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Greater Detection for Better Decisions

Development of a NGS-based CE-IVD test for pathogen detection

iDTECT Dx blood

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iDTECT™ Blood: sample-to-report metagenomics

TAT : 48 h

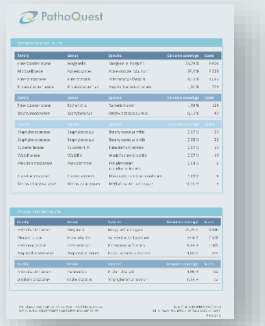
Blood sample

Sample preparation

Significant enrichment in pathogen nucleic acids

Patent application filed

Sequencing MiSeq®



BioIT workflow and report generation

- Cloud-based software
- Automated from FastQ files to report
- Curated pathogens database

Copyrighted

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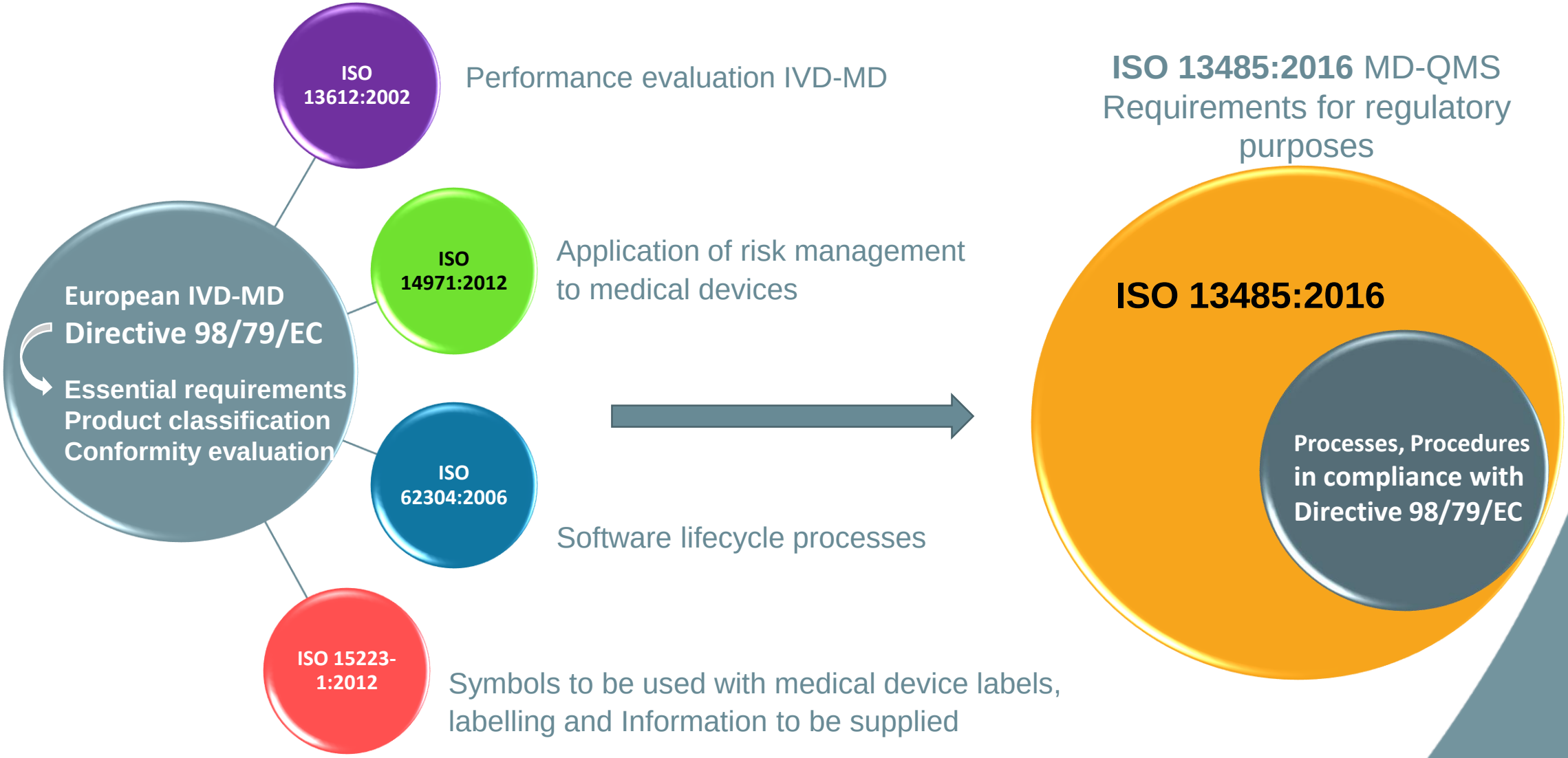
Normative References for iDTECT conception - development



Management of a IVD-MD from Design and Development to Market

Go/No Go

18 to 36 months

Initiation	Feasability	Development	Transfer Industrialization	Clinical and Medico-Economic performances	Market

Unmet need
Identification
Product Profile
definition

Prototype
Functional specifications
Perfomance definition

Prototype
Verification
Validation

Bridging studies
Deployments
Scale up

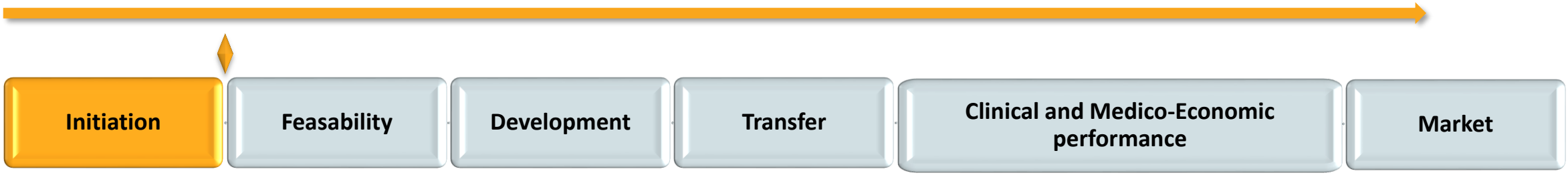
Clinical Performance Definition

Reimbursement dossier

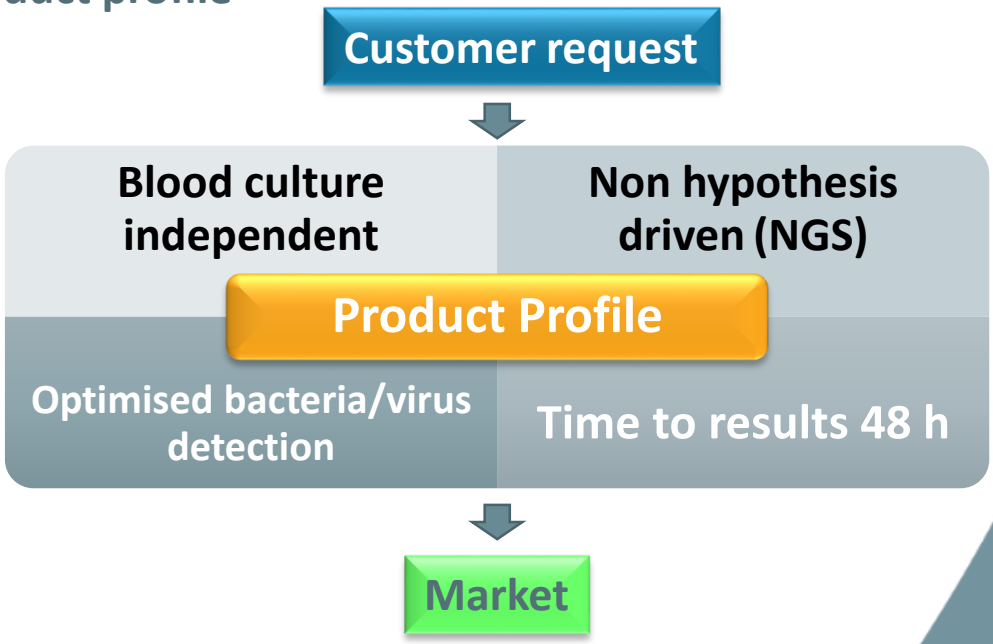
Risk Analysis / Risk Management

Change Control Management

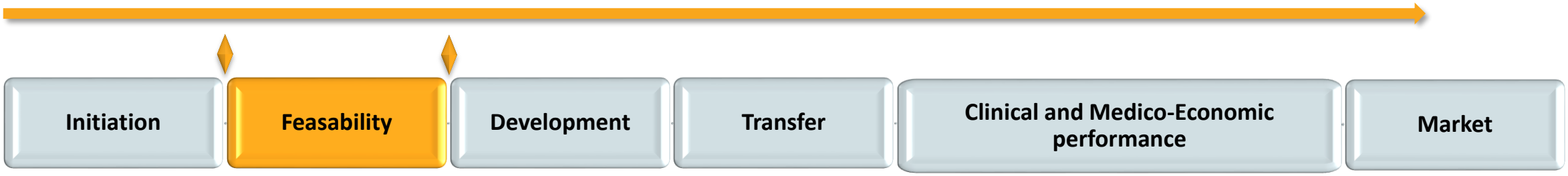
Initiation Phase – Project Overview



- **Identification of the unmet need and definition of the product profile**
- **Intended use :** patients with a suspected infection
- **Regulatory Plan :** normative references
- **Project Planning and Budget**
- **Commercial model definition**



Feasability Phase – Proof of Concept Definition



- **Risk analysis initiation**

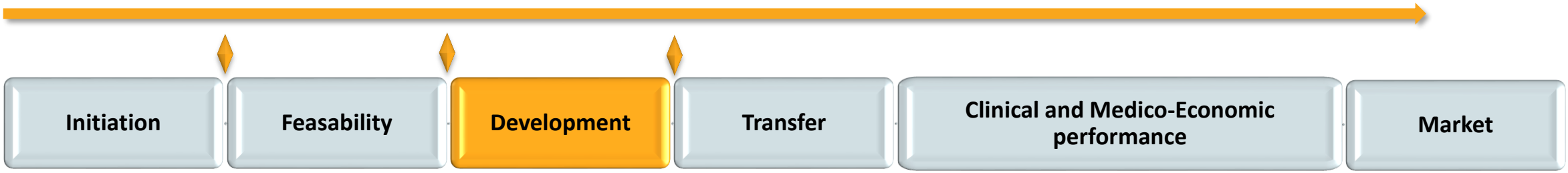
- **Functionnal specifications definition:**

Sample Processing	BioIT Pipeline
Whole blood sample collection and storage	Pathogen database
Whole blood sample processing	Pathogen identification software
Spiking toolbox : pathogen models	Scoring: Identification Confidence Index
Controls	

- **Performance evaluation :**
  - Spiked samples: LoD per pathogen model
  - Biological samples: comparison to conventional diagnostic decision algorithm

Main Deliverable : Design Input Requirements Plan

Development Phase–Prototype Validation-Verification -1



- **Risk analysis, D.I.R and regulatory plan updates**

- **Performance evaluation :** clinical study (n° 130101B-41) 101 patients - **Hopitals Necker and Pompidou** (Paris, Fr)

Patients suspected of infectious disease requiring microbiological investigations AND suffering from an immuno-suppressive conditions

- ✓ observational and prospective over 30 days, 2 time points: day 1 and day 30
- ✓ identifcation of bacteria and viruses
- ✓ performance comparison to conventional pipeline : blood culture, other cultures, PCR ….
- ✓ determination of clinical relevance of identified pathogens by a Clinical Adjudication Committee

Development Phase–Prototype Validation-Verification-2

Primary outcome – day 1

Patients with clinically relevant pathogens

	Standard Procedures Positive	Standard Procedures Negative	Total nb of patients
UNGS - Positive	9	27	36
UNGS - Negative	2	63	65
Total nb of patients	11	90	101

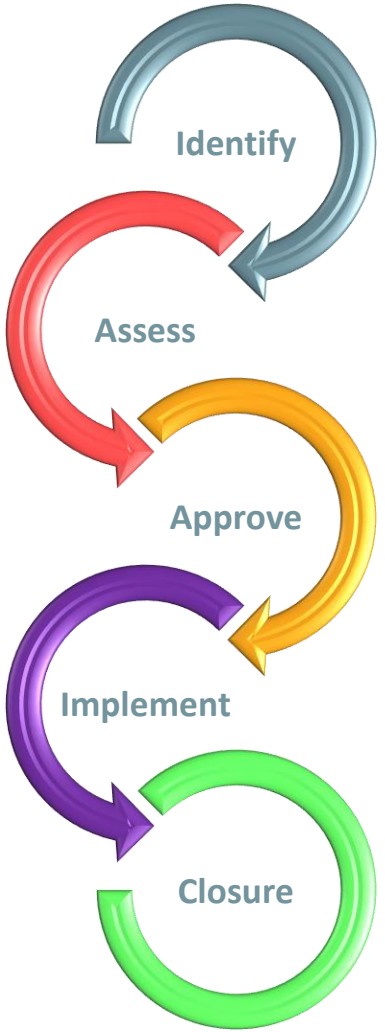
= 1 CMV, 1 E.coli

NPV = 97%

Parize P et al, Clin Microbiol Infect. 2017

Development Phase - Prototype Validation-Verification -3

Change Control Management



Need for prototype 1 improvement

- To increase analytical sensitivity
- To fit with clinical lab equipment
- To optimize report interpretation

Action plan

- Addition of a detergent as adjuvant to nucleases
- Random amplification improvement
- Technology transfer (Ion Torrent to Illumina)
- Scoring method development

Go

Objective : at least equivalent performances

Prototype 2/ iDTECT validation

- Development and Validation studies
- Analytical performance verifications (repeatability/reproducibility, robustness)

Integration into QMS

Proton Instrument – Ion Torrent

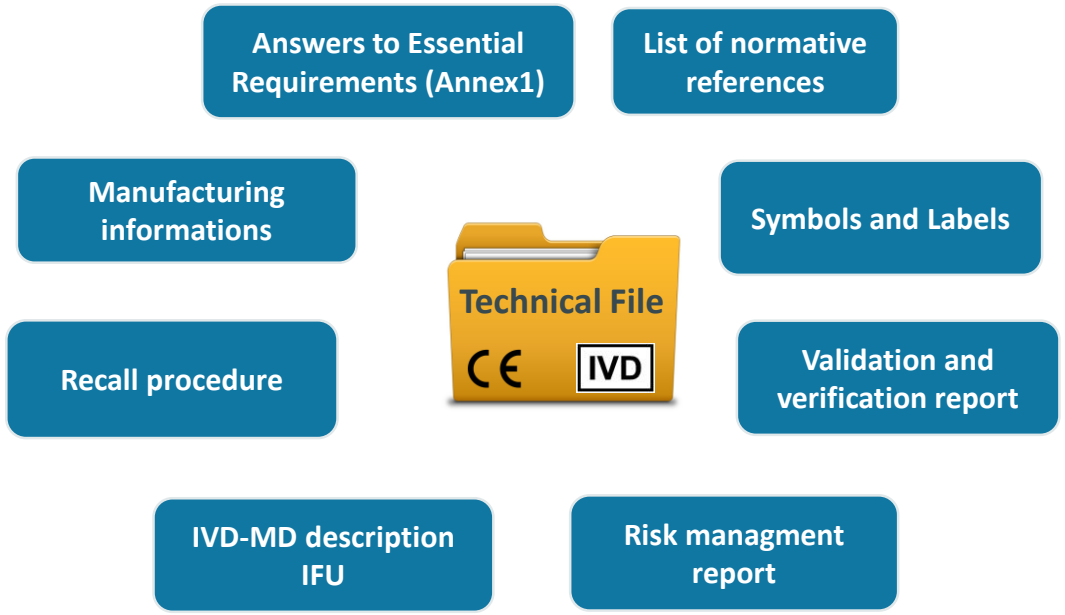
MiSeq Instrument - Illumina

Development Phase – CE Marking

★ CE-IVD Q4 2016

Initiation	Feasability	Development	Transfer	Clinical and Medico-Economic performance	Market

Main Deliverables : D.I.R plan, D.I.R report, D.O.R report, Validation and Verification report and Risk Managment Report



Conformity evaluation

Directive 98/79/EC
Annex 3

Release of Conformity Certificate

- Device is not part of Annex II
- Not a device for self-testing
- Software : class C

iDTECT™ Software

Bioinformatic analysis: < 20 min per sample

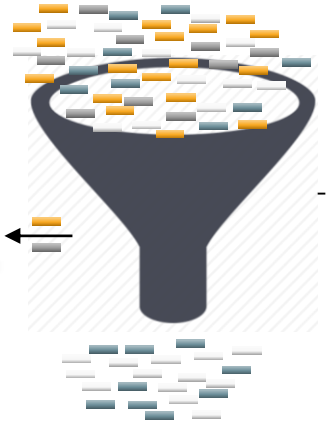
From patient to iDTECT report

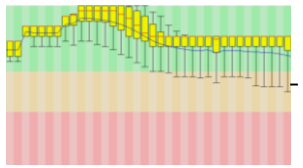
Patient

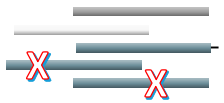
Sample preparation

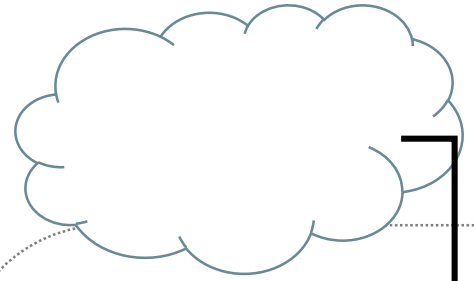
Sequencing

Hardware proxy









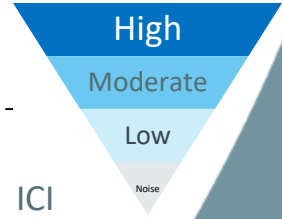
Datacenter

Pathogens assignation

Score

iDTECT db

Report generation



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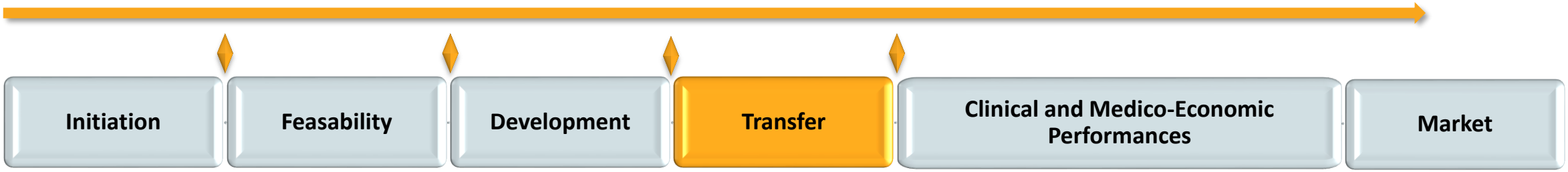
Transfert Phase – Industrialization of iDTECT™ Blood



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Specialized Diagnostic Laboratories

Hôpitaux Universitaires SAINT-LOUIS LARIBOISIÈRE FERNAND-WIDAL

Cerba HealthCare

Memorial Sloan Kettering Cancer Center

Clinical Phase–Medico-economic evaluation - IDENTIFY

French multicentric study

1. Evaluation of the febrile episod
2. Antimicrobial treatment and adjustments
3. Hospital resource utilisation (days in types of wards, additional imaging or biological tests)

objectives

iDTECT™ pipeline – current and future

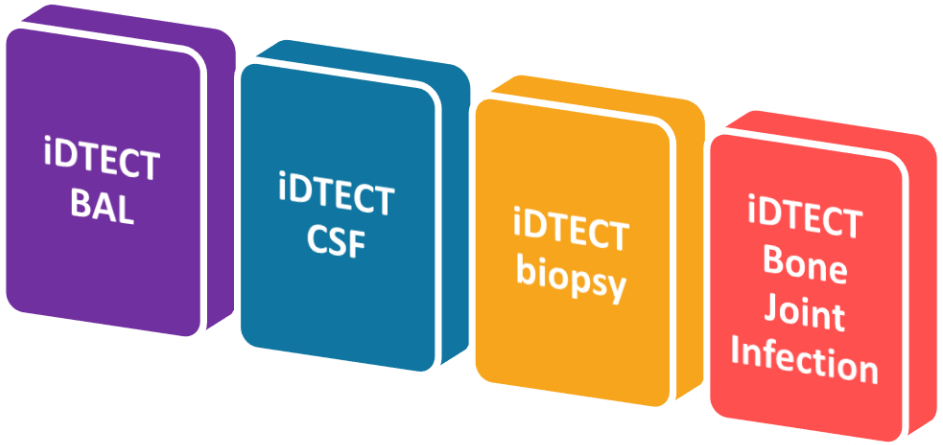
iDTECT™ Blood

CE IVD Q4 2016

Target population

- **Febrile Neutropenic (current)**
- **Stem Cell transplantation**
- **Solide organ transplantation**
- **Endocarditis**

Other sample types (selection ongoing)



Conclusion

- iDTECT™ development in compliance with the Directive 98/79/EC
- iDTECT™ Blood is currently deployed in private/hospital specialized laboratories
- A clinical and medico-economic utility study in febrile neutropenic patients will be initiated in Q1 2018
- Other indications of iDTECT™ Blood are currently under evaluation
- Selection among other sample types for the next iDTECT CE-IVD development is ongoing