

# ATMP manufacture practical introduction

Gene and Cell Therapy Product (ATMP) Drug Development



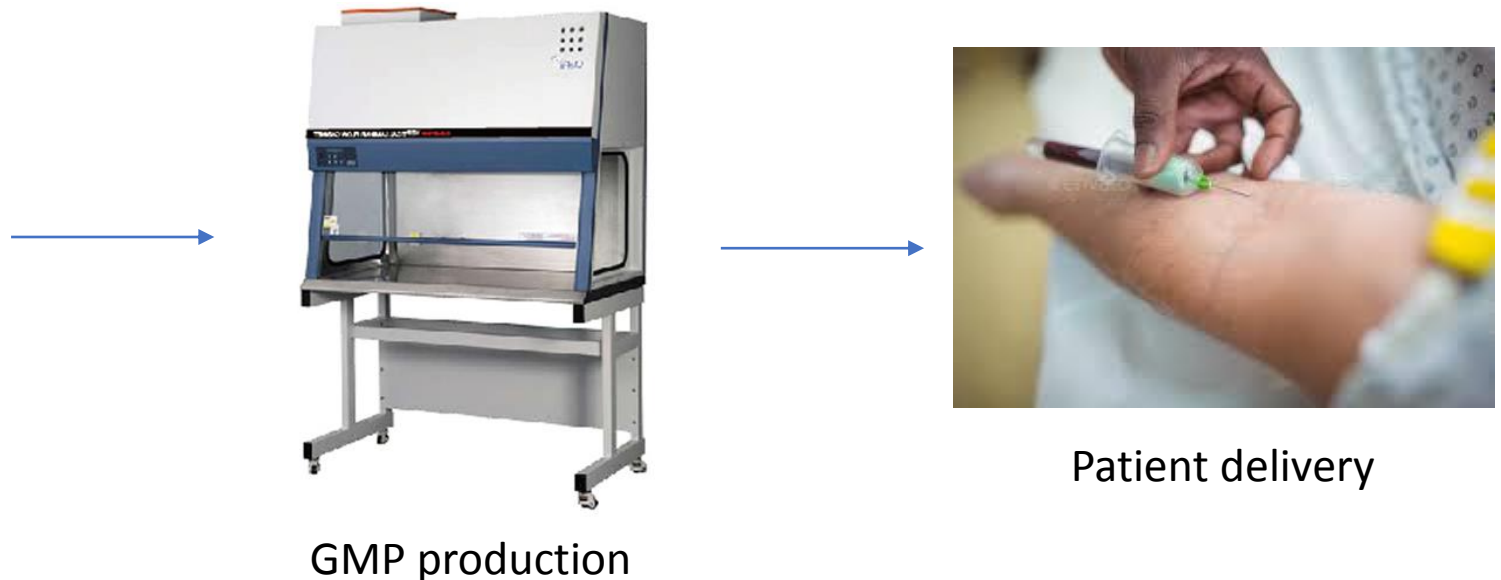
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# Manufacturing a sterile product



- You want to treat a patient with a cell or gene therapy product that you will manufacture
- What if the treatment works but the product is not sterile?
- How to minimise the risk for microbial transfer to the product (via the personnel/material)?



# Making you 'sterile'



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Imagine 'microbial contamination as the paint – it's all over you!

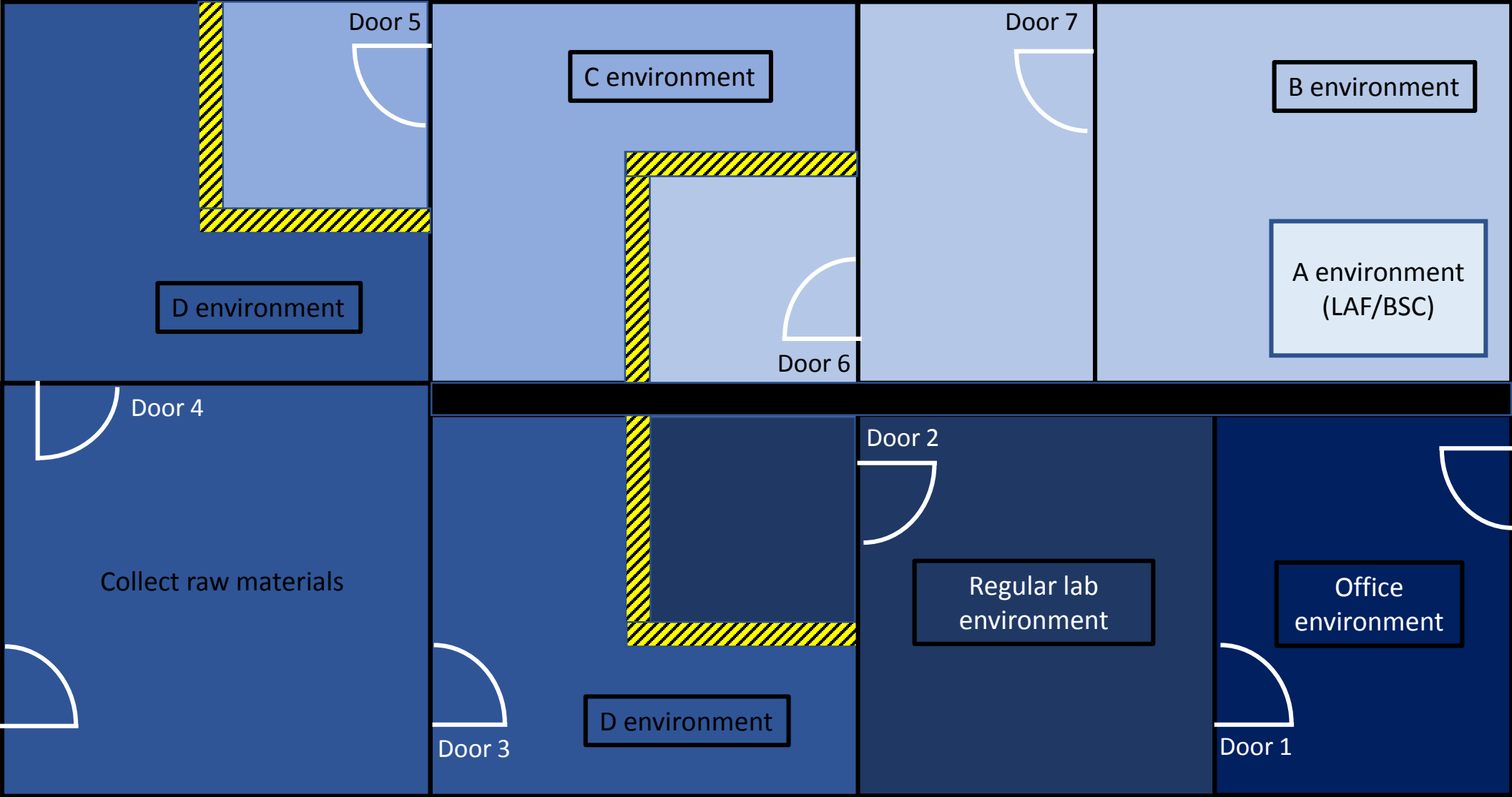
By the end of this process you want to have as little 'paint' entering the cleanroom as possible

# Basic cleanroom floor plan



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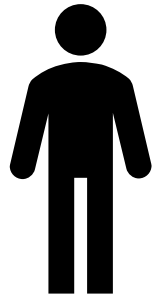


# Making you 'sterile'



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- Change your shoes
- Put lab coat over clothes



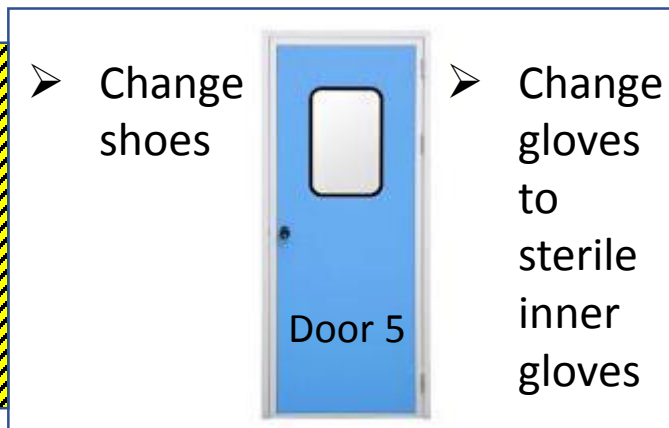
- Remove lab coat, clothes, makeup, jewellery
- Wash hands
- Put on 'undergarment', new lab coat, socks and shoes



- Collect sterile outer clothing
- Collect raw materials



- Remove lab coat
- Put on headcover
- Put on mask
- Put on non-sterile gloves – spray with EtOH



- Change shoes

- Change gloves to sterile inner gloves



- Put on sterile outer clothing and shoes
- Put on sterile outer gloves



C environment

B environment

A environment

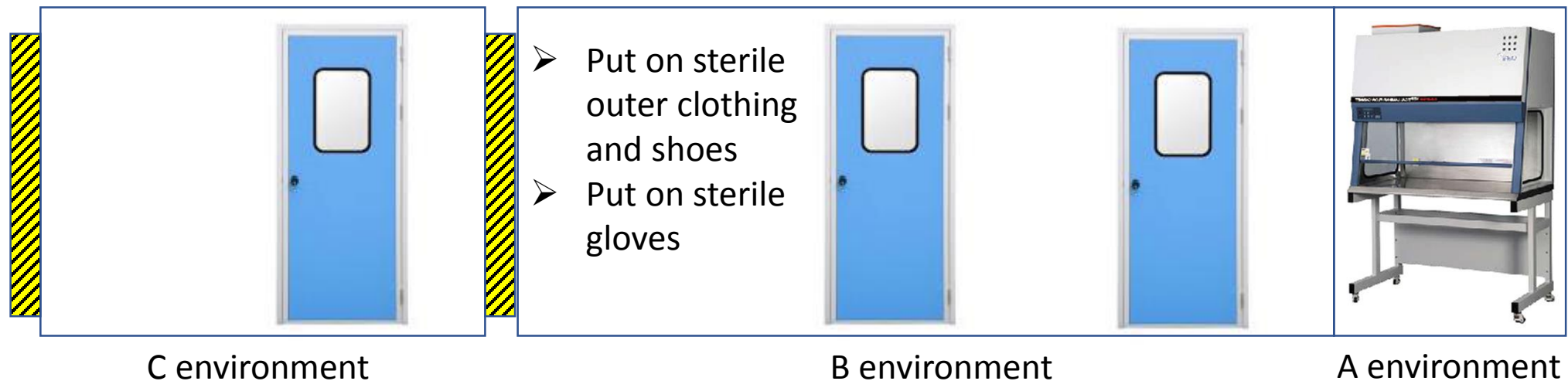
# Making 'you' sterile - gowning



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- <https://www.youtube.com/watch?v=m3QDxlZluAU>
- From 2:59



# Making 'you' sterile - gowning



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# Ensuring raw materials stay sterile



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- CoA, CoO, risk assessment, batch control
- Triple packing, no paper – otherwise spray, spray, spray

- Collect raw materials
- Spray with EtOH
- transport on EtOH cleaned trolley



- remove outer layer packaging
- C person transfers to C EtOH cleaned trolley



C environment

- Remove next layer packaging
- B person transfers to B EtOH cleaned trolley



B environment

- B person opens last layer of packaging at LAF entrance, A person removes from packaging without leaving A environment



A environment


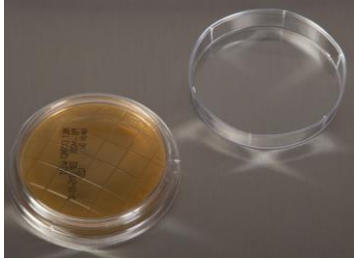


# Ensuring production environment is sterile




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- Microbial air monitoring during production
- Press plates at the end of production on surfaces in the room that have been touched/utilised
- Press plates on the fingers of the 'B person'

B environment



- Particle counter in the LAF
- Sedimentation plates in the work space
- Press plates at the end of production on the LAF work surface
- Press plates on the fingers of the 'A person'



A environment

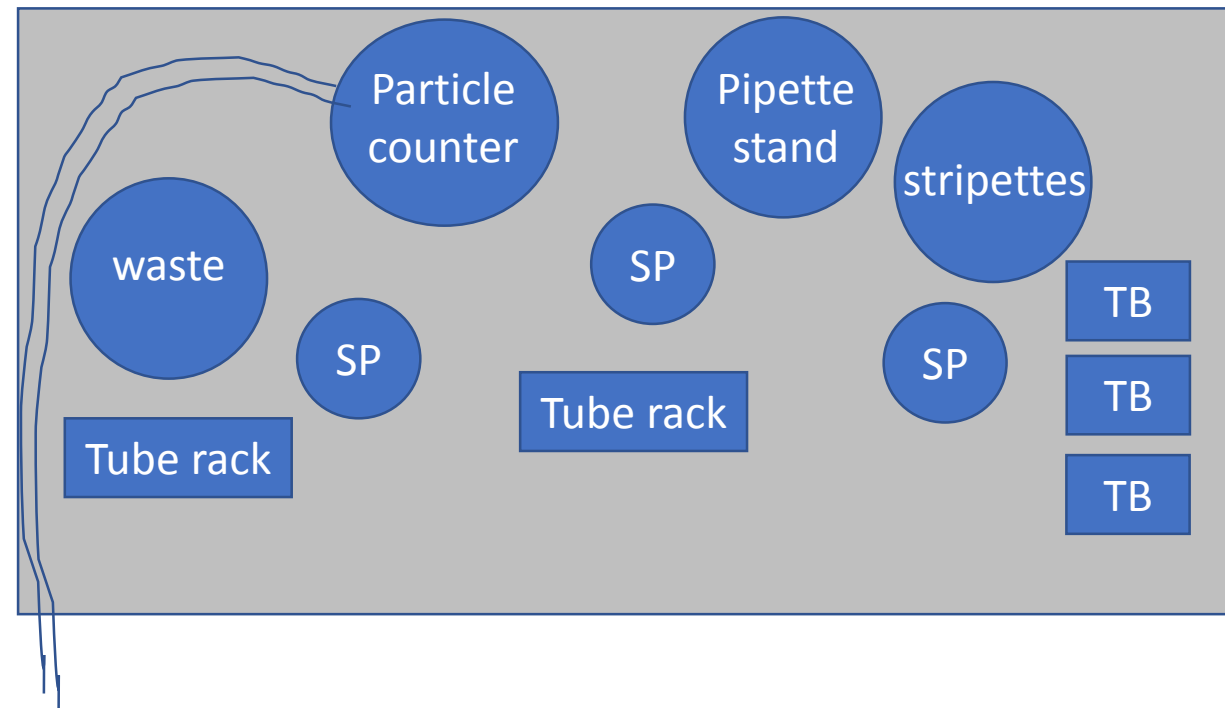
# Working in the LAF/BSC – A person



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- SP – sedimentation plate
- TB – tip box
- Particle counter and tube going to system outside LAF
- Sterile gloves are put on into the A environment and then hands are not removed
- If you remove a hand glove must be changed



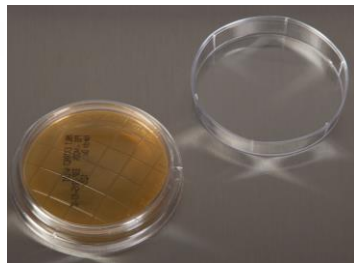
A environment

# Assisting the A person – B person



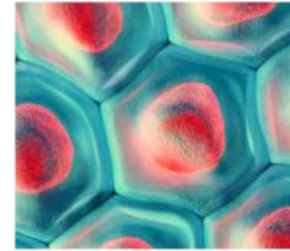
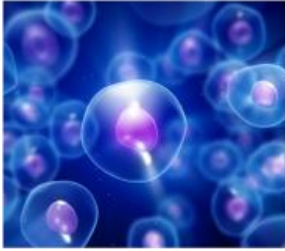
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- Responsible for providing instruction to A person
- Responsible for providing reagents to A person by opening package at A/B interface without entering hands or packaging into hood
- Responsible for marking in batch protocol when a step has been performed – initials and date for each step
- If you make a mistake ~~cross~~ and initial and date



Step	Preparations for thawing of one vial of the WCB: 2-5 days before thawing	Date, Sign.
1. →	Make sure that stock solutions are aliquoted and that the materials list (last page) are completed with IG#/batch#/preparation date, expiration dates etc.	
2. →	Thaw 1 x 5mL 521-CTG at +4°C. It is stable undiluted 3 months at +4°C.	
3. →	Thaw a bottle <u>NutriStem</u> at +4°C.	
Step	Preparations for thawing of one vial of the WCB: 1-5 days before thawing	Date, Sign.
4. →	Coat two T25 flask with 521-CTG: <ul style="list-style-type: none"> <li>•→ Take out DPBS +/- from +4°C</li> <li>•→ Add 2.5mL DPBS +/- to a T25 flask and then add 500-µL 521-CTG (100 µg/mL) and mix well.</li> <li>•→ Label the flask "521-CTG". Put in a sterile bag and store at +4°C (for maximum one week).</li> </ul>	
5. →	Put sterile water in a beaker and place at 37°C overnight.	

B environment



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