FIND

# TECHNOLOGY TRANSFER TO MANUFACTURING

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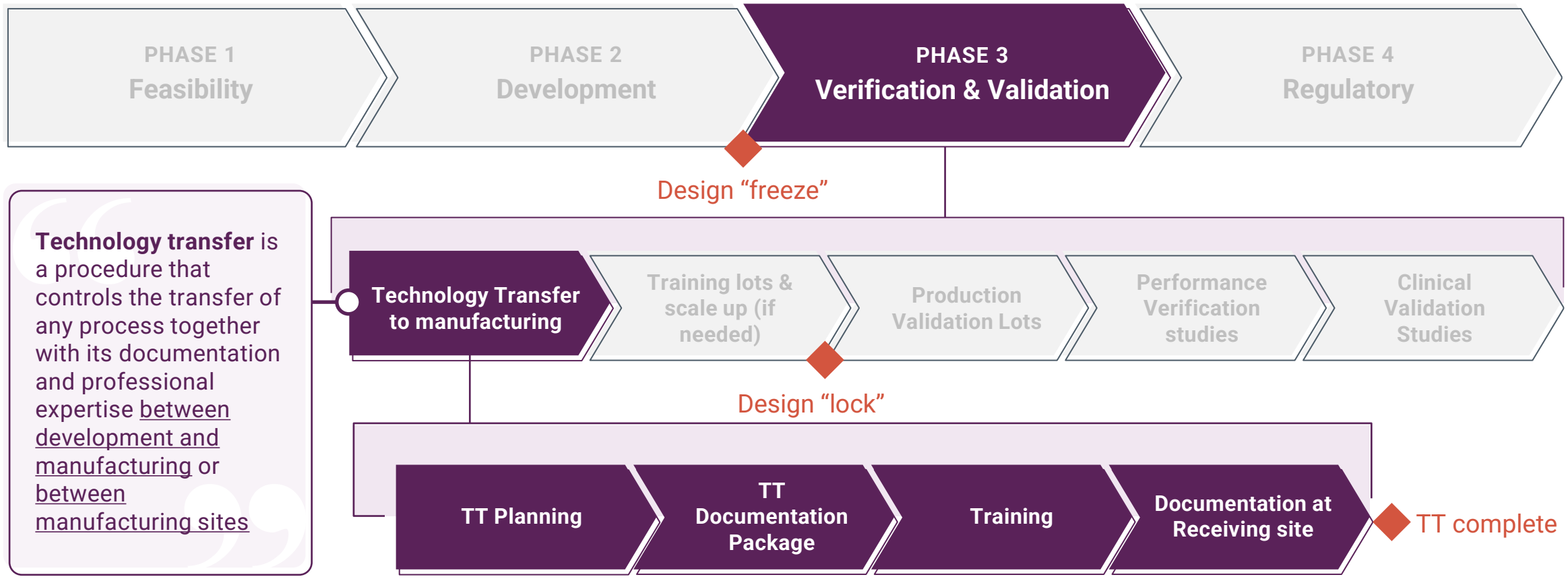
# TOPICS

1. Technology Transfer to manufacturing
2. Technology Transfer scenarios
3. Technology Transfer team
4. Example: transfer a lateral flow test from company A to company B
5. Technology Transfer steps
6. Considerations for a successful Technology Transfer

FIND PHASE GATE SYSTEM EXAMPLE

# PRODUCT DEVELOPMENT: VERIFICATION AND VALIDATION PHASE



**This approach can be controversial - Is this the right approach?**

We'll explore both sides:

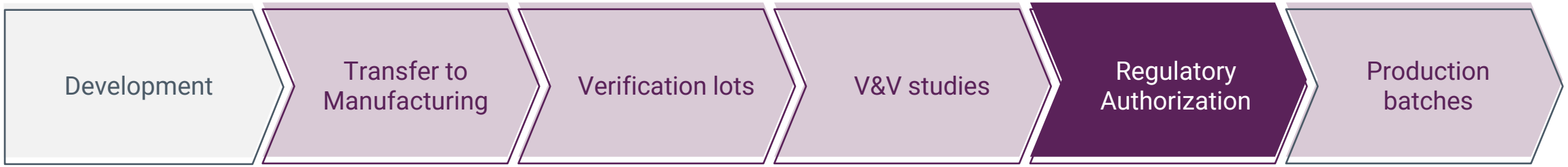
- Regulatory before Tech Transfer to manufacturing
- Regulatory after Tech Transfer to manufacturing

WHEN? SCENARIOS

# TECHNOLOGY TRANSFER TO MANUFACTURING

## SCENARIO 1:

V&V data for submission to Regulatory Authorization is generated using lots produced by manufacturing team using manufacturing line.




## SCENARIO 2:

V&V data for submission to Regulatory Authorization is generated using lots produced by R&D team using R&D line. Technology transfer happens after obtaining regulatory authorization but before product launch.

WHEN? SCENARIOS

# TECHNOLOGY TRANSFER TO MANUFACTURING

## WHY DO WE RECOMMEND SCENARIO 1 vs SCENARIO 2

- If V&V data is obtained using lots made by manufacturing team on the final manufacturing line, the V&V performance data reflects the way all future lots will be produced; no significant changes are expected that can affect the claimed performance using this line.
- To minimize unnecessary costs, you must have a thorough gate/design review after development to be sure you only transfer a test that meets design and regulatory requirements.

## WHAT TO HAVE IN MIND IF YOUR MODEL IS SCENARIO 2

- You must evaluate the impact of changing production lines on device performance and demonstrate that the device produced on the (new) manufacturing line meets your product claims (i.e. that no changes in performance occurred during the tech transfer). Worst case, you could need to re-validate analytical and/or clinical test performance
- If any significant change is identified, you should determine if you need to notify the regulatory authority; they may require evidence that device performance has not changed before allowing you to sell the product.

WHEN? SCENARIOS

# USE OF SAME LINE FOR R&D AND MANUFACTURING

## ADVANTAGES

1. **Cost efficiency** – specially when low volumes are produced
2. **Exact same equipment** is used – no significant changes due to the equipment
3. **Faster time-to-market** - the transition from prototype to final product is smoother and quicker.
4. **Improved communication** - proximity between R&D and production teams facilitates better communication

## DISADVANTAGES

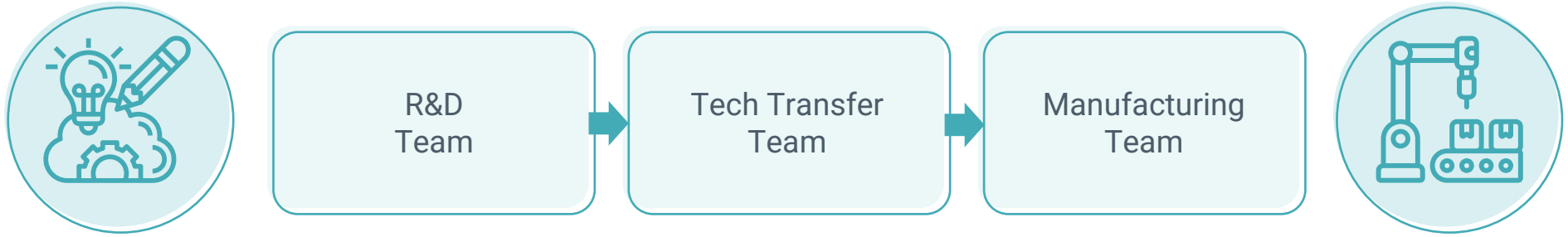
1. **Resource constraints** - share the same resources (e.g., space, equipment, personnel) might lead to competition for these resources
2. **Risk of disruption** - if issues arise in one area will directly impact the other (e.g., R&D delays)
3. **Risk of contamination** – R&D team might be working on innovative test that can contaminate a production batch

# RECOMMENDATIONS

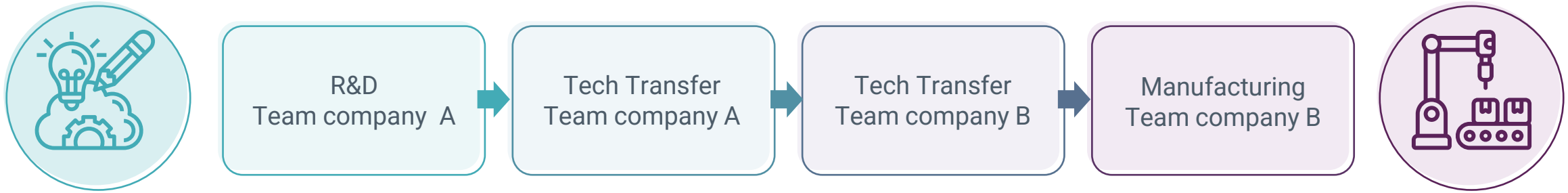
- When possible, we recommend two separate lines (one for R&D and one for Manufacturing) especially when production volumes start to increase, to minimize risks of contamination and do not disturb production plans with R&D work.
- If R&D and Manufacturing lines use different processes and/or different equipment it is important to produce V&V lots on the manufacturing line to minimize changes in product performance after regulatory approval.
- If R&D must use the Manufacturing line, there must be excellent control on the R&D work (e.g. line clearance procedures, visible labelling of equipment and materials for R&D use, cleaning validations or swab out of equipment/parts that could contaminate production batches).

# TECHNOLOGY TRANSFER TO MANUFACTURING SCENARIOS

**Technology transfer from R&D to manufacturing in the same company:**

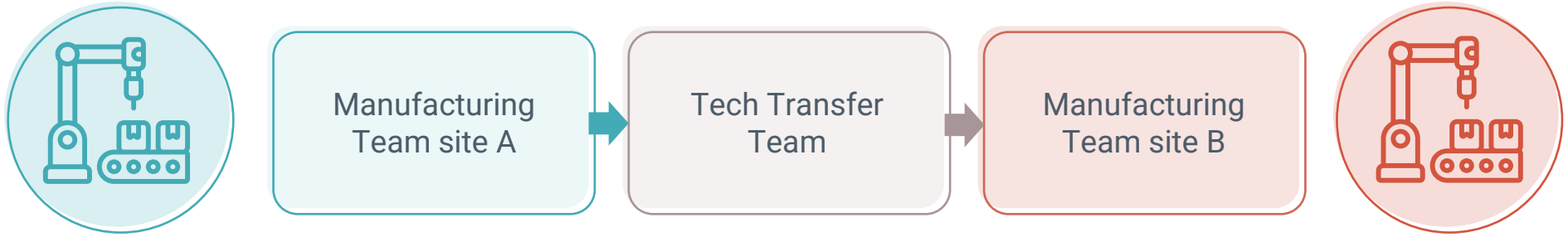



**Technology transfer from R&D in company A to manufacturing in company B:**

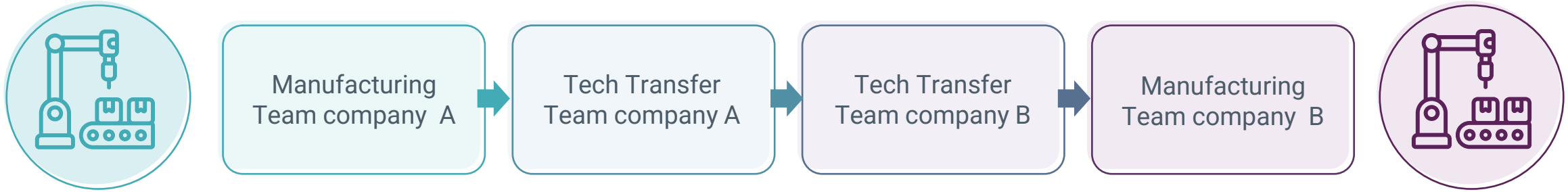


# OTHER SITUATIONS THAT MAY REQUIRE TECHNOLOGY TRANSFER

**Technology transfer to a new manufacturing site from the same company:**




**Transfer an existing product to a third-party:**



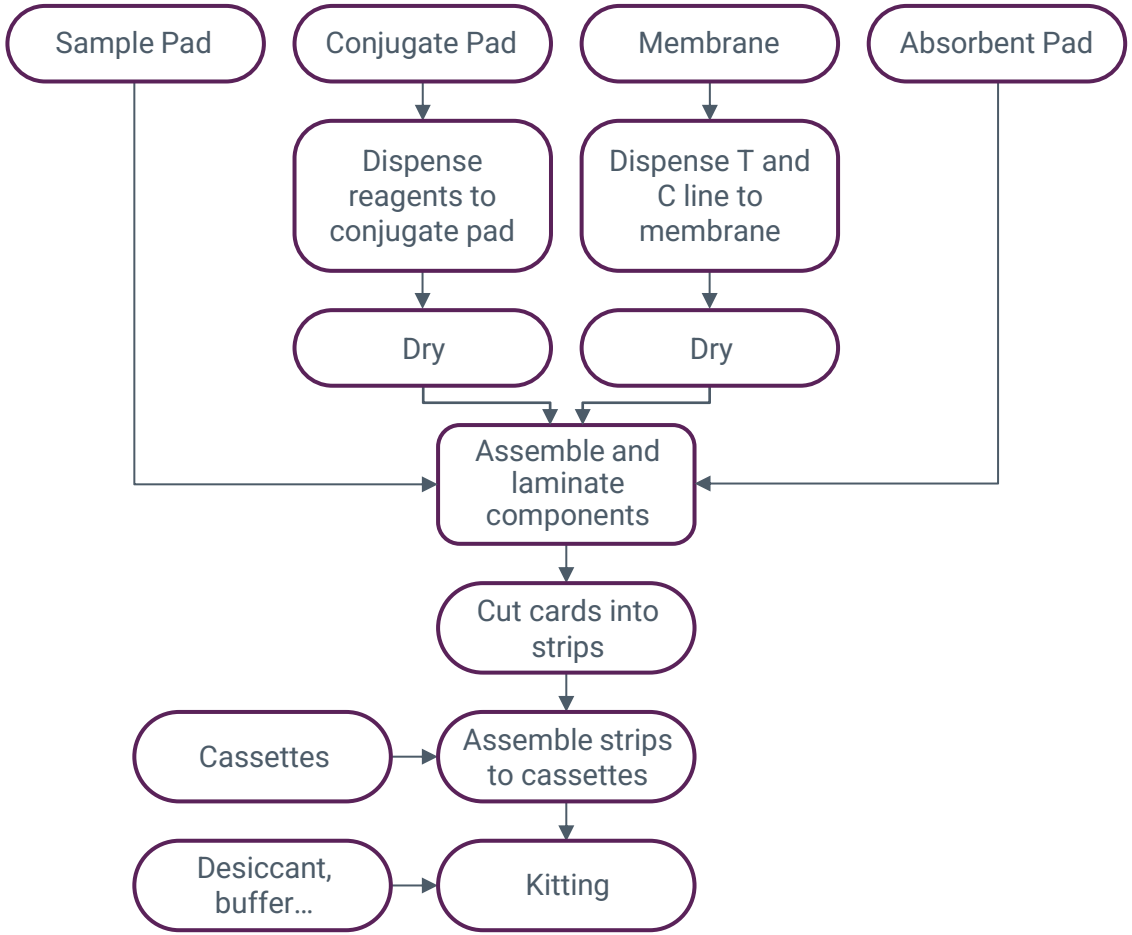
# TECHNOLOGY TRANSFER TEAM

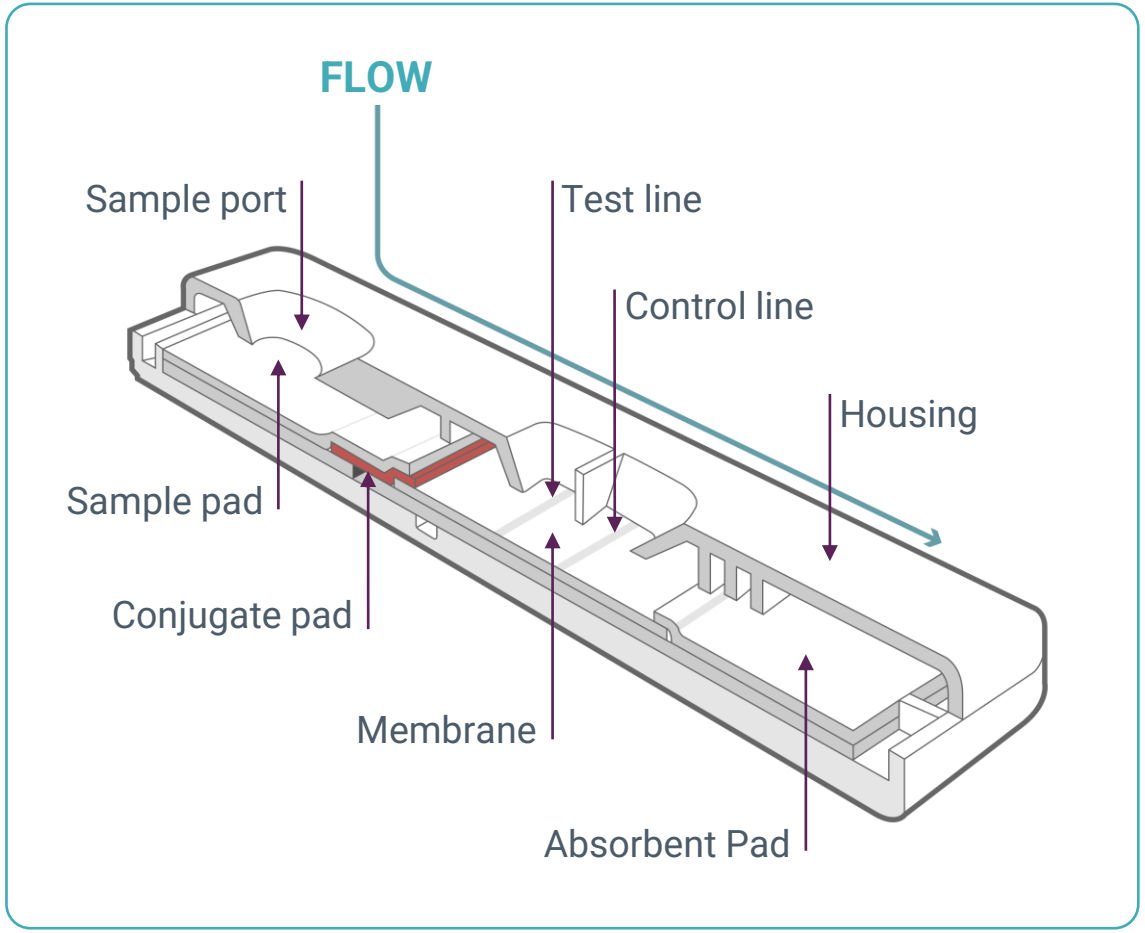
| Roles | Responsibilities |
|---|---|
| **R&D representative** | ▪ Central focus for transfer activities.<br>▪ Generates all documentation and brings the process “know-how”. |
| **QA representative** | ▪ Reviews documentation to determine compliance with regulatory authorities<br>▪ Review analytical methods with QC representative to determine capability, equipment training requirements.<br>▪ Initiates conversion of transfer site documentation into local QA system. |
| **Manufacturing representative** | ▪ Reviews process instructions (with R&D representative) to confirm capacity and capability.<br>▪ Considers any safety implications.<br>▪ Considers impact on local standard operating procedures (SOPs).<br>▪ Considers training requirements of operators. |
| **Engineering representative** | ▪ Reviews (with manufacturing representative) equipment requirement.<br>▪ Initiates required engineering modifications.<br>▪ Reviews preventative maintenance and calibration impact. |
| **QC representative** | ▪ Reviews analytical requirements.<br>▪ Availability with instruments.<br>▪ Responsible for analytical method transfer. |

*“An overview on technology transfer of pharmaceutical industry” Shalini Sivadasan, et.al. International Journal of Pharmaceutical Science and Research, January 2020, 11(2):573-579*

EXAMPLE

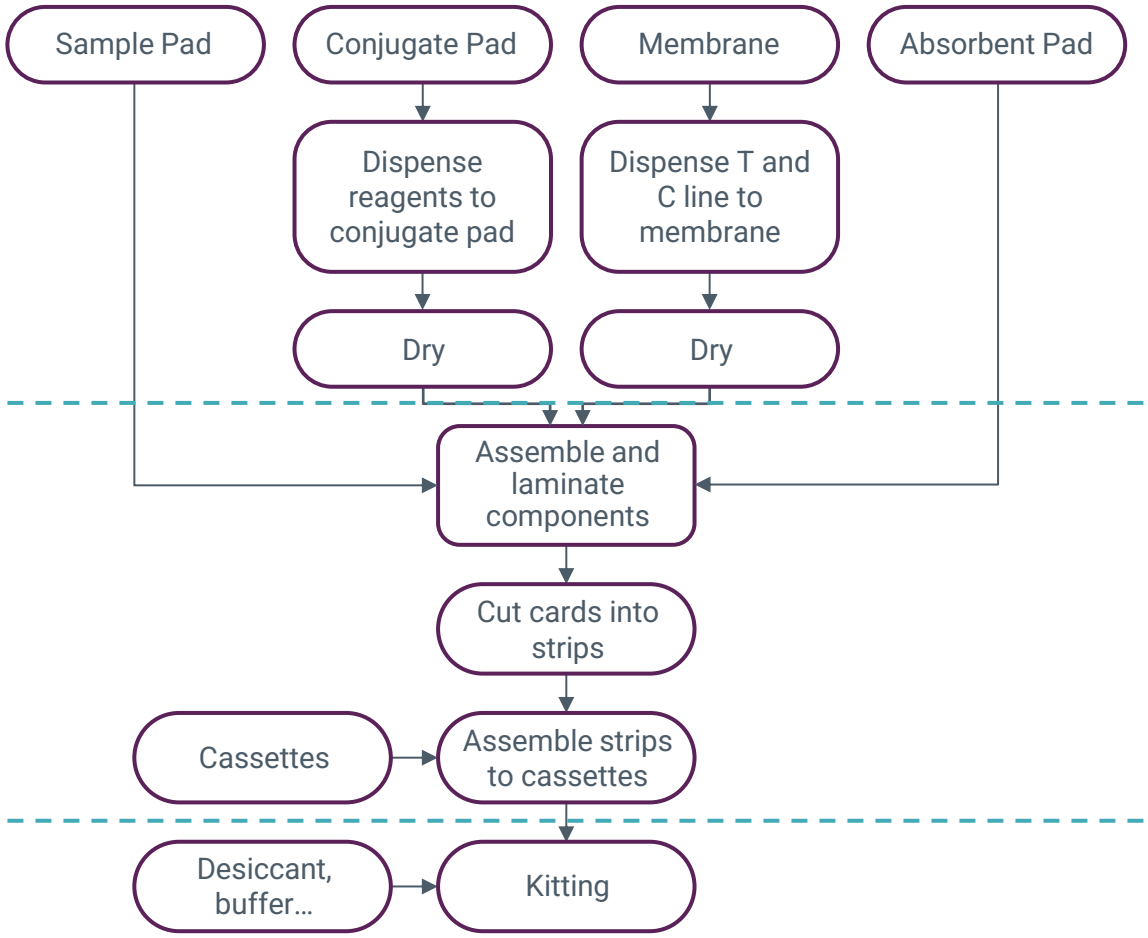
# LATERAL FLOW TEST TRANSFER FROM COMPANY A TO COMPANY B



EXAMPLE

# LATERAL FLOW TEST TRANSFER FROM COMPANY A TO COMPANY B



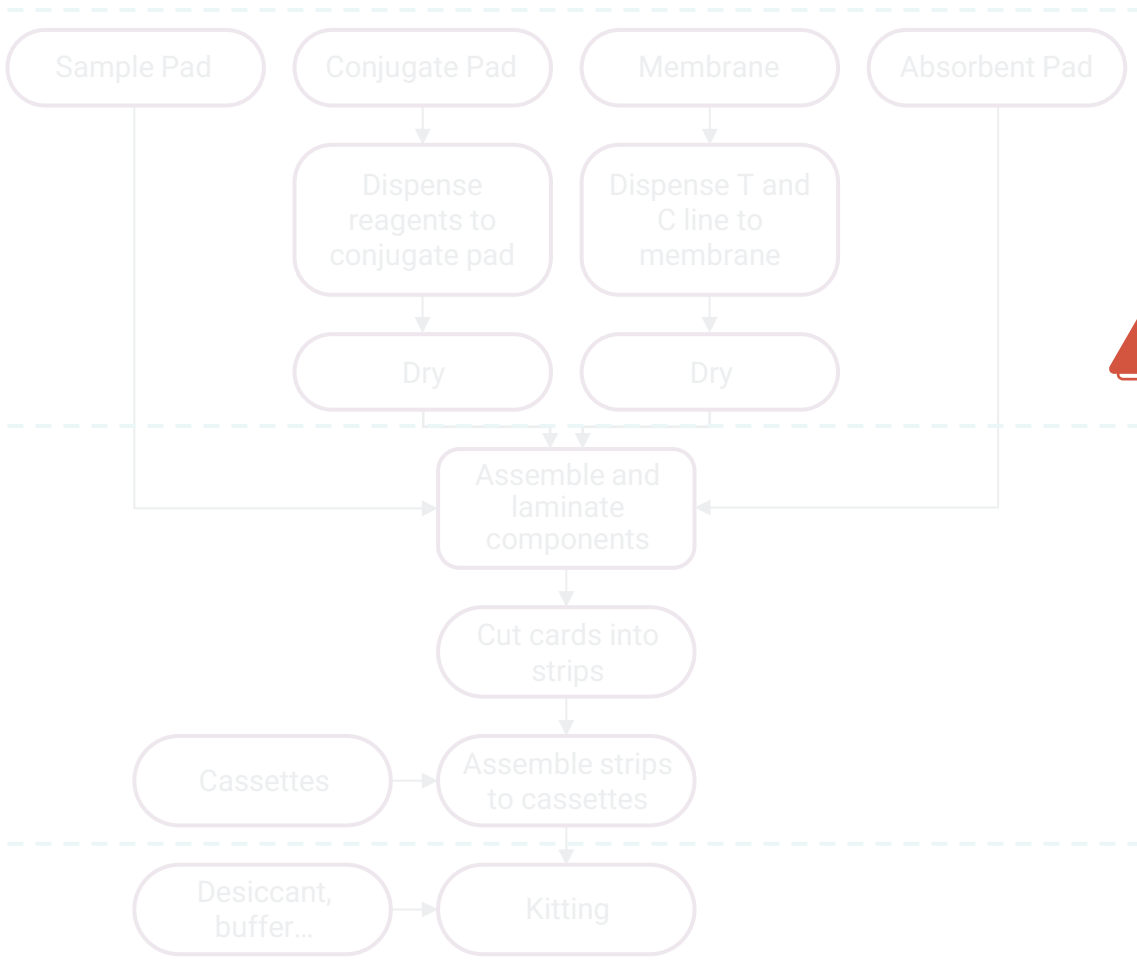

**3** **End-to-end transfer**

**2** **Transfer from semi-finished product (un-cut sheet)**

**1** **Finished product (packaging) – OEM product –**

EXAMPLE

# LATERAL FLOW TEST TRANSFER FROM COMPANY A TO COMPANY B




3 **End-to-end transfer**

**IN ALL CASES RECEIVING UNIT IS THE LEGAL RESPONSIBLE:**

- Accountable for product performance
- Safety standards
- Compliance with regulations

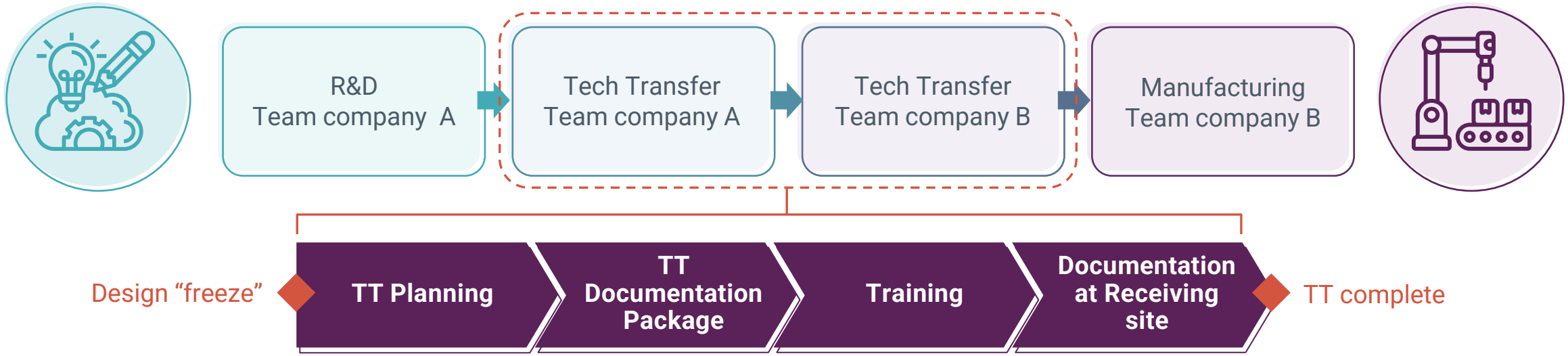
For OEM products, there may be contractual agreements between companies specifying responsibilities.




1 **Finished product (packaging) – OEM product –**

EXAMPLE

# END-TO-END LFT TECHNOLOGY TRANSFER FROM COMPANY A TO B



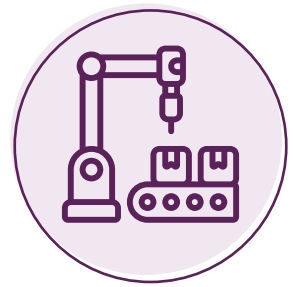

During **Technology Transfer Negotiation**, as a Receiving unit:

- Ensure there is a market need for the test.
- Request analytical and clinical performance data (internal or public) that demonstrates tests performance claims.
- If possible, get your technical team to run some test at your facility to confirm performance and have internal technical fee d-back.
- Understand the needs and risks of the transfer (e.g. does it require design changes that may affect performance?).
- Estimate time and cost for the tech transfer (be realistic!).

EXAMPLE

# END-TO-END LFT TECHNOLOGY TRANSFER FROM COMPANY A TO B

**TT Planning** → TT Documentation Package → Training → Documentation at Receiving site



- Create the TT team (if it does not exist): ensure it has the correct expertise, and all members have the availability to take the task.
- Sending and Receiving plan together the Technology Transfer steps.
- Agree on documents that Sending unit will transfer to the Receiving unit as part of the TT Documentation package:
  - Design and Development Plan
  - Product Requirements Document
  - Design Inputs Document
  - Risk Management Plan and Risk Assessment Document
  - Traceability Matrix
  - Raw Material Specifications and Supplier Qualification
  - Bill of Materials / COGs
  - R&D reports
  - Technology Transfer Plan
  - Manufacturing Procedures
  - Manufacturing SOPs
  - QC Testing Procedures

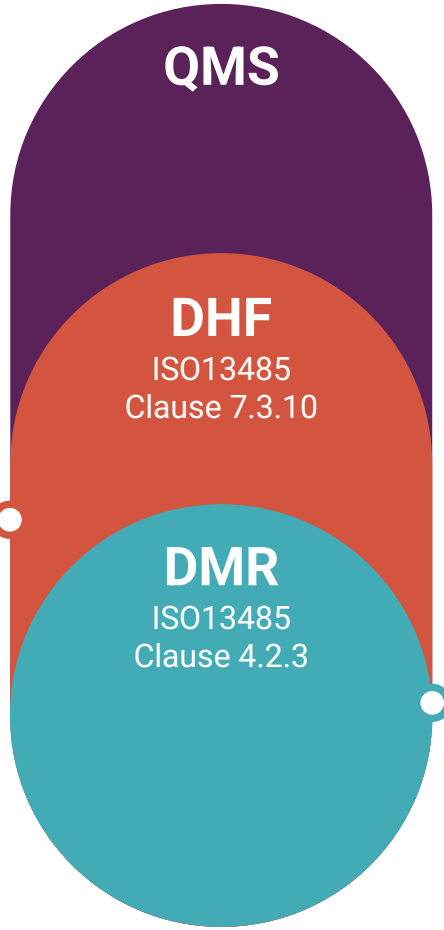
**REMEMBER:**
For stringent regulatory agencies (like WHO PQ, FDA, IVDR), Receiving unit is responsible of the Design History File for all development phases independently of who executed them.

# DESIGN HISTORY FILE VS DEVICE MASTER RECORD

## TECH TRANSFER FROM SENDING UNIT

### DESIGN HISTORY FILE

- **Purpose:** Documents the entire design and development process of an IVD
- **Contents:** Includes records of design inputs, outputs, verification, validation, risk analysis, design reviews, and design changes
- **Focus:** Demonstrates that the device was developed in accordance with the approved design plan and regulatory requirements
- **Audience:** Primarily used by regulatory bodies to ensure the design controls and development process were followed.



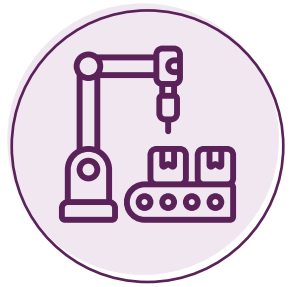

## TECH TRANSFER TO MANUFACTURING

### DEVICE MASTER RECORD

- **Purpose:** Serves as the comprehensive "recipe" for manufacturing an IVD
- **Contents:** Includes manufacturing processes, equipment specifications, materials, quality assurance procedures, and packaging and labeling instructions
- **Focus:** Ensures consistent production and quality of the device by detailing how it is made and controlled
- **Audience:** Used by the manufacturing team to produce the device and may be reviewed by regulatory bodies during inspections or audits

# END-TO-END LFT TECHNOLOGY TRANSFER FROM COMPANY A TO B

TT Planning → **TT Documentation Package** → Training → Documentation at Receiving site

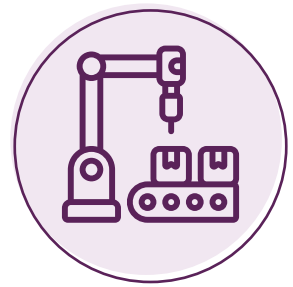


As a Receiving until, when reviewing **TT Documentation Package** you must check**:**

- R&D reports demonstrate test performance
- Test COGs is alignment to your market needs and commercial strategy
- All raw material suppliers are qualified and deliver in your country to an acceptable price. Any change on raw material will trigger a Design Change and may affect test performance.
- Understand the risk of any change to the product materials or specifications and leverage the expertise of the sending team.
- Manufacturing team fully understand SOPs and have no questions.
- Identify if any of the instruments used during the manufacturing process are different and the engineering team needs to either perform equivalence studies or buy new equipment before starting the transfer.
- The Manufacturing and Engineering team from the Receival unit might benefit of a visit to the Sending unit to fully understand the process

# END-TO-END LFT TECHNOLOGY TRANSFER FROM COMPANY A TO B

TT Planning → TT Documentation Package → **Training** → Documentation at Receiving site



Training can happen remotely or in-person at the Receiving unit site:

- 3 training lots: For the first lot, Sending unit demonstrates and Receiving unit follows. For the second lot, Receiving unit builds and Sending unit supervise and assist. For the third lot, Receiving unit builds alone following SOPs with no support.
- All training lots are QC based on analytical and clinical performance specifications.
- Training report is generated identifying any issue observed during the training and recommendations how to mitigate the issues.

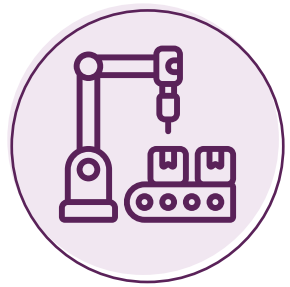
**TOP TIPS:**

**As Receiving unit, we recommend you to:**

- Request intermediate materials to measure progress and trouble-shoot during the training lots production.
- Use all the raw materials pre-qualified by the Sending unit during the training.
- Have a lot of test produced at the Sending unit to QC side-by-side with the training lots.

# END-TO-END TECHNOLOGY TRANSFER FROM COMPANY A TO B

TT Planning → TT Documentation Package → Training → **Documentation at Receiving site**



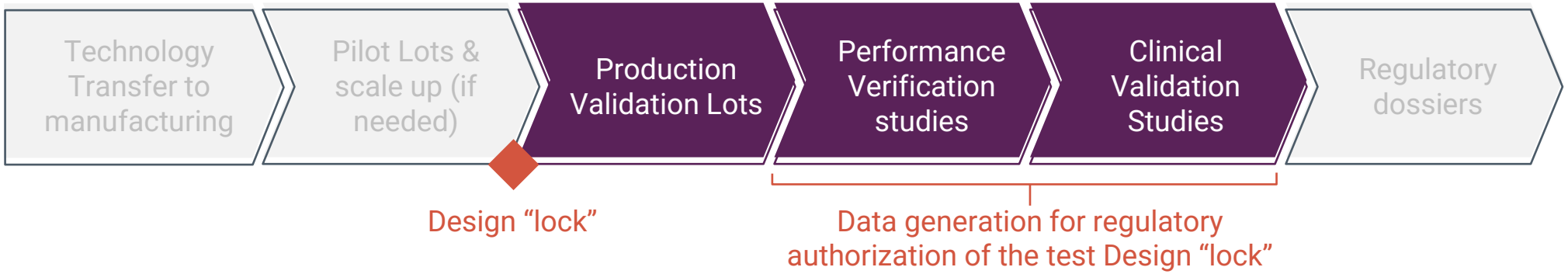
- Integrate Sending Unit SOPs (with modifications, if any) to the Receival Unit QMS system.
- Complete manufacturing plan.
- Finalize manufacturing validation plan and protocols (include equipment and processes).

**IMPORTANT:**
Design and Risk team review before and after transfer to ensure all is well documented in the Receiving unit QMS system.

# END-TO-END TECHNOLOGY TRANSFER FROM COMPANY A TO B


- R&D lots are smaller in size than manufacturing lots, therefore a scale up it is most of the times needed:
  - Scale up all processes to your manufacturing volumes before Verification and Validation studies.
  - Some processes are not easy to scale up and should be identified during the Tech Transfer phase.
  - Scale up can be done by steps through Pilot Lots.
  - Test performance to ensure it was not affected by the scale up.
  - Perform Manufacturing Latitude (or optimals) to ensure robustness between lots.

# END-TO-END TECHNOLOGY TRANSFER FROM COMPANY A TO B




- If during the verification and validation phase there is a Design Change, all studies will need to be done again with the new Design version. Examples:
  - Change of one critical component supplier
  - Change cassette/cartridge design
- If a design change occurs when product is in the market, equivalence studies need to be provided to demonstrate the change did not affect test performance. Examples:
  - Expansion of operation temperature
  - Adding a new sample type
  - Production in a new Manufacturing site

# SUCCESS OF TECHNOLOGY TRANSFER

## It depends on:

- Communication – open communication between all team members.
  - Direct communication between technical members.
  - Effective and timely communication with regulators (e.g., need for side inspections before release lots of manufactured material).
- Sending and receiving unit.
  - Technology transfer is not a “one way street”.
  - The sending unit and receiving unit must be equally involved in the process to ensure success.
- Full time dedicated technology transfer team.
- Design and Risk team review before and after transfer to ensure all is well documented in the Receiving unit QMS system.

# KEY TAKEAWAYS

**1**

Technology Transfer is a critical phase that requires a fully dedicated team with the correct expertise.

**2**

Ultimate legal responsibility is for the Receival unit, therefore is extremely important you have full control and understanding of the product Design History File.

**3**

A common difficulty in LMIC is procurement of raw materials at competitive prices. It is extremely important to revise suppliers and COGs before TT agreement.

**4**

Accepting a TT with poor quality evidences will have an impact in cost and timelines.

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# QUESTIONS & FEEDBACK