Corso di Biotecnologie applicate
A.A. 2025-2026

Stefano Ceschia

Alifax Srl (Sede di Nimis, Udine)

Trieste, 02st April 2026

OUTLINE

1. General introduction about Alifax, Research and Design activities

2. Main areas of interest in Alifax

   a) ESR (scope of the test, biological mechanisms, clinical importance)

   b) Microbiology (Antimicrobial Stewardship, MDROs, Clinical microbiology workflow)

   c) Introduction of new products in the market

3. Design process (Project Vision, Stakeholder needs, Usability, Safety, Performance)

4. From Design to Manufacturing and Sells: Process Validation, Safety, Registrations

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LEADER ITALIANO DELL’IVD

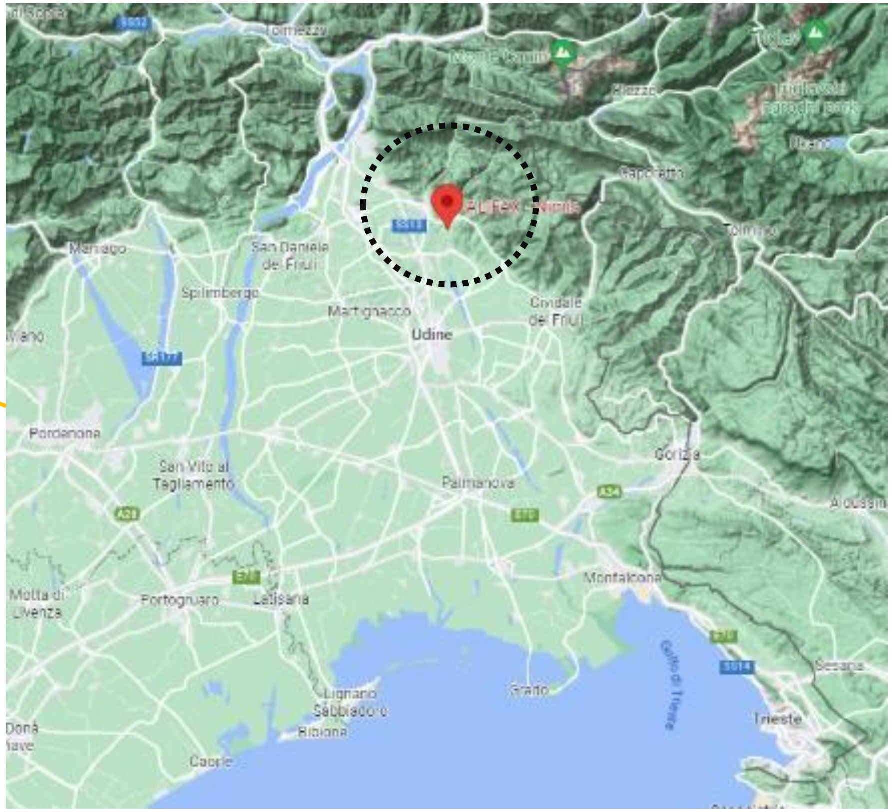
- Alifax opera nella progettazione, produzione e commercializzazione di dispositivi IVD per la diagnostica di laboratorio clinico.

- Distribuisce in Italia prodotti IVD di terzi come importatore e distributore

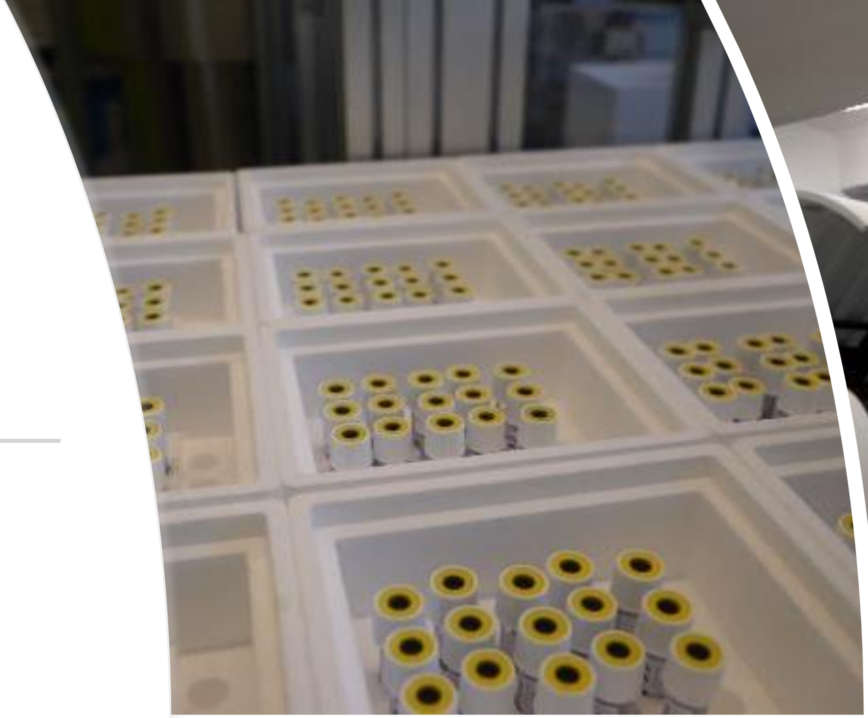
- Commercializza in Italia e nel mondo i prodotti a proprio marchio

ALIFAX DESIGN AND MANUFACTURING SITE

Alifax has a large facility in Nimis (UD) dedicated to the reasearch, development, design and production of IVD products and service

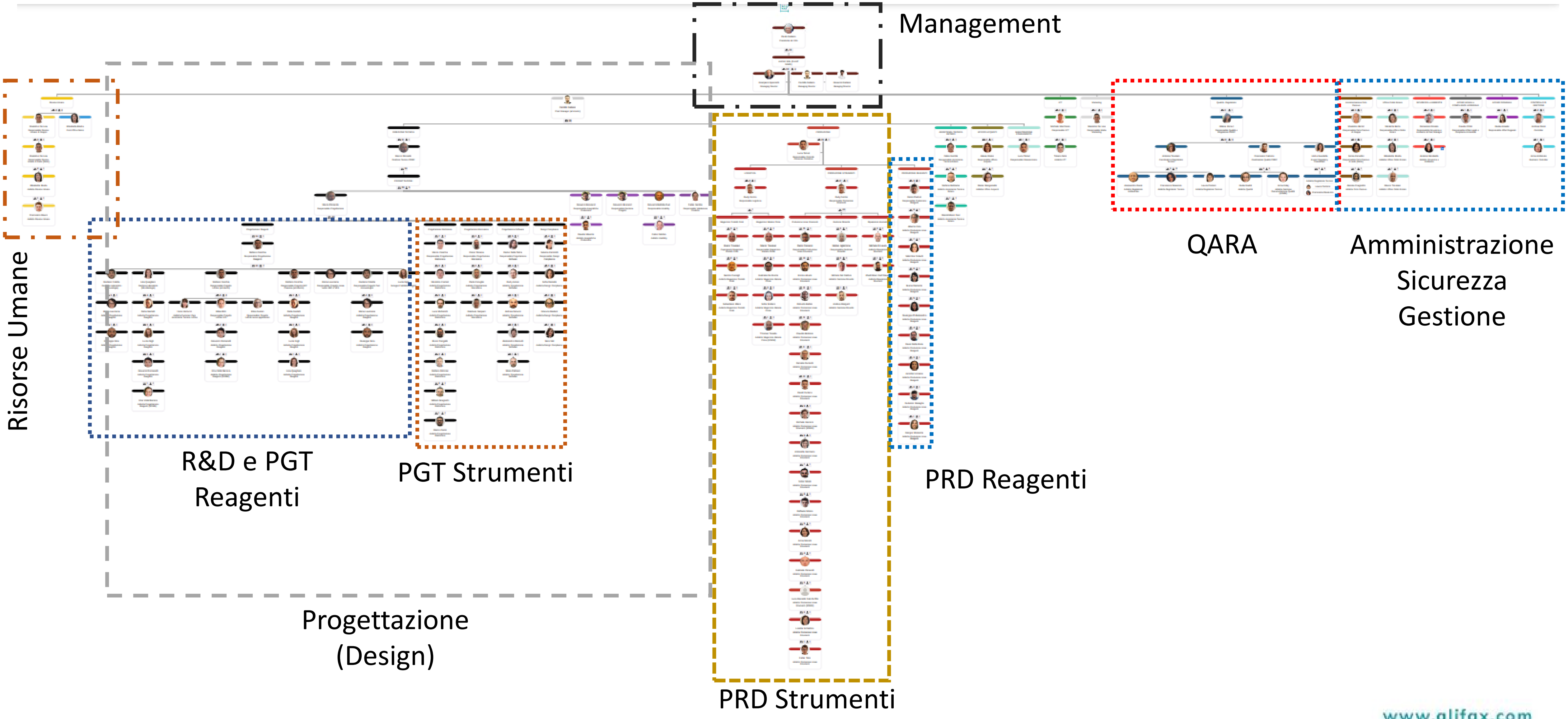


- Approximately 100 persons involved in:
  - R&D;
  - Design;
  - Manufacturing;
  - Quality Assurance & Regulatory affairs (QARA);
  - Administration and logistics



ORGANIZZAZIONE INTERNA

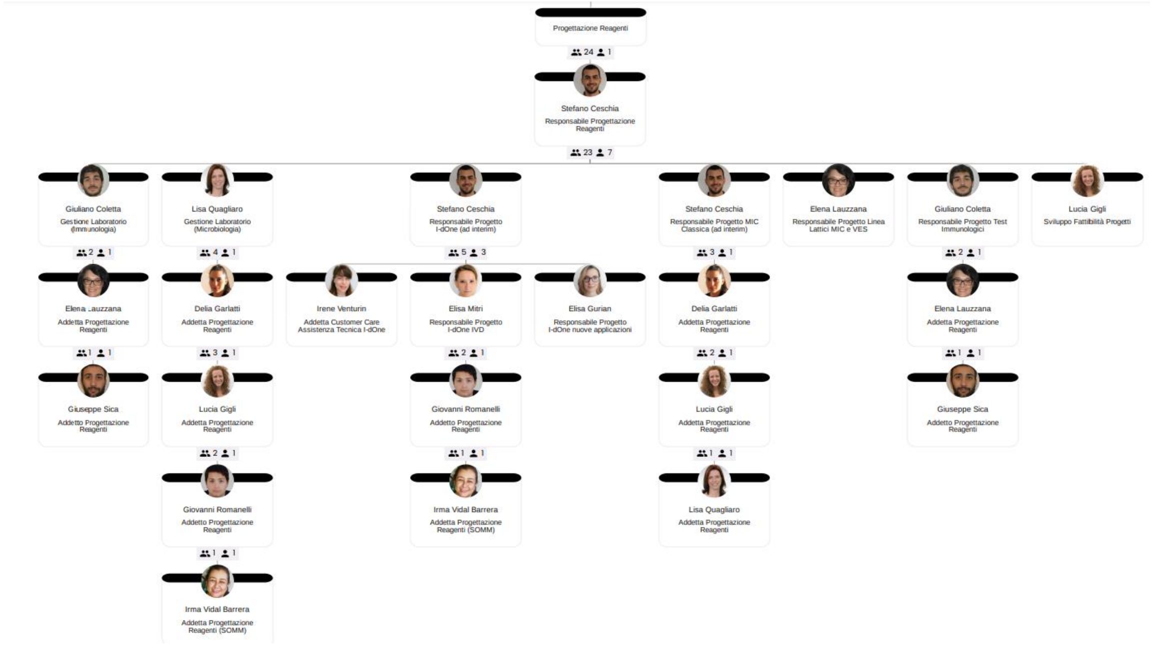
INSIDE INNOVATION



PROGETTAZIONE REAGENTI

- **Professionalita'**:
  - *Biologi;*
  - *Chimici;*
  - *Biotecnologi;*
  - *Tecnici di laboratorio;*

- **Grado di formazione**:
  - *Laurea magistrale;*
  - *PhD*
  - *Post-Doc*



L'UFFICIO RICERCA E SVILUPPO
SEDE DI NIMIS

- **Scopo dell'ufficio:**
  - sviluppo di nuovi test sugli strumenti a marchio Alifax;
  - ricerca e testing di nuove tecnologie applicabili all'ambito clinico diagnostico;
  - sviluppo di nuovi dispositivi tramite progetti di prototipizzazione ed industrializzazione.

- **Composizione:**
  - Attualmente impiegate 13 persone di diversa estrazione formativa

- **Background:**
  - 4 risorse con titolo PhD in ambito chimica / biofisica
  - 9 laureati in ambito Biologia, Biotecnologie, Chimica industriale

RELAZIONI INTER-UFFICIO

Progettazione Elettronica

Progettazione Meccanica

Produzione reagenti

Qualità e regolatorio

Progettazione Software

Validazioni ospedaliere

Utilizzatore finale

COORDINAMENTO MULTIDISCIPLINARE

Progettazione Elettronica

Progettazione Meccanica

Produzione reagenti

Qualità e regolatorio

Progettazione Software

Validazioni ospedaliere

Utilizzatore finale

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ALIFAX'S PRODUCT LINES

- ESR
- MICROBIOLOGY
- IMMUNOLOGY

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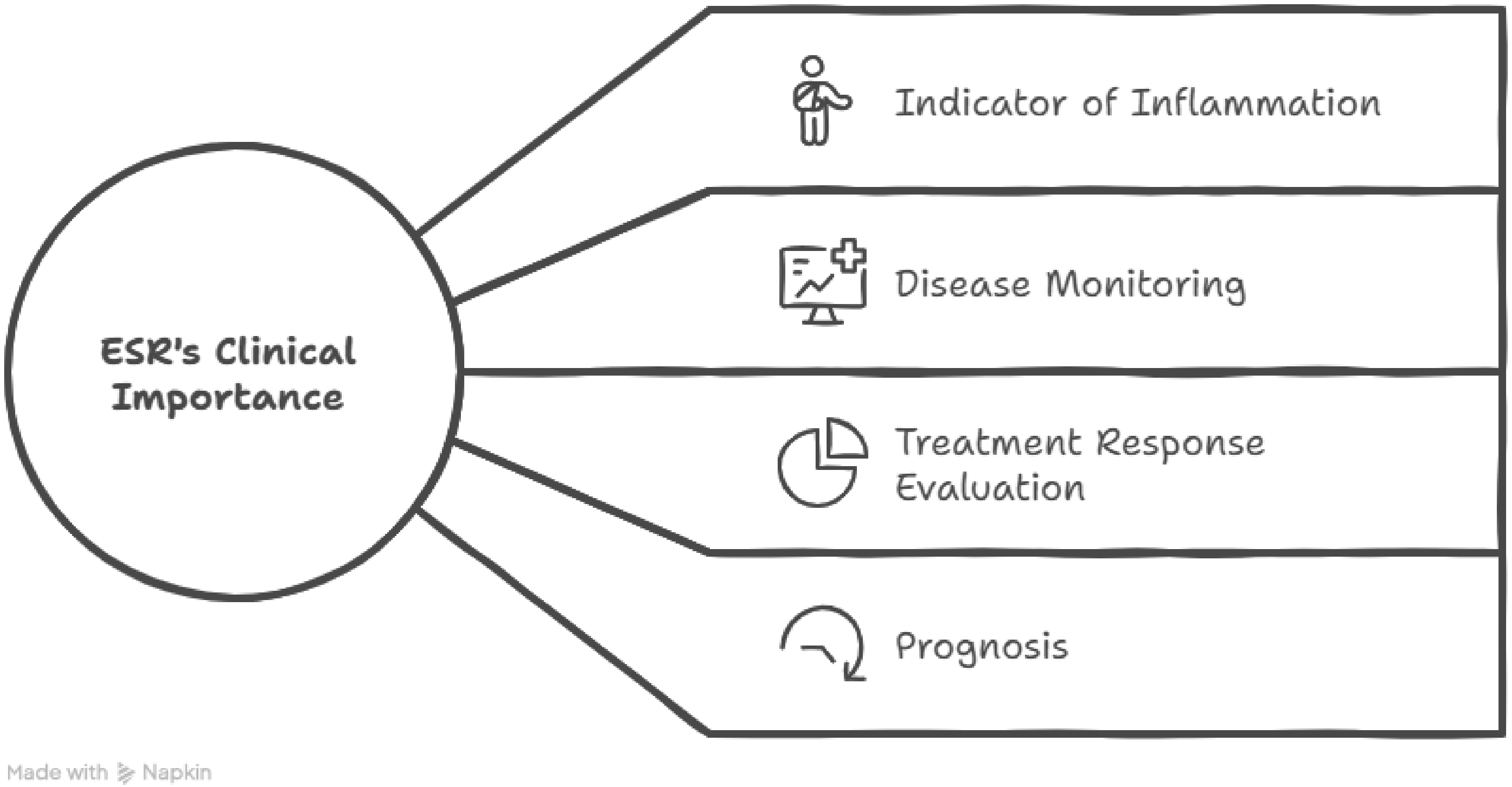
Exploring the Multifaceted Role of ESR



A Bit of History

- Even the ancient **Greeks and Romans** noticed a different blood sedimentation in various medical disorders
- During the **Middle Ages** and the **Renaissance** physicians describe in specific diseases of blood clots covered with whitish liquid called "crusta inflammatoria“
- In **1772 William Hewson** in **1832 and Herman Nasse** observe that the sedimentation in blood samples without fibrinogen is much slower than the whole blood samples
- In **1894, Edmund Biernacki** (1866-1912), a Polish physician, first noted the increased sedimentation rate of blood from ill individuals and realized that this increase was due to the **presence of fibrinogen** in the individual's blood sample.

Edmund Biernacki
(1866-1912)

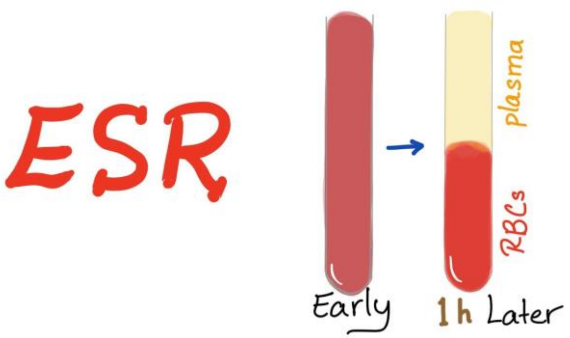
A Bit of History

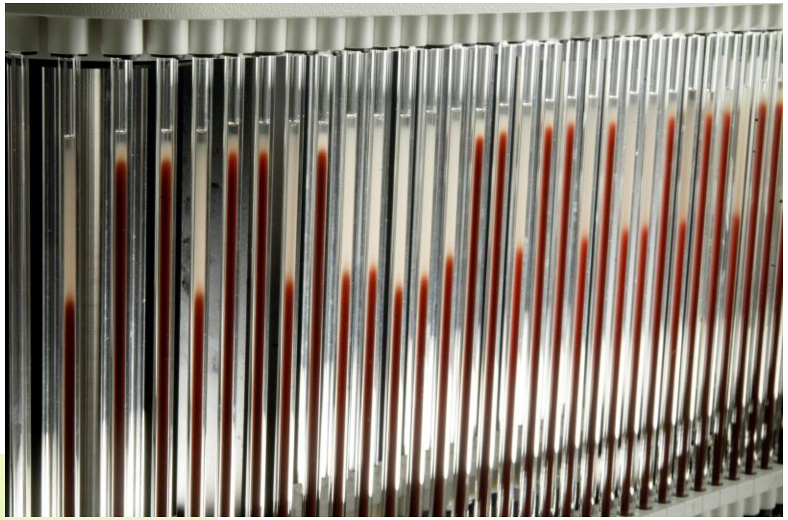
- In **1918, Robin Fahraeus** (1888-1968) furthered Biernacki's work. His initial motivation to study the ESR of blood was as a **pregnancy test**, but his interest expanded to the study of the ESR test in his patients.
- In **1921, Alf Westergren** (1881-1968) refined the technique of performing the ESR test and reported its usefulness in determining the prognosis of patients with **tuberculosis**.
- In **1935, Maxwell M. Wintrobe** (1901-1986) published a variation of the ESR methodology and, at one time, this method was in wide use.

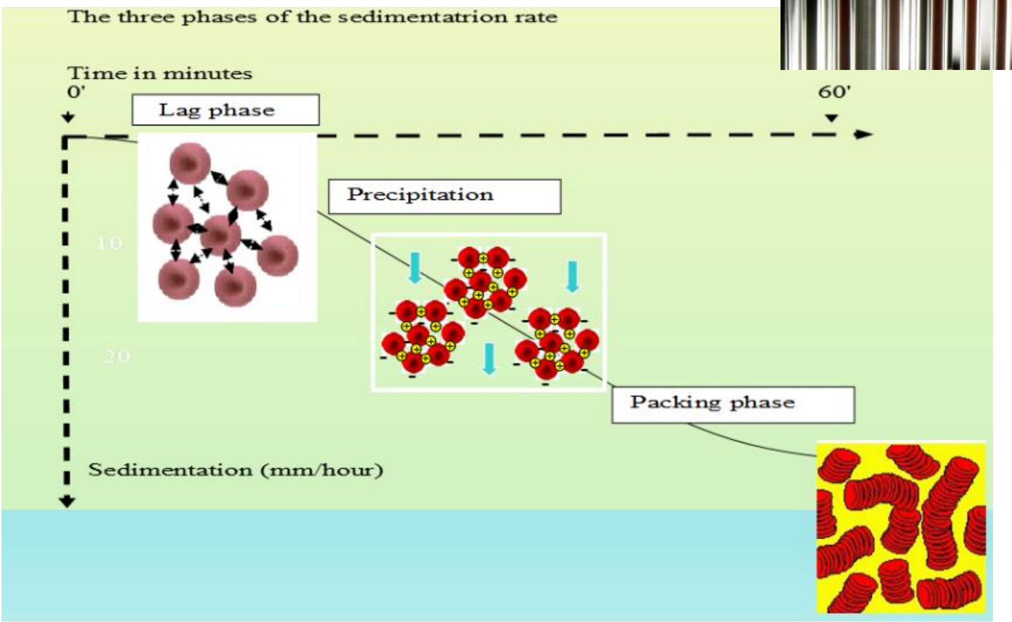
National Museum of the History of Science and Medicine (The Netherlands) Erythrocyte sedimenttion rate equipment stand (CEMI 1920)

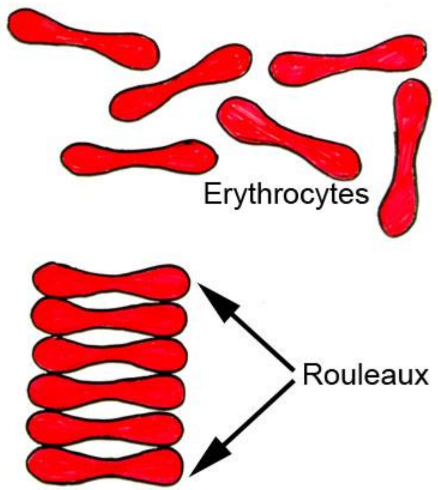
ESR

THE STANDARD METHOD



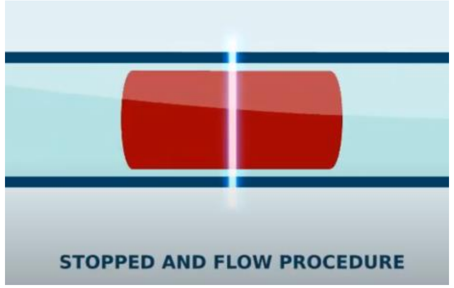


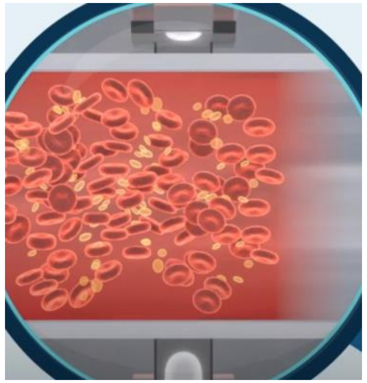


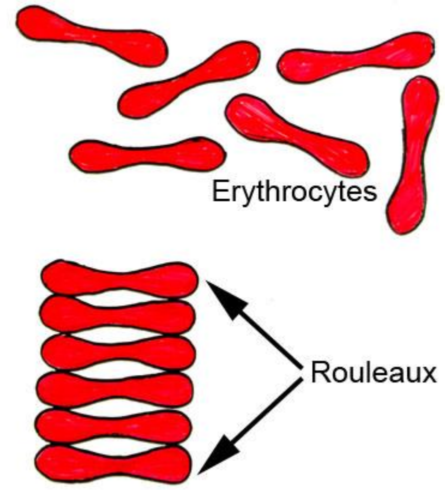


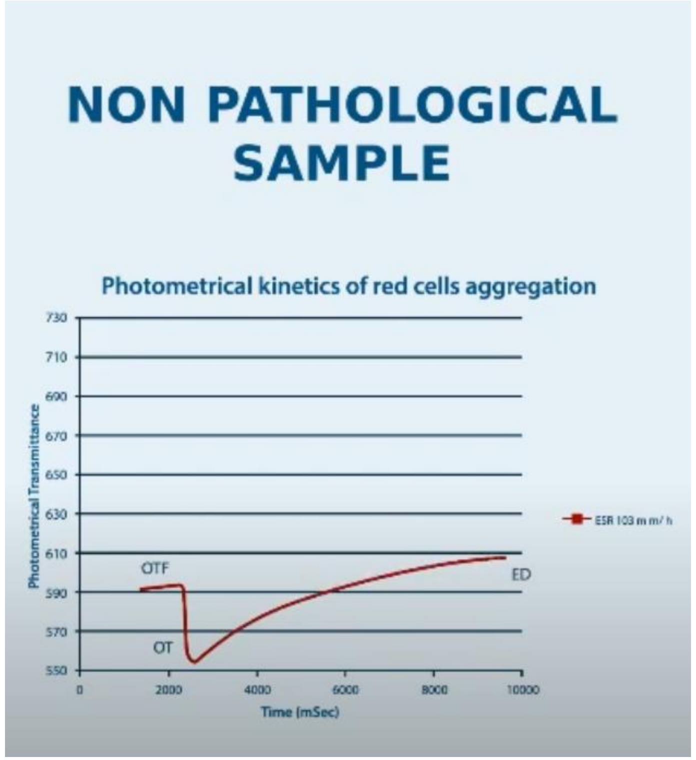
ESR

ALIFAX METHOD

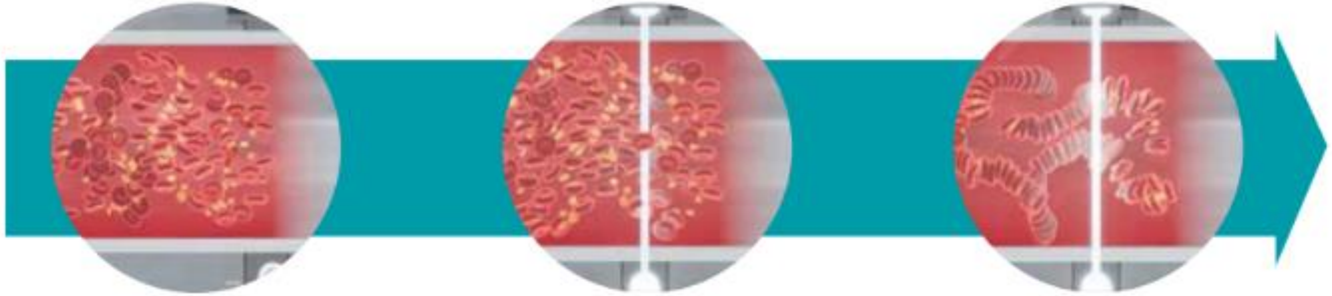








PRODOTTI A MARCHIO ALIFAX
LINEA EMATOLOGIA – VES IN 20’’



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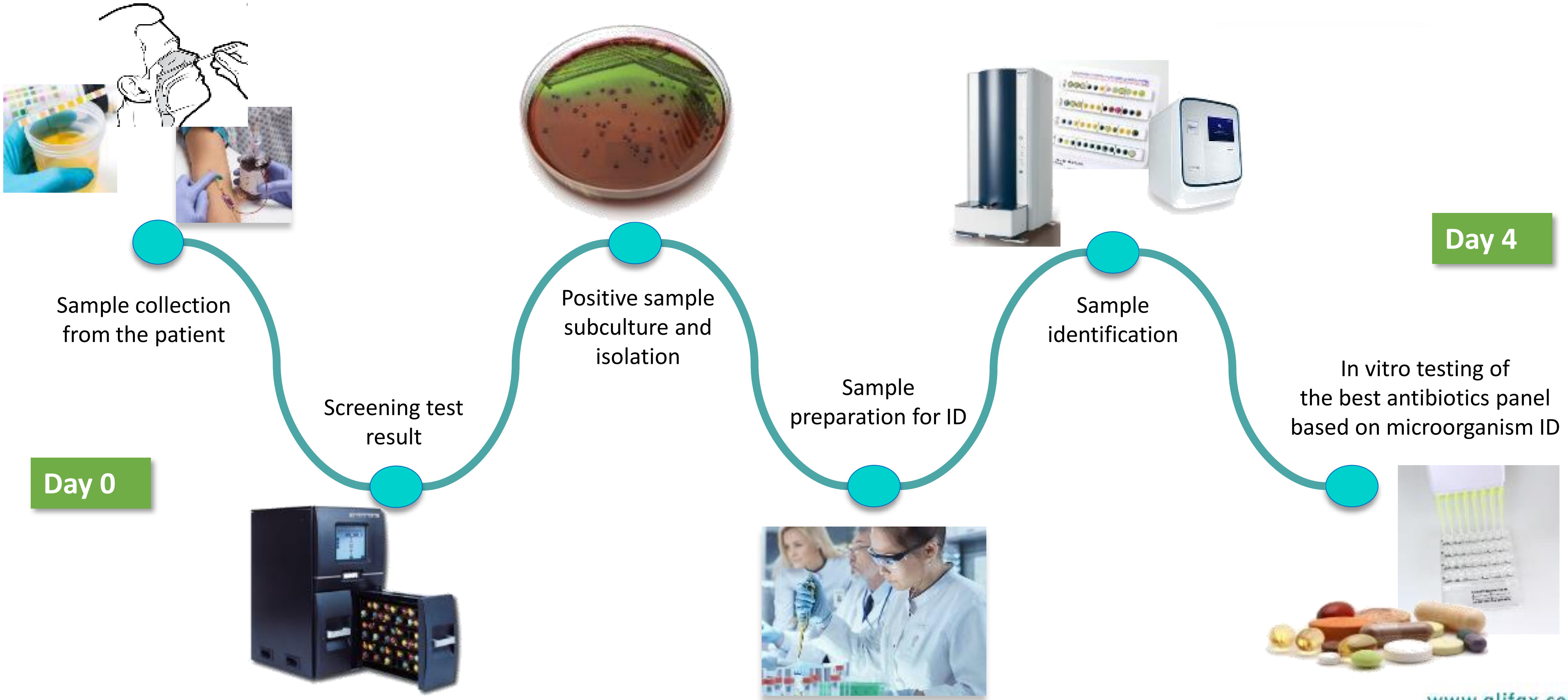
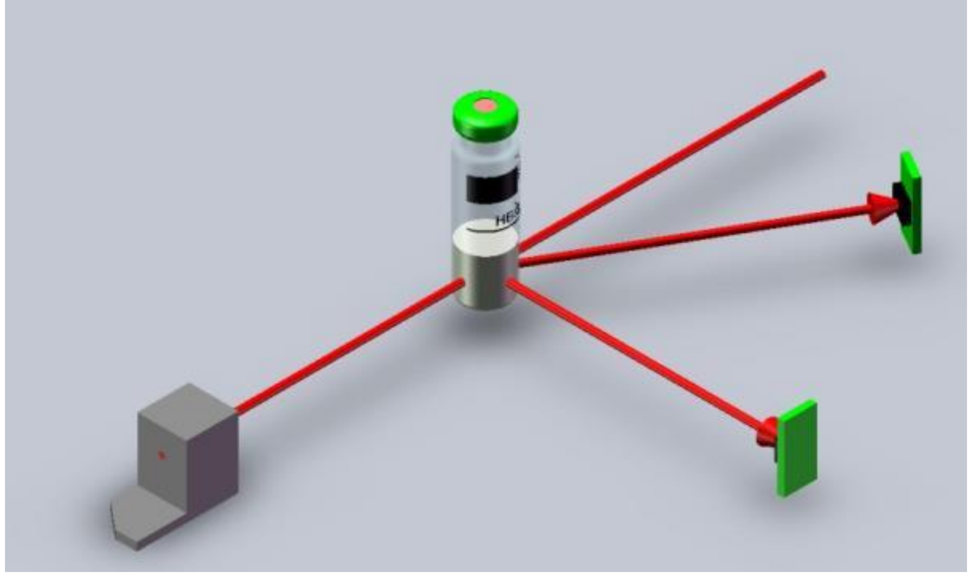
GENERICO FLUSSO DIAGNOSTICO IN LABORATORIO MICROBIOLOGIA

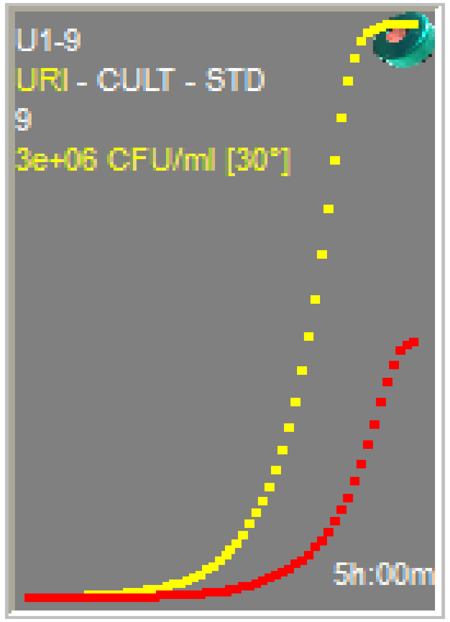


TECNOLOGIA BREVETTATA

I segnali di scattering vengono analizzati, elaborati e convertiti in curve di crescita tracciate in **tempo reale**

L'elaborazione matematica fornisce non solo una **valutazione qualitativa della presenza/assenza di microrganismi,** ma anche una valutazione **quantitativa della quantità iniziale di batteri espressa in CFU/ml**





INSIDE INNOVATION

Dispersione di Rayleigh

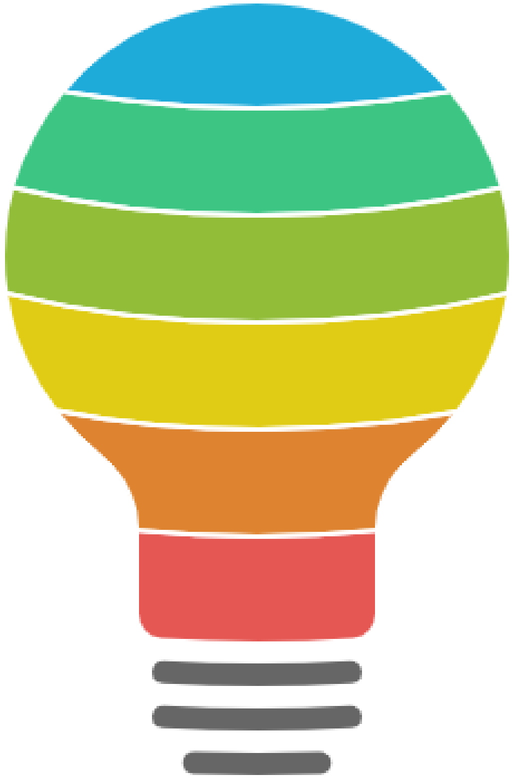
Dispersione di luce da particelle più piccole della lunghezza d'onda

Dispersione di Brillouin

Dispersione di luce da onde sonore in un materiale

Dispersione di Thomson

Dispersione di luce da elettroni liberi



Dispersione di Mie

Dispersione di luce da particelle della lunghezza d'onda o più grandi

Dispersione di Raman

Analisi di luce da vibrazioni molecolari

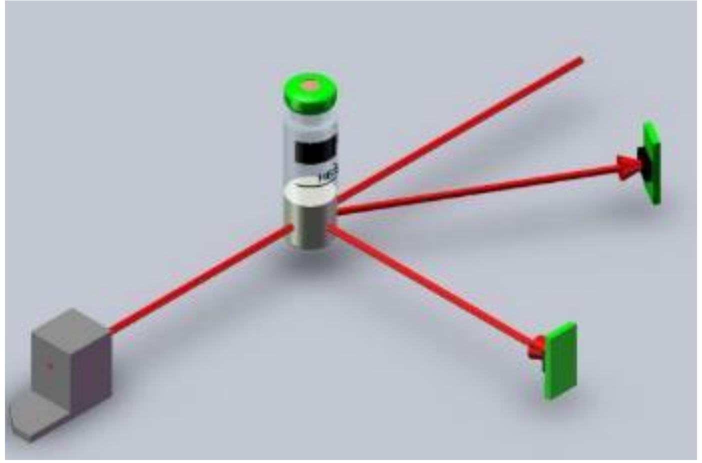
Dispersione di Compton

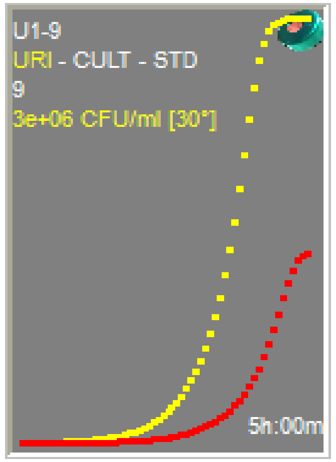
Dispersione di luce da particelle cariche

lightscattering

PRODOTTI A MARCHIO ALIFAX
LINEA BATTERIOLOGIA CLASSICA

- Rilevazione rapida di microorganismi in sospensione mediante letture Laser Light Scattering
- Sviluppo di tecnologie integrate per movimentazione campioni, dispensazione e semina automatica.
- Flessibilità di reagenti per lo svolgimento di molteplici test di laboratorio





INSIDE INNOVATION

PRODOTTI A MARCHIO ALIFAX
LINEA BATTERIOLOGIA CLASSICA

ALIFAX NEL FLUSSO DIAGNOSTICO – LINEA CLASSICA

Sample collection from the patient

Day 0

Screening test result

Positive sample subculture and isolation

Sample preparation for ID

Sample identification

Day 2

In vitro testing of the best antibiotics panel based on microorganism ID

IDENTIFICHIAMO I BISOGNI DIAGNOSTICI

Urinary Tract Infections (UTIs): Verso una Diagnosi Rapida e Decentralizzata

Superare le barriere del laboratorio centrale per una terapia mirata fin dal primo giorno.

INSIDE INNOVATION

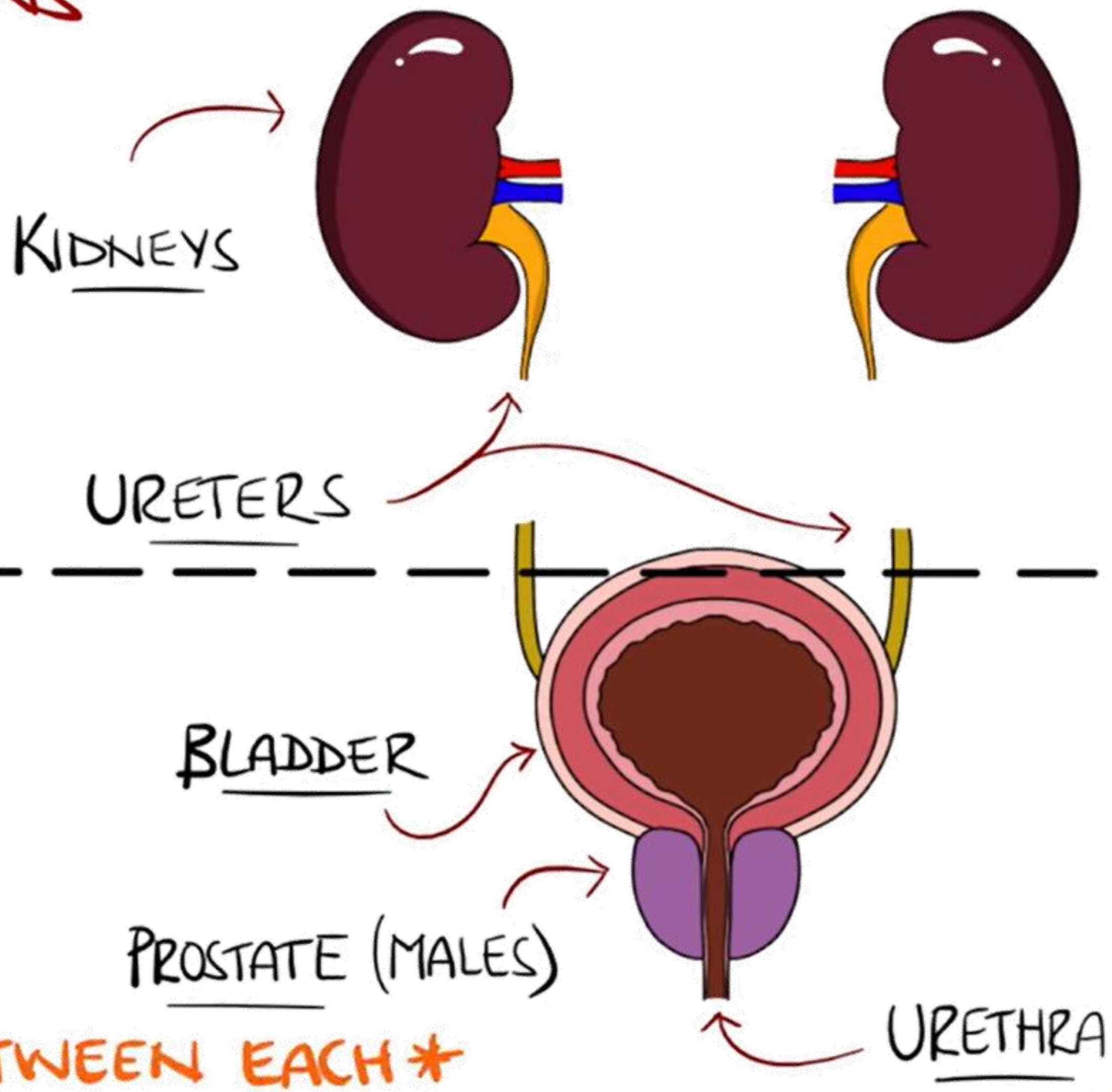
URINARY TRACT INFECTIONS

UPPER UTI

1) PYELONEPHRITIS (KIDNEY)
2) URETERITIS

LOWER UTI

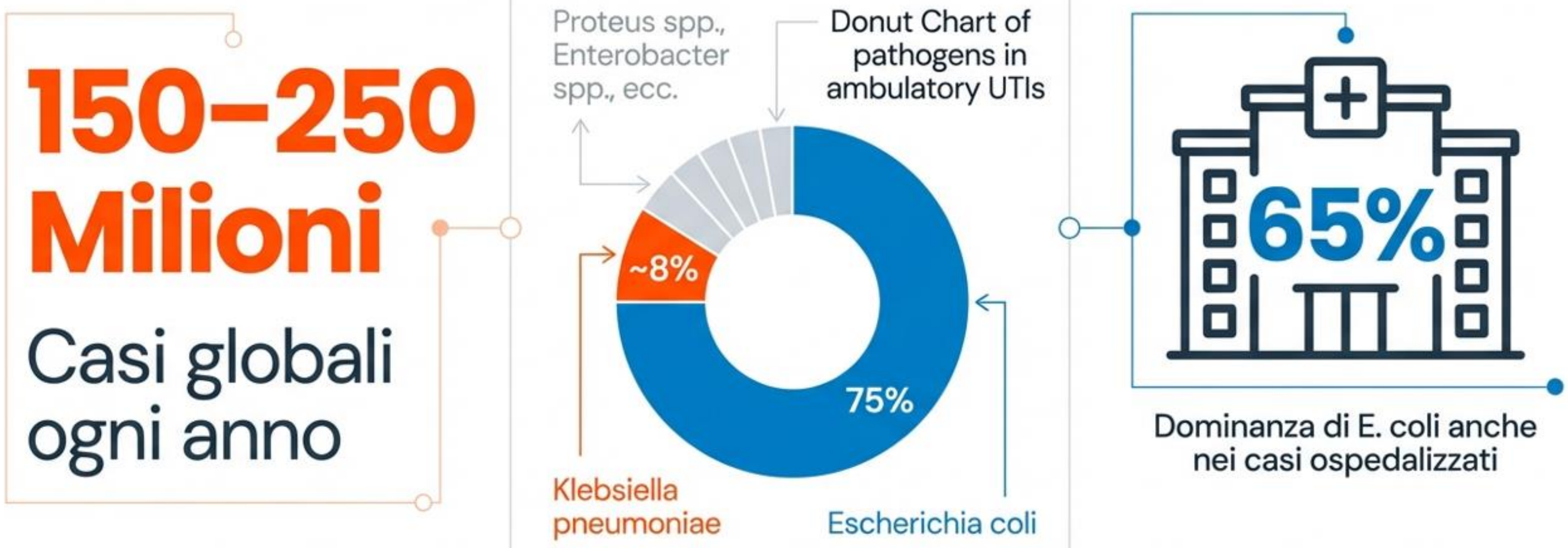
1) CYSTITIS (BLADDER)
2) PROSTATITIS
3) URETHRITIS



INFECTIONS MAY SPREAD BETWEEN EACH

IVU Non Complicate (uUTI)	IVU Complicate (cUTI)
Profilo Paziente Donne sane, pre-menopausa.	**Profilo Paziente** Pazienti con anomalie strutturali, catetere, insufficienza renale, gravidanza.
Fattori di Rischio Rapporti sessuali, uso di spermicidi, genetica.	**Fattori di Rischio** Cateterizzazione (CAUTI), ostruzioni, immunosoppressione.
Rischio Complicazioni Basso, spesso autolimitante.	**Rischio Complicazioni** Alto (Pielonefrite, Urosepsi, Danno renale).

Infezioni Associate a Catetere (CAUTI)
Le infezioni associate a catetere rappresentano il 30-80% delle infezioni acquisite, con un rischio che aumenta del 10% per ogni giorno di cateterizzazione nelle donne.



Impatto Globale: Le infezioni delle vie urinarie rappresentano una delle patologie infettive più diffuse al mondo, generando costi astronomici e un massiccio consumo di antibiotici.

INSIDE INNOVATION

1. Colonizzazione

I patogeni residenti nell'intestino colonizzano l'uretra tramite specifiche adesine.

2. Moltiplicazione e Biofilm

La risposta infiammatoria fallisce. Formazione di biofilm protettivo nella vescica (Cistite). Sintomi: Disuria, ematuria.

3. Pielonefrite

L'infezione risale agli ureteri fino ai reni. Sintomi: Febbre, dolore lombare acuto.

4. Urosepsi (Rischio Critico)

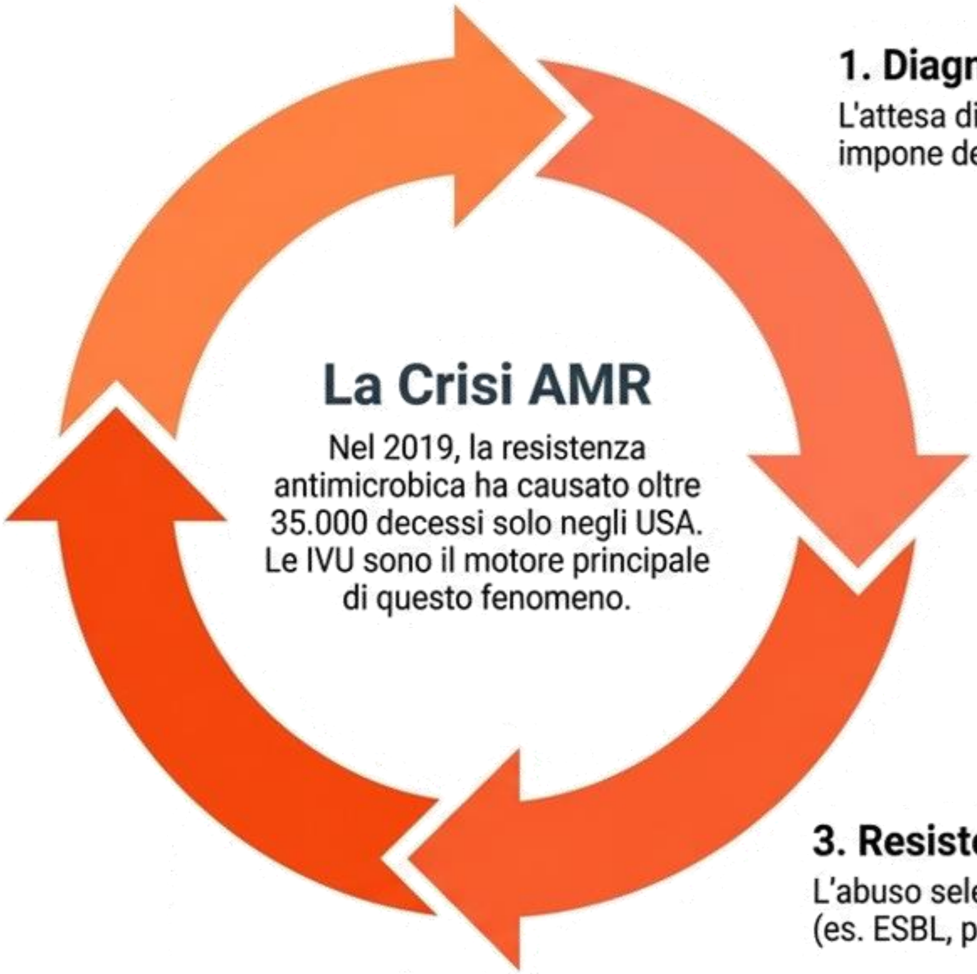
I batteri superano la barriera epiteliale renale ed entrano nel flusso sanguigno.

I patogeni residenti nell'intestino colonizzano l'uretra tramite specifiche adesine. (Sintomi lievi)

L'infezione risale agli ureteri fino ai reni. Sintomi: Febbre, dolore lombare acuto.

L'importanza della tempistica: Intercettare l'infezione allo stadio 1 o 2 previene danni permanenti e blocca l'escalation verso l'urosepsi.

Il Ciclo Vizioso dell'AMR: Un Motore di Crisi



1. Diagnosi Tardiva
L'attesa di 48-72h per l'urinocoltura impone decisioni cliniche immediate.

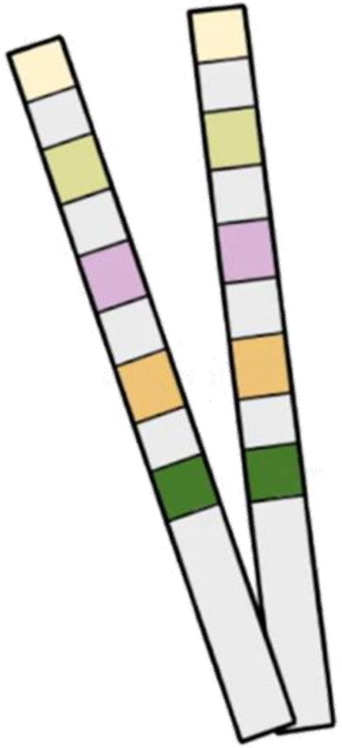
2. Terapia Empirica
Prescrizione "alla cieca" di antibiotici a largo spettro (es. fluorochinoloni, ampicillina). Oltre il 30% delle prescrizioni risulta inappropriato.

3. Resistenza Antimicrobica (AMR)
L'abuso seleziona ceppi multi-resistenti (es. ESBL, patogeni KPC).

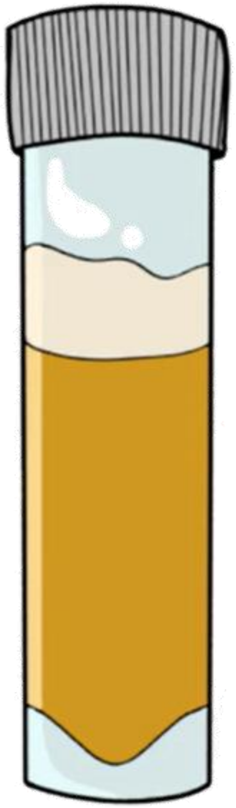
4. Fallimento Terapeutico
Infezioni ricorrenti, prolungamento dei sintomi e necessità di terapie di salvataggio.

DIAGNOSIS

* CLINICAL SYMPTOMS AND URINE INVESTIGATIONS *



1. URINE DIPSTICK
   - POSITIVE WBC / NITRITES AND BLOOD SUGGESTIVE OF UTI
   - NOT RELIABLE IN >65 YEARS OR CATHETERIZED
2. URINE CULTURE
3. IMAGING
   - STRUCTURAL / FUNCTIONAL CAUSE SUSPECTED
   - US / CT



I Vantaggi (Il Gold Standard)

- Alta Sensibilità
- Basso Costo
- Profilo di Suscettibilità (AST) completo

Il Prezzo del Ritardo

48-72 Ore

Urinocoltura Tradizionale. Un test eccellente per guidare la terapia a lungo termine, ma clinicamente inutile per il triage del paziente sintomatico nel giorno 1.
L’infezione viaggia più veloce dei tempi di incubazione.

Pregi

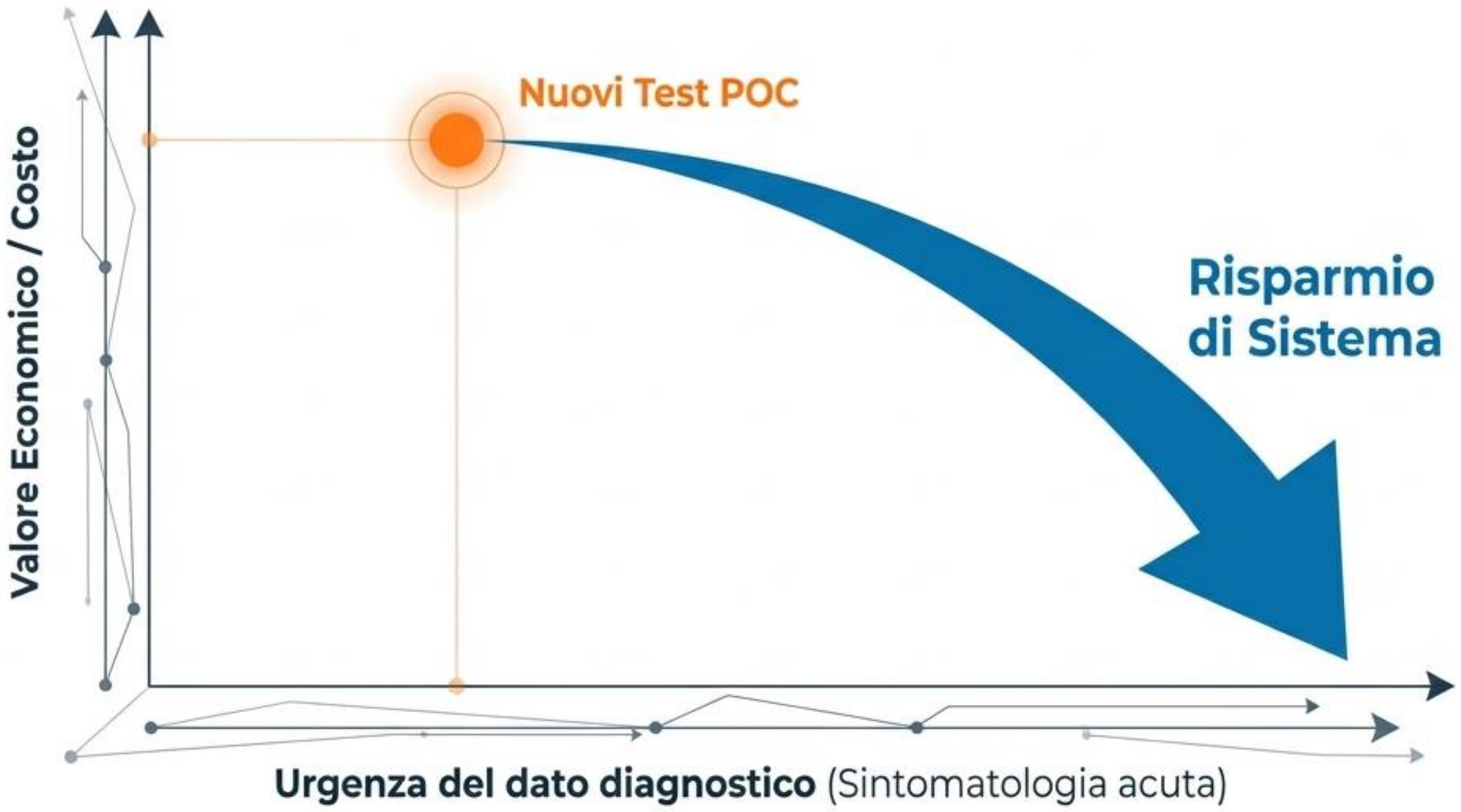
- Minuti
- Basso costo
- Utili per rilevare nitriti e leucociti con **alto valore predittivo negativo**.

Il Falso Senso di Sicurezza

- **Nessuna** identificazione del patogeno.
- **Nessun dato** sulla suscettibilità antibiotica (AST).
- Scarsa precisione quantitativa.

Metodi POC Attuali. I test a **striscia reattiva (Dipstick)** confermano l'infiammazione, ma lasciano il medico **completamente cieco** nella scelta dell'antibiotico mirato.

CAMBIO DEL PUNTO DI VISTA



Bilancio Costo vs. Urgenza. Un test molecolare POC ha un costo unitario superiore a un'urinocoltura standard. Tuttavia, prescrivere la terapia corretta al giorno 1 evita fallimenti terapeutici, visite al pronto soccorso, e lo sviluppo di ceppi multi-resistenti (un onere stimato in 5 miliardi di dollari annui solo negli USA).

INSIDE INNOVATION

INTASAMENTO DELLE ATTIVITA' DI LABORATORIO

Proc (Bayl Univ Med Cent). 2024 Feb 8;37(2):312–316. doi: 10.1080/08998280.2023.2288788

Lab testing overload: a comprehensive analysis of overutilization in hospital-based settings

Tanveer Shaik [a], Ramsha Mahmood [a], Sai Gautham Kanagala [b], Harmanjit Kaur [c], Vaidehi Mendpara [d], Vasu Gupta [e], Priyanka Aggarwal [f], Fnu Anamika [g], Nikita Garg [h], Rohit Jain [i]

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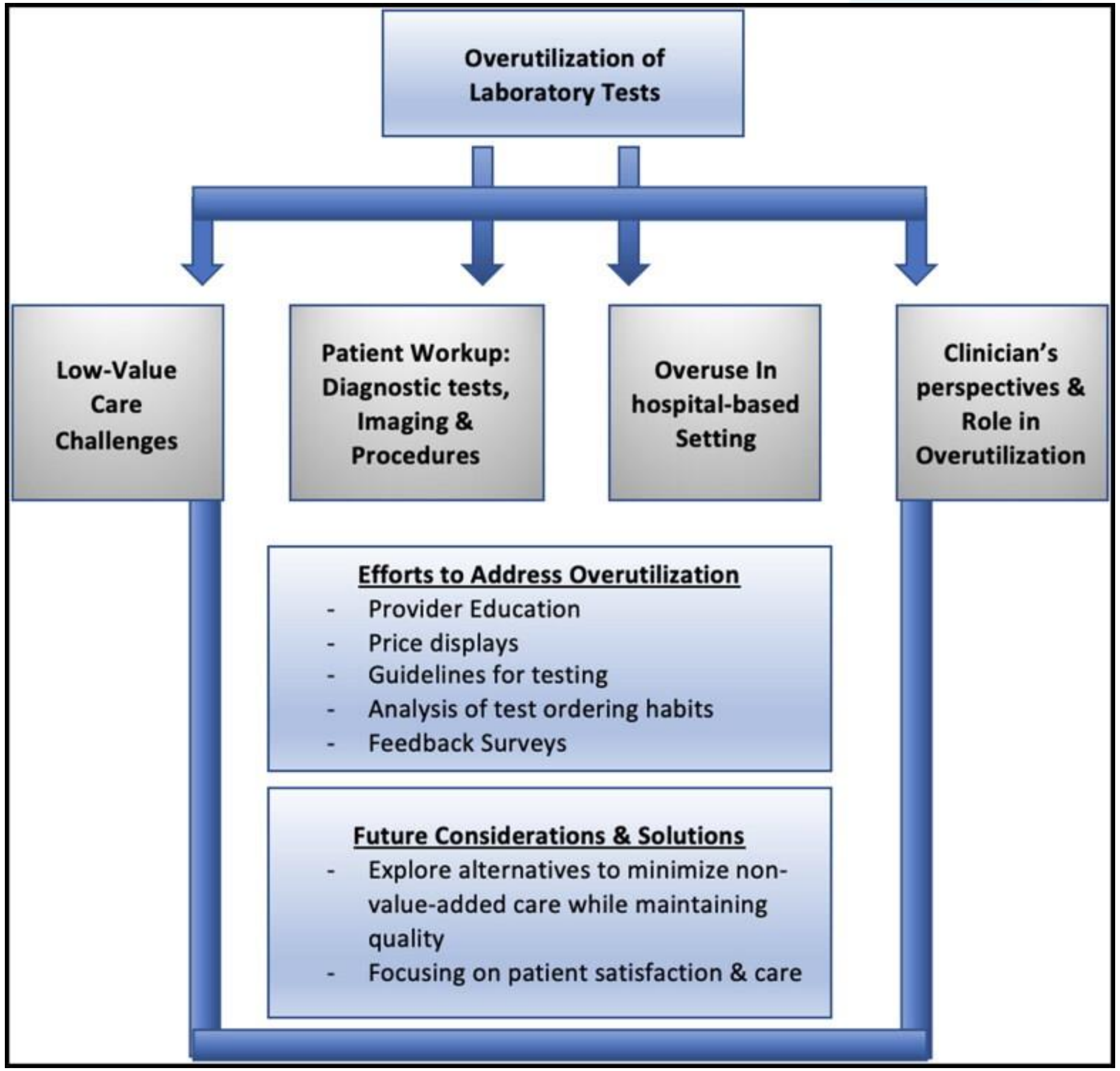
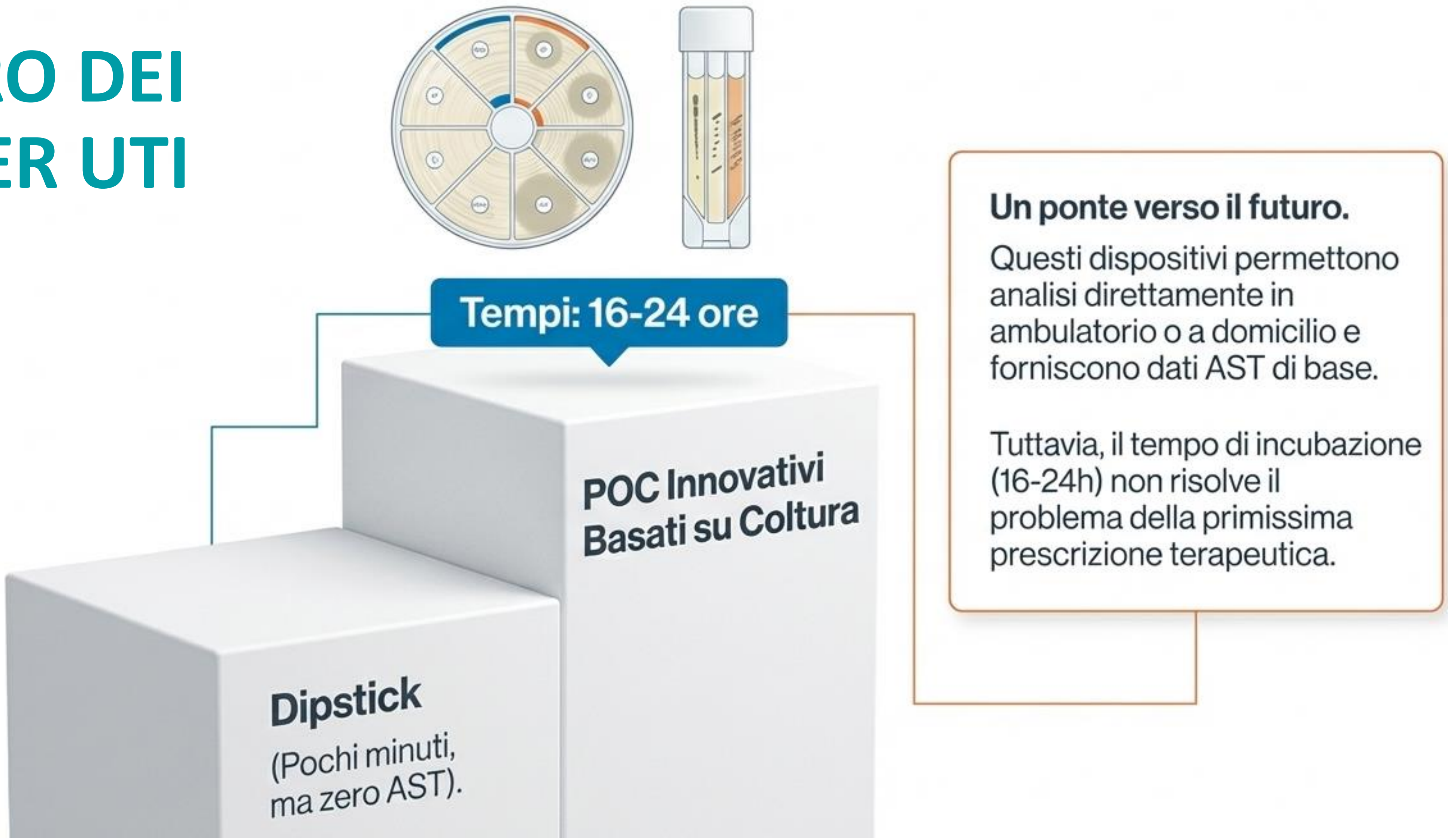
PMCID: PMC10857549 PMID: 38343466



ALI FAX

INSIDE INNOVATION

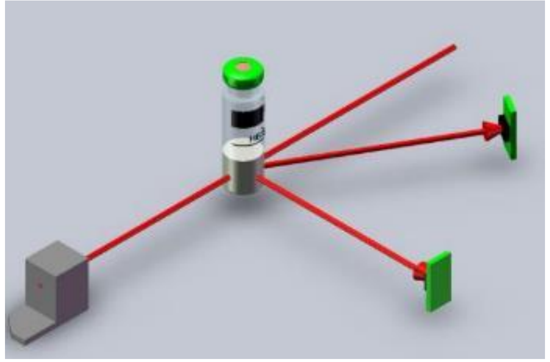
FUTURO DEI POC PER UTI



La Strategia di Decentralizzazione: Efficienza e Rapidità Diagnostica

La Strategia di Decentralizzazione. Trasferire il potere diagnostico dal laboratorio centrale direttamente alle mani del Medico di Medicina Generale (MMG). La medicina territoriale diventa il primo e definitivo fronte.

COME REALIZZARE UN POC? IDEE….



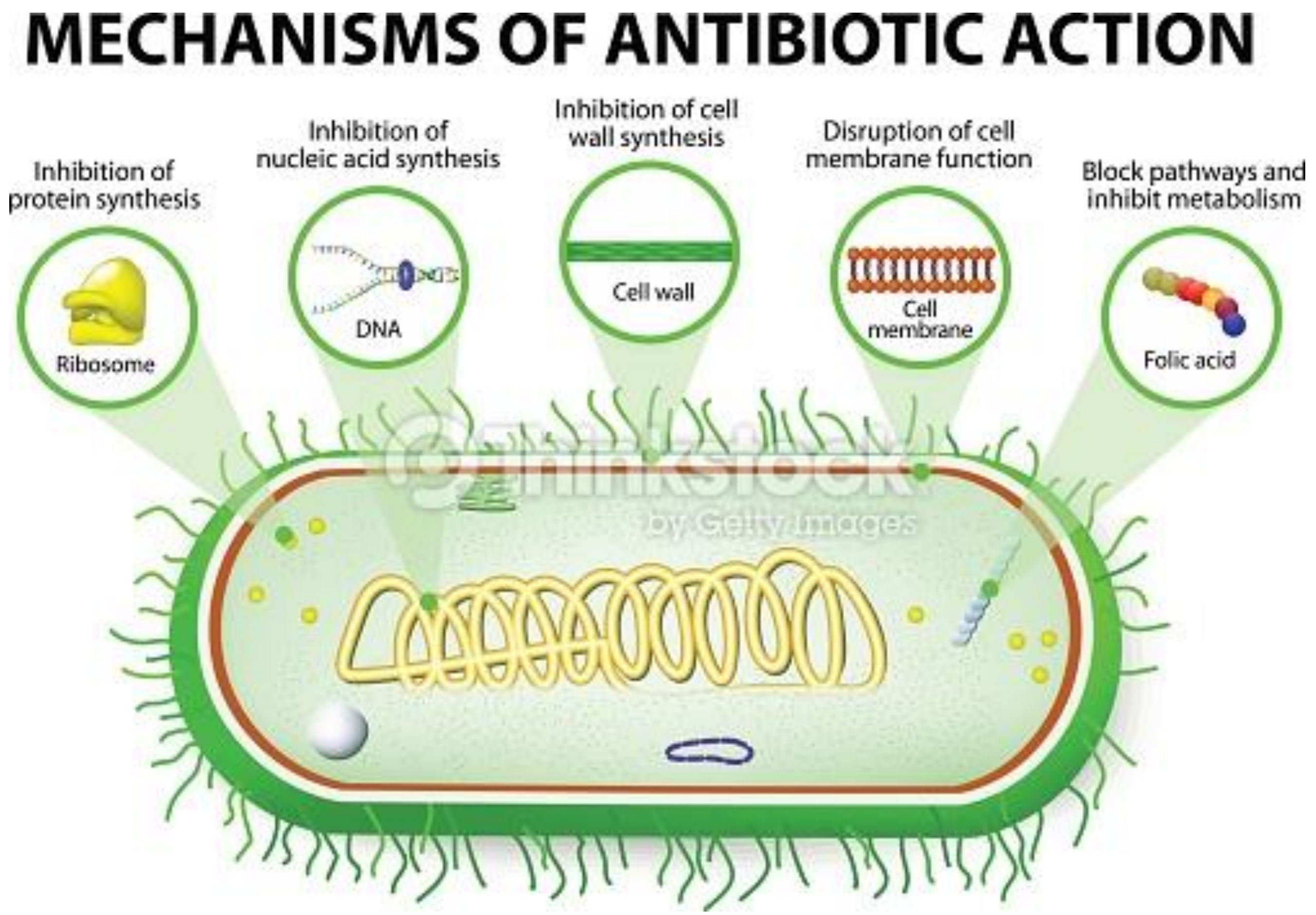
- Miniaturizzare
- Abbattere i costi
- Aumentare le risposte diagnostiche disponibili
- Interfacciamento con sistema sanitario centrale
- User Friendly per personale non di laboratorio
- Impossibilità di errore
- Risultati affidabili e completi

ANTIBIOTIC RESISTANCE

5 MILLION CASES WORLDWIDE

25,OOO DEATHS IN EUROPE

700,000 DEATHS WORLDWIDE



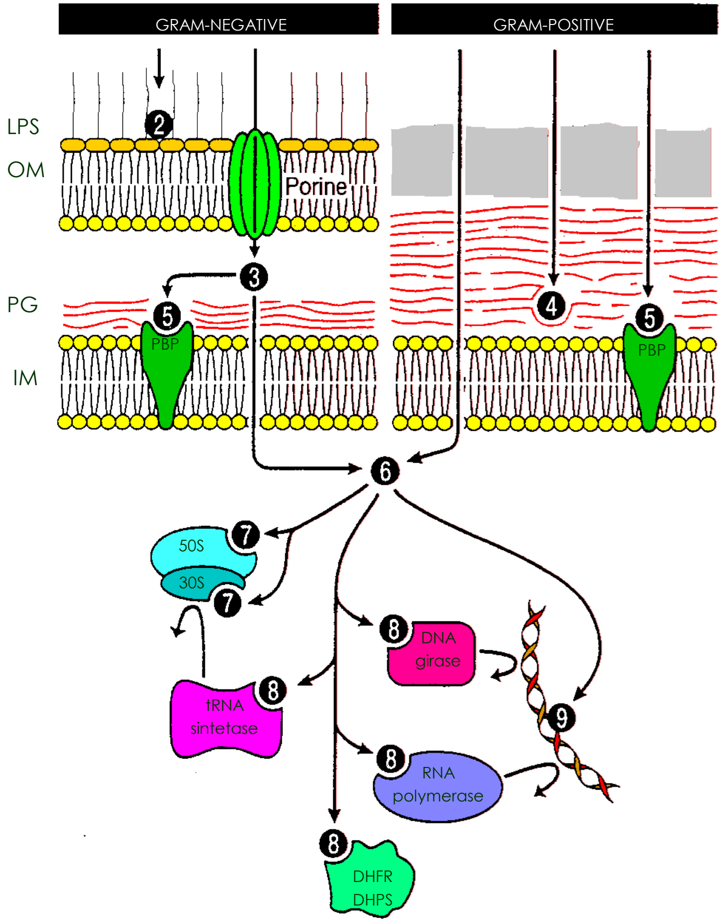
- β-lactams

- Penicillins
- β-lactam/β-lactamase inhibitor combination
- Cephems
- Penems
- Monobactams

- Non-β-lactams

- Aminoglycosides
- Folate pathway inhibitors
- Glycopeptides
- Lipopeptides
- Macrolides
- Nitroimidazoles (only against strictly anaerobic bacteria)
- Oxazolidinones
- Quinonoles
- Streptogramins
- Tetracyclines
- Single-drug classes

Antimicrobial agent classes



The antibiotic resistance of bacteria is the ability to be or to become resistant to antibiotics.

May be 2 kinds:

- Intrinsic (natural)
- Acquired
    - Genetic mutation (chromosomal)
    - Antibiotic induction
    - New genes intake (esogenic)

Mechanisms of resistance

The main mechanisms used by bacteria are:

- Enzimatic inactivation of drug (eg. beta-lactamase)
- Antibacterial target alteration (eg. PBP, ribosomes)
- Lower cellular permeability (eg. LPS, EPS)
- Active efflux of the drug

TIME

Essay: THE FUTURISTS: Looking Toward A.D. 2000

Friday, Feb. 25, 1966

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Nearly all experts agree that bacterial and viral diseases will have been virtually wiped out. Probably arteriosclerotic heart disease will also have been eliminated. Cells have only a few secrets still hidden from probers, who are confident that before the year 2000 they will have found the secret that causes cancer. The most exciting, and to some the most frightening, prospect is the chemical and electrical treatment of the brain. Dr.

TIME MAGAZINE 1966 Feb 25

nature

International weekly journal of science

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Journal home > Archive > insight > Full text > Figure 2

FIGURE 2. Leading causes of death worldwide.

From the following article:
The challenge of emerging and re-emerging infectious diseases
David M. Morens, Gregory K. Folkers & Anthony S. Fauci
Nature **430**, 242-249(8 July 2004)
doi:10.1038/nature02759

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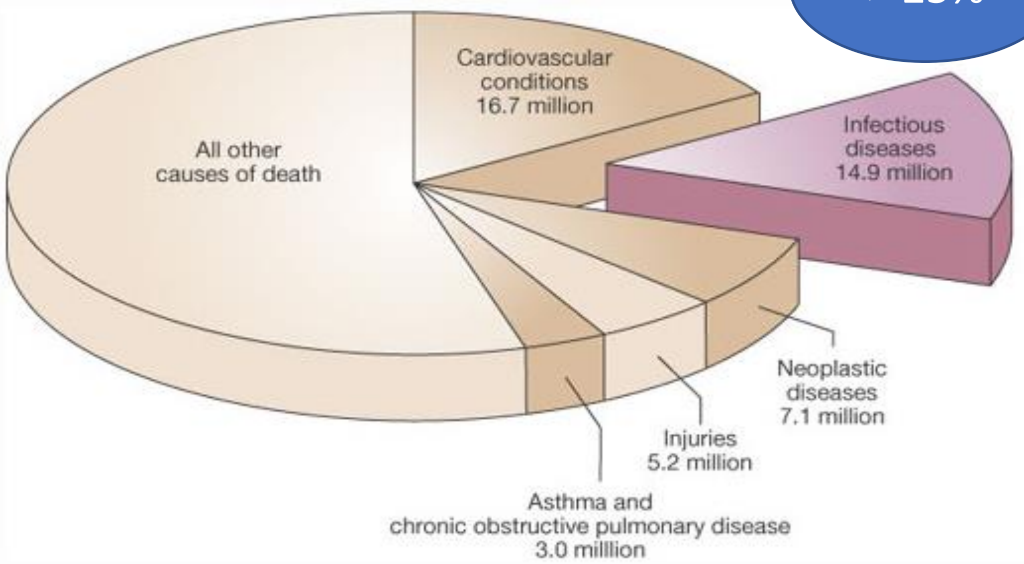


Infectious diseases	Annual deaths (million)
Respiratory infections	3.96
HIV/AIDS	2.77
Diarrhoeal diseases	1.80
Tuberculosis	1.56
Vaccine-preventable childhood diseases	1.12
Malaria	1.27
STDs (other than HIV)	0.18
Meningitis	0.17
Hepatitis B and C	0.16
Tropical parasitic diseases	0.13
Dengue	0.02
Other infectious diseases	1.76

About 15 million (>25%) of 57 million annual deaths worldwide are the direct result of infectious disease. Figures published by the World Health Organization (see http://www.who.int/whr/en and ref. 7).

Nature 2004

	Resistant Pathogen	2017 Threat Estimate	2018 Threat Estimate	2019 Threat Estimate	2017-2019 Change	2020 Threat Estimate and 2019-2020 Change
URGENT	Carbapenem-resistant *Acinetobacter*	8,500 cases 700 deaths	6,300 cases 500 deaths	6,000 cases 500 deaths	Stable*	7,500 cases 700 deaths **Overall: 35% increase*** **Hospital-onset: 78% increase***
URGENT	Antifungal-resistant *Candida auris*	171 clinical cases†	329 clinical cases	466 clinical cases	Increase	754 cases **Overall: 60% increase**
URGENT	*Clostridioides difficile*	223,900 infections 12,800 deaths	221,200 infections 12,600 deaths	202,600 infections 11,500 deaths	Decrease	Data delayed due to COVID-19 pandemic
URGENT	Carbapenem-resistant Enterobacterales	13,100 cases 1,100 deaths	10,300 cases 900 deaths	11,900 cases 1,000 deaths	Decrease*	12,700 cases 1,100 deaths Overall: Stable* **Hospital-onset: 35% increase***
URGENT	Drug-resistant *Neisseria gonorrhoeae*	550,000 infections	804,000 infections	942,000 infections	Increase	Data unavailable due to COVID-19 pandemic
SERIOUS	Drug-resistant *Campylobacter*	448,400 infections 70 deaths	630,810 infections	725,210 infections	Increase	Data delayed due to COVID-19 pandemic‡ 26% of infections were resistant, a 10% decrease
SERIOUS	Antifungal-resistant *Candida*	34,800 cases 1,700 deaths	27,000 cases 1,300 deaths	26,600 cases 1,300 deaths	Decrease*	28,100 cases 1,400 deaths **Overall: 12% increase*** **Hospital-onset: 26% increase***
SERIOUS	ESBL-producing Enterobacterales	197,400 cases 9,100 deaths	174,100 cases 8,100 deaths	194,400 cases 9,000 deaths	Increase*	197,500 cases 9,300 deaths **Overall: 10% increase*** **Hospital-onset: 32% increase***
SERIOUS	Vancomycin-resistant Enterococcus	54,500 cases 5,400 deaths	46,800 cases 4,700 deaths	47,000 cases 4,700 deaths	Stable*	50,300 cases 5,000 deaths **Overall: 16% increase*** **Hospital-onset: 14% increase***

	Resistant Pathogen	2017 Threat Estimate	2018 Threat Estimate	2019 Threat Estimate	2017-2019 Change	2020 Threat Estimate and 2019-2020 Change
SERIOUS	Multidrug-resistant *Pseudomonas aeruginosa*	32,600 cases 2,700 deaths	29,500 cases 2,500 deaths	28,200 cases 2,400 deaths	Decrease*	28,800 cases 2,500 deaths Overall: Stable* **Hospital-onset: 32% increase***
SERIOUS	Drug-resistant nontyphoidal *Salmonella*	212,500 infections 70 deaths	228,290 infections	254,810 infections	Increase	Data delayed due to COVID-19 pandemic‡ 14% of infections were resistant, a 3% decrease
SERIOUS	Drug-resistant *Salmonella* serotype Typhi	4,100 infections <5 deaths	4,640 infections	6,130 infections	Increase	Data delayed due to COVID-19 pandemic‡ 85% of infections were resistant, a 10% increase
SERIOUS	Drug-resistant *Shigella*	77,000 infections <5 deaths	215,850 infections	242,020 infections	Increase	Data delayed due to COVID-19 pandemic‡ 46% of infections were resistant, a 2% increase
SERIOUS	Methicillin-resistant *Staphylococcus aureus*	323,700 cases 10,600 deaths	298,700 cases 10,000 deaths	306,600 cases 10,200 deaths	Stable*	279,300 cases 9,800 deaths Overall: Stable* **Hospital-onset: 13% increase***
SERIOUS	Drug-resistant *Streptococcus pneumoniae*	12,100 invasive infections 1,500 deaths†	See pathogen page if comparing data over time	12,000 invasive infections 1,200 deaths	Stable	Data delayed due to COVID-19 pandemic
SERIOUS	Drug-resistant Tuberculosis (TB)	888 cases 73 deaths†	962 cases 102 deaths	919 cases	Stable	661 cases Decrease‡
CONCERNING	Erythromycin-resistant group A *Streptococcus*	5,400 infections 450 deaths†	See pathogen page if comparing data over time	6,200 infections 560 deaths	Increase	Data delayed due to COVID-19 pandemic
CONCERNING	Clindamycin-resistant group B *Streptococcus*	13,000 infections 720 deaths†	See pathogen page if comparing data over time	15,300 cases 940 deaths	Increase	Data delayed due to COVID-19 pandemic

MDR Bacteria Responsable of Hospital Aquired Infections

E: *Enterococcus faecium*
S: *Staphylococcus aureus*
K: *Klebsiella pneumoniae*
A: *Acinetobacter baumannii*
P: *Pseudomonas aeruginosa*
E: *Enterobacter species*

World Health Organization (WHO) list, 2017

MDRO infections represent a growing global health problem, further intensified in recent years by the pandemic, which due to an unpredictable emergency has increased the selective pressure and decreased the active surveillance in the hospital environment.

Alarming increase in resistant infections during hospitalization from 2019 to 2020*

Carbapenem-resistant Enterobacterales	**35%**
ESBL-producing Enterobacterales	**32%**
Vancomycin-resistant Enterococcus	**14%**
Methicillin-resistant Staphylococcus aureus	**13%**

It is more urgent than ever to prioritize efforts towards resistance containment and support the One Health program to improve the detection, characterization and rapid response to emerging AMR.

* COVID-19: U.S. Impact on Antimicrobial Resistance, Special Report 2022

ANTIBIOTIC RESISTANCE?

IT'S AN ONGOING PROCESS WITH A DRAMATIC ESCALATION

MDR: Multi Drug Resistance

THE WORST SCENARIO:

XDR: Extensive Drug Resistance

RESISTANCE TO ALL ANTIBIOTICS, EXCEPT 1 OR 2

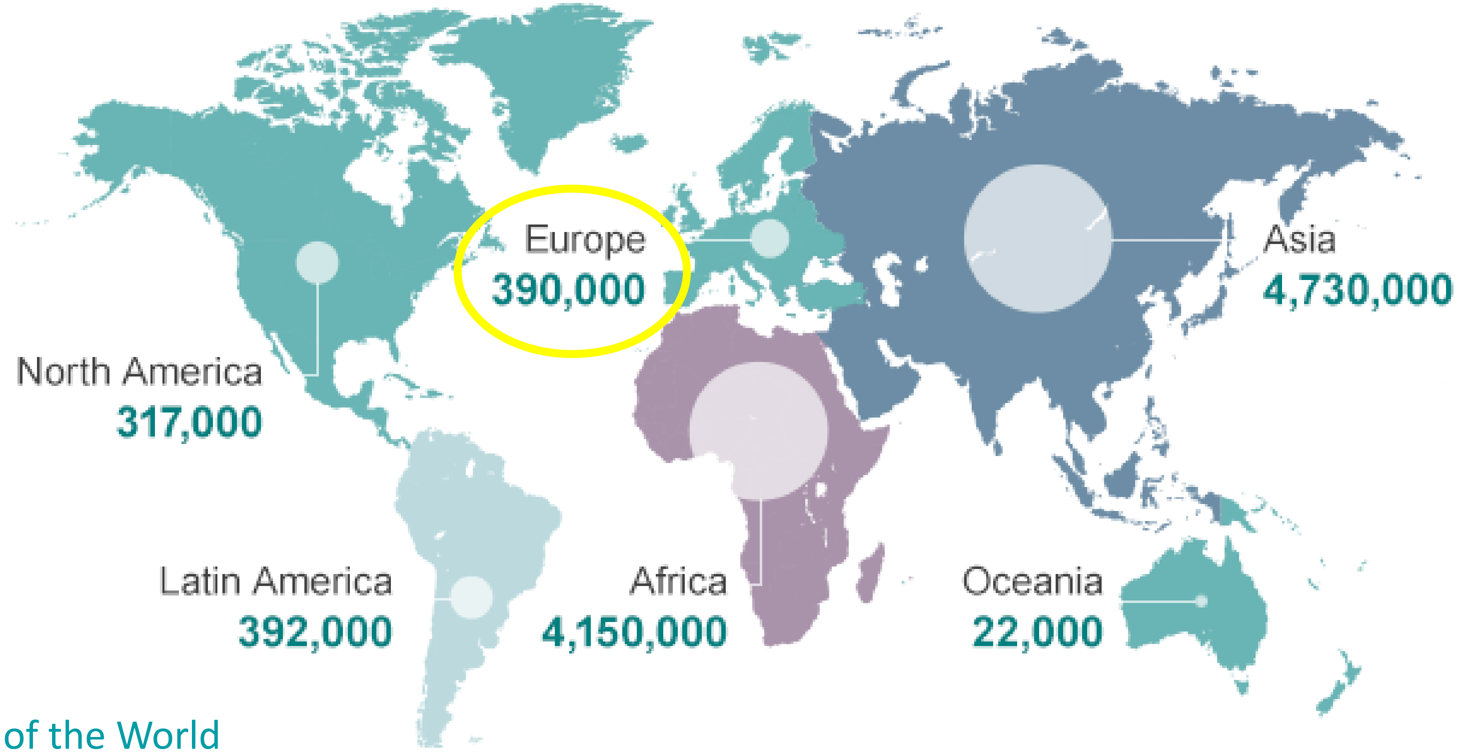
PDR: Pan Drug Resistance

RESISTANCE TO ALL ANTIBIOTICS

WHY IS ANTIMICROBIAl RESISTANCE A GLOBAL CORCERN?

INSIDE INNOVATION

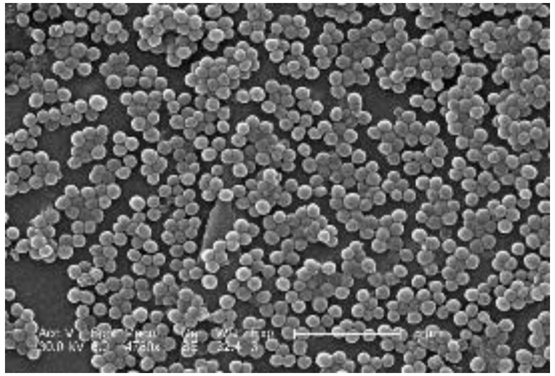
Deaths attributable to antimicrobial resistance every year by 2050



2.4 Million people could lose their lives in Europe, North America And Australia in the period 2015-2050. According to the forecasts, Italy, Greece and Portugal would rank among the top of OCSE countries for the highest mortality rates from AMR

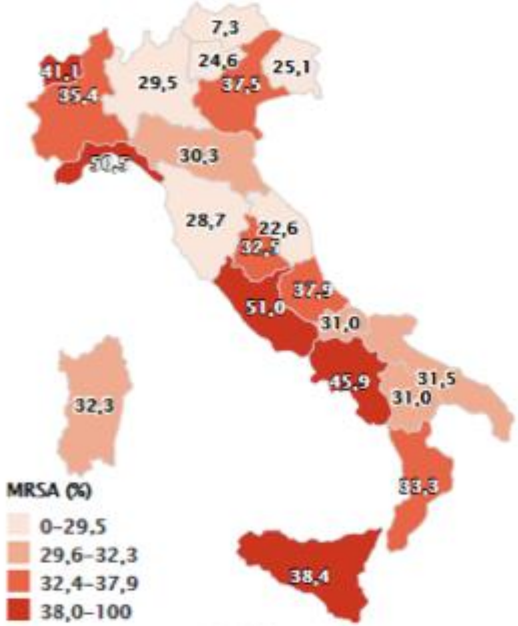
According to the forecasts of the World Bank, **the economic impact of the AMR** could exceed that of the financial crisis of 2008-2009.

MRSA
METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS



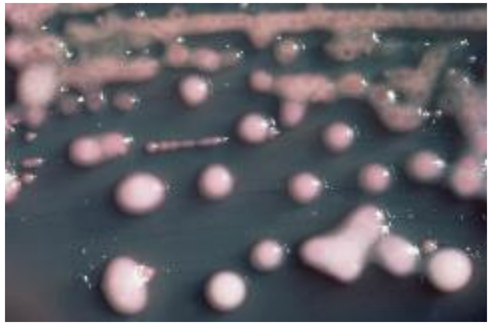
People with methicillin-resistant Staphylococcus aureus infections are 64% more likely to die than people with drug-sensitive infections (WHO 2020)

GOLD STANDARD:
Chromogenic selective media culture from nasal, throat, inguinal swab (direct or enriched) + Confirmation Test



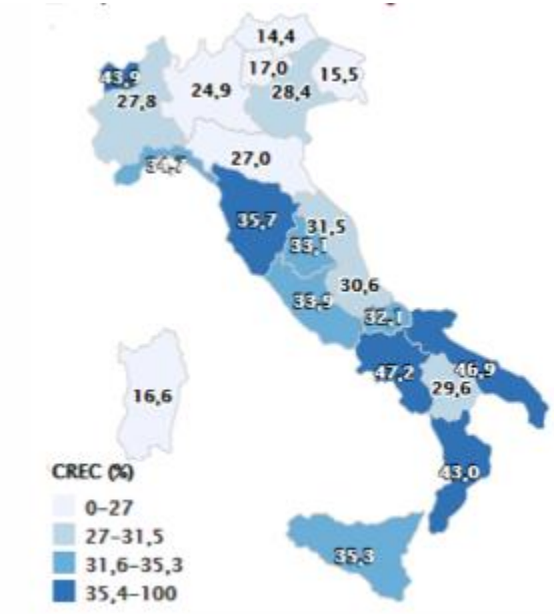
TURN AROUND TIME (TTR):
24h, 48h, and 72h

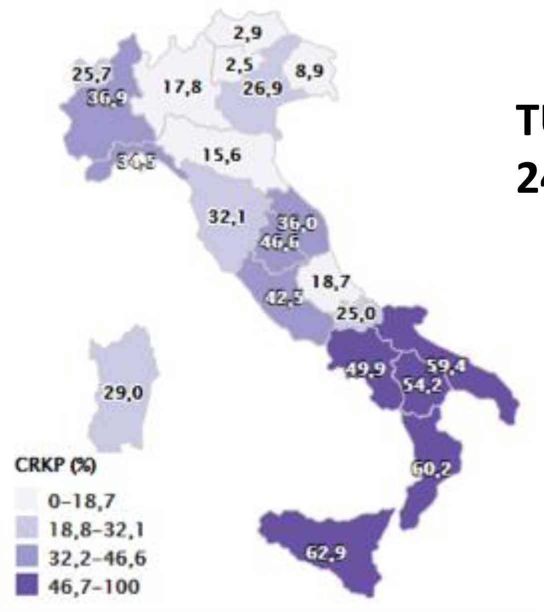
CPE
CARBAPENEMASE-PRODUCING ENTEROBATERALES



Resistance in carbapenem antibiotics treatment has spread to all regions of the world. They are a major cause of hospital-acquired infections such as pneumonia, bloodstream infections, and infections in newborns and intensive-care unit patients. In some countries, such as in some region of Italy, carbapemen antibiotics do not work in more than half of the patients treated due to infections with resistant microorganisms.

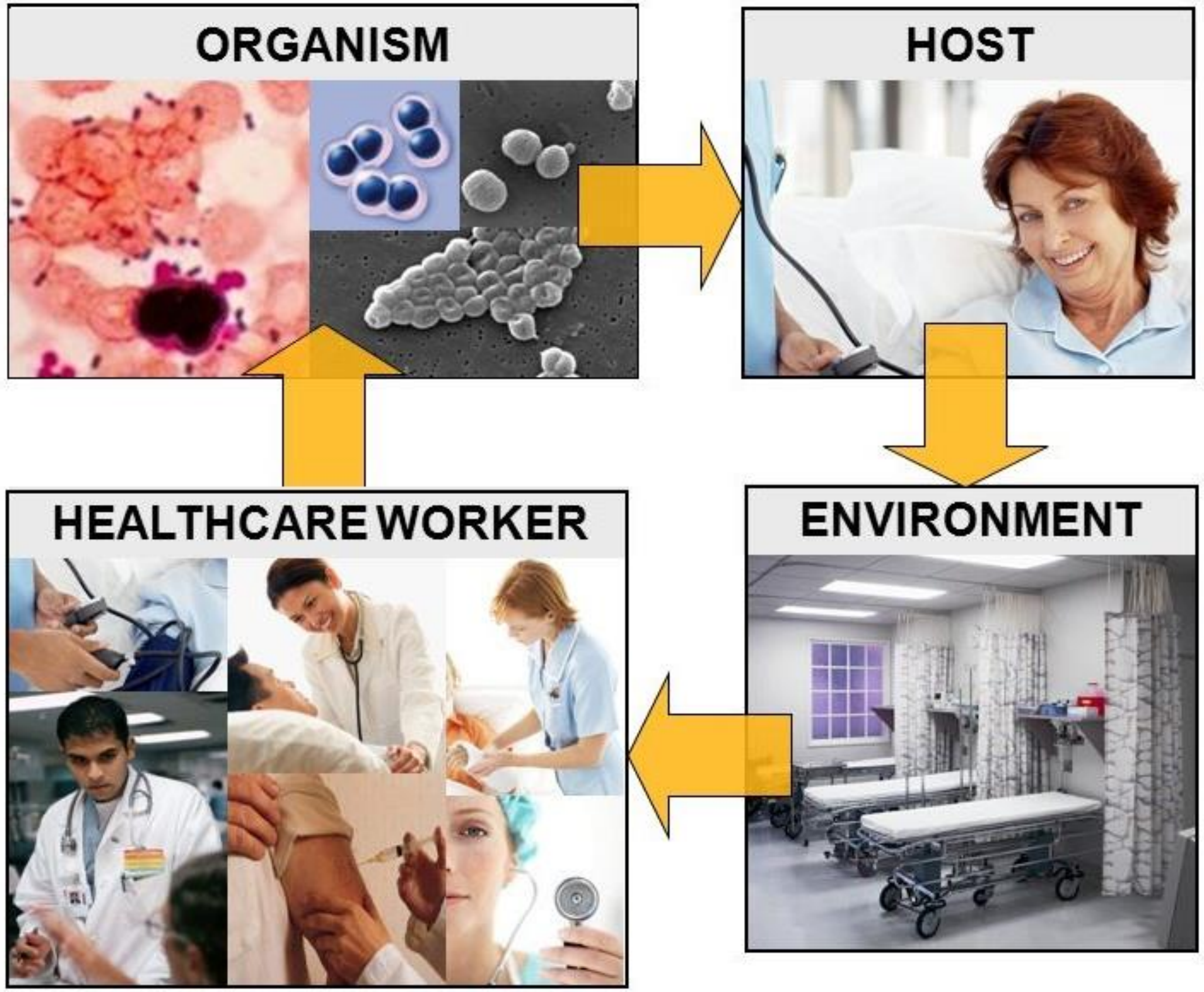
GOLD STANDARD:
Chromogenic selective media culture from rectal swab + Confirmation Test





TURN AROUND TIME (TTR):
24h, 48h, and 72h

MDRO Cycle of Transmission



MDRO spreading induces:

- <u>Higher mortality in critical settings;</u>
- Increased hospitalizations;
- Higher costs of patient management

ANTIMICROBIAL STEWARDSHIP

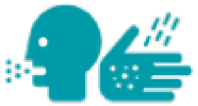
CAUSE DELLE RESISTENZE ANTIMICROBICHE

ECCESSO DI PRESCRIZIONI DI ANTIBIOTICO

MANCATA ADERENZA ALLA TERAPIA PRESCRITTA

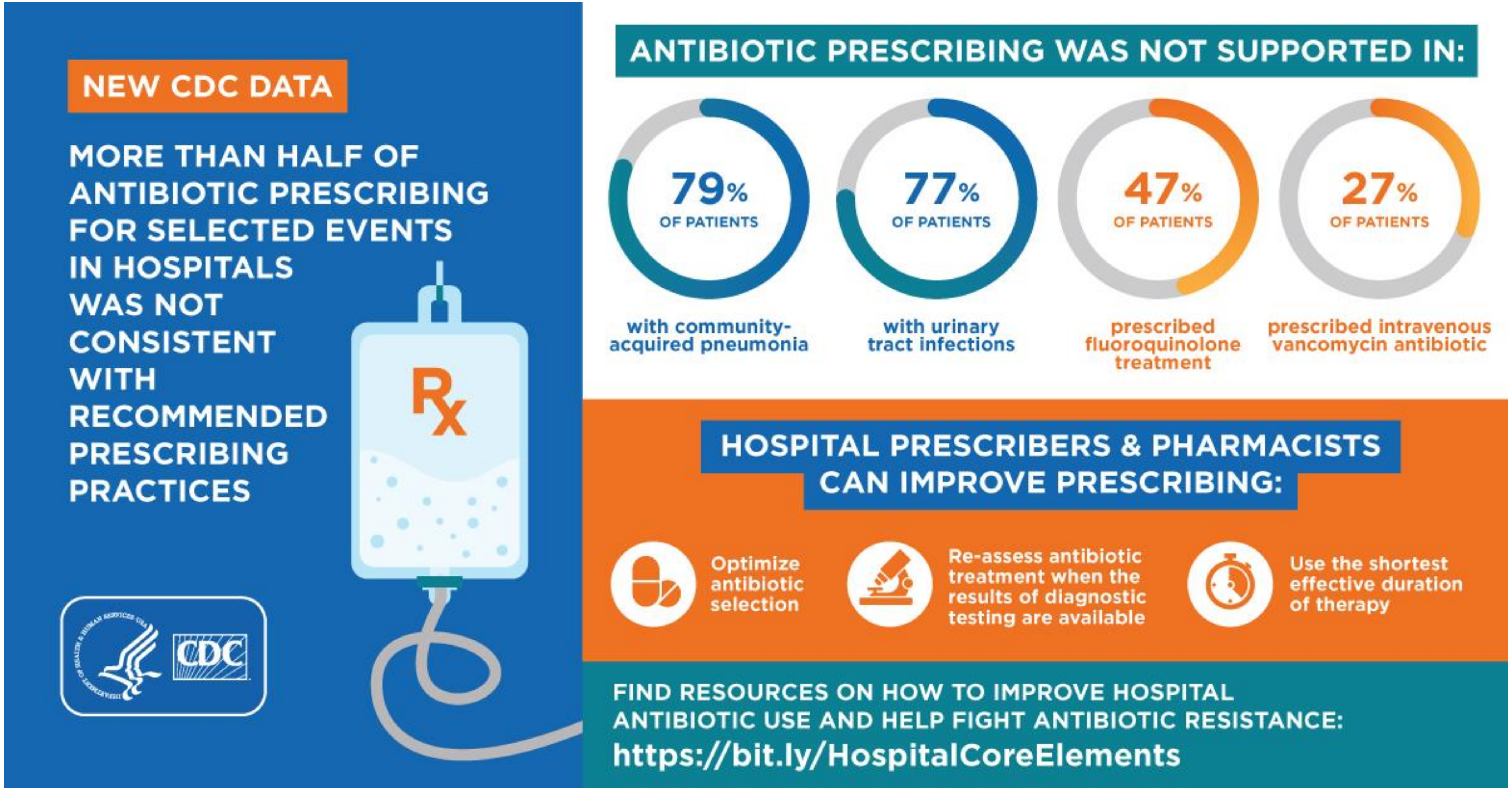
ABUSO DI ANTIBIOTICI IN ALLEVAMENTO

RIDOTTO CONTROLLO DELLE INFEZIONI OSPEDALIERE



SCARSA OSSERVANZA DELLE REGOLE DI IGENE

CARENZA DI METODOLOGIE DIAGNOSTICHE RAPIDE EFFICACI

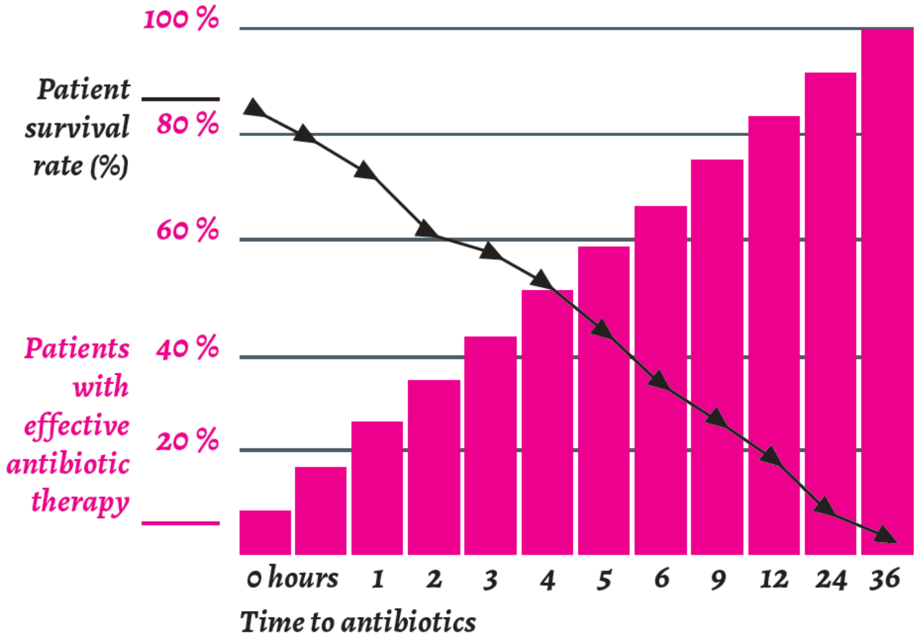

NEW CDC DATA
MORE THAN HALF OF ANTIBIOTIC PRESCRIBING FOR SELECTED EVENTS IN HOSPITALS WAS NOT CONSISTENT WITH RECOMMENDED PRESCRIBING PRACTICES
Rx
CDC
ANTIBIOTIC PRESCRIBING WAS NOT SUPPORTED IN:
79% OF PATIENTS
with community-acquired pneumonia
77% OF PATIENTS
with urinary tract infections
47% OF PATIENTS
prescribed fluoroquinolone treatment
27% OF PATIENTS
prescribed intravenous vancomycin antibiotic
HOSPITAL PRESCRIBERS & PHARMACISTS CAN IMPROVE PRESCRIBING:
Optimize antibiotic selection
Re-assess antibiotic treatment when the results of diagnostic testing are available
Use the shortest effective duration of therapy
FIND RESOURCES ON HOW TO IMPROVE HOSPITAL ANTIBIOTIC USE AND HELP FIGHT ANTIBIOTIC RESISTANCE:
https://bit.ly/HospitalCoreElements

Dati 2019

Mortality Risk with Increasing Delays in Initiation of Effective Antimicrobial Therapy

Give the right therapy in a short time could save the life of the critical patient

In the case of systemic bacterial infections, **the time for the diagnosis is a decisive factor for the survival of the patient since the delay of adequate antibiotic therapy increases the likelihood of patient death of 7.5% for each hour of delay and exponentially after 24 hours after the onset of hypotension** (Kumar, Crit Care Med 2006; 34: 1589-96).

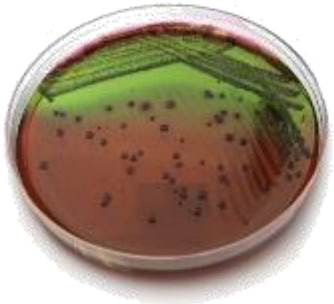


ANALISI CLINICA EMOCOLTURE

Day 0

Sample collection from the patient

Screening test result



Positive sample subculture and isolation

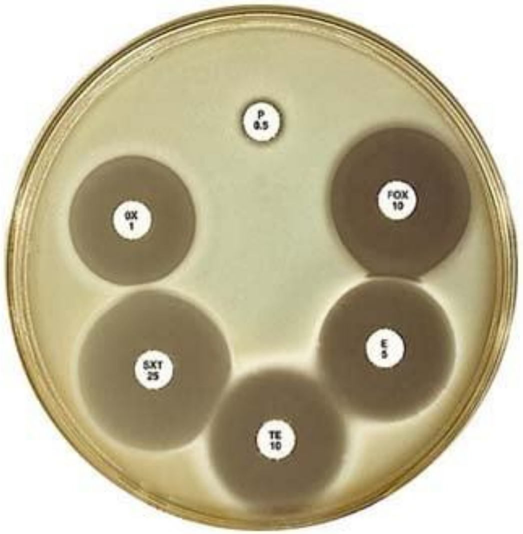
Sample preparation for ID

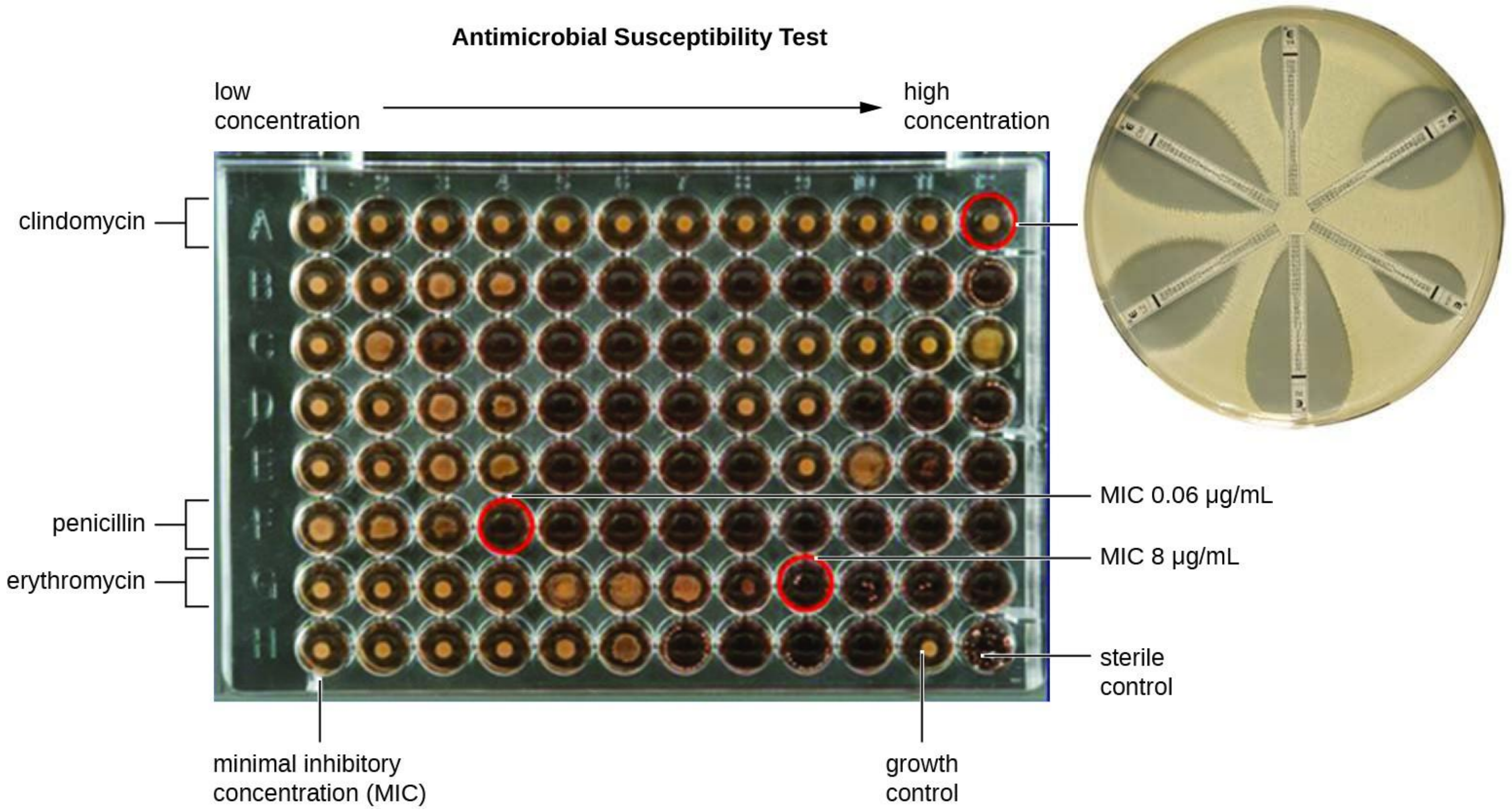
Sample identification

Day 4

In vitro testing of the best antibiotics panel based on microorganism ID

ANTIBIOGRAMMA E MIC



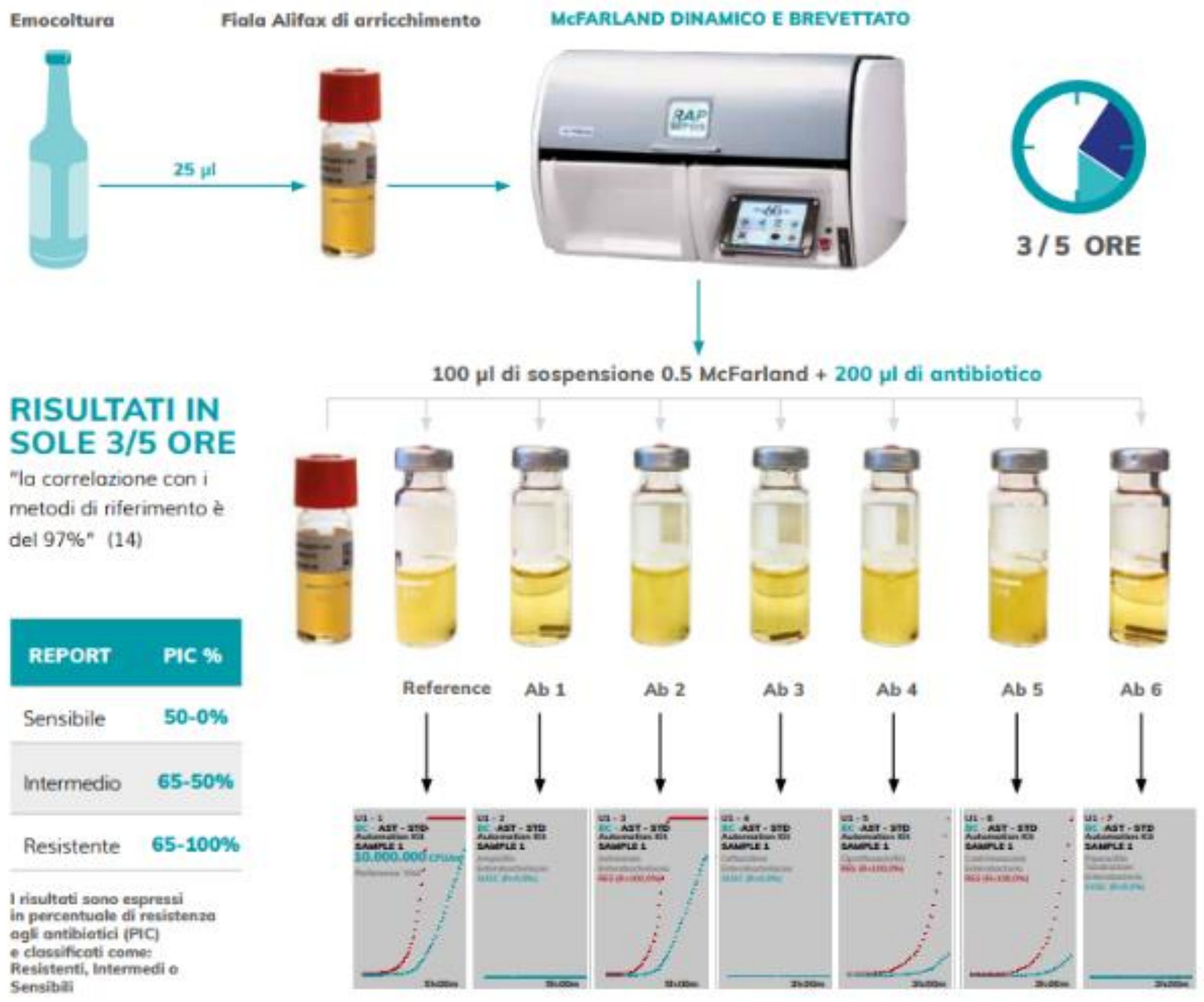


Sia test qualitativi che quantitavi per l'esecuzione dell'antibiogramma richiedono un'incubazione O/N

GESTIONE DEL PAZIENTE CRITICO
SELEZIONE TERAPEUTICA

- Valutazione rapida delle migliori scelte terapeutiche per il paziente critico grazie alla tecnologia Laser Light Scattering

RAP SEPSIS

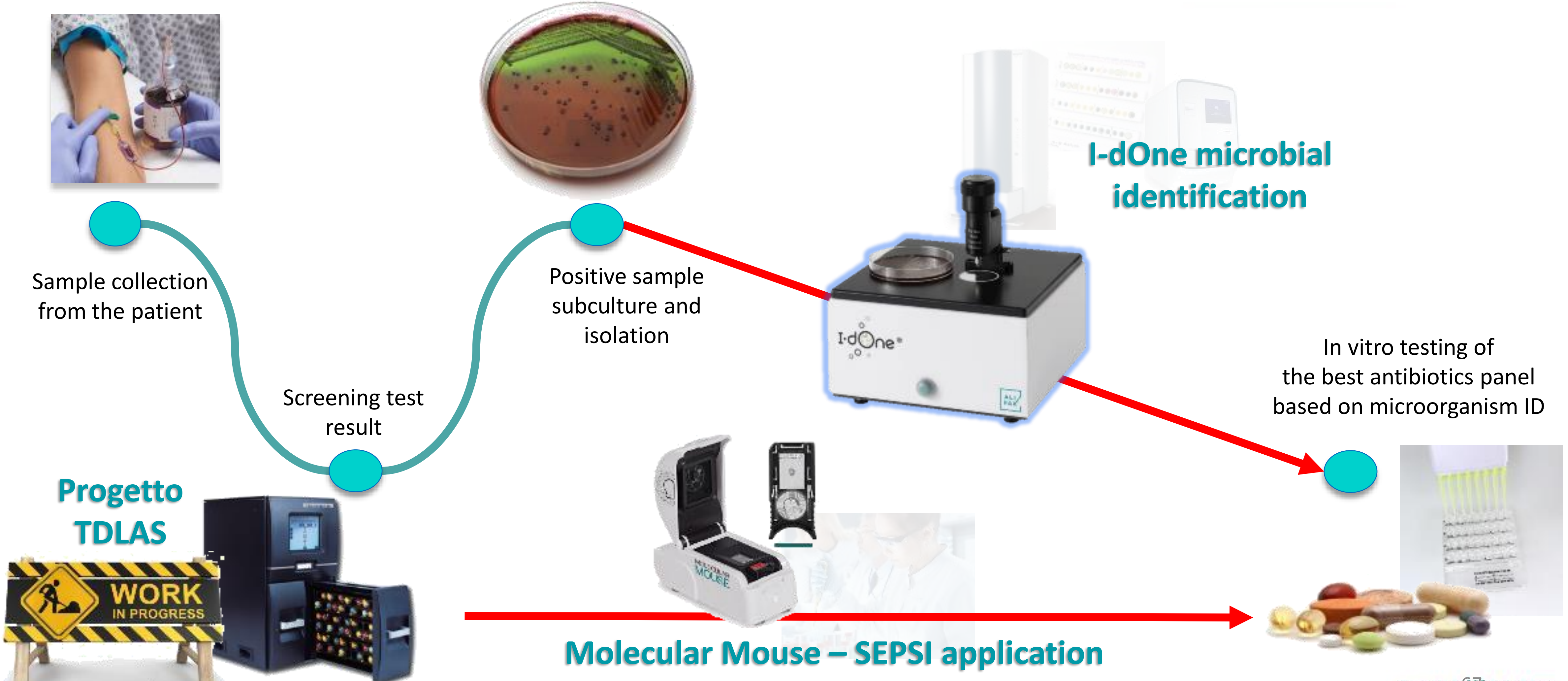


	RAP SEPSIS Fenotipico	TRADITIONAL AST Fenotipico	BIOLOGIA MOLECOLARE Genotipico
Turnaround time (TAT)	**3 o 5 ore**	48-72 ore	1-2 ore
Report	**Sensibile e resistente**	Sensibile e resistente	Solo le resistenze note
Utilità dei resultati	**RAP SEPSIS Fornisce risultati clinici rilevanti**	Utile per la conferma definitiva e per gli studi epidemiologici	Risultati clinicamente utili SOLO per le resistenze note, non info sulla sensibilità
Pannelli di antibiotici	**PERSONALIZZABILE per il paziente**	Pannelli	Non applicabile
Automazione	**Sistema di inoculo Walk-away, McFarland e lettura**	Lettura Semi-automatica	Semi-automatico
Costi	**€€€**	€€	€€€€€

INSIDE INNOVATION

ALIFAX NEL FLUSSO DIAGNOSTICO – LINEA CLASSICA

ALIFAX NEL FLUSSO DIAGNOSTICO – NUOVA GENERAZIONE PRODOTTI

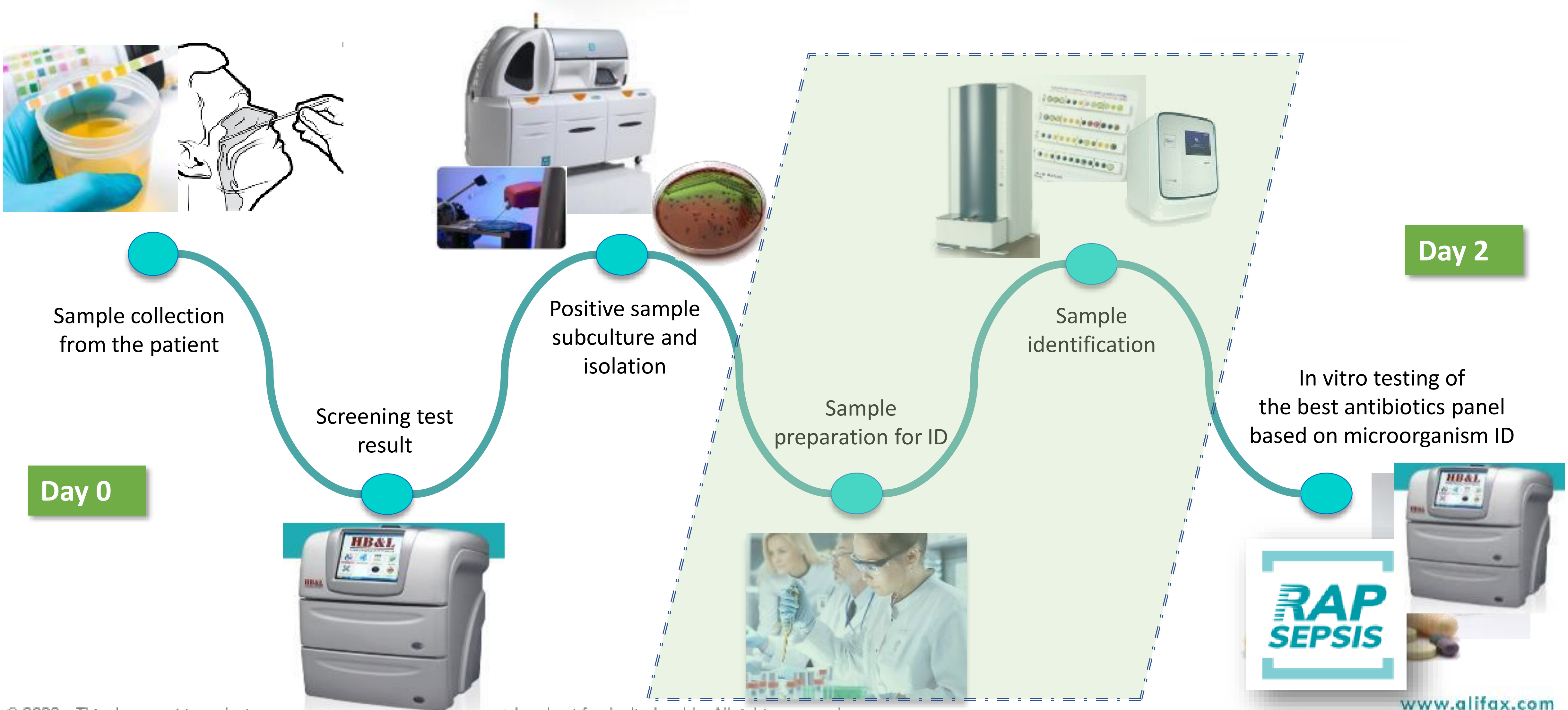


OUTLINE

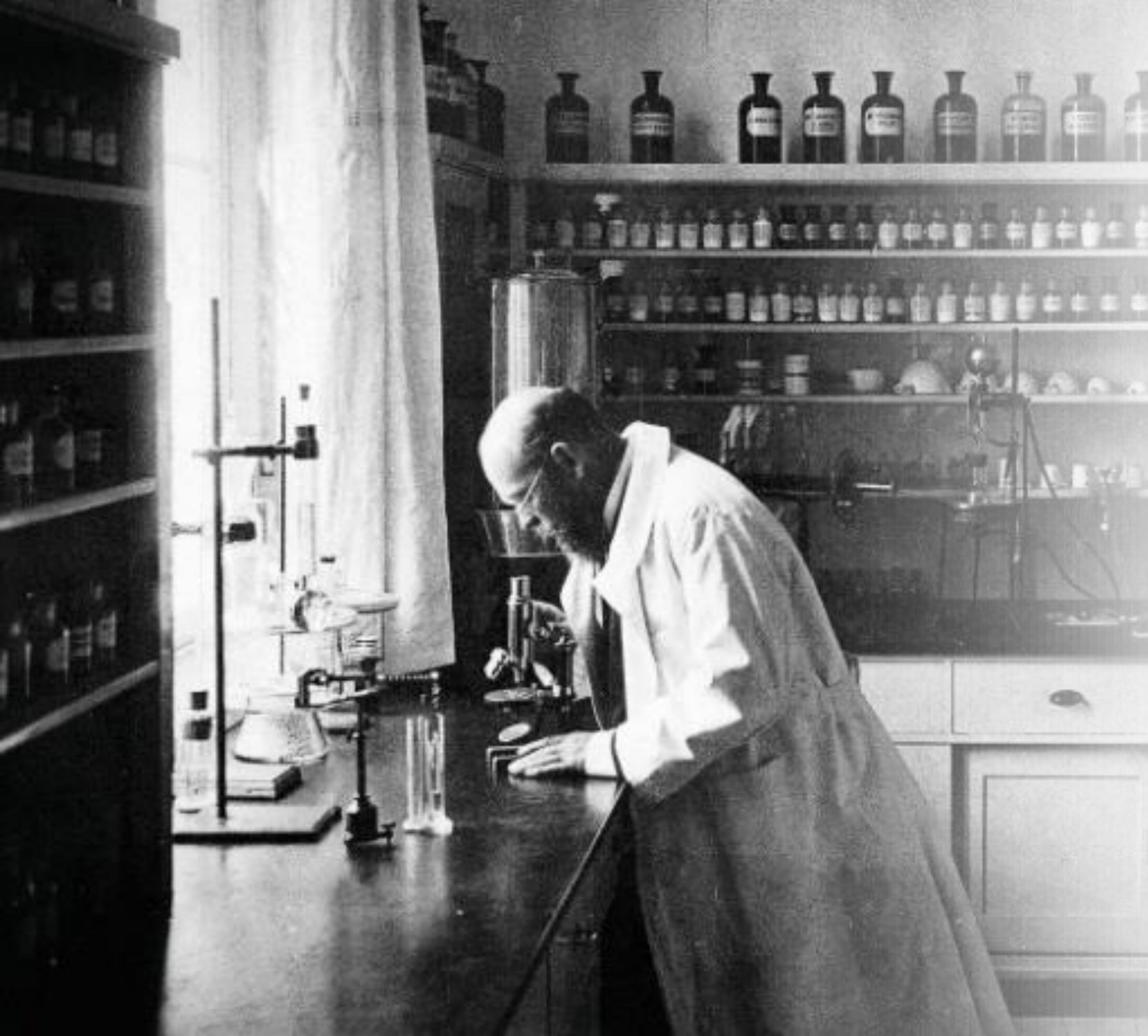
1. General introduction about Alifax R&D and Design
2. Main areas of interest in Alifax
   a) ESR (scope of the test, biological mechanisms, clinical importance)
   b) Microbiology (Antimicrobial Stewardship, MDROs, Clinical microbiology workflow)
   c) Introduction of new products in the market
3. Design process (Project Vision, Stakeholder needs, Usability, Safety, Performance)
4. From Design to Manufacturing and Sells: Process Validation, Safety, Registrations

INSIDE INNOVATION

ALIFAX NEL FLUSSO DIAGNOSTICO NUOVE APPLICAZIONI



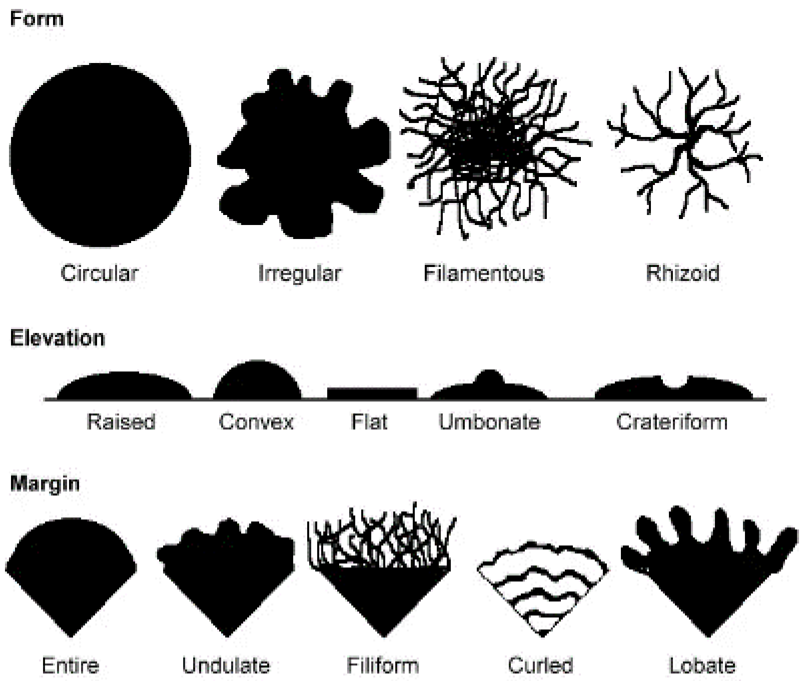
www.alifax.com

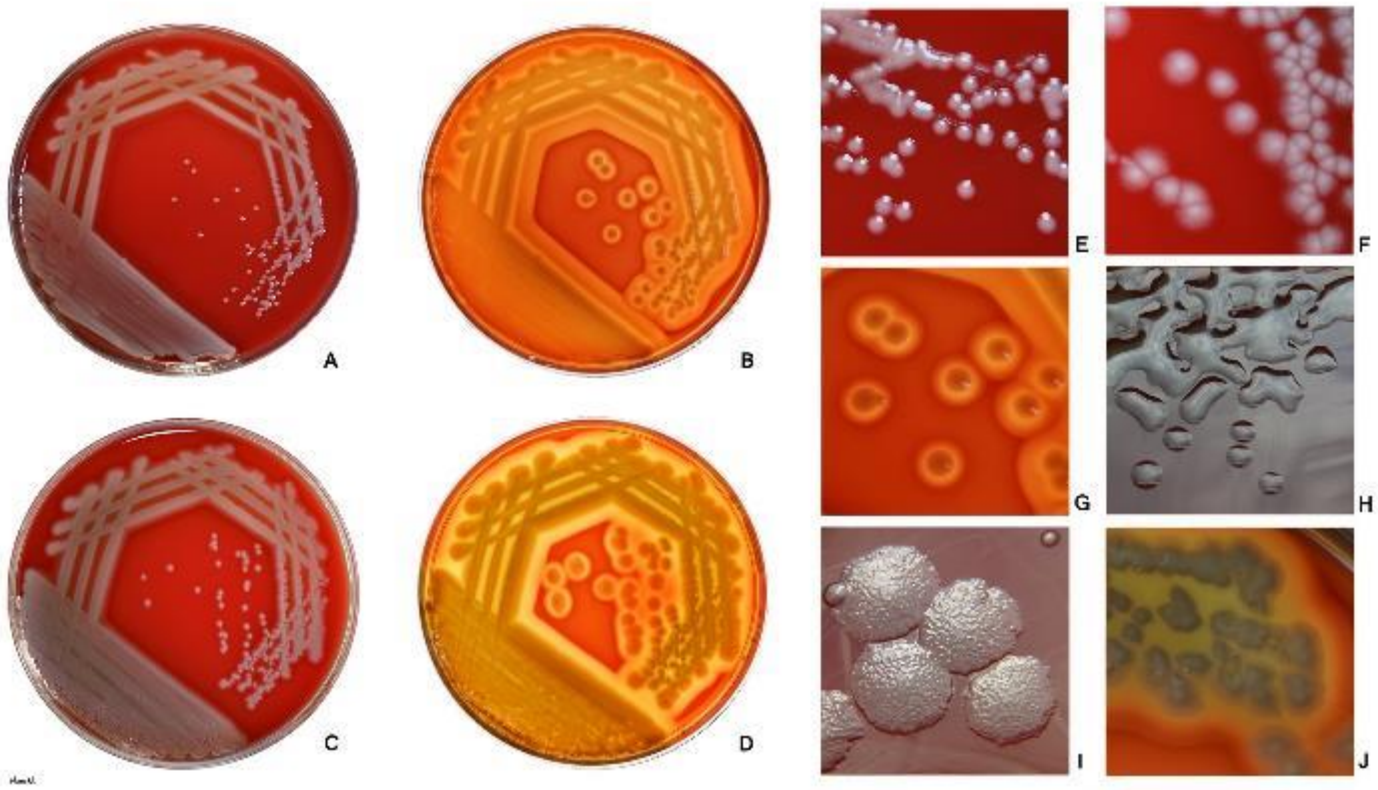


IDENTIFICAZIONE MICROBICA

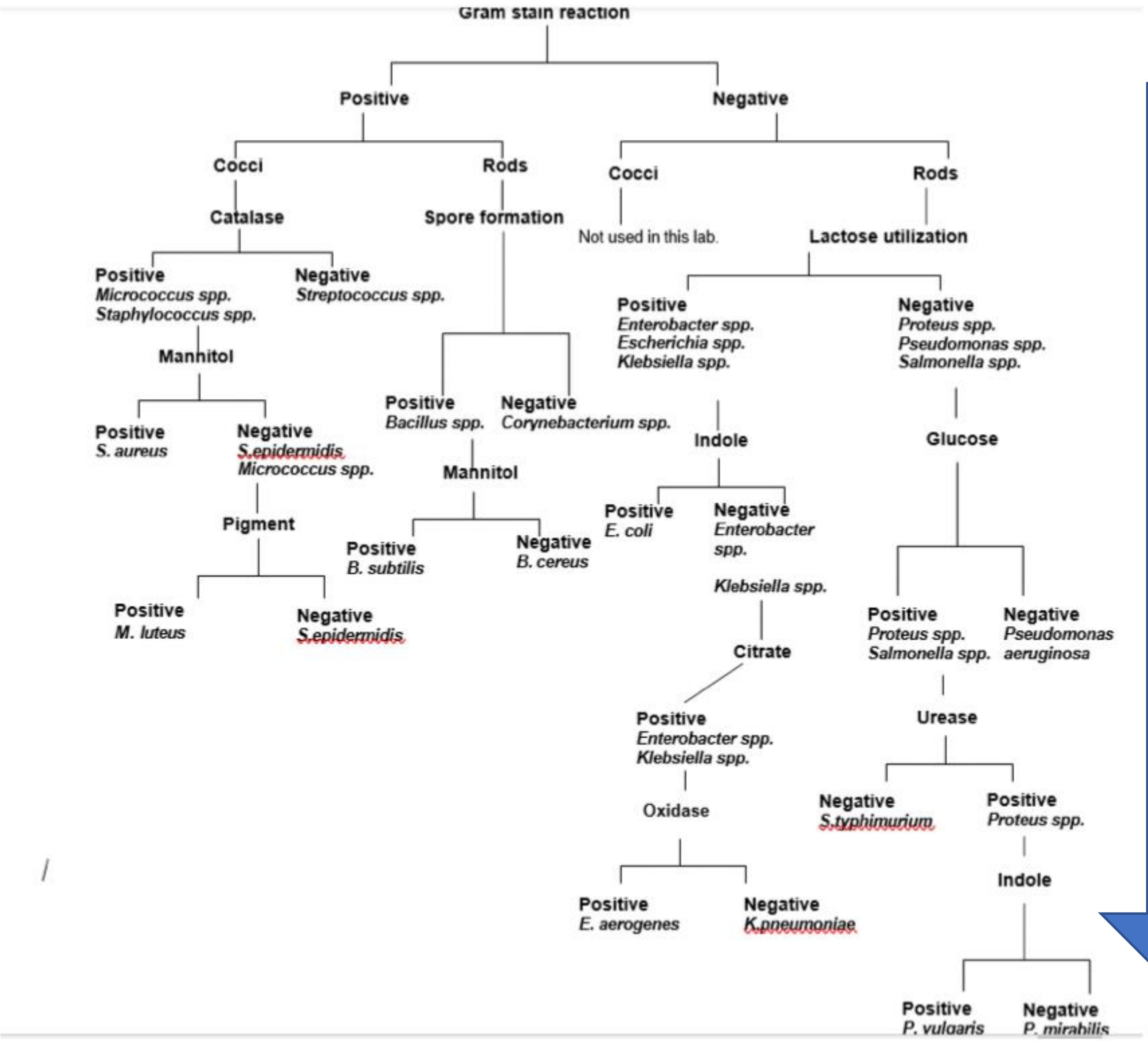
- **Robert Koch (1843 – 1910)**
- Ritenuto, assieme al suo collega e rivale Louis Pasteur, il fondatore della moderna batteriologia e microbiologia a seguito dello sviluppo della teoria microbica delle malattie

IDENTIFICAZIONE MICROBICA - VISIVA

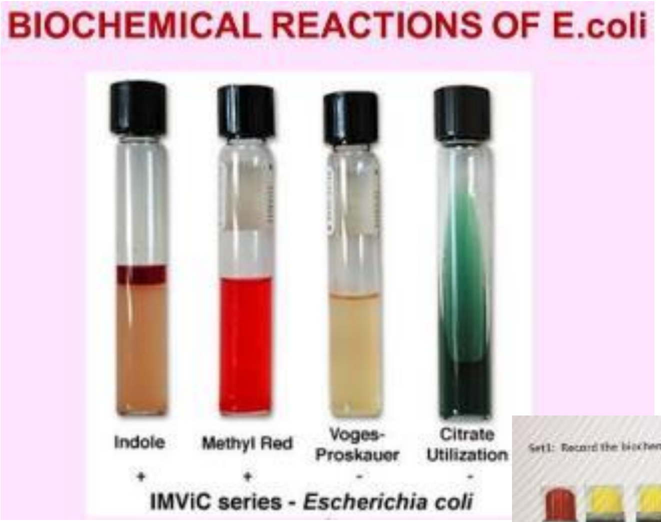


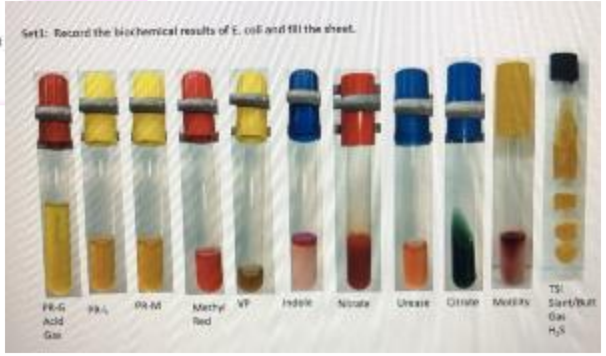


IDENTIFICAZIONE MICROBICA – BIOCHIMICA MANUALE



Test Biochimici eseguiti in funzione di algoritmi di identificazione basati su letteratura.
Metodo macchinoso, time-consuming e molto prono ad errori

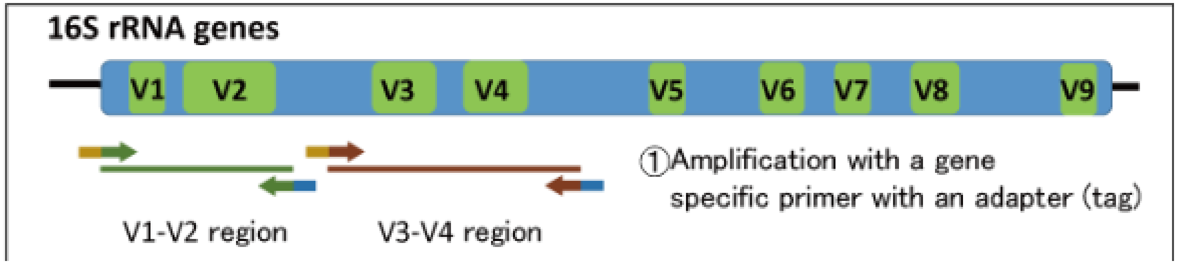




IDENTIFICAZIONE MICROBICA – BIOCHIMICA AUTOMATIZZATA

24/48 ore
€

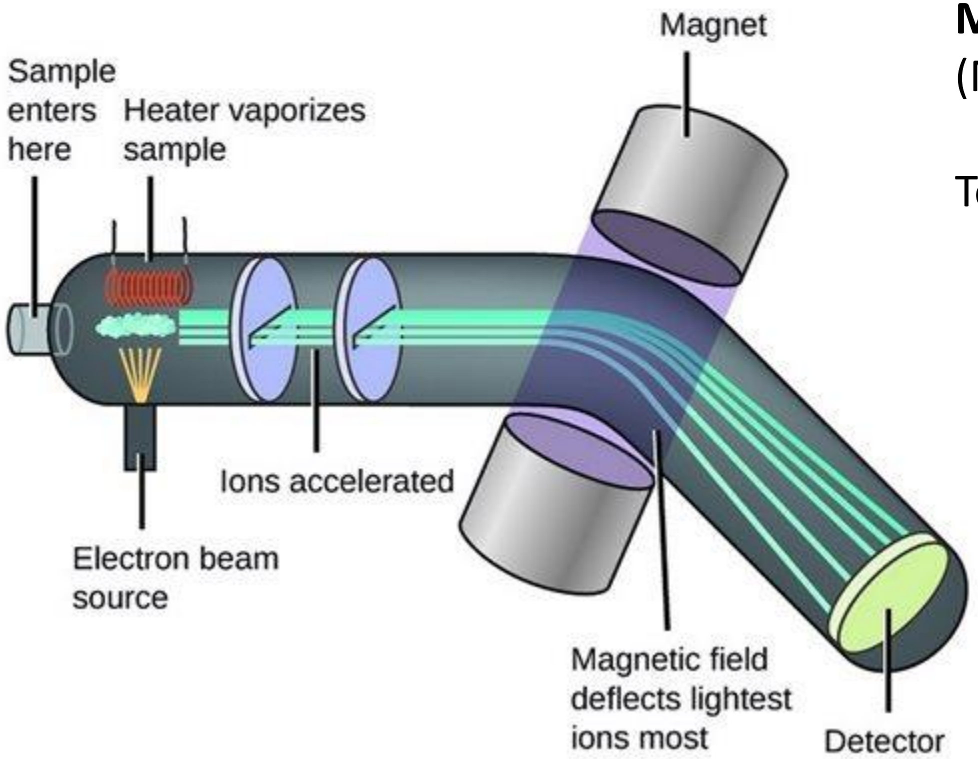
IDENTIFICAZIONE MICROBICA – BIOLOGIA MOLECOLARE



HOURS
€€€€

IDENTIFICAZIONE MICROBICA – SPETTROMETRIA DI MASSA

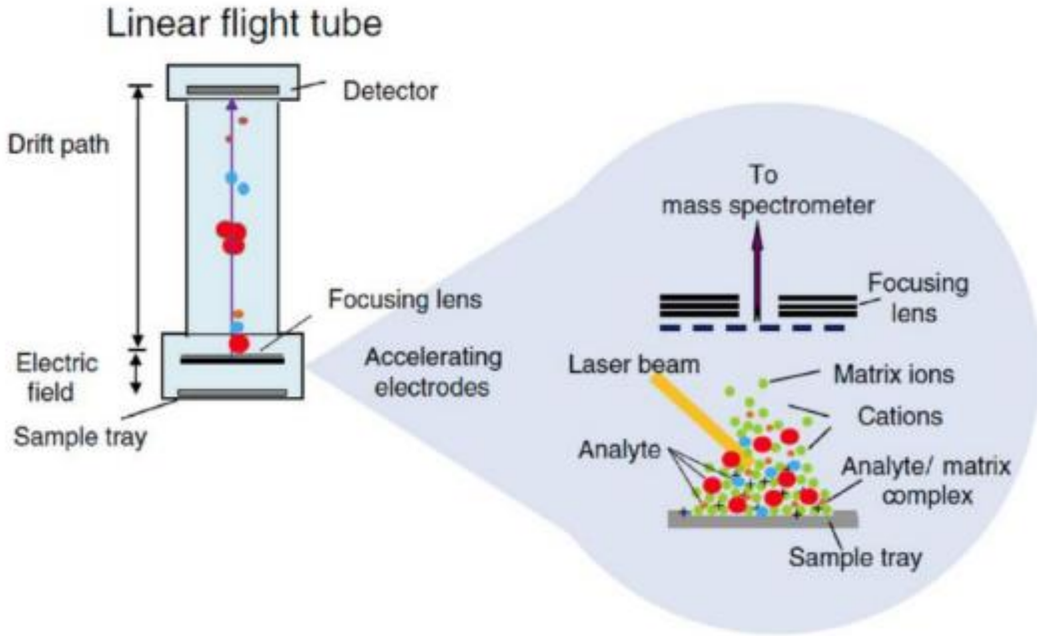
INSIDE INNOVATION



HOURS
€€€

MALDI-ToF
(Matrix Assisted Laser Desorption Ionization – Time of Flight)

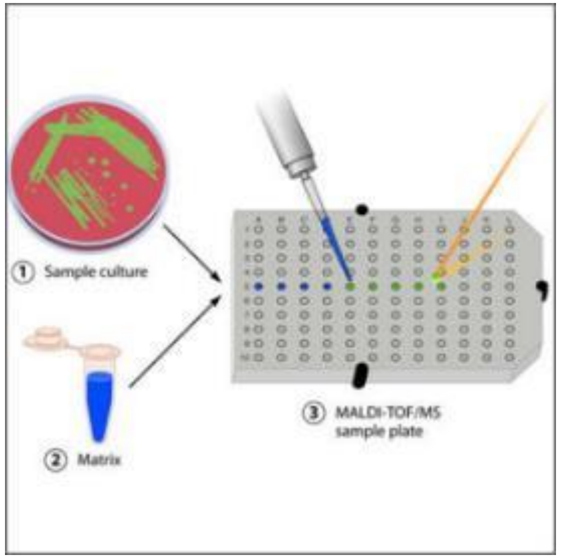
Tecnologia nata negli anni 80 per scopi di ricerca



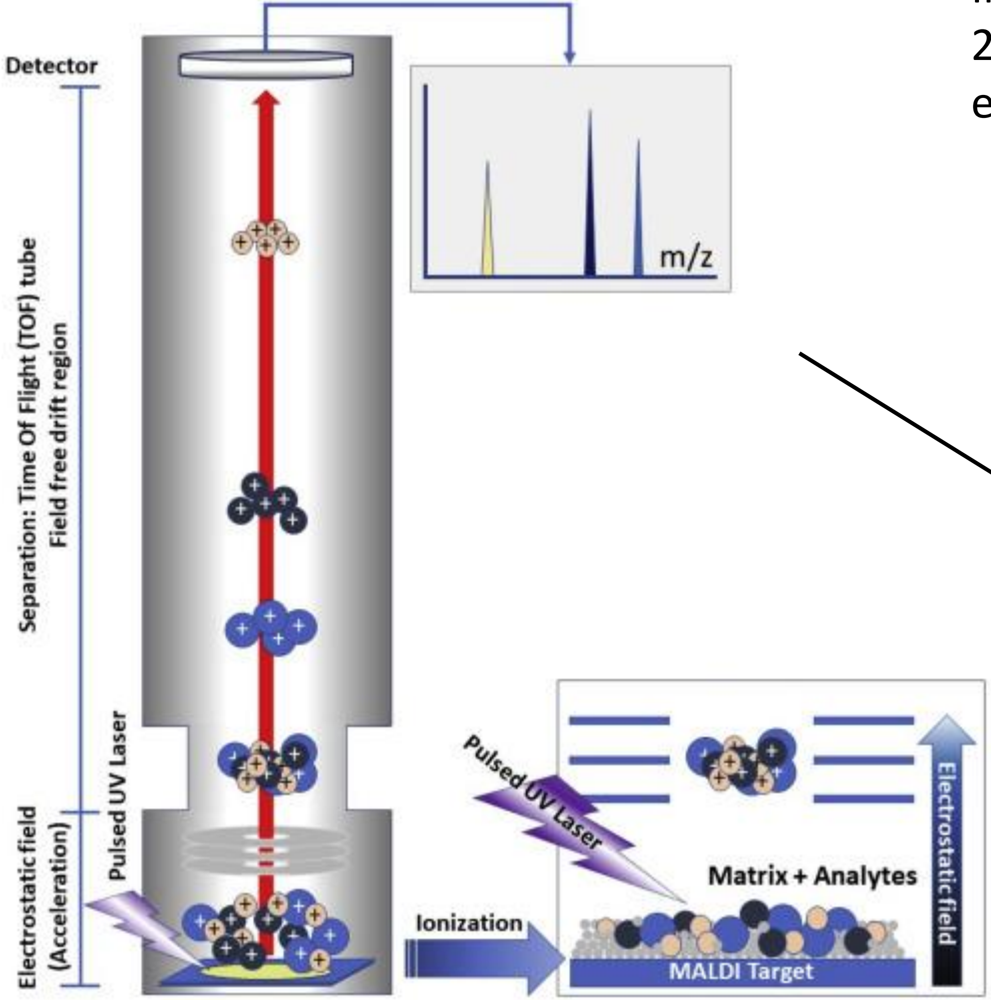
IDENTIFICAZIONE MICROBICA – SPETTROMETRIA DI MASSA

INSIDE INNOVATION

1

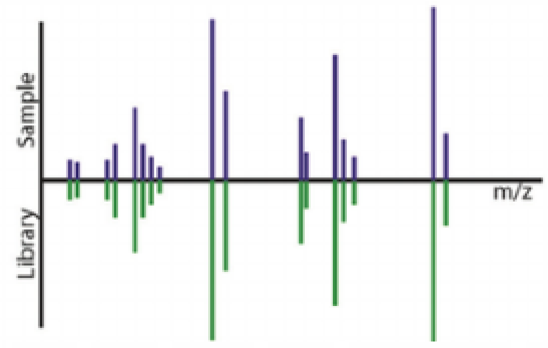


2



Introdotto in microbiologia dopo il 2000 da grandi aziende come Bruker e Biomerieux

3



Output

Sample	Rate	Matched Pattern	Score Value
ID	1	Bacteria starin#	XXXX
	2	Bacteria starin#	XXXX
	3	Bacteria starin#	XXXX


microflex


BIOMÉRIEUX

CONTESTO DEL LABORATORIO DIAGNOSTICO MICROBIOLOGICO

INSIDE INNOVATION

IDEA

REALTA’

MICROBIAL ID SCENARIO

	Time to ID	Sample preparation	Costs per test	Purchase & Maintenance	ID capacity	Dimensions
Biochemical	🕘 🕘 🕘	🕘 🕘 🕘	€ €	€ €	⚙ ⚙	↖ ↗ ↖ ↗ ↙ ↘ ↙ ↘
Molecular method (PCR)	🕘	🕘	€ € €	€ €	⚙ ⚙ ⚙	↖ ↗ ↙ ↘
MALDI-TOF	🕘	🕘	€	€ € €	⚙ ⚙ ⚙	↖ ↗ ↖ ↗ ↖ ↗ ↙ ↘ ↙ ↘ ↙ ↘

MICROBIAL ID SCENARIO

INSIDE INNOVATION

	Time to ID	Sample preparation	Costs per test	Purchase & Maintenance	ID capacity	Dimensions
Biochemical	🕒 🕒 🕒	🕒 🕒 🕒	€ €	€ €	⚙ ⚙	↖ ↗ ↖ ↗ ↙ ↘ ↙ ↘
Molecular method (PCR)	🕒	🕒	€ € €	€ €	⚙ ⚙ ⚙	↖ ↗ ↙ ↘
MALDI-TOF	🕒	🕒	€	€ € €	⚙ ⚙ ⚙	↖ ↗ ↖ ↗ ↖ ↗ ↙ ↘ ↙ ↘ ↙ ↘

COSA SERVE QUINDI??

INSIDE INNOVATION

	Time to ID	Sample preparation	Costs per test	Purchase & Maintenance	ID capacity	Dimensions
Biochemical			€ €	€ €		
Molecular method (PCR)			€ € €	€ €		
MALDI-TOF			€	€ € €		
ALIFAX IDEALE			€	€		

ABBIAMO GIA' TUTTE LE SOLUZIONI?

Idea

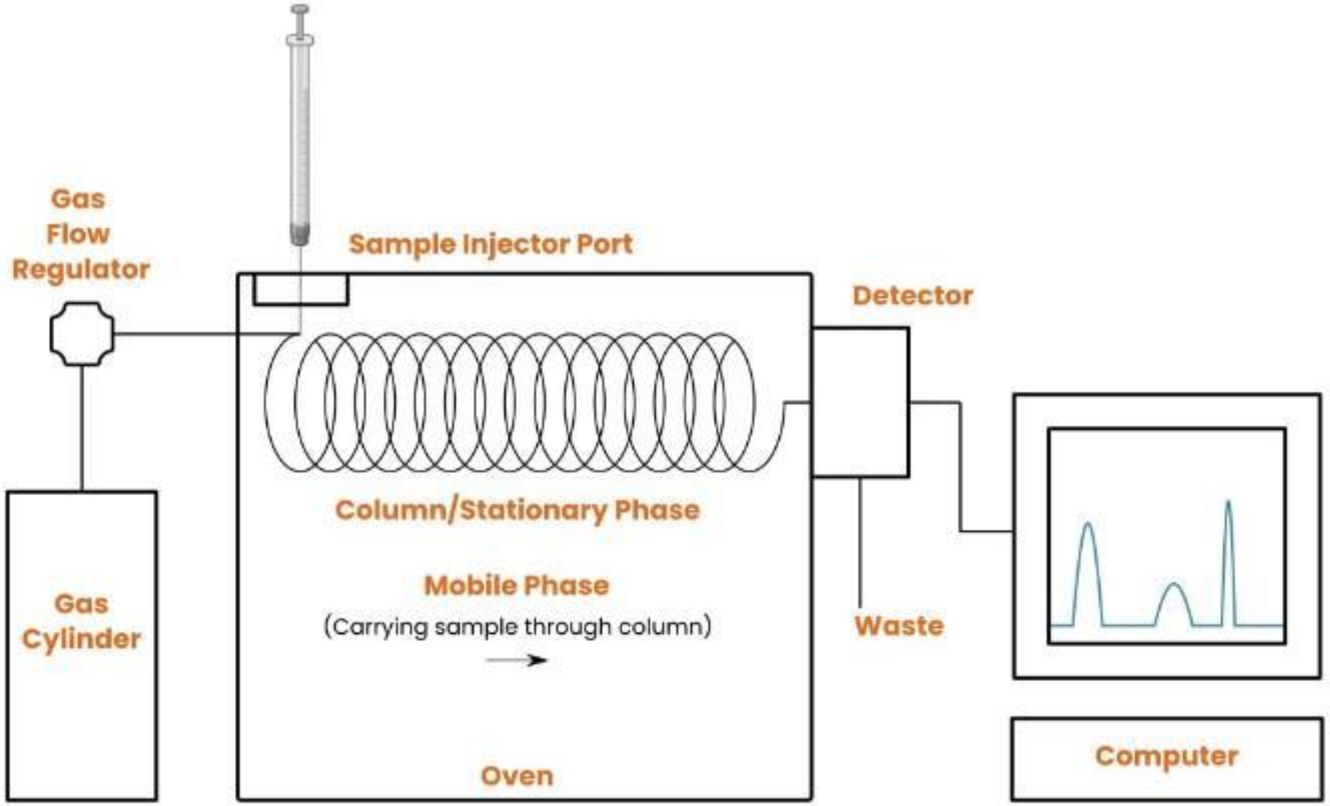
Sviluppo

Prodotto

Fattibilità

TENTATIVO 1: GAS CROMATOGRAFIA

Micro GC per analisi gas prodotti dal metabolismo microbico



INSIDE INNOVATION

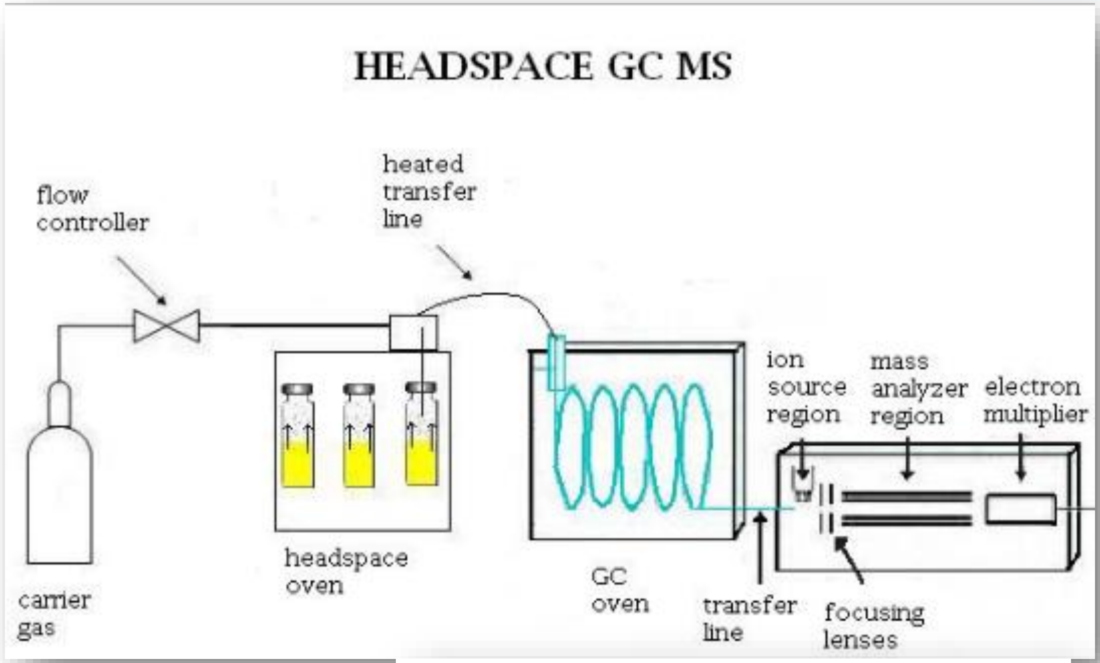
TENTATIVO 1: GAS CROMATOGRAFIA

Svantaggi

- Ridotta informazione delle componente misurabili;
- Elevata manutenzione attrezzatura;
- Necessità di gas «carrier» costantemente disponibile (costi, reperibilità, sicurezza)
- Prelievo campione richiedeva crescita in ambiente chiuso e sigillato, diverso da routine.

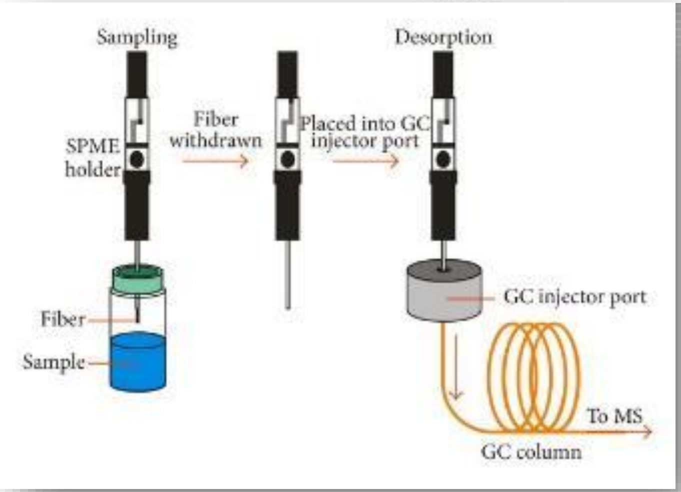
	Time to ID	Sample preparation	Costs per test	Purchase & Maintenance	ID capacity	Dimensions
ALIFAX IDEALE						↖ ↗ ↙ ↘

TENTATIVO 2: HEAD SPACE GC-MS



GC-MS per analisi metaboliti spazio di testa

Campionamento **SPME** (solid-phase micro extraction) da coltura liquida



TENTATIVO 2: HEAD SPACE GC-MS

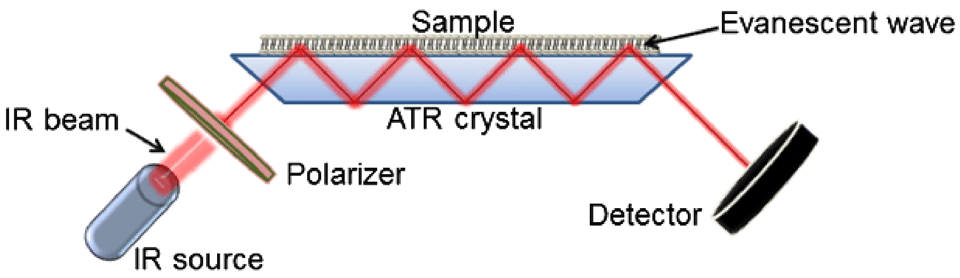
Svantaggi

- Costo attrezzatura necessaria e manutenzione;
- Utilizzo di sistema di campionamento SPME da sostituire di frequente;
- Necessità di gas «carrier» costantemente disponibile (costi, reperibilità, sicurezza);
- Prelievo campione richiedeva crescita in ambiente chiuso e sigillato, diverso da routine;
- Elevata variabilità di campionamento operatore dipendente.

	Time to ID	Sample preparation	Costs per test	Purchase & Maintenance	ID capacity	Dimensions
ALIFAX IDEALE						

TENTATIVO 3: SPETTROSCOPIA INFRAROSSA

Analisi di assorbimento spettroscopia infrarossa FTIR da colonia isolata con campionamento in ATR

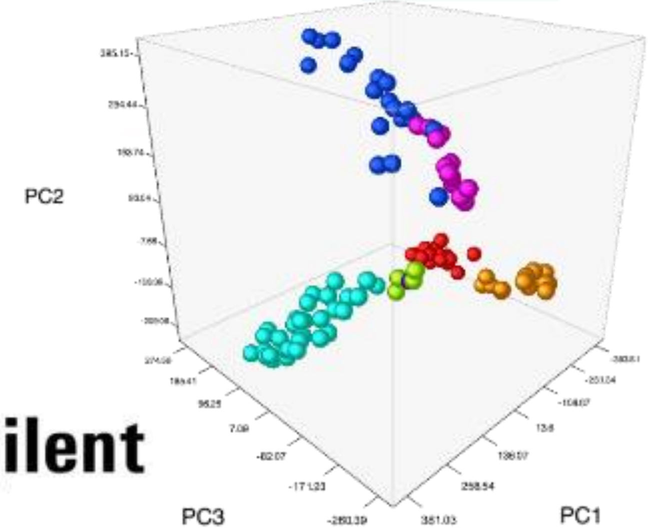


ATR: *Attenuated Total Reflection*
FTIR: *Fourier-transform infrared spectroscopy*

TENTATIVO 3: ATR-FTIR

Vantaggi

- ✓ Primi risultati molto promettenti fin da subito;
- ✓ Disponibilità hardware a costo contenuto e performance adeguate;
- ✓ Presenza di esperti disponibili a collaborare per attività di sviluppo;
- ✓ Campionamento estremamente robusto e indipendente da operatore;
- ✓ Assenza di consumabili, reattivi, manutenzione.



Agilent

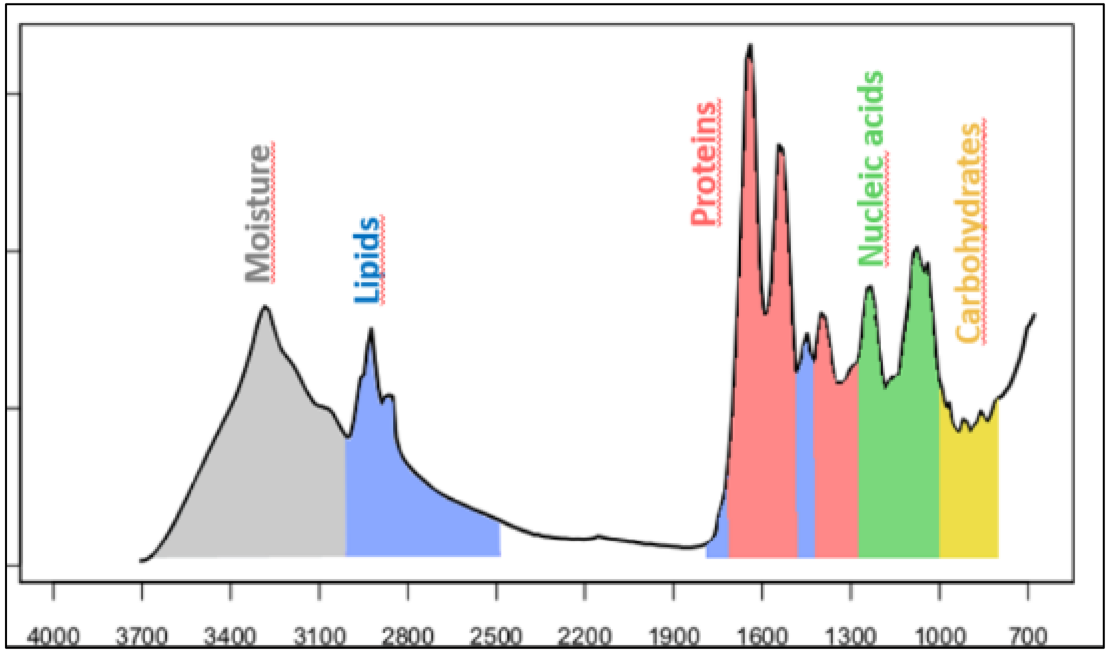
Elettra Sincrotrone Trieste

	Time to ID	Sample preparation	Costs per test	Purchase & Maintenance	ID capacity	Dimensions
ALIFAX IDEALE						

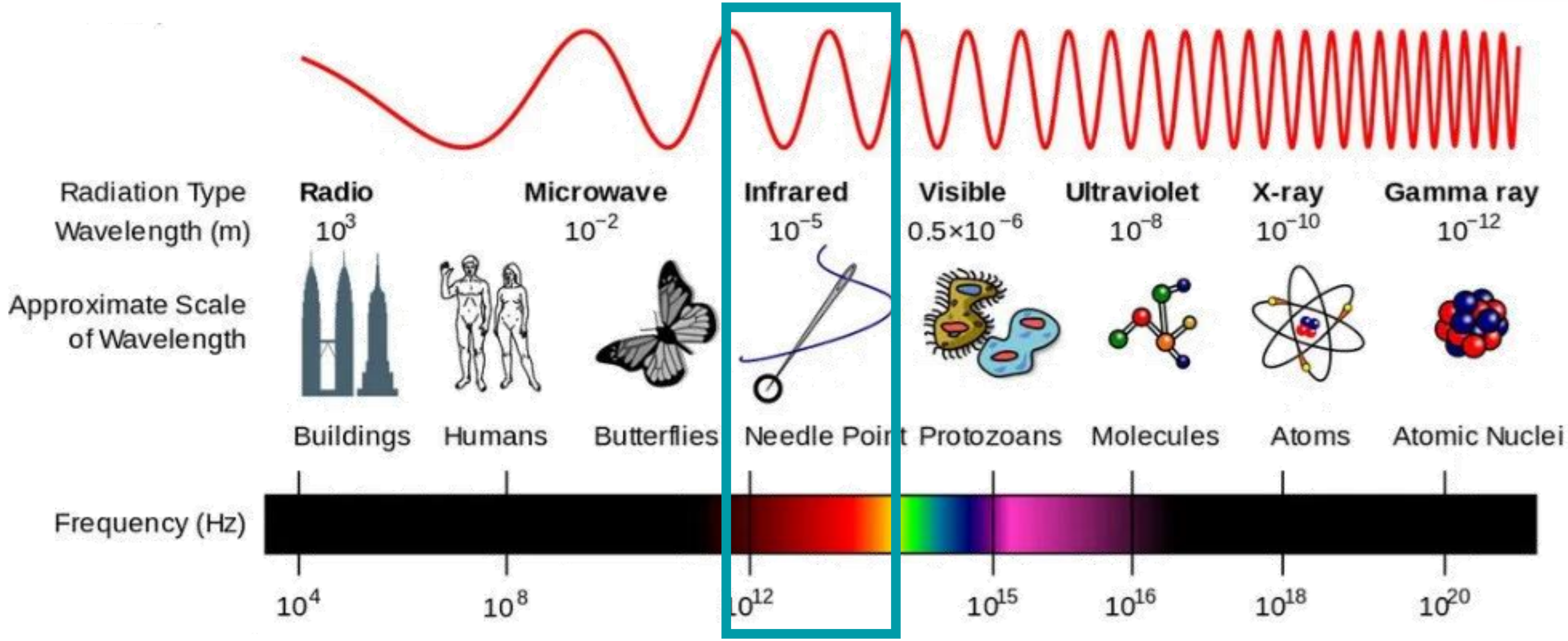
FAIL FAST.
FAIL CHEAP.
TRY AGAIN.

I-dOne

Sistema di identificazione microbica basato sull'interpretazione di spettri di assorbimento infrarosso tramite ATR-FTIR



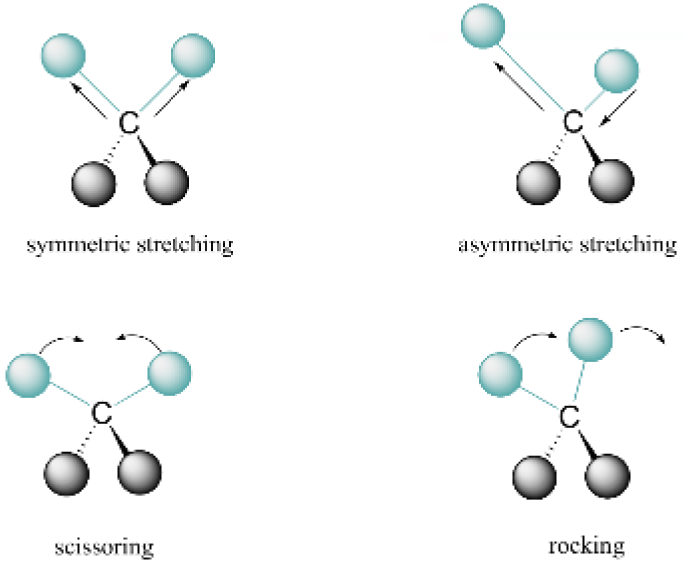
TECNOLOGIA_1
RADIAZIONE INFRAROSSA



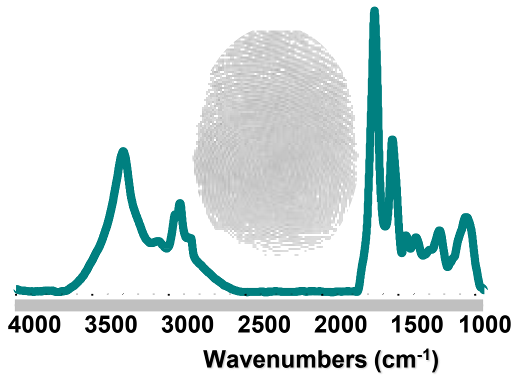
IR RANGE:
1-10 μm

TECNOLOGIA_2
ASSORBIMENTO INFRAROSSO

Bonds absorb InfraRed energy by increasing their vibrational state in relation to their specific molecular structure.

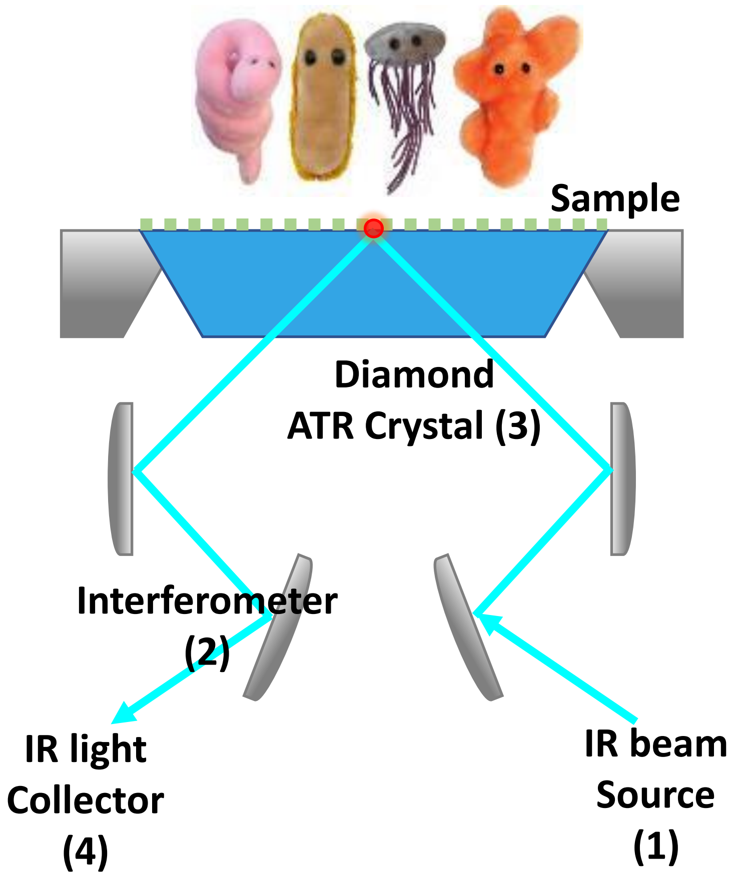


The InfraRed spectrum of a bacterial sample is considered to be its most characteristic physical property and serves as its molecular fingerprint for definitive identification.



TECNOLOGIA_3
SISTEMA ROBUSTO DI CAMPIONAMENTO

The **ATR**-FTIR Approach (ATR: Attenuated Total Reflection)



We illuminate the sample from the bottom of a reading crystal on which the sample is placed. At the interface between crystal and sample the absorption of the IR light occur by the sample. **The capacity of the incident light to penetrate the sample is called evanescent wave.** The residual beam is thus collected from the detector. The difference between the absorption profile with and without the sample makes the absorption spectrum.

Advantage: the penetration depth of the IR light is independent from the sample. IR light is able to penetrate the sample for hundreds of nanometers. Thus:

- Intensity does not depend on sample concentration
- A very small amount of sample is enough

ATTIVITA’ TECNICHE DI SVILUPPO

INSIDE INNOVATION

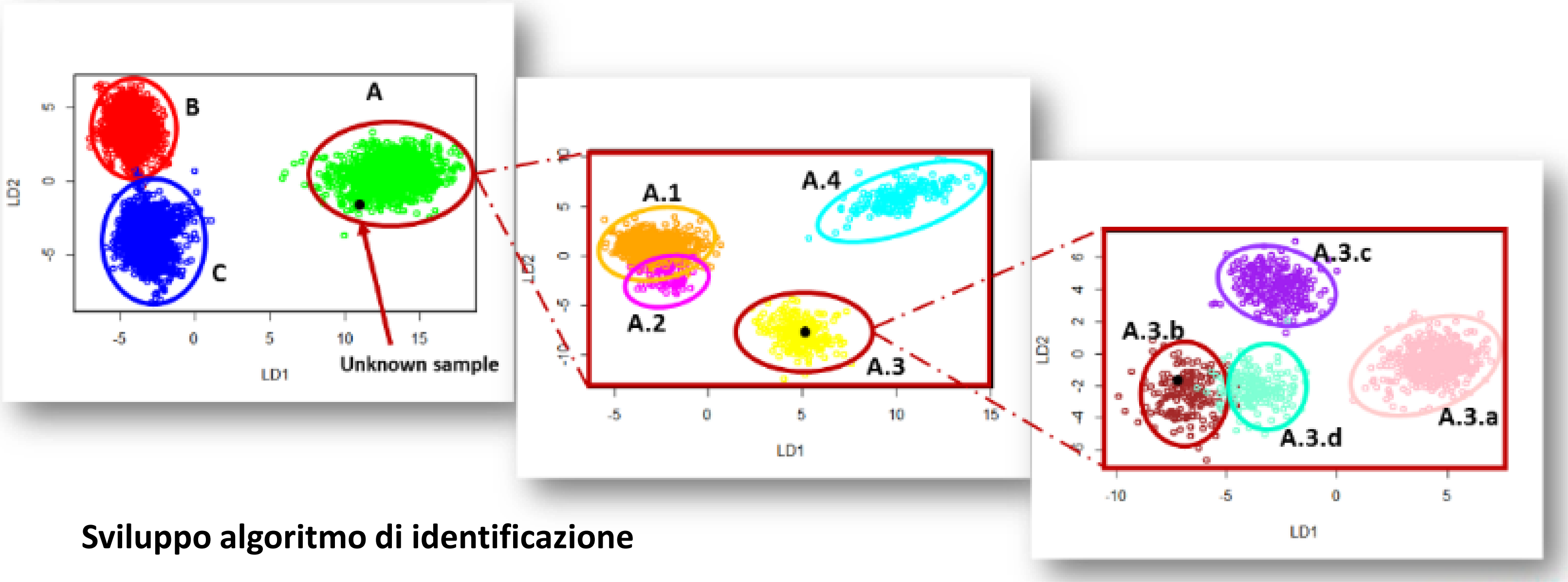
Raccolta ceppi microbici

ID di riferimento

Crescita in diverse condizioni

Misura spettri IR

Creazione database di riferimento con oltre 20.000 spettri (in crescita costante)



Sviluppo algoritmo di identificazione

ALI FAX

INSIDE INNOVATION

I-DONE: STORIA DI UN PROGETTO

Luglio 2016

- *Prima DEMO strumento AGILENT*

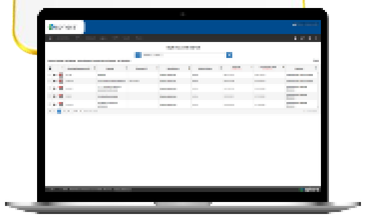
Settembre 2016

- Inizio collaborazione scientifica con Elettra

Elettra Sincrotrone Trieste

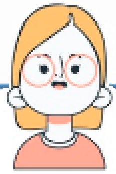
Novembre 2016

- Inizio collaborazione con Software House per sviluppo primo prototipo software



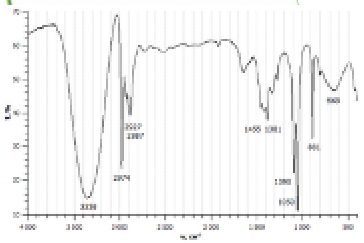
Gennaio 2017

- Inserimento risorse per attività di laboratorio



Anno 2017

- Sviluppo software per raccolta dati e creazione libreria di riferimento



Luglio 2018

- *Sottoscritto contratto con Agilent*

Agilent Technologies

Agosto 2018

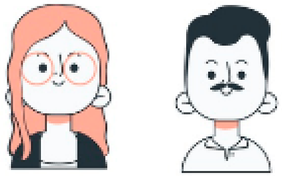
- *Inizio sperimentazione clinica presso laboratori italiani*

Gennaio 2019

- Inserimento Risorse per attività di laboratorio

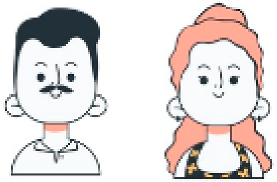
Febbraio 2019

- Inserimento Risorse per sviluppo algoritmi e gestione progetto



Novembre 2019

- Integrazione Risorse per sviluppo algoritmo e raccolta dati



CONTINUA

COME ARRIVARE A UN PRODOTTO?

Sample collection from the patient

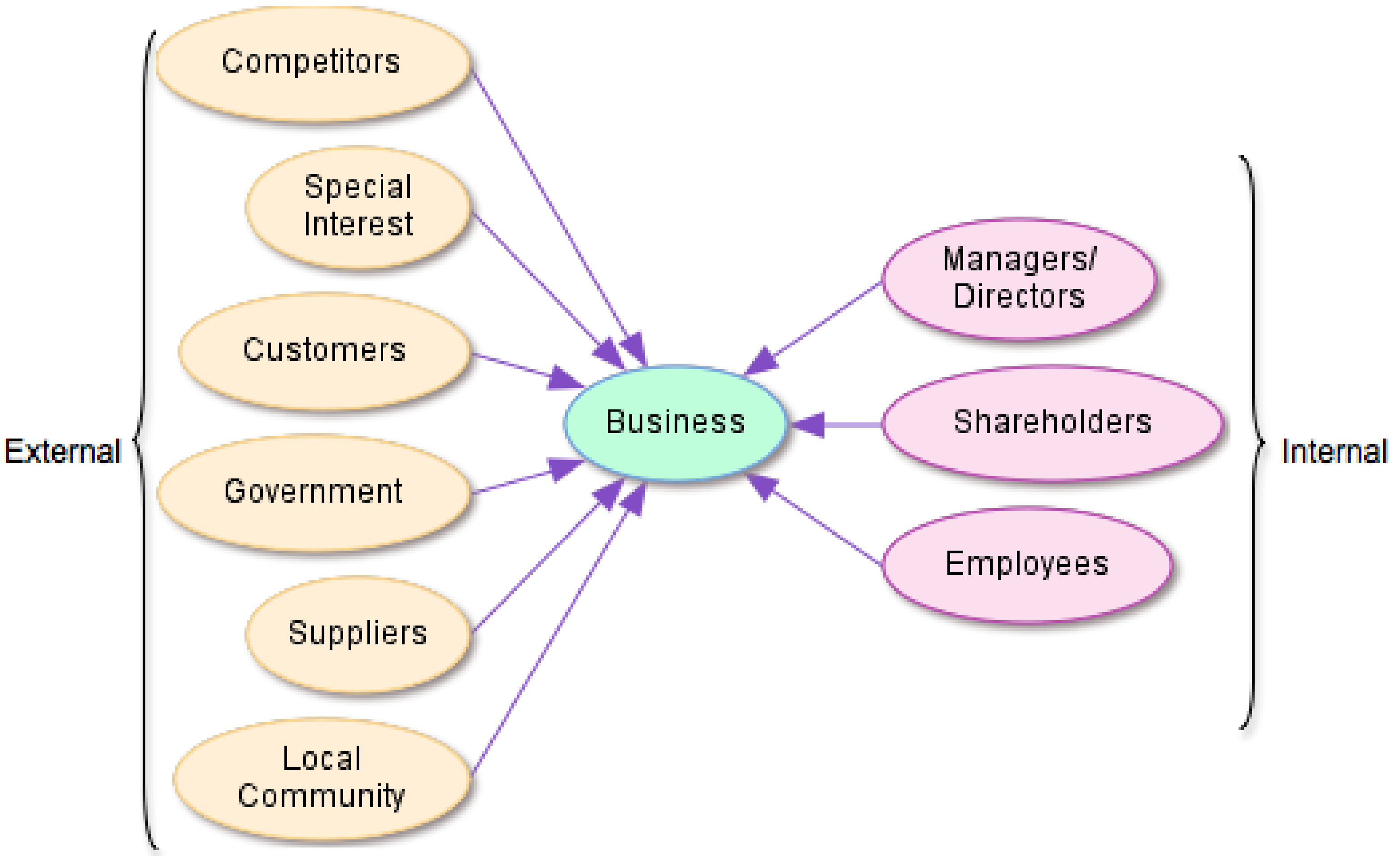
Screening test result

Positive sample subculture and isolation

I-dOne microbial identification

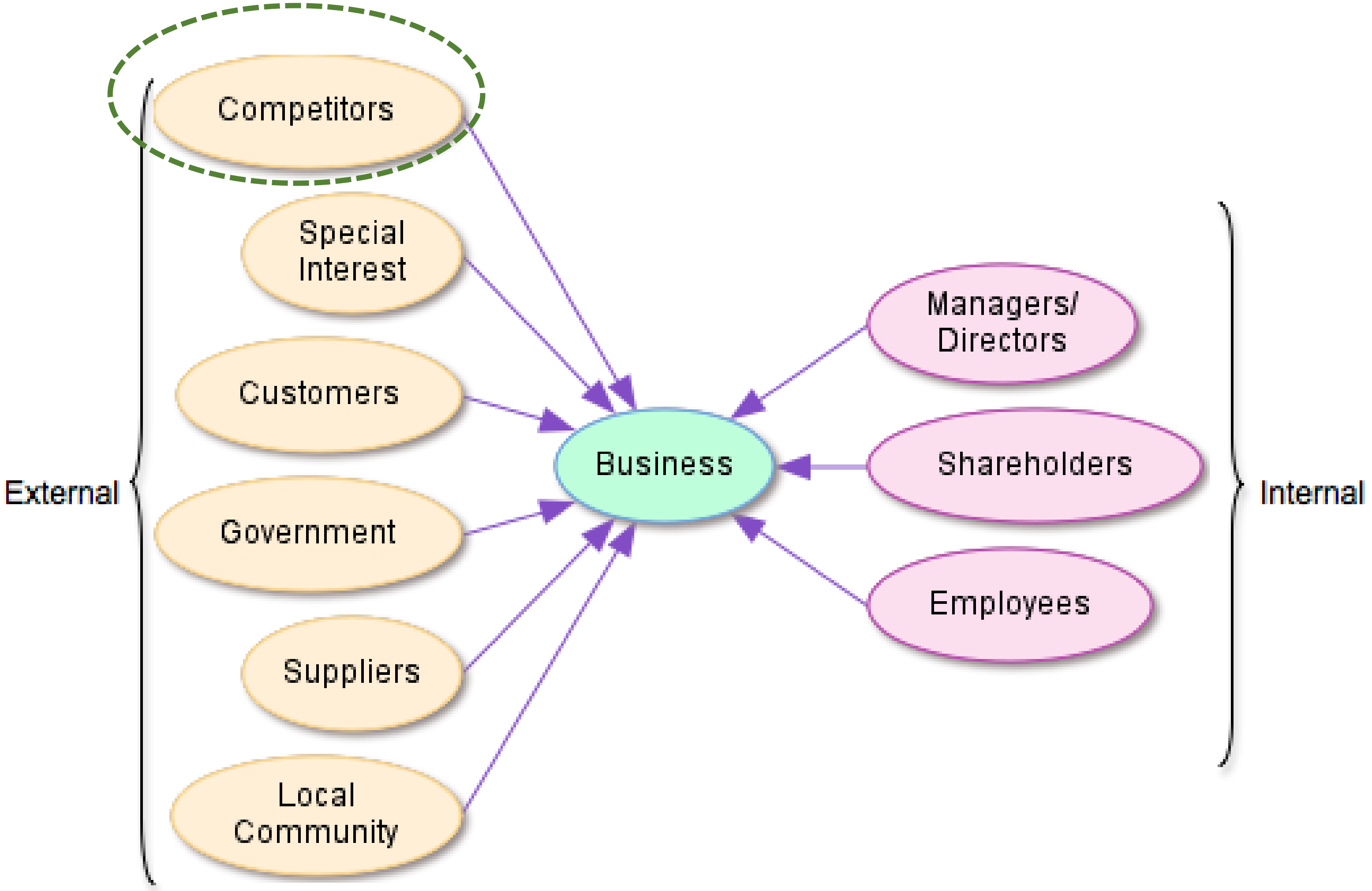
In vitro testing of the best antibiotics panel based on microorganism ID

STAKEHOLDER DI PROGETTO



Stakeholder (portatore di interesse) è genericamente qualsiasi soggetto o gruppo coinvolto in una qualsiasi iniziativa economica, una società o altro progetto, e in generale con interessi legati all’esecuzione o dall’andamento dell'iniziativa stessa.

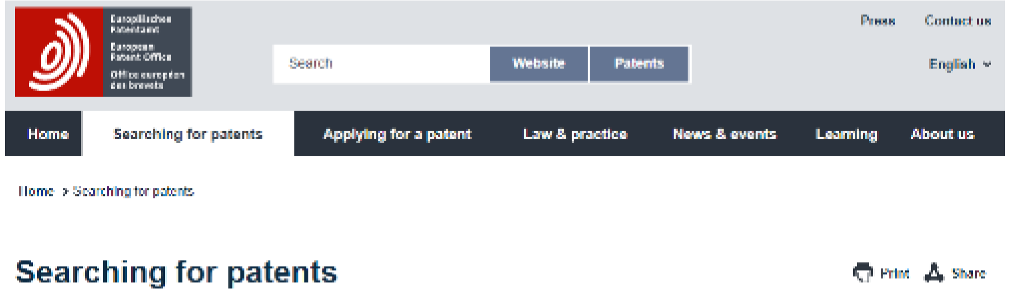
STAKEHOLDER DI PROGETTO



TUTELARSI DAI COMPETITORS

INSIDE INNOVATION

https://www.epo.org/searching-for-patents.html

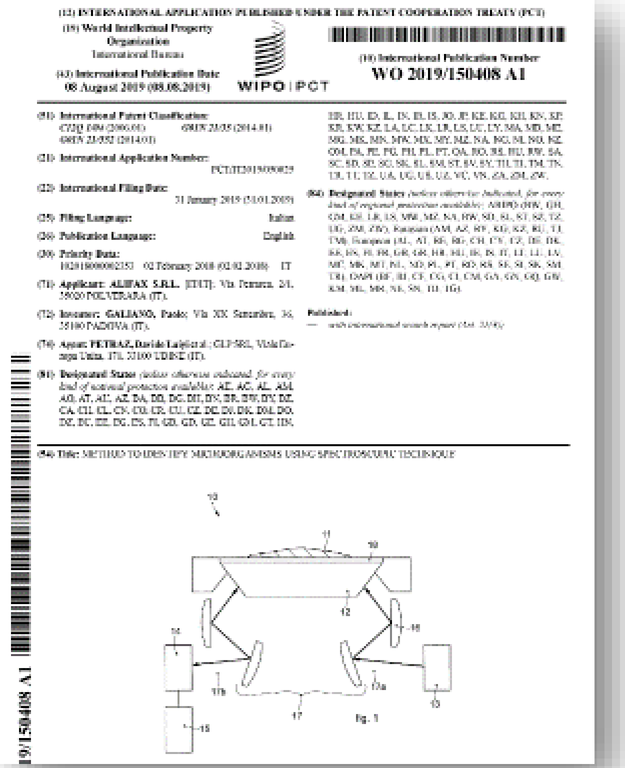


https://patents.google.com/

Google Patents

IP CONSULTING

Verificare lo spazio brevettuale disponibile per sviluppare la propria idea in area non coperte da *competitors* e **tutelare le proprie applicazioni** tramite la scrittura di brevetti


(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
08 August 2019 (08.08.2019)

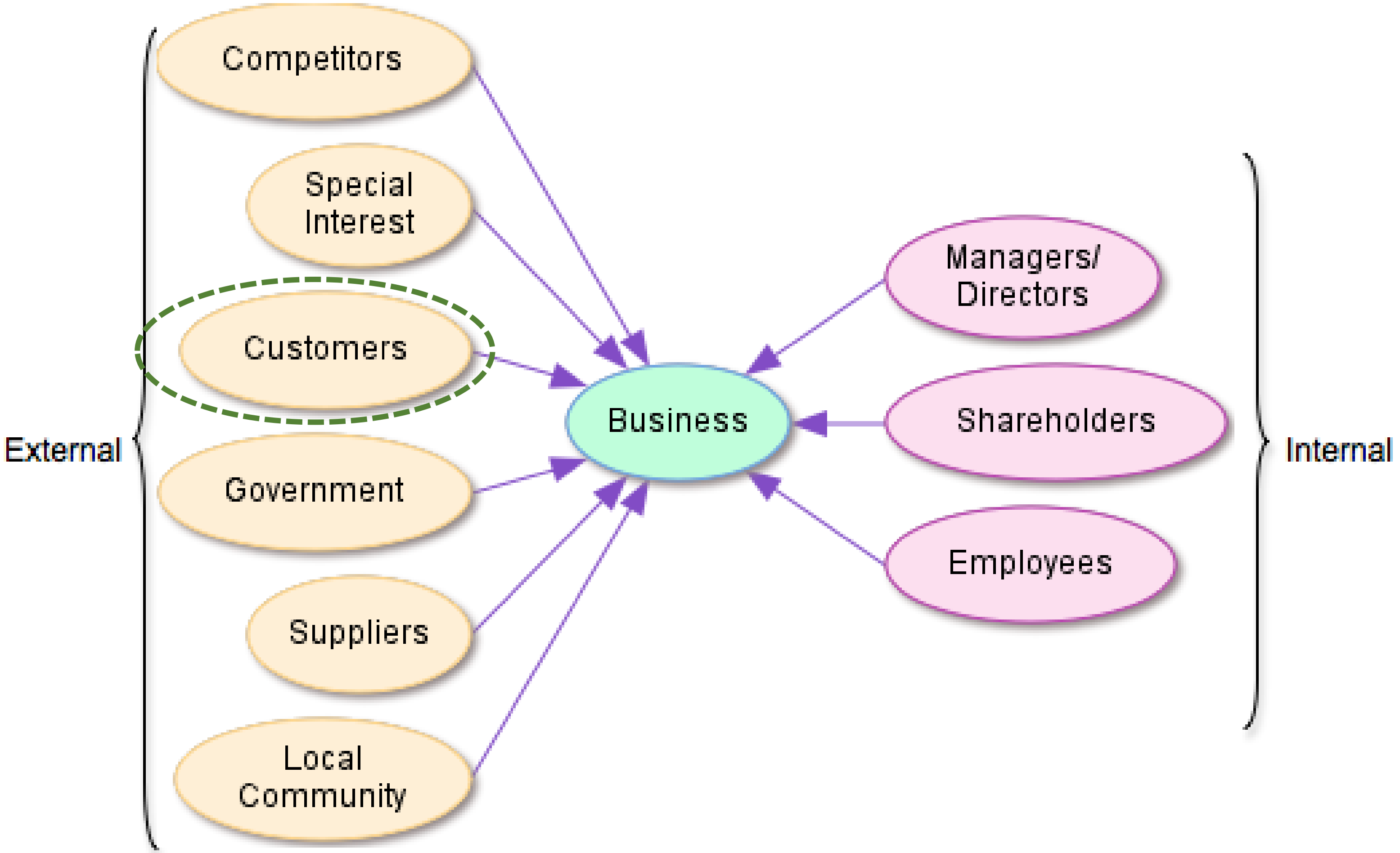
WIPO | PCT

(10) International Publication Number
WO 2019/150408 A1

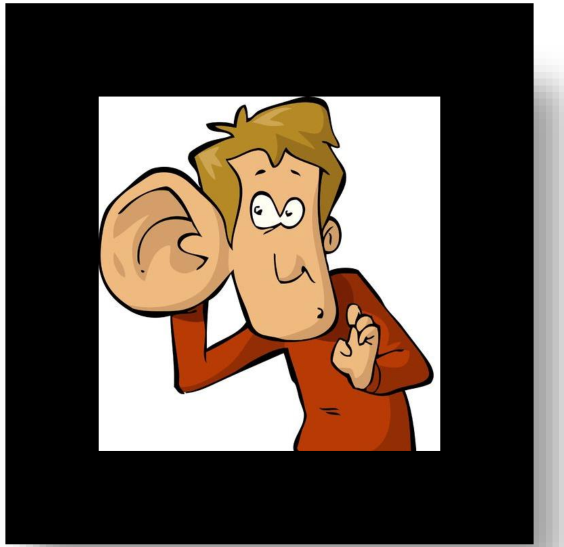
(71) Applicant: ALIFAX S.R.L.

(54) Title: METHOD TO IDENTIFY MICROORGANISMS USING SPECTROSCOPIC TECHNIQUE

ALTRI STAKEHOLDER DI PROGETTO



IDENTIFICARE I CUSTOMER (USER) NEEDS



DEFINIRE GLI USER NEEDS DI PRODOTTO

Chi sono gli user????

DEFINIRE GLI USER NEEDS DI PRODOTTO

Chi sono gli user????

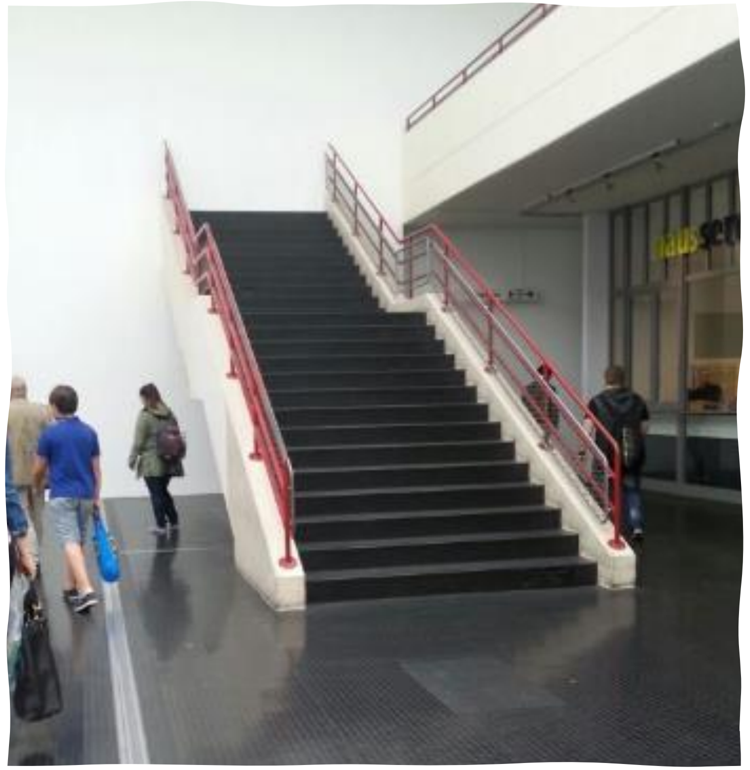
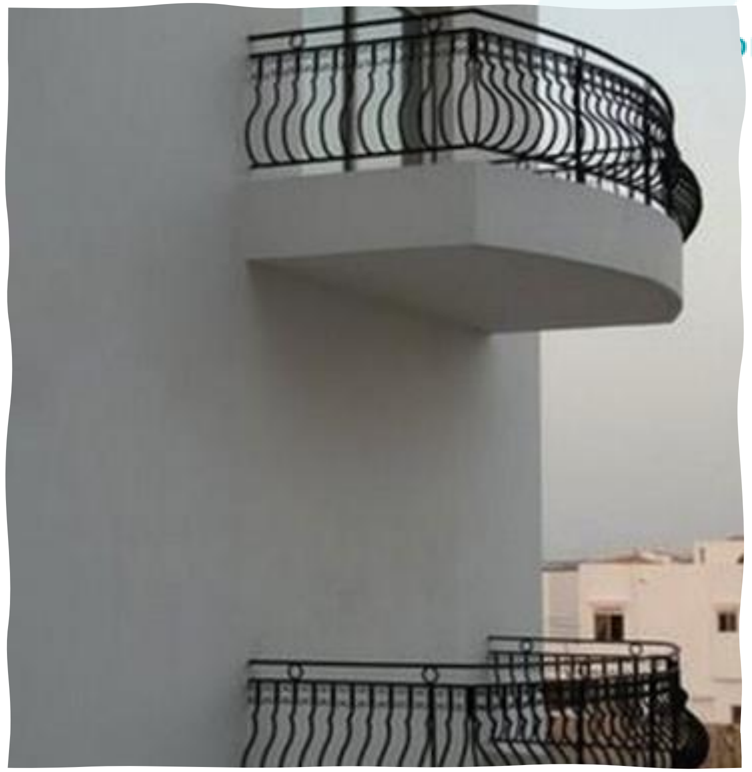
- **Addetto Produzione**
- **Magazzino e Logistica (movimentazione, stoccaggio)**
- **Commerciale (promozione, impatto emotivo prodotto)**
- **Installatore (facile, veloce, completo)**
- **Utilizzatore di laboratorio (usabilità)**
- **Direttore del laboratorio (vantaggio)**
- **Assistenza Tecnica (accessibile, semplice)**

DEFINIRE GLI USER NEEDS DI PRODOTTO

INSIDE INNOVATION

Chi sono gli user????

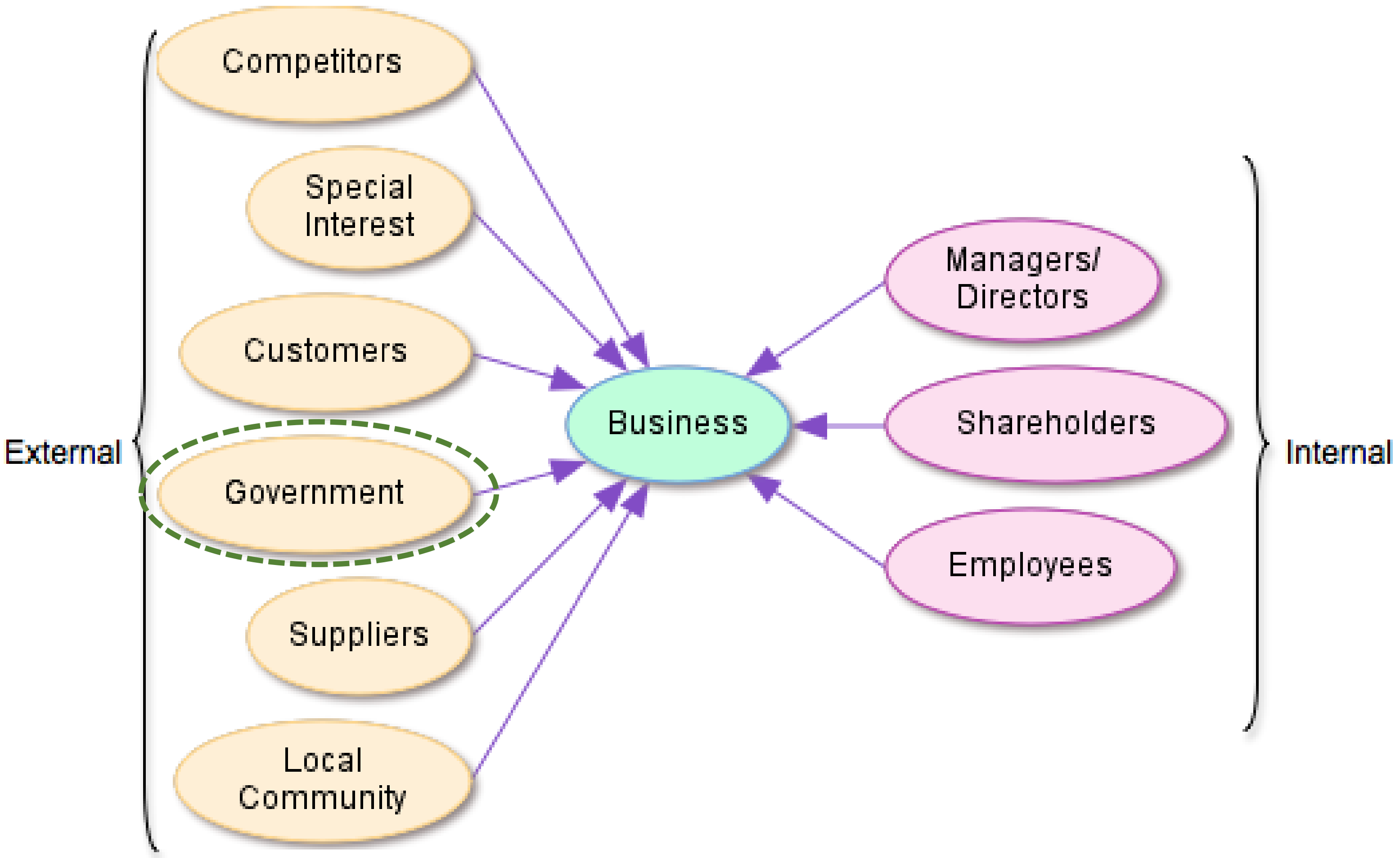
- Addetto Produzione
- Magazzino e Logistica (movimentazione, stoccaggio)
- Commerciale (promozione, impatto emotivo prodotto)
- Installatore (facile, veloce, completo)
- Utilizzatore di laboratorio (USABILITA')
- Direttore del laboratorio (vantaggio)
- Assistenza Tecnica (accessibile, semplice)

USABILITA’ COME FUNZIONE

USABILITA' COME RIDUZIONE DI ERRORI

ALTRI STAKEHOLDER DI PROGETTO



IVDR – REG EU 746/2017

Regolamenta e guida nello sviluppo di un dispositivo IVD:

- Definizione dell'Intended Use del dispositivo
- Assegnazione della classe di rischio del dispositivo
- Rispetto dei requisiti minimi di Sicurezza e Performance
- Esecuzione di prove di verifica e validazioni cliniche

GENERAL SAFETY AND PERFORMANCE REQUIREMENTS

CHAPTER I, **GENERAL REQUIREMENTS**
1. Devices shall achieve the performance intended by their manufacturer and shall be designed and manufactured in such a way that, during normal conditions of use, they are suitable for their intended purpose. They shall be safe and effective and shall not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety, taking into account the generally acknowledged state of the art.

ALI FAX

INSIDE INNOVATION

GENERAL SAFETY AND PERFORMANCE REQUIREMENTS

CHAPTER I, **GENERAL**
1. Devices shall achi intended by their manufa designed and manufactu during normal conditions their intended purpose. effective and shall not co condition or the safety o health of users or, where provided that any risks w their use constitute acce against the benefits to th with a high level of prote taking into account the g of the art.

CHAPTER II, **REQUIREMENTS REGARDING DESIGN AND MANUFACTURE**		
10. Chemical, physical and biological properties		
10.1. Devices shall be designed and manufactured in such a way as to ensure that the characteristics and performance requirements referred to in Chapter I are fulfilled. Particular attention shall be paid to:		
(a) the choice of materials and substances used, particularly as regards toxicity and, where relevant, flammability;		
(b) the compatibility between the materials and substances used and biological tissues, cells and body fluids, taking account of the intended purpose of the device and, where relevant, absorption, distribution, metabolism and excretion;		
(c) the compatibility between the different parts of a device which consists of more than one implantable part;		

INSIDE INNOVATION

GENERAL SAFETY AND PERFORMANCE REQUIREMENTS

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(b) the compatibility between the materials substances used and biological tissues, ce body fluids, taking account of the intended of the device and, where relevant, absorpti distribution, metabolism and excretion;
(c) the compatibility between the different a device which consists of more than one implantable part;

11. **Infection and microbial contamination**
11.1. Devices and their manufacturing processes shall be designed in such a way as to eliminate or to reduce as far as possible the risk of infection to patients, users and, where applicable, other persons. The design shall: (a) reduce as far as possible and appropriate the risks from unintended cuts and pricks, such as needle stick injuries, (b) allow easy and safe handling, (c) reduce as far as possible any microbial leakage from the device and/or microbial exposure during use, and (d) prevent microbial contamination of the device or its content such as specimens or fluids.
11.2. Where necessary devices shall be designed to facilitate their safe cleaning, disinfection, and/or re-sterilisation.

GENERAL SAFETY AND PERFORMANCE REQUIREMENTS

INSIDE INNOVATION

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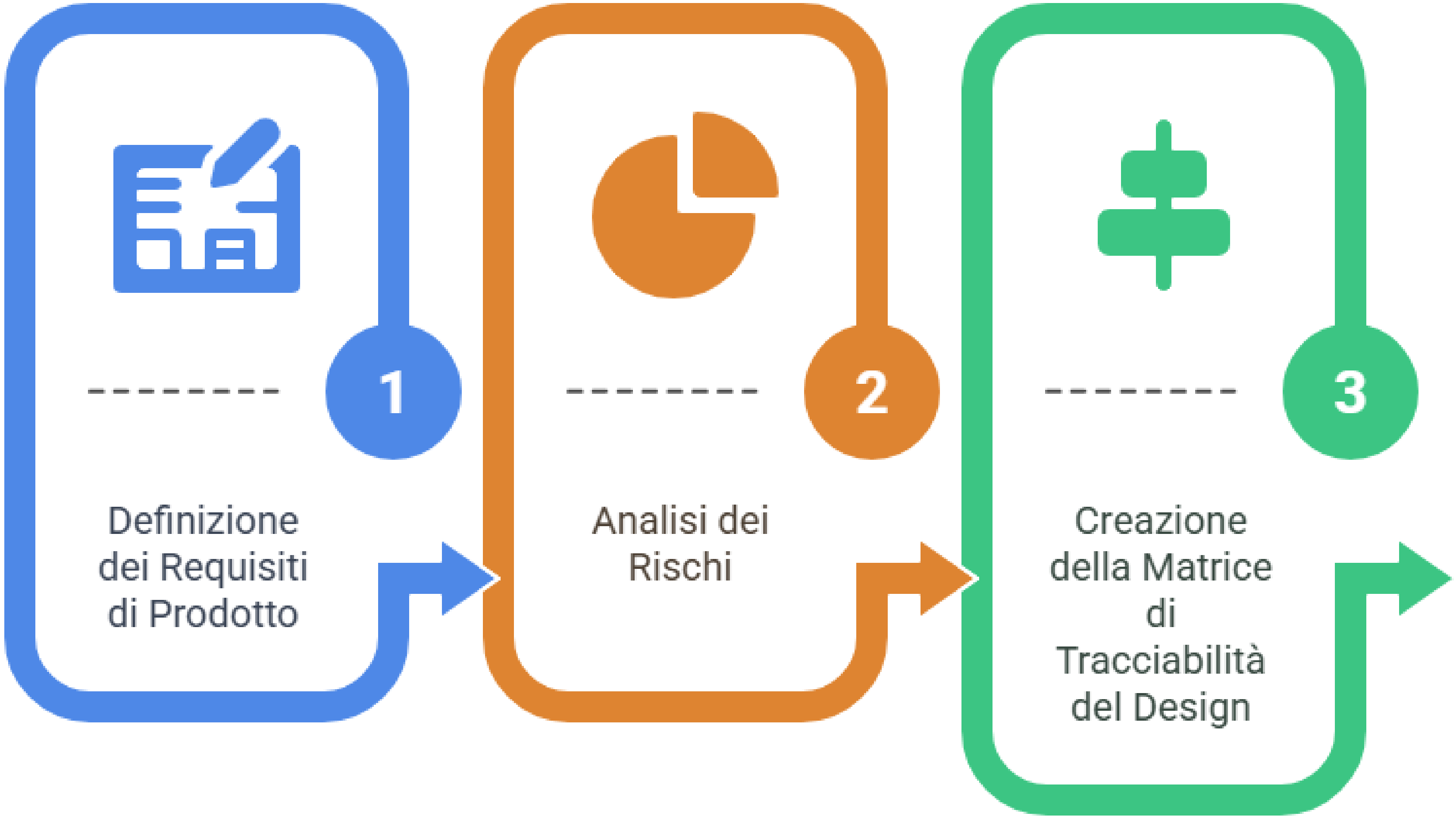
(d) prevent microbial contamination of the device or its content such as specimens or fluids.

11.2. Where necessary devices shall be designed to facilitate their safe cleaning, disinfection, and/or re-sterilisation.

17. Electronic programmable systems — devices that incorporate electronic programmable systems and software that are devices in themselves

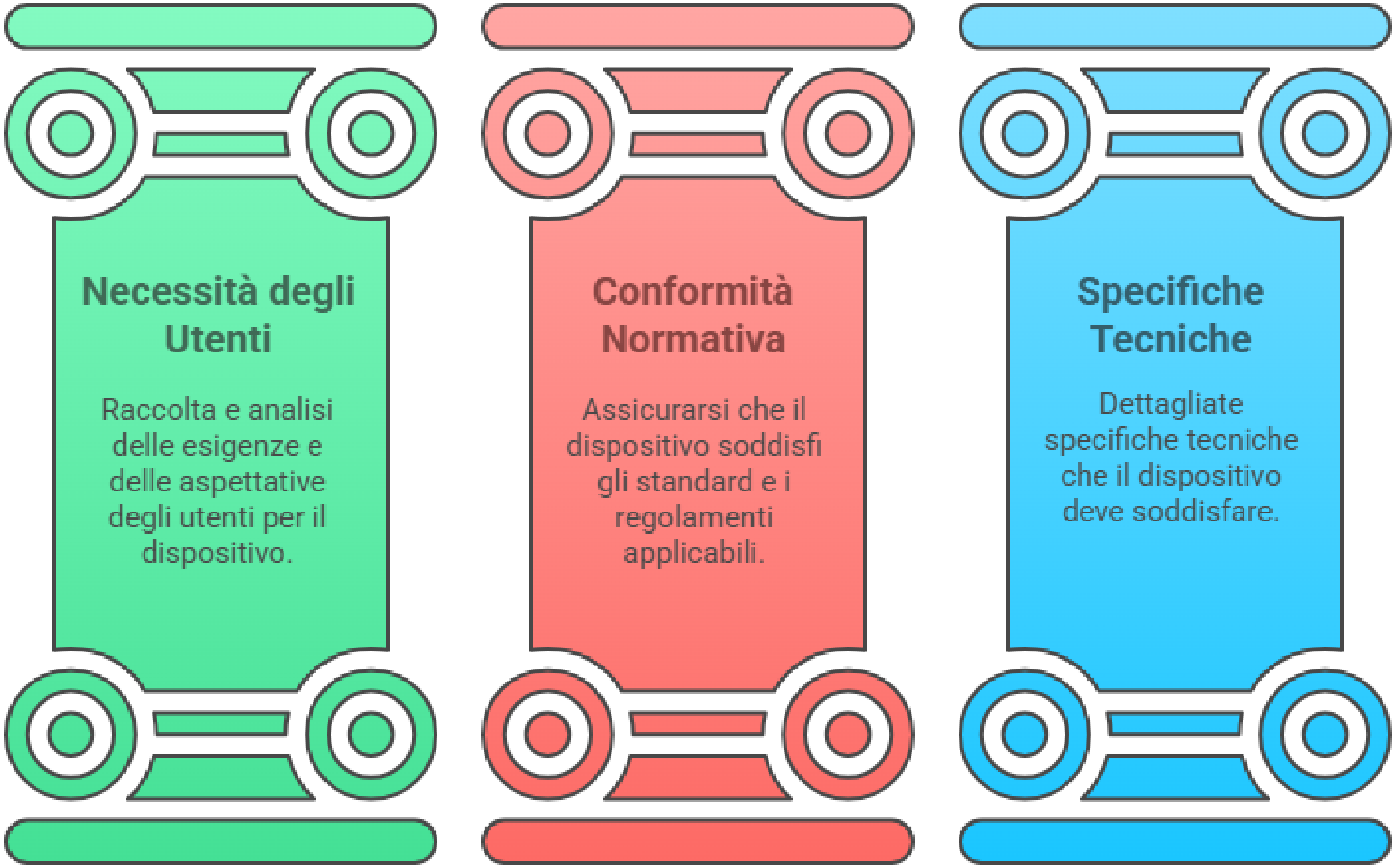
17.1. Devices that incorporate electronic programmable systems, including software, or software that are devices in themselves, shall be designed to ensure repeatability, reliability and performance in line with their intended use. In the event of a single fault condition, appropriate means shall be adopted to eliminate or reduce as far as possible consequent risks or impairment of performance.

DAI REQUISITI AL PRODOTTO



INSIDE INNOVATION

Fondamenti Essenziali per la Progettazione di Dispositivi Diagnostici



Gestione dei Rischi nel Design dei Dispositivi Diagnostici

Matrice di Tracciabilità del Design

Matrice di Tracciabilità del Design

Collega requisiti, design e test

Tracciabilità dei Requisiti

Garantisce che i requisiti non vengano trascurati

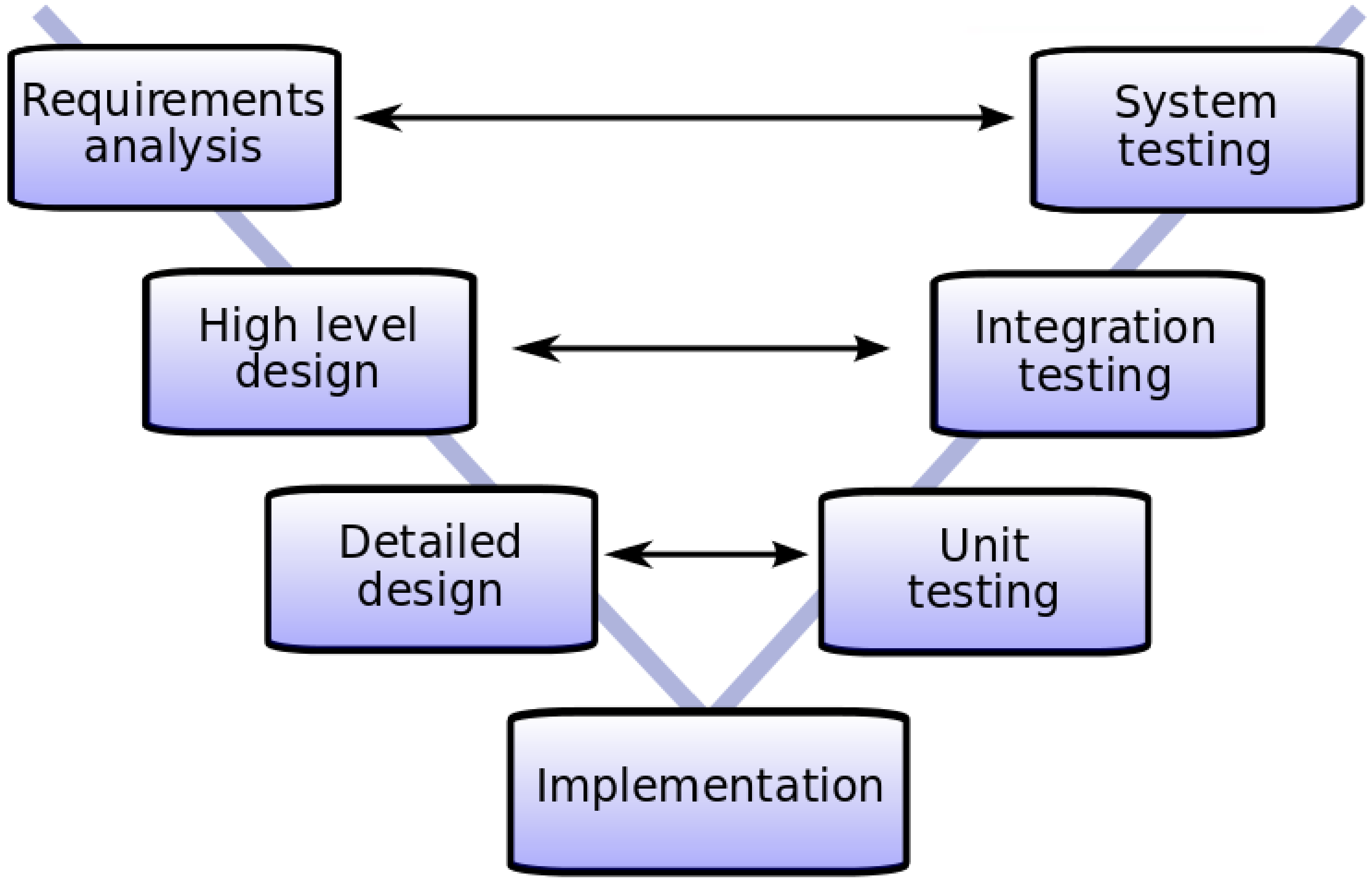
Valutazione dell'Impatto

Facilita la gestione dei cambiamenti e la mitigazione dei rischi

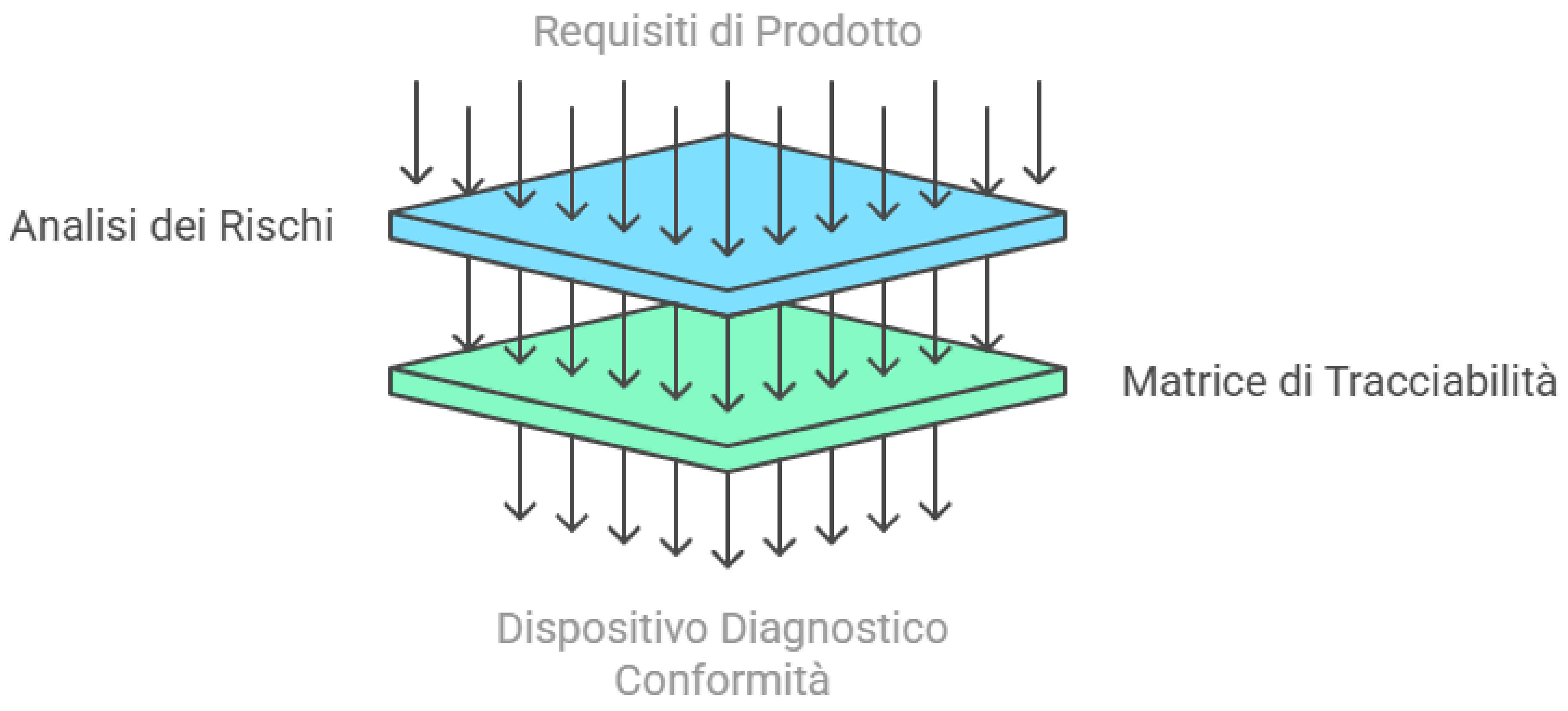
DESIGN TRACEABILITY MATRIX

INSIDE INNOVATION

- User needs
- Stakeholder needs
- Analisi dei rischi
- Requisiti Normativi



Processo di Design di un Dispositivo Diagnostico



OTTENIMENTO DI UN PRODOTTO

Sample collection
from the patient

Screening test
result

Positive sample
subculture and
isolation

I-dOne (Alifax) identification

In vitro testing of
the best antibiotics panel
based on microorganism ID

Al prossimo incontro…

ALI
FAX