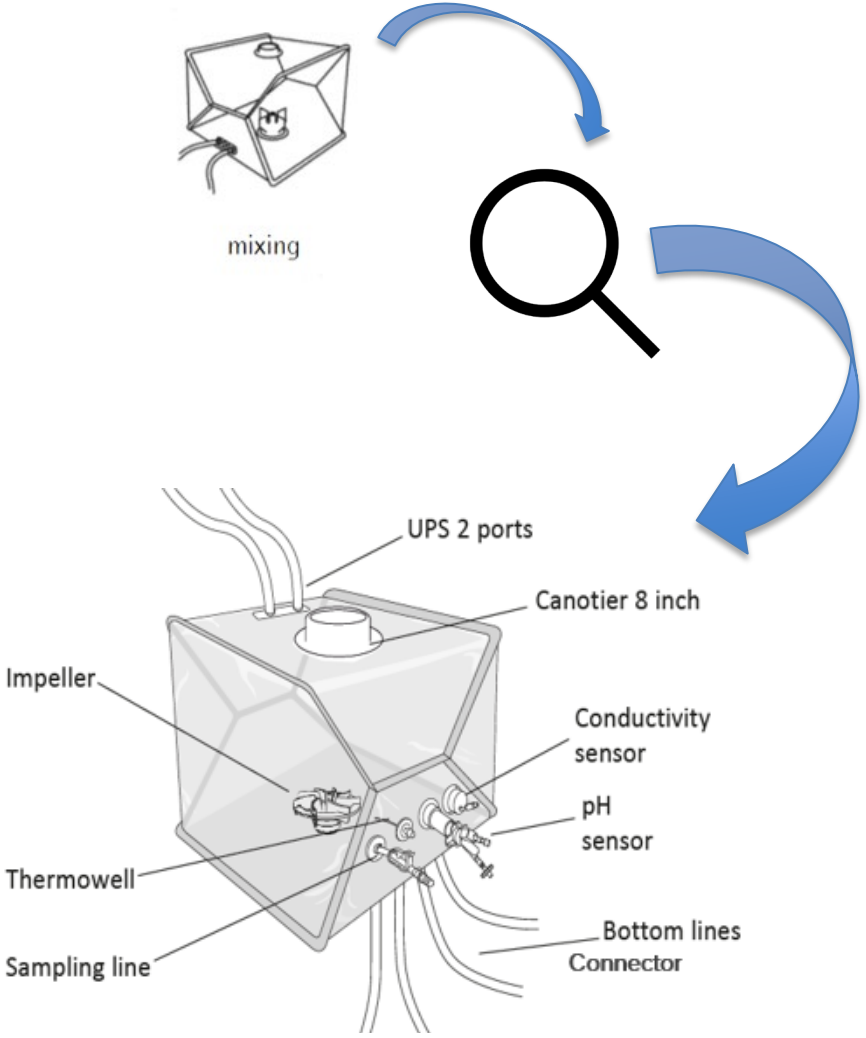
- | | |
|--|--|
| <ul style="list-style-type: none"> • Sterilization, cleaning • Possible cross contamination • Low flexibility | <ul style="list-style-type: none"> → Sterilized, only hardware-cleaning → Avoid cross contamination → High flexibility: set of different designs → Critical: extractables & leachables |
|--|--|



Bag manufacturing

Bag details

- Complex assembly of **different components** made of **different material**
- HDPE, PE, EvOH, PP, EVA
PSU, LLDPE, Si,
- Film material
- Extractables & Leachables



Bag manufacturing

Extractables & Leachables

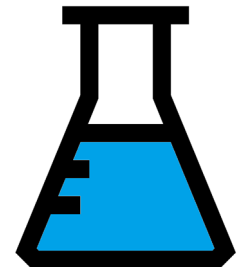


Extractables

- Extractables are **compounds that can be extracted from a container closure system, drug packaging component or any other contact surface.**

This **extraction** is happening during **harsh conditions** such as **heat, extraction solvents** or any other **highly-concentrated buffers or solutions.**

Extractables **can be potential Leachables.**



Bag manufacturing

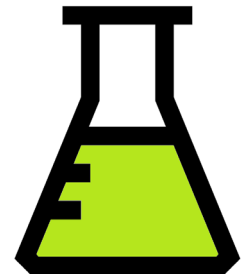
Extractables & Leachables



Leachables

- Leachables are **compounds that passively migrate or leach into the drug product over time** as a result of direct contact of the drug formulation with the surfaces (packaging, container closure system, etc.)

Leachables are generally **a subset of Extractables** - but not always.

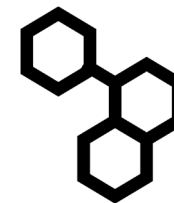
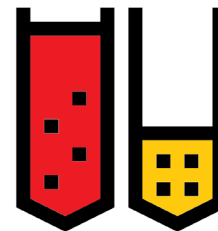


Bag manufacturing

Extractables & Leachables



- Tests and studies usually **done by the manufacturer** results stated in validation / E&L guides for the customers
Sartorius provides **in house studies** and **risk assessment** via an extractable simulator.
- Customers do their **own tests**
- **independent laboratories**



Bag manufacturing

Extractables & Leachables



- **Typical solvents** – examples

1M Hydrochloric Acid

1M Sodium Hydroxide

4M NaCl

1% Polysorbate 80

Ethanol

WFI

10 % Dimethyl sulfoxide (DMSO)

4M Ammonium Sulfate

- **Test method** e.g.:

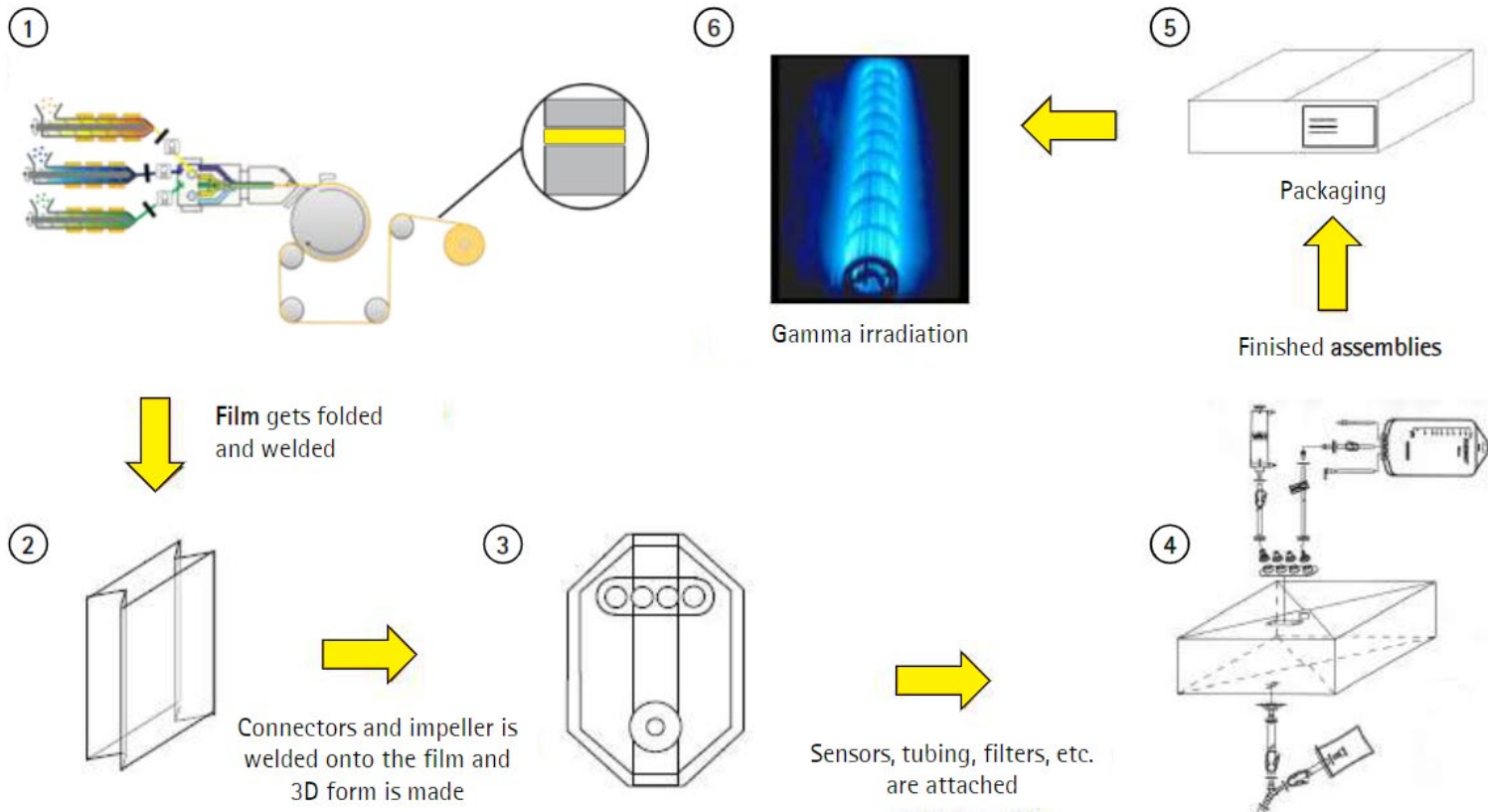
gas/liquid/ion chromatography

& mass spectrometry & flame ionization detector

Bag manufacturing Production Process

Extractables & Leachables

Silicon -> anti blocking agent for PE
linear and branched alkane -> from PE resins



Bag manufacturing

Film material



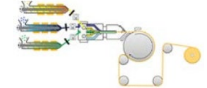
Two main types of film materials on the market
regarding product contact

- EVA → ethyl vinyl acetate
 - Main characteristics: robust, elastic but poor barrier to gases
 - Well known, long time on the market
- PE → polyethylene
 - Main characteristics: robust, flexible, good water vapor and alcohol barrier properties
 - Well known from packaging industry and clinical use

Specifications
and control of
raw material



Control of the
critical process
parameters

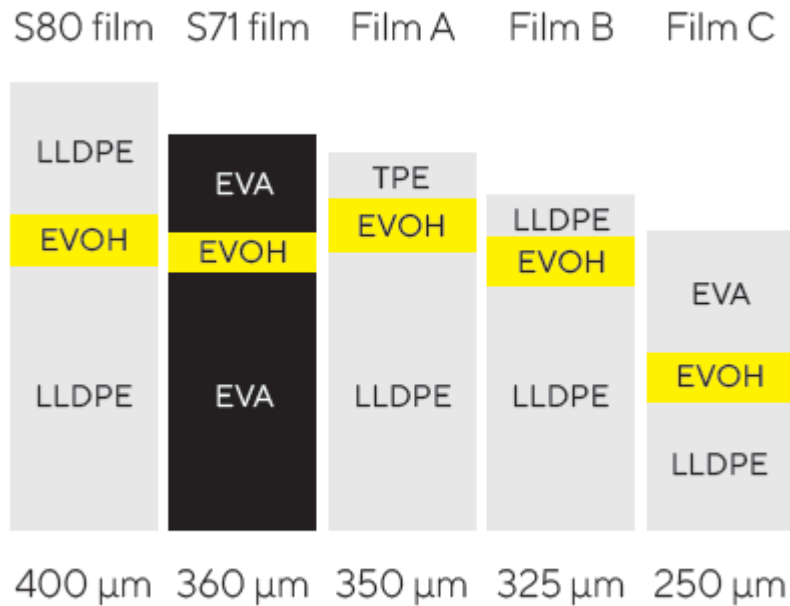


Specifications
and control of
film quality
attributes



Bag manufacturing

Film material



- EVOH → ethyl vinyl alcohol
- LLDPE → linear low-density polyethylene
- TPE → thermoplastic elastomer

Bag manufacturing

Film material



Process & application requirements

- Robustness
- Ease of use
- Biocompatibility
- Purity
- Cleanliness
- Compatibility
- Adsorption
- Stability
- Sterility



Raw material science, film & bag expertise

S80 film | PE 400 µm

Backbone	LLDPE	<p>Flexsafe® Bags & Cultibags</p>
	EVOH	
Contact Layer	LLDPE	

S71 film | EVA 300 – 360 µm

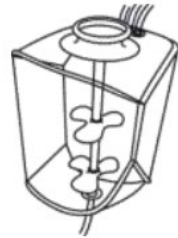
Backbone	EVA	<p>Flexboy® & Celsius® Bags</p>
	EVOH	
Contact Layer	EVA	



Bag quality attributes

- Strength
- Flexibility
- Weldability
- Cell growth
- Extractables
- Particles
- Gas Barrier
- Chemical resistance
- Bioburden

Single-Use bag types & Hardware → live demonstration



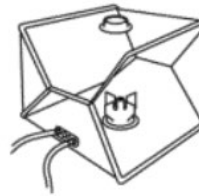
3D cell cultivation



storage / shipping



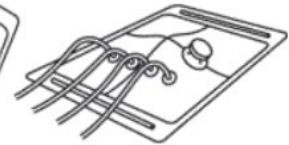
holding



mixing



freezing



2D cell cultivation



References

- Pictures from Sartorius if no reference is stated below the picture
- Sartorius documentation: data sheets, application notes, validation guides
→ if you are interested in having a detailed look into the documents please contact:
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