

# IVD PRODUCT LIFECYCLE

♦ Olga Ordeig







## **TOPICS**

- 1 Definition of in-vitro diagnostics
- 2 Definition of product lifecycle & product development
- 3 Phase gate system: why is important
- 4 Examples of IVD phase gate systems
- 5 Define scope of the training
- 6 Why do diagnostic companies fail?



## **DEFINITION OF IN VITRO DIAGNOSTICS**

#### MEDICAL DEVICES

Medical devices are any form of appliance, instrument, software, or device used by patients and healthcare professionals to be used for medical purposes.

Supporting live



Monitoring

Diagnosis





**Treatment** 

## IN VITRO DIAGNOSTICS (IVDS)

An in vitro diagnostic device is a subset of medical devices specifically intended to examine specimens derived from the human body, such as blood, saliva, tissue, and other samples.

Diagnosis or prognosis





Predisposition health condition

Disease progression monitoring





Therapeutic decision



# TYPE OF IVD BY DIAGNOSTICS TECHNIQUES

# **Molecular Diagnostics**

Detect genetic material (DNA, RNA) based on amplification techniques.

Blood, oral swabs, sputum, feces, ...

Covid-19 (PCR), TB, HPV, bacteria screen



#### **Immunoassays**

Detect substances such as proteins, hormones, or pathogens using antibodies or/and antigens.

Blood, oral swabs, urine, feces, ...

Pregnancy test, malaria, Covid-19 Ag



# Clinical Chemistry

Measure chemical components (e.g., enzymes, hormones, electrolytes) based on a (bio-)chemical / enzymatic reaction.

Mostly blood, urine and may be others

Glucose, Cholesterol, Iron, Blood gases



# Cell-based (e.g. Hematology, Culture & AMR tools)

utilize living cells or cell cultures to assess biological responses

Mostly blood

CBC, bacteria ID/AST(phenotypic), blood culture





## TYPE OF IVD BY COMPLEXITY

## **Laboratory IVD**

- Laboratory equipment is needed
- Training of skill personnel
- >3 manual steps



#### **Near POC**

- Basic/minimal lab equip. requirements
- Minimal training
- Benchtop/desktop units, mains power
- Semi-automated (1-3 manual steps)



#### **True POC**

- No lab equipment
- No training
- Can be carried
- Battery-operated devices
- Kits including disposable sample materials
- Fully automated (sample in-sample out)



#### **Instrument free POC**

- No instrument or power requirements
- Fully disposable
- Fully automated testing processes



**Increasing complexity** 

#### **Increasing accessibility**



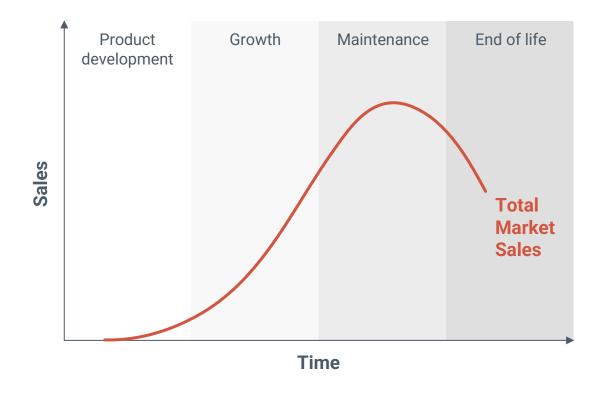


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## PRODUCT LIFECYCLE

The product lifecycle is the succession of stages that a product goes through during its existence, starting from development and ultimately ending in decline.

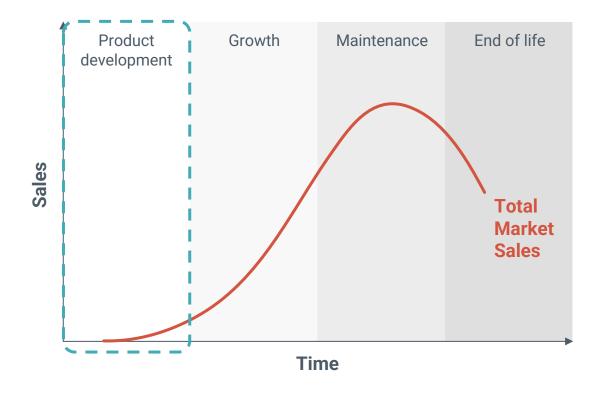


- Product Development is the stage where a new product is ideated, tested and introduced to the market.
- During the **Growth** stage, customers have accepted the product in the market and costumers are beginning to truly by in.
- The Maintenance stage is when sales start to level off from the rapid growth period.
- The End of Life stage is when competitors have begun to take a portion of the market and the product experiences a decline in sale.



## PRODUCT DEVELOPMENT

During the next days we will focus on the **product development phase**, and how to bring to market quality-assured products minimizing the risks of failure.



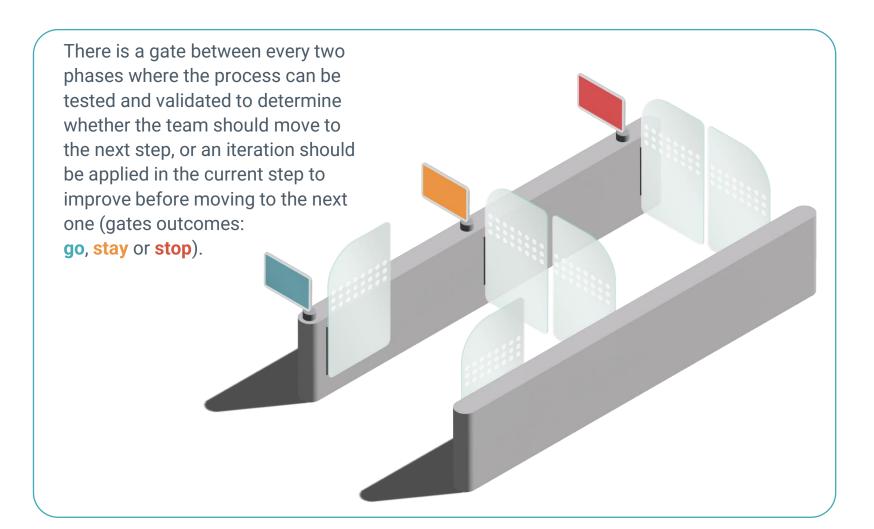
- This stage can be long, depending on the complexity of the product, how new it is, and the competition.
- It is a difficult stage and isn't always a success.
- It is also a phase where companies spend a lot of money without bringing any revenue because the product isn't been sold yet.



## PHASE GATE SYSTEM

The **Phase Gate System** is a project management technique that is used to guide a product from conception to launch over several phases.

These phases are separated by so-called 'gates'; the decision points for whether or not to proceed to the next phase.





## WHY PHASE GATING IS IMPORTANT



Ensure systematic progression of product development.



Provides
structural
checkpoints at
different phases
of development,
ensuring that
each phase is
thoroughly
evaluated and
meets predefined
criteria before
advancing to
the next.



Enhances quality control and reduces risk.



Ensures resources are allocated effectively.



Promotes communication between teams.



Improves overall project efficiency and success.





## FIND EXAMPLE

FIND divides the product development of an IVD in 6 phases and requires a review at the end of each phase before moving to the next one.

PHASE 2 PHASE 3 PHASE 0 PHASE 1 PHASE 4 PHASE 5 Concept **Feasibility Development** Verification & Regulatory **Implementation Validation** Transfer IVD test Exploration of new Selection of Late prototype Dossier Implementation and biomarkers. reagents and development to to manufacturer submission, scale up of the IVD in reagents and/or development of demonstrate ("design lock"). Regulatory target countries. Postperformance that Final verification Authorization market surveillance technologies. early prototypes to demonstrate and validation for review and and additional meets product functionality. requirements regulatory approval. studies. ("design freeze"). submission.

#### IVD PHASE GATE SYSTEM



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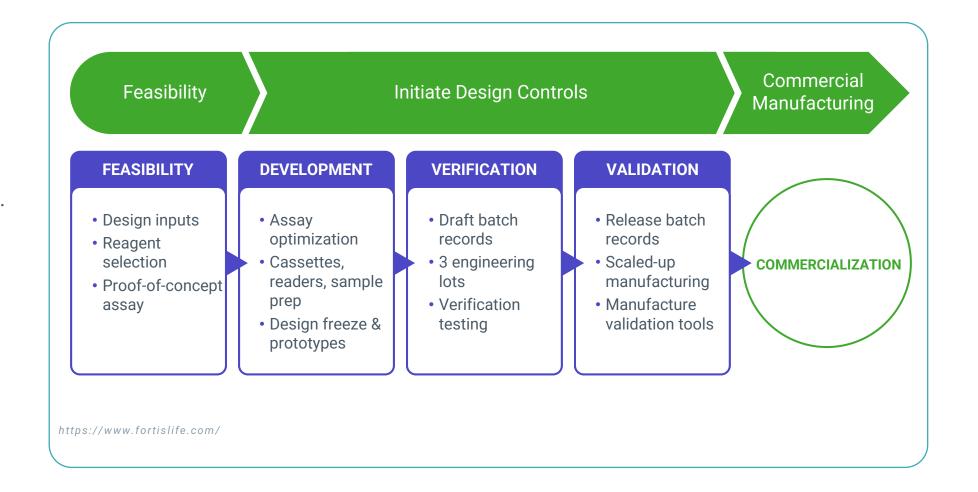
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## **COMPANIES USE DIFFERENT TERMINOLOGIES**

This is an example of a company that provides end-to-end immunodiagnostic and molecular diagnostic assay development and manufacturing services.

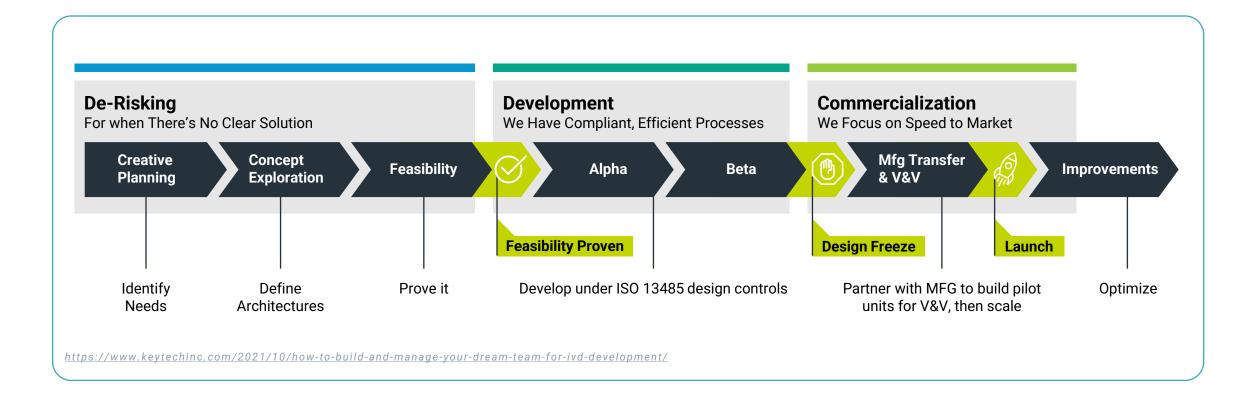






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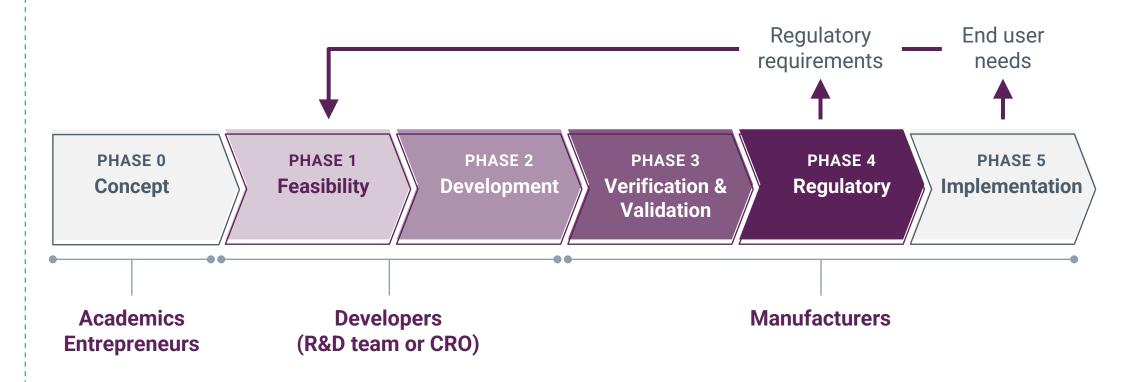
This example is from an end-to-end product development service company for medical devices, including IVDs.





# SCOPE: FEASIBILITY TO REGULATORY

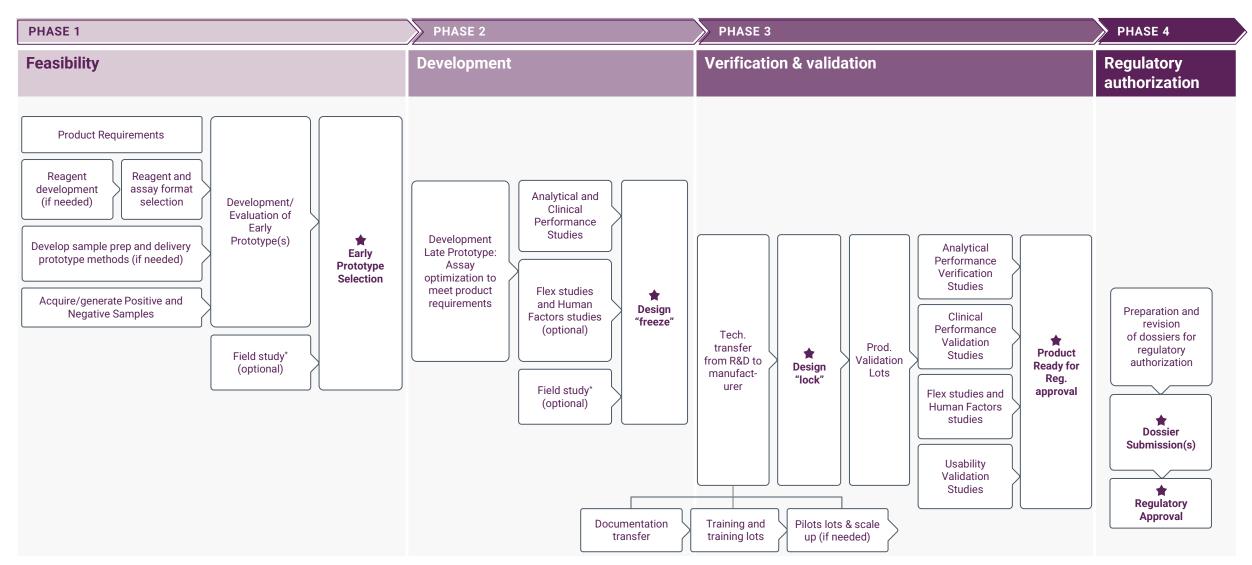
In this training we will focus on the most relevant phases for an IVD manufacturer: from Feasibility to Regulatory.







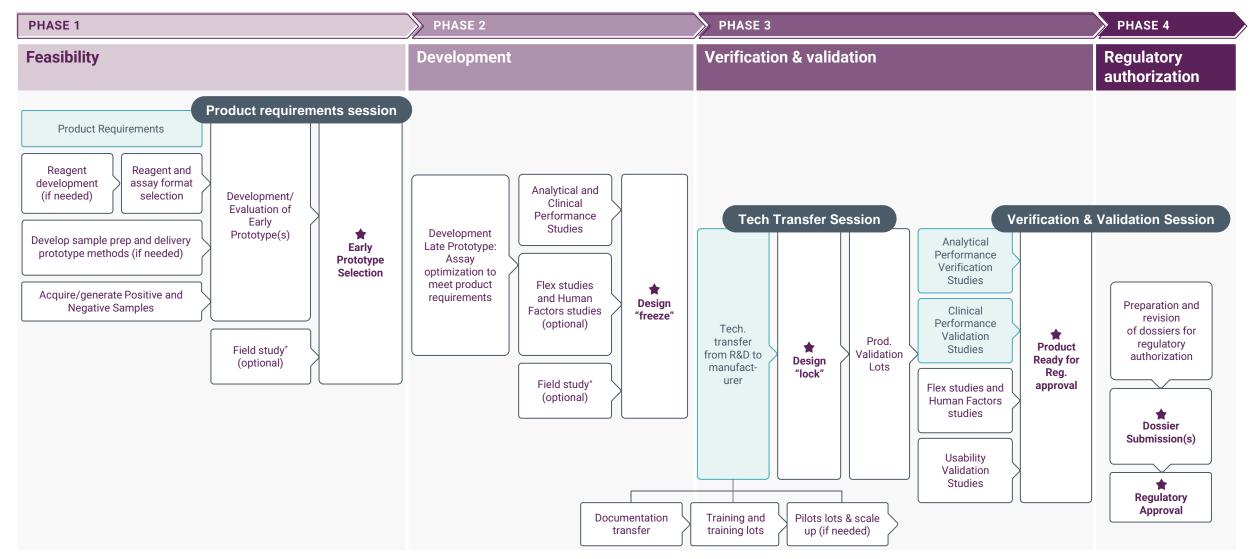
# LATERAL FLOW TEST EXAMPLE





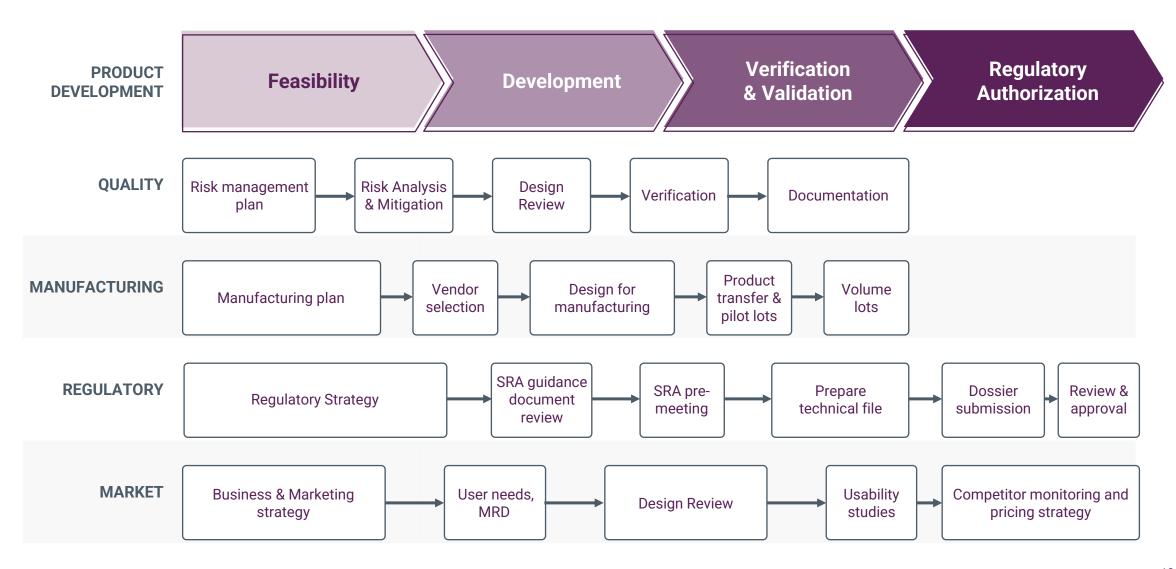


# LATERAL FLOW TEST EXAMPLE



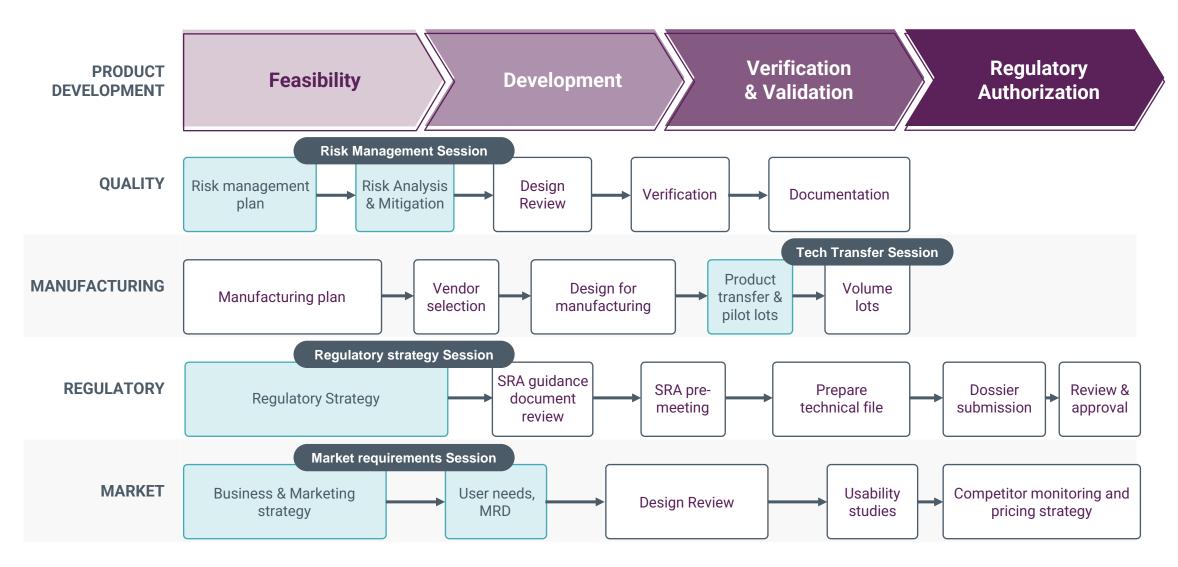


## **BEYOND PRODUCT DEVELOPMENT**





## **BEYOND PRODUCT DEVELOPMENT**







# PRODUCT DEVELOPMENT: FEASIBILITY PHASE

PHASE 1 Feasibility

PHASE 2

Development

Verification & Validation

PHASE 4
Regulatory

Work in **feasibility phase** supports development and evaluation of an **early prototype** to demonstrate by laboratory studies that the IVD is reasonably likely to:

- 1. meet the performance characteristics set in the draft product requirements document
- 2. be manufacturable
- serve its intended use

Testing and performance evaluation with real patient samples is strongly recommended. Preliminary stability studies should also be performed.

- Market Requirements
   Document
- Product Requirements
   Document
- Detailed Design and Development Plan
- Regulatory strategy
- Preliminary manufacturability assessments

A properly completed **Feasibility Phase** will reduce the likelihood of project timeline slippage in Development



#### FIND PHASE GATE SYSTEM

# PRODUCT DEVELOPMENT: DEVELOPMENT PHASE

PHASE 1 easibility PHASE 2

Development

Verification & Validation

PHASE 4
Regulatory

Design "freeze"

Work in **development phase** supports further development of a **late prototype** of the IVD which is designed to work and look as the finish product.

Performance (both analytical and clinical) in this phase must meet product requirements.

Project risk analysis is conducted, and all risks are mitigated to a tolerable level.

The development phase culminates with a verified prototype ("design freeze") ready to transfer to manufacturing.

- Update Market Requirements
   Document
- Final Product Requirements Document
- Update Design and Development Plan
- Update Regulatory Strategy
- Draft Performance Evaluation Plan (including analytical and clinical)
- Complete manufacturing processes

A properly completed **Development Phase** mitigates the risk that the IVD test will fail V&V after transfer to manufacturing



#### FIND PHASE GATE SYSTEM

# PRODUCT DEVELOPMENT: VERIFICATION AND VALIDATION PHASE

PHASE 1
Feasibility

PHASE 2

Development

PHASE 3
Verification & Validation

PHASE 4
Regulatory

Design "freeze"

Design "lock"

Work in **Verification & Validation phase** is initiated with the **technology transfer** from R&D to manufacturing through **pilot lots**. Once the performance of the test at manufacturers is confirmed ("**design lock**"), **validation lots** are produced, and the final Analytical Verification and Clinical Validation studies are done.

**Performance** (both analytical and clinical) in this phase must meet **product requirements**.

Project risk analysis is completed, and all risks are mitigated to a tolerable level.

- Complete Performance Evaluation Plan (including analytical and clinical)
- Analytical Verification, Clinical Validation and Usability Protocols.
- Manufacturing tests are validated
- Study reports

A properly completed **Verification & Validation Phase** improves the likelihood to obtain regulatory authorization



#### FIND PHASE GATE SYSTEM

# PRODUCT DEVELOPMENT: REGULATORY AUTHORIZATION PHASE

PHASE 1
Feasibility

PHASE 2

Development

Verification & Validation

PHASE 4
Regulatory

Work in **Regulatory Authorization phase** is initiated with the **preparation and revision of the dossiers** for submission to regulatory authority and/or WHO PQ as per the approved regulatory strategy; and culminates in receipt of the approval(s).

- Design History File complete
- Submission dossiers





# **EXAMPLE OF MANUFACTURER DOCUMENTATION REQUIREMENTS**

			Design & Developme			
	Phase 0 (Concept)	Phase 1 (Feasibility)	Phase 2 (Development)	Phase 3 (Verification and Validation)	Phase 4 (Regulatory Authorization)	Phase 5 (Implementation
Product Requirements Document	Optional	Initiate	Complete	Update AR	Update AR	Update AR
Design Input Document	Optional	Initiate	Complete	Update AR	Update AR	Update AR
Marquet Requirement Document	Optional	Initiate	Complete	Update AR	Update AR	Update AR
Analytical Performance Verification Protocols	_	-	Preliminary	Complete FS	Update AR	Update AR
Clinical Performance Validation Protocols	_	_	Preliminary	Complete FS	Update AR	Update AR
Usability Validation Protocols	_	_	_	Complete FS	Update AR	Update AR
Risk Assessment/Failure Modes and Effects Analysis (FMEA): Design (d)FMEA, [manufacturing] process (p)FMEA	-	Initiate dFMEA	Initiate pFMEA Update dFMEA	Complete FS	Update AR	Update AR
Human Factors Evaluation Protocols	_	_	_	Complete FS	Update AR	Update AR
Flex Studies Protocol	_	_	_	Complete FS		
Manufacturing Validation Plan	_	_	_	Complete	_	_
Manufacturing Validation Protocols	_	_	_	Complete FS	_	_







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Diagnostics Report January 2018

> by Mickey Urdea Rich Thayer

Halters Associates worked over the last decade with many companies, and they noticed that several diagnostics companies that initially appeared to be on a path to success ultimately failed.

In 2018, the Bill & Melinda Gates Foundation asked Halteres to conduct a study to help them understand why diagnostics companies fail:



GROUP 1
"Successes"

Companies that had reached commercial sustainability for at least 3 years.

GROUP 2 "Failures"

Companies either out of business entirely or whose assets were sold for small sums.

GROUP 3
"Zombies"

Companies that despite having product(s) in the market, the authors felt were likely to eventually fail.



## DIAGNOSTICS COMPANY GROWTH PHASES: 0 TO 4

PHASE 0	Design Phase – Concept  Concep		Performance (Sens / Spec / Repro) specifications fill an unmet need	Customer needs are understood (Voice of the Customer)		
PHASE 1	Feasibility and Planning	Experienced leadership / employee team capable of addressing business / tech challenges	All inventions have been completed to achieve final product / scale / COGs targets	Menu strength (one product vs. multiple). Company has back up plan in event of failure		
PHASE 2	Design and Development	Disciplined development processes (Design Control, Quality System)	Supply chain process, COGs targets, capital needs. Product designed for manufacturability	Robust IP, freedom to operate		
PHASE 3	Validation and Launch Readiness Established manufacturing and design control processes		Clinical studies supporting regulatory approval AND commercial/ reimbursement strategy	Market entry strategy in place, specific initial customers identified		
PHASE 4	Complete plans for commercial positioning and targeted launch		Reimbursement and / or payment strategy with clear objectives, budget and timelines. Partners identified	Operations robust and stable enough to transfer to sustaining operations. Have sufficient cash planed to profitability or liquidation		



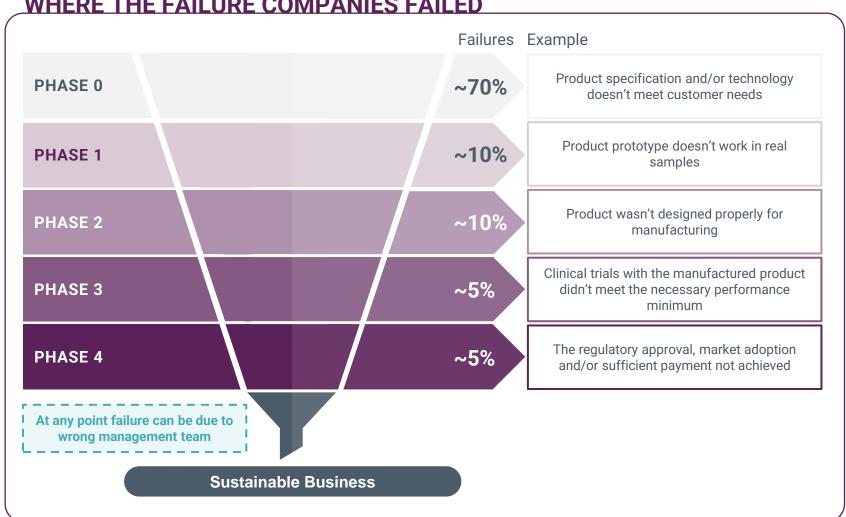
# Successful companies had clear criteria successes across each of the five phases, from conception in phase 0 to commercialization in phase 4.



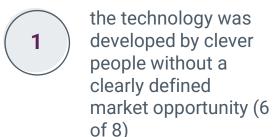
Most failures
were due to
founders believing
that they had
product concepts
that customers
would want without
actually conducting
'user needs' studies
(phase 0 criterion).



### WHERE THE FAILURE COMPANIES FAILED



For the Failures, many of the problems occurred early in the Phase 0 activities (8 of 15):

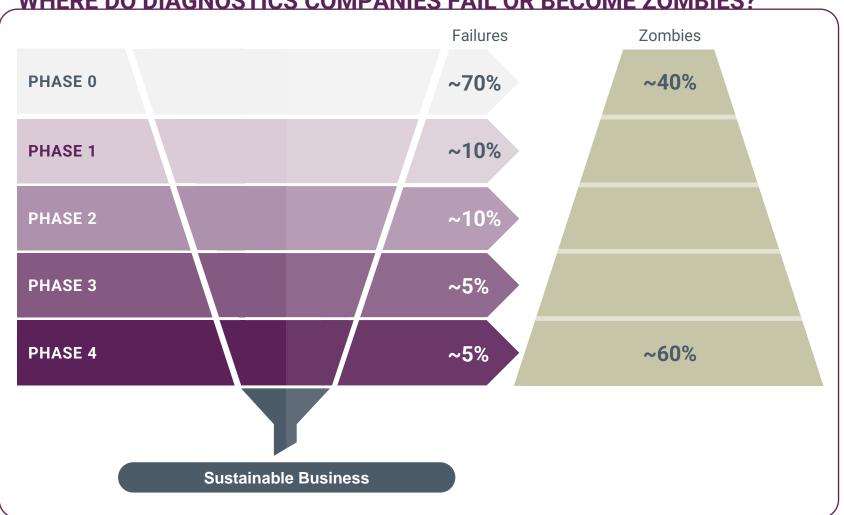


a market opportunity was clearly defined but the technology simply failed to provide adequate performance (2 of 8).

The other 7 of the 15 Failures had troubles at other points along the way.



#### WHERE DO DIAGNOSTICS COMPANIES FAIL OR BECOME ZOMBIES?



Less than half of the Zombies made mistakes in the Phase 0 category. Instead, the problems were identified mostly in Phase 4, Commercialization.

In each case senior management was able to find cash to keep them going but they failed to make them sustainable.



## READING

Peabody J, Burgon T, Paculdo D, et al. Postmortems on diagnostic testing start-ups: reports of commercial successes and failures and the case of the Zombie life science company.

**DIAGNOSTICS** 

ORIGINAL RESEARCH

Postmortems on diagnostic testing start-ups: reports of commercial successes and failures and the case of the Zombie life science company

John Peabody , <sup>1,2</sup> Trevor Burgon, <sup>1</sup> David Paculdo, <sup>1</sup> Othman Ouenes, <sup>1</sup> Enrico de Belen, <sup>1</sup> Mike Richey, <sup>3</sup> Richard M Thayer, <sup>3</sup> Mickey Urdea <sup>3</sup>





## **Market Failures in Diagnostic Ecosystems for LMIC Year 2022**

They map the nine main market failures across the stages of the diagnostics ecosystem value chain, indicated by colored blocks:

I	Limited Investment	Insufficient workforce	Deterring regulations	Inefficient purchasing and procurement	Operational inefficiencies	Limited infrastructure and technology	High costs	Low trust	Limited government support and policy development
1 RESEARCH AND DEVELOPMENT		Health and biomedical researchers	Intellectual property						
2 MANUFACTURING			Approvals pathways and QMS	Raw materials supply	Production scale and costs				
3 PROCUREMENT AND DISTRIBUTION				Delayed funding cycles and high opportunity costs	Connection gaps between stakeholders	Distribution networks and product forecasting			
4 SERVICE DELIVERY AND USER ADOPTION		Health care workforce				Health service accessibility	End user affordability		





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# Research and development MARKET FAILURES



# Manufacturing MARKET FAILURES



- ◆ Insufficient workforce: Limited and unstained investment in academia, research, and innovation in LMICs results in limitations in training and career opportunities for R&D professionals.
- ◆ Intellectual property: Diagnostic products are often imported from HICs, which benefit from stronger IP protections. The reliance on overseas IP increases shipping and distribution costs, which are passed on to the end-user.

- Limited Investment: Regional manufacturers have limited growth opportunities due to lack of scalable and sustainable demand for diagnostic products in local and regional markets.
- ♠ Approvals pathways and quality management systems: Inefficient and fragmented regulatory systems across LMICs create barriers for local manufacturers to enter and scale up within these markets.
- Raw material: Limited domestic availability of raw materials and products leaves regional manufacturers highly reliant on imports from HICs.
- Production scale and costs: Sustainable operations require appropriate infrastructure and technology, high utility rates of machinery, and predictable demand.



## READING

Market failures and opportunities for increasing access to diagnostics in low-and middle-income countries

https://www.path.org/our-impact/resources/market-failures-and-opportunities-for-increasing-access-to-diagnostics-in-low-and-middle-income-countries/





1

A well-established
Phase Gate System
minimizes the risks
for a product to fail
before or after
reaching the
market.

2

Product Development
Phases must be
defined by each
company to adapt to
their products and
processes.

3

Most IVD companies fail because the developed product does not meet the user needs.

4

Define regulatory pathway on the early product development phases minimize development cost and time.

