Companion Diagnostics contra AMR?

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AMR INSIGHTS®
TOWARDS A WORLD FREE FROM AMR

Emerging Antimicrobials and Diagnostics in AMR
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Introduction & **Contact**

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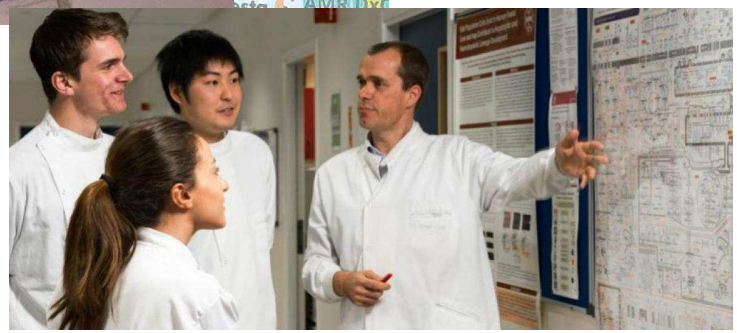


TACKLING ANTIMICROBIAL RESISTANCE ON TEN FRONTS

http://amr-review.org

- Public awareness
- Sanitation and hygiene
- Antibiotics in agriculture and the environment
- Vaccines and alternatives
- Surveillance
- Rapid diagnostics

"I call on the governments of the richest countries to mandate now that by 2020, all antibiotic prescriptions will need to be informed by up-to-[date] surveillance information [and] a rapid diagnostic test wherever one exists."

[R] Review May 19, 2016 – Tackling Drug-[R]esistant Infections Globally: final report and recommendations

There has been very little progress on the review's central and most expensive recommendations for transforming research and development incentives for antibiotics, vaccines and diagnostics.

Review of Progress on Antimicrobial Resistance: Background and Analysis, Charles Clift, Centre on Global Health Security | October 2019, Chatham House

HM Government

Tackling antimicrobial resistance 2019–2024

The UK's five-year national action plan

Published 24 January 2019

HM Government

Contained and controlled

The UK's 20-year vision for antimicrobial resistance

Published 24 January 2019

"… be able to report on the percentage of prescriptions supported by a diagnostic test or decision support tool by 2024."

For Dx: UK AMR Diagnostics Collaborative

Variability of **Antibiotic Prescription** for Febrile Children

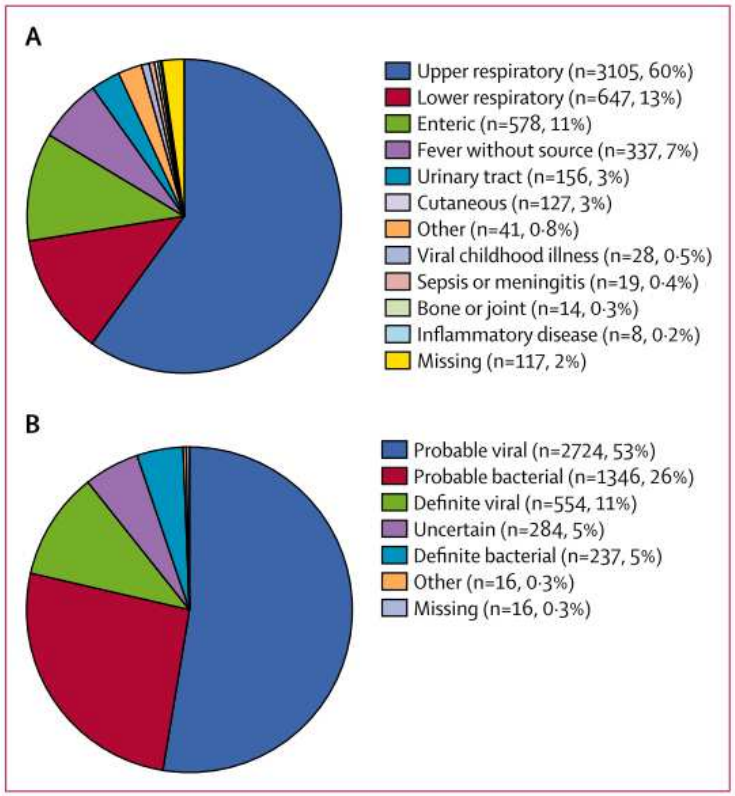
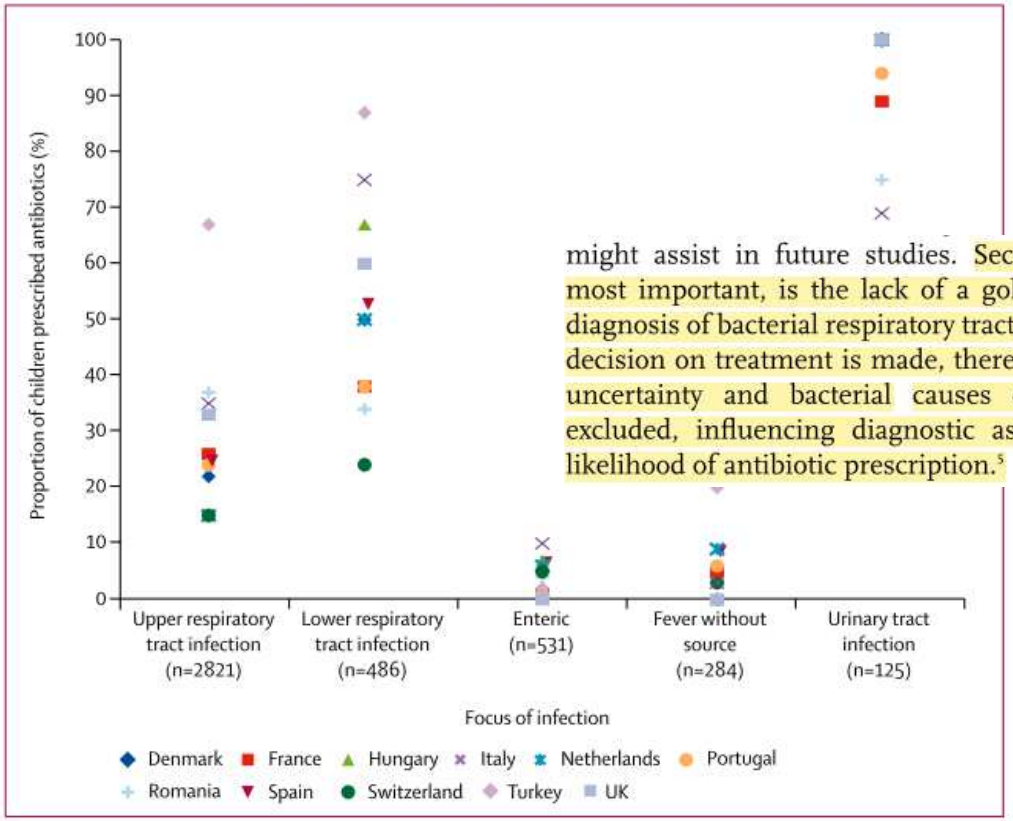


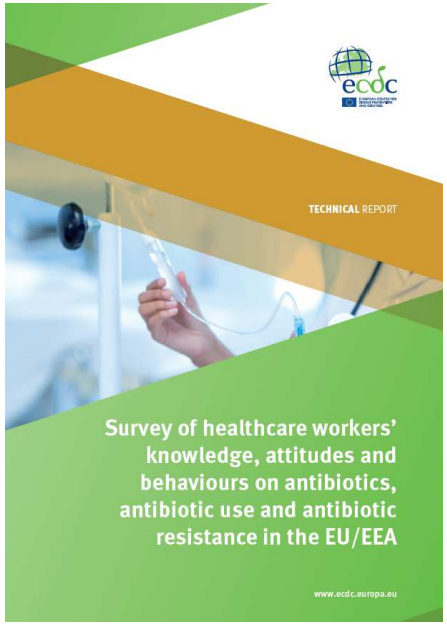
Figure 2: **Frequency of probable focus (A) and cause (B) of infection in all 5177 children studied**



might assist in future studies. Second, and probably most important, is the lack of a gold standard for the diagnosis of bacterial respiratory tract infections. When a decision on treatment is made, there is often diagnostic uncertainty and bacterial causes can often not be excluded, influencing diagnostic assessment and the likelihood of antibiotic prescription.[5]

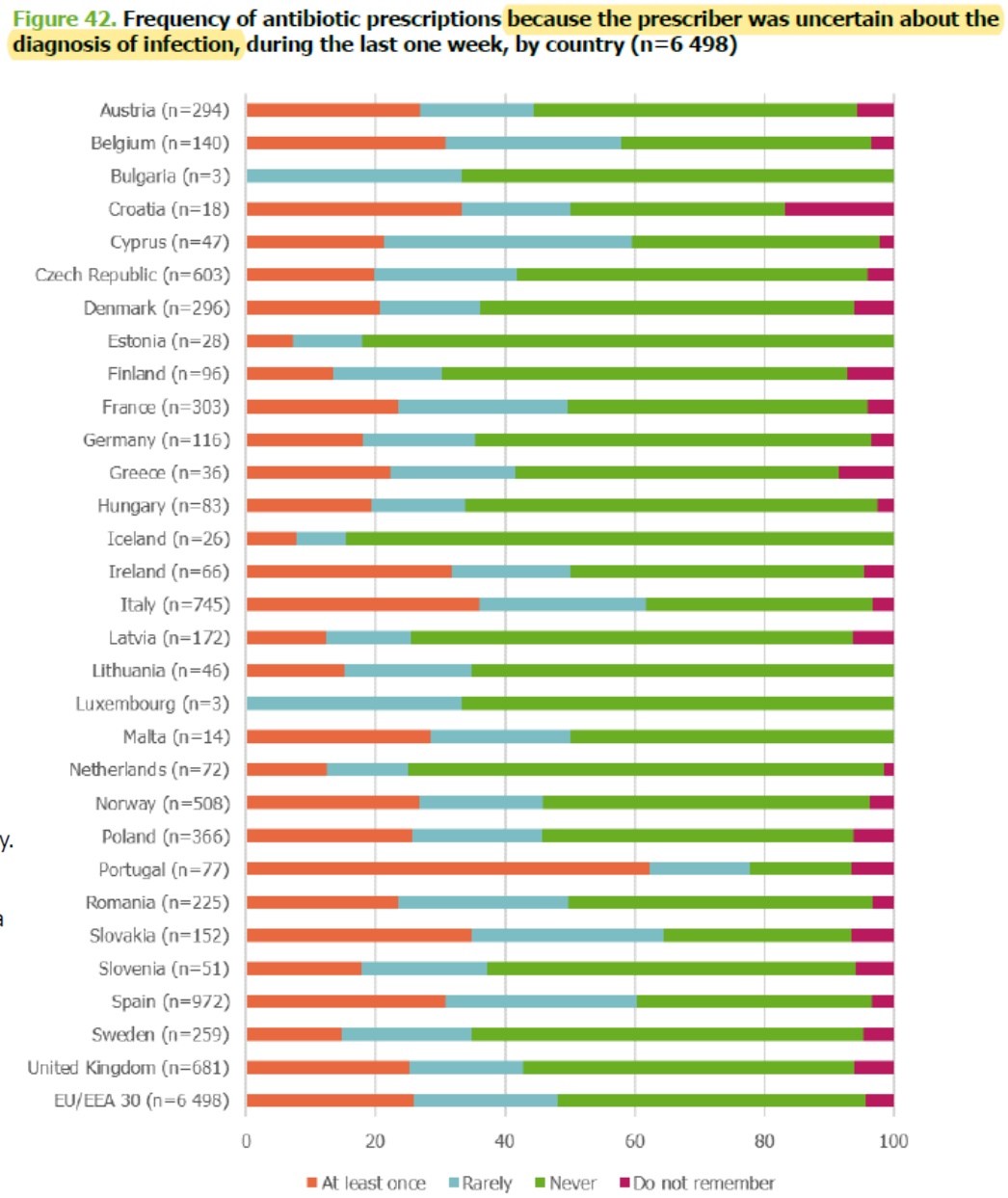
Figure 3: **Variability in antibiotic prescription across countries for the most frequent foci of infection in 4560 children without comorbidities**

Antibiotic prescription for febrile children in European emergency departments: a cross-sectional, observational study. van de Maat J, van de Voort E, Mintegi S, Gervaix A, Nieboer D, Moll H, Oostenbrink R; Research in European Pediatric Emergency Medicine study group. Lancet Infect Dis. 2019 Feb 28. pii: S1473-3099(18)30672-8



Diagnostic uncertainty leads to antibiotic use

Regarding prescribers' motivations to initiate antibiotic prescriptions, 31% of prescribers said they would have preferred not to prescribe an antibiotic at least once in the week prior to completing the survey, but did so anyway. The most common reason for this was 'fear of patient deterioration or fear of complications': 43% reported that these fears affected their prescribing decision at least once per week, and 11% at least once per day. This varied across countries, with the highest proportion stating such fears as a factor for initiating prescribing at least once a week reported in Slovakia, and the lowest proportions in the Netherlands and Sweden. Other drivers included an uncertain diagnosis (26%); impossible to follow up on the patient (23%); limited time to explain the reason why antibiotic is not indicated (10%); and maintaining the patient relationship (8%).



European Centre for Disease Prevention and Control. Survey of healthcare workers' knowledge, attitudes and behaviours on antibiotics, antibiotic use and antibiotic resistance in the EU/EEA. Stockholm: ECDC; 2019.

The **Diagnostic Spectrum** in Clinical Microbiology

Phenotypic
- Gram staining
- Culture
- Biochemistry

Non phenotypic
- Immunoassays
- Molecular
- Mass Spec
- Imaging
- Sequencing

Host Response
- Biomarkers
- Gene expression

Specimen - Culture
Whole Blood - Blood Culture
Automation, Integration, Sample to Answer
ID, ID/AST, AMR
Lab - POCT

Some **Molecular Diagnostic Systems** in Use or With Potential for Infectious Disease Diagnostics


www.drw-ltd.com


www.biocartis.com


www.cepheid.com


www.nanosphere.com


www.molecular.roche.com


www.check-points.com


www.curetis.com


www.alere-i.com


www.alere.com


www.biomerieux-diagnostics.com

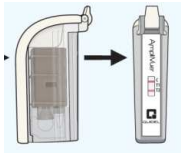

www.luminexcorp.com


www.stat-dx.com


www.bosch-vivalytic.com


www.blink-dx.com


www.twistdx.co.uk


www.quidel.com


www.optigene.com


www.meridianbioscience.com


www.mybinxhealth.com


www.genefluidics.com


www.daktaridx.com


www.genmarkdx.com


www.mobidiag.com


nanoporetech.com


www.dnae.co.uk


www.rheonix.com


www.corisbio.com


www.genepoc-diagnostics.com


spindiag.de


www.chipcare.ca


www.quantumdx.com


www.cubedlabs.com


www.genedriveplc.com


www.ivd-plattform.de


www.bigteclabs.com


gbscience.com

AMR Dx Global Network

AMR Dx Global
jpiamr | vri
a virtual research institute project

- Addressing Barriers for Development and Implementation of Rapid Diagnostics to Tackle AMR → Teaching and Training
- Visit our survey:

AMR Diagnostics-Teaching and Training

https://edin.ac/2Qk37Vb

AMR Diagnostics Teaching & Training Resource - Self Registration

https://edin.ac/376Vd7N

@BachmannTill

WHO AMR Diagnostics **TPP Public Consultation**

Target Product Profile for a Multiplex Platform for **Identification and Resistance Testing/AST** of Prioritized Bacterial Pathogens

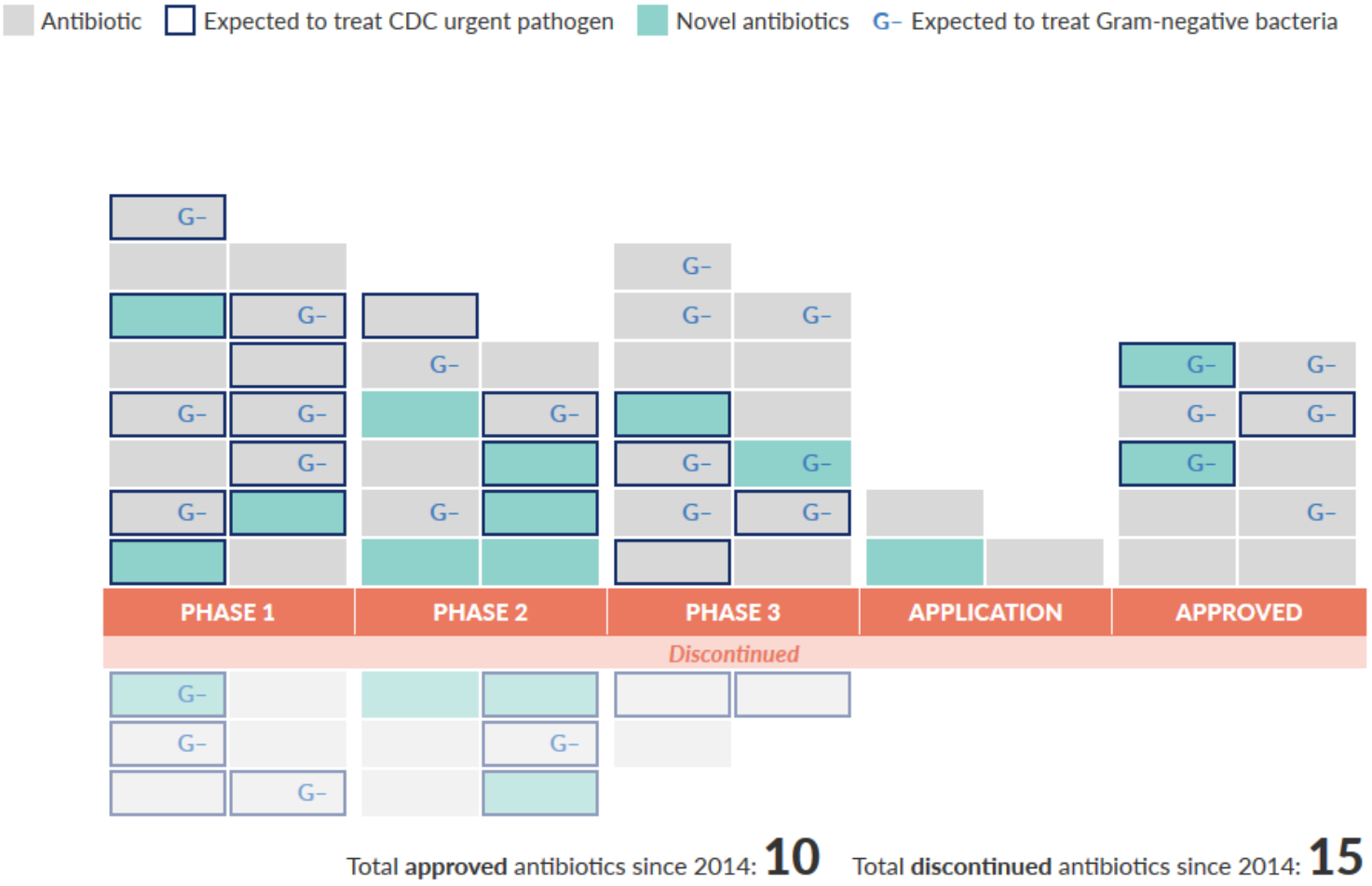
	Characteristic	Minimum Requirement	Optimal Requirement
	Scope of the Platform		
1	**Intended Use**	For purposes of patient management and antibiotic stewardship,[1] detection and identification of (i) multiple prioritized bacterial pathogens[2] associated with clinical syndromes, such as bloodstream, respiratory, urinary tract infections (UTIs), and gastrointestinal infections (GIs), and either (ii) genetic determinants of antibiotic susceptibility/resistance *or* phenotypic antimicrobial susceptibility (AST)[3] with respect to select antibiotics for the pathogens identified.	For purposes of patient management and antibiotic stewardship, detection and identification of (i) multiple prioritized bacterial pathogens associated with clinical syndromes, such as bloodstream, respiratory, UTIs, and GIs, and either (ii) genetic determinants of antibiotic susceptibility/resistance *or* phenotypic AST with respect to the full range of antibiotics for the pathogens identified.
2	**Description of System**	The system will consist of an instrument[4] designed for use in combination with a self-contained, disposable assay cartridge(s)[5] containing all required reagents to execute a test from sample to result.	
3	**Target Use Setting**	Level 2[6] Healthcare Facility (District Hospital or above) defined as having a functioning laboratory with trained personnel, water, electricity with intermittent surges and/or outages, limited climate control, dust, and medical staff onsite; The target use setting does not include mobile testing facilities.	

Target Product Profile for a Platform to **Detect Phenotypic Antimicrobial Susceptibility** of Prioritized Bacterial Pathogens to Facilitate Antibiotic Stewardship

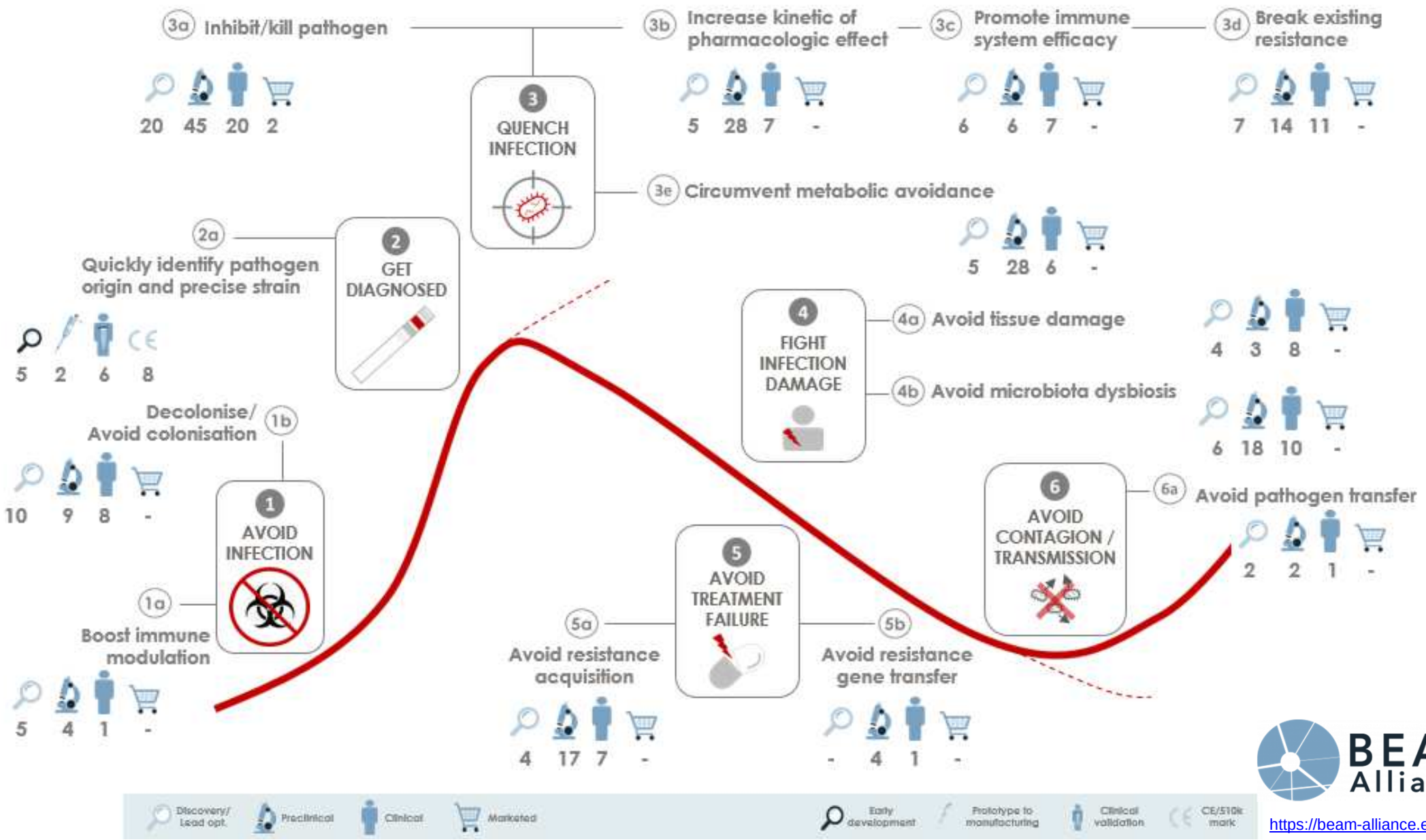
	Characteristic	Minimum Requirement	Optimal Requirement
	Scope of the Platform		
1	**Intended Use**	A reflex test to detect phenotypic antimicrobial susceptibility (AST) of prioritized bacterial pathogens[15] associated with clinical syndromes, such as bloodstream, respiratory, urinary tract, and gastrointestinal infections following positive identification of such pathogens on a separate test or test platform in order to facilitate antibiotic stewardship.[16]	
2	**Description of System**	The system will consist of an instrument[17] designed for use in combination with a self-contained, disposable assay cartridge(s)[18] containing all required reagents to execute a test from sample to result.	
3	**Target Use Setting**	Level 2[19] Healthcare Facility (District Hospital or above) defined as having a functioning laboratory with trained personnel, water, electricity with intermittent surges and/or outages, limited climate control, dust, and medical staff onsite.	
4	**Target User**	Trained laboratory personnel (e.g., 1-2 year certificates)	
5	**Target Population**	Adults to children >5 months of age, including immunocompromised individuals	Same, plus neonates (including premature infants) up to 6 months of age
	Instrument		
6	**Instrument Design**	Single integrated instrument with port(s) capable of interfacing with one or more cartridge designs for detection of antimicrobial susceptibility of prioritized bacterial pathogens to achieve the intended use.	
7	**Size**	Small, table-top instrument (50 cm x 75 cm by 50 cm, or smaller)	
8	**Weight**	≤ 25 kg	≤ 10 kg
9	**Power Requirements**	Local 110-220 AC mains power, plus uninterruptable	Same, with rechargeable battery back-up (8-hour operation);

http://www.who.int/news-room/detail/15-05-2018-first-ever-who-list-of-essential-diagnostic-tests-to-improve-diagnosis-and-treatment-outcomes

Antibiotics in Development 2018



https://www.pewtrusts.org/en/research-and-analysis/data-visualizations/2019/five-year-analysis-shows-continued-deficiencies-in-antibiotic-development



BEAM Alliance

https://beam-alliance.eu/pipeline/

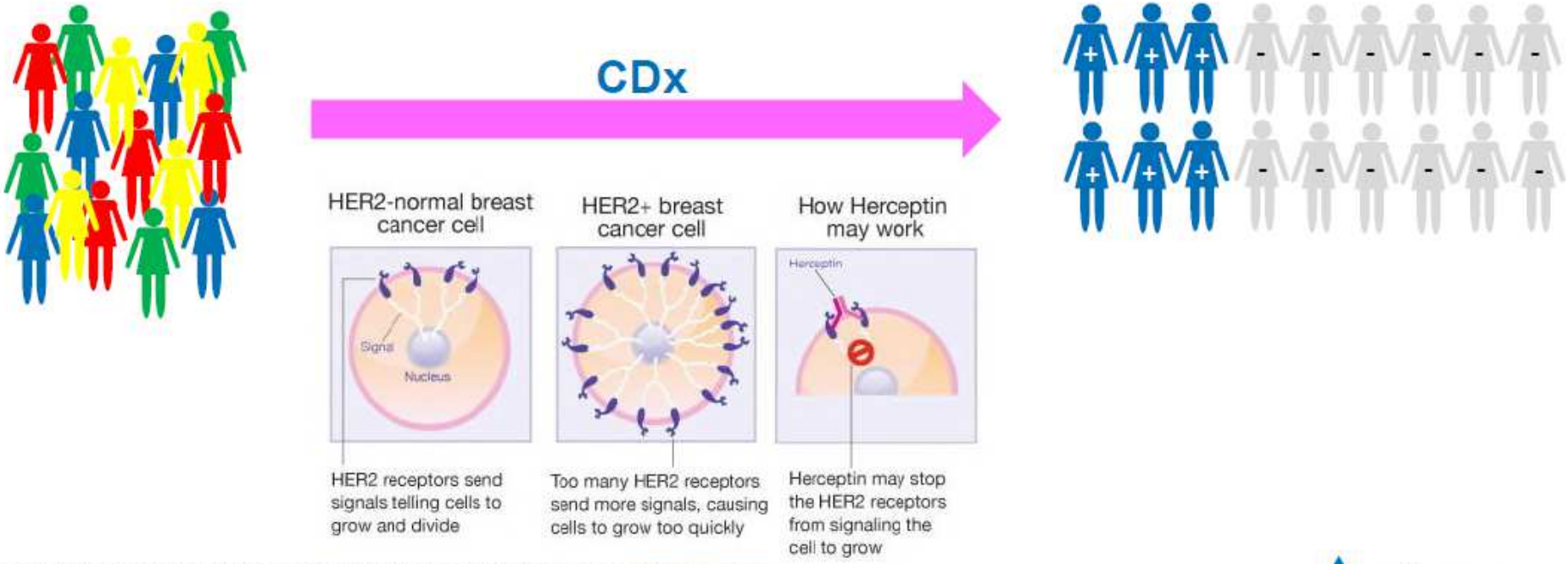
Companion Diagnostics

A companion diagnostic is a diagnostic test (Dx) which helps a therapeutic (Rx) product to meet their labelled safety and effectiveness claim

Companion Diagnostics/IVD's

What is a Companion Diagnostic (CDx) ?

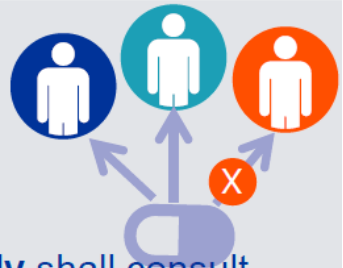
First simultaneous FDA-approval of CDx (HER2 Assay) and Rx (Herceptin) 1998 in the US by Roche.



TÜVRheinland®
Precisely Right.

Companion Diagnostics: New EU definition

EUROPEAN MEDICINES AGENCY



Art. 2(7) IVDR

"(7) 'companion diagnostic' means a device which is **essential for the safe and effective use** of corresponding medicinal product to:

(a) **identify**, before and/or during treatment, **patients** who are most likely to **benefit from the corresponding medicinal product**, or

(b) **identify**, before and/or during treatment, **patients** likely to **be at increased risk of serious adverse reactions** as a result of treatment with the corresponding medicinal product."

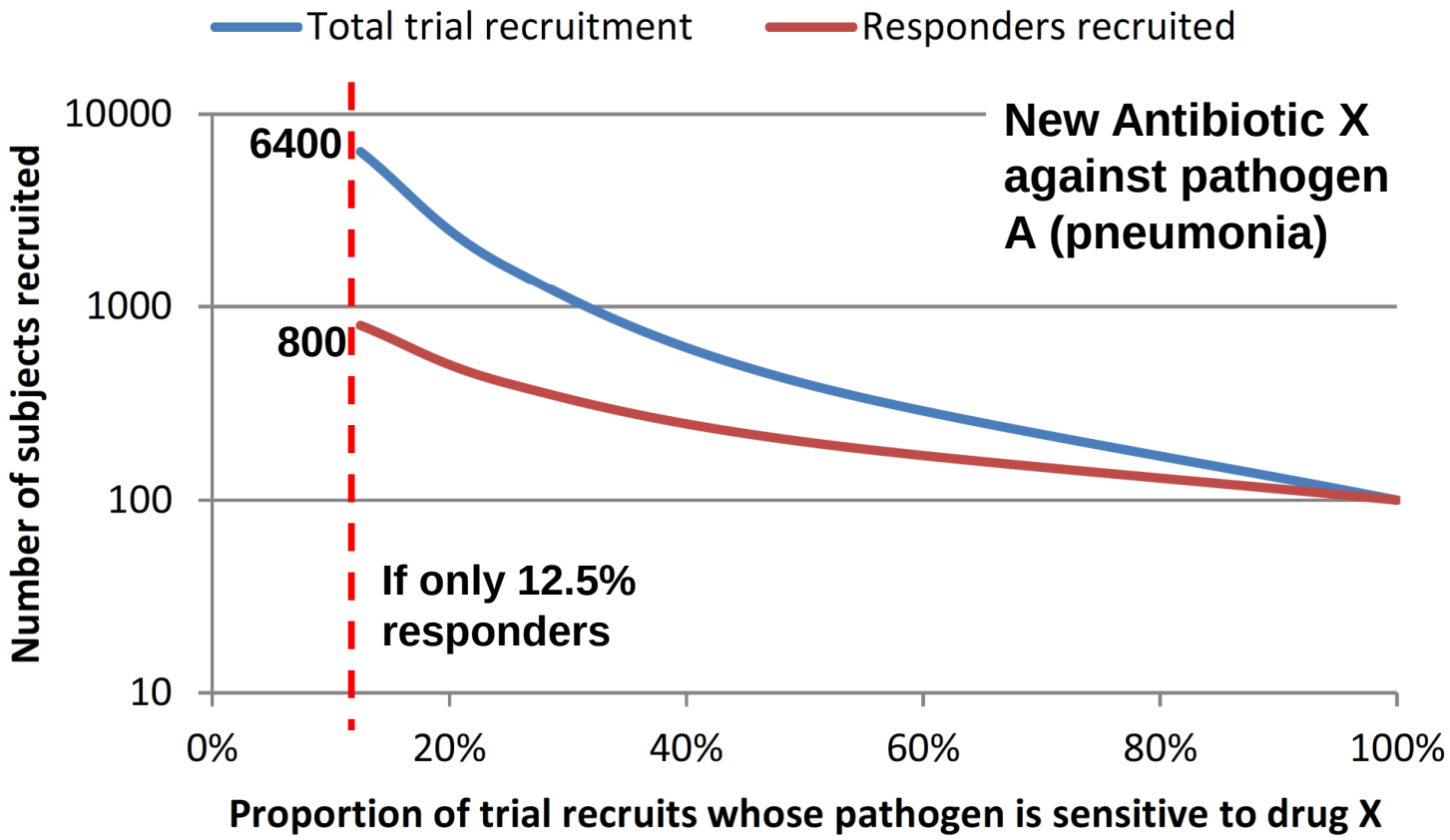
IVDR Article 48(3)

For **companion diagnostics** the **notified body** shall consult the concerned **competent authority** designated in accordance with Directive 2001/83/EC or the European Medicines Agency (**EMA**), as applicable

ANNEX IX, Chapter II - 5.2.

The **notified body** shall, before issuing an **EU technical documentation assessment certificate** for the companion diagnostic and on the basis of the **draft summary of safety and performance** […] consult one of the competent authorities […] regarding the suitability of the device in relation to the medicinal product concerned.

Enriching the Clinical Trial Sample for Likely Responders Reduces Trial Size



Independent review on anti-microbial resistance; regulation-innovation interactions and the development of Antimicrobial drugs and diagnostics for human and animal diseases main report Joyce Tait, Ann Bruce, James Mittra, John Purves and Jack Scannell, Innogen Institute 2014

January 13, 2016

Cepheid Announces Diagnostic Collaboration With MedImmune And COMBACTE To Facilitate Clinical Trials Of New Monoclonal Antibodies To Prevent Serious Infectious Diseases

GeneXpert Systems and Xpert Tests Expected to Enhance Efficiency of Clinical Trials

SUNNYVALE, Calif., Jan. 13, 2016 /PRNewswire/ --Â Cepheid (Nasdaq: CPHD) today announced a collaboration with MedImmune, the global biologics research and development arm of AstraZeneca, and COMBACTE, a European public/private partnership set up to promote the development of new drugs in the anti-infectives field, to develop a series of rapid diagnostic tests to identify *Staphylococcus aureus* (*S. aureus*) and *Pseudomonas aeruginosa* (*P. aeruginosa*) in respiratory secretions of mechanically ventilated patients.Â These tests will be used to help identify patients for MedImmune's MEDI4893 and MEDI3902 clinical programs, which are being conducted within the COMBACTE consortium to explore the use of biologics in preventing ventilator associated pneumonia (VAP) infections in intensive-care-unit (ICU) patients.

MEDI4893 is a novel monoclonal antibody that targets alpha toxin produced by *S. aureus* and is currently being investigated by MedImmune and COMBACTE for the prevention of nosocomial pneumonia caused by *S. aureus*.Â MEDI3902 is a bispecific antibody under investigation for the prevention of nosocomial pneumonia caused by *P. aeruginosa*, a highly drug-resistant bacterium.Â Â The Xpert® tests are expected to help identify patients colonized with *S. aureus* or *P. aeruginosa* before they have clinical signs of pneumonia, so that these patients can be enrolled in the respective MEDI4893 or MEDI3902 clinical trials.

"Utilizing rapid diagnostics is a key component in effectively targeting serious healthcare-associated pathogens in our MEDI4893 and MEDI3902 clinical trials," said Steve Projan, head of Infectious Diseases and Vaccines, Innovative Medicines unit at MedImmune.Â "We believe that the combination of rapid diagnostics and pathogen-specific antibodies will help physicians identify patients at risk and prevent serious and life-threatening infections in a way that is not possible today.Â By developing diagnostic tests through this collaboration with Cepheid, we can ensure that novel life-saving antibodies are delivered to patients who need them in a rapid and efficient manner."

As part of the collaboration, Cepheid has adapted its existing Xpert MRSA/SA skin and soft tissue infection (SSTI) test cartridge for use in respiratory sample types for detection of patients with respiratory colonization with *S. aureus* and MRSA.

Entasis Therapeutics Receives Positive Feedback from FDA End-of-Phase 2 Meeting for ETX2514SUL; Signs Rapid Diagnostic Agreement with bioMérieux

Entasis to incorporate BIOFIRE® FILMARRAY® System, a rapid molecular diagnostic platform, into ETX2514SUL Phase 3 clinical trial, on track to initiate in 1Q 2019

February 05, 2019 08:00 ET | **Source:** Entasis Therapeutics Holdings Inc.

WALTHAM, Mass., Feb. 05, 2019 (GLOBE NEWSWIRE) -- Entasis Therapeutics Holdings Inc. (NASDAQ: ETTX), a clinical-stage biopharmaceutical company focused on the discovery and development of novel antibacterial products, today announced a successful End-of-Phase 2 meeting with the U.S. Food and Drug Administration (FDA) regarding ETX2514SUL for the treatment of patients with pneumonia and bloodstream infections caused by carbapenem-resistant *Acinetobacter baumannii*. A Gram-negative bacterium causing severe infections, *A. baummanii* is associated with high mortality, rapidly-increasing rates of antibiotic resistance, growing significance as a hospital-acquired infection, and limited treatment options. Following this meeting, Entasis remains on track to initiate its Phase 3 clinical trial for ETX2514SUL in the first quarter of 2019.

Further, Entasis announced an agreement with bioMérieux, a world leader in the field of *in vitro* diagnostics, pursuant to which Entasis will incorporate BIOFIRE® FILMARRAY® Instruments and BIOFIRE® FILMARRAY® Pneumonia Panels into its global Phase 3 trial for ETX2514SUL for enrollment optimization. The BIOFIRE System is an FDA-cleared and CE-marked multiplex PCR system that integrates sample preparation, amplification, and detection into one closed system. The BIOFIRE System requires only two minutes of hands-on time and has a total run time of approximately 45 to 75 minutes, depending on the panel. The BIOFIRE Pneumonia Panel and the BIOFIRE® FILMARRAY® Pneumonia Panel *plus* received FDA clearance and CE-Marking in November 2018. The BIOFIRE Pneumonia Panels enable fast, accurate, and comprehensive syndromic testing for lower respiratory tract infections and can identify 33 targets, including *A. baumannii*, direct from sputum (including endotracheal aspirate) and bronchoalveolar lavage (including mini-BAL) sample types.

"We are extremely pleased with the outcome of our End-of-Phase 2 meeting with the FDA and excited to incorporate the BIOFIRE System into our Phase 3 clinical trial," said Robin Isaacs, Chief Medical Officer, Entasis Therapeutics. "With our successful

FIND AND UK GOVERNMENT SPEARHEAD NEW DIAGNOSTICS INITIATIVES TO FIGHT ANTIMICROBIAL RESISTANCE; FIND LAUNCHES DIAGNOSTICS USE ACCELERATOR

Nov 2018

Drug-resistant gonorrhoea is an urgent public health issue;[1] new gonorrhoea antibiotics are in development, but they will require stewardship to ensure their efficacy is preserved as long as possible. FIND will facilitate the development and rapid feasibility assessment of high-priority companion diagnostics needed to support delivery and roll out of these new drugs, particularly through the differentiation of gonorrhoea and chlamydia infections.

Target product profile for a rapid, low-cost diagnostic to distinguish gonorrhoea from Chlamydia infection at primary care		
Characteristic	**Minimal**	**Optimal**
SCOPE		
1. Intended use	To detect Neisseria gonorrhoea (NG) only or NG and Chlamydia trachomatis (CT) infection to improve syndromic patient management and to facilitate appropriate antibiotic use	Same as minimum plus to assist in screening to identify previously undetected NG or NG and CT infections to support public health management
2. Target use setting	Primary health care settings including health posts (Level 1[1]); to be used after initial clinical evaluation (referring to Step 2 in the WHO Vaginal/Urethral Discharge Flowchart[2]) to guide treatment decision	
3. Test format / Equipment	A non-instrumented, single use, disposable diagnostic test preferred; Ideally no additional power required for operation, but if required, battery power with 8-hour operation between charges. Reader optional and only appropriate if its inclusion supports enhanced test performance (see Appendix 1 for reader requirements)	
4. Target users	The target users include community health workers with minimal training and any health worker with a similar or superior training level	
5. Target analytes	Identification of NG or NG and CT	Same as minimal, plus detection additional sexually transmitted infections (e.g. Mycoplasma and trichomonas) ideal

SpeeDx, QuantuMDx Collaborate with FIND on POC Molecular Diagnostics for STIs

Nov 07, 2019 | staff reporter

Axxin, DCN Dx

Save for later

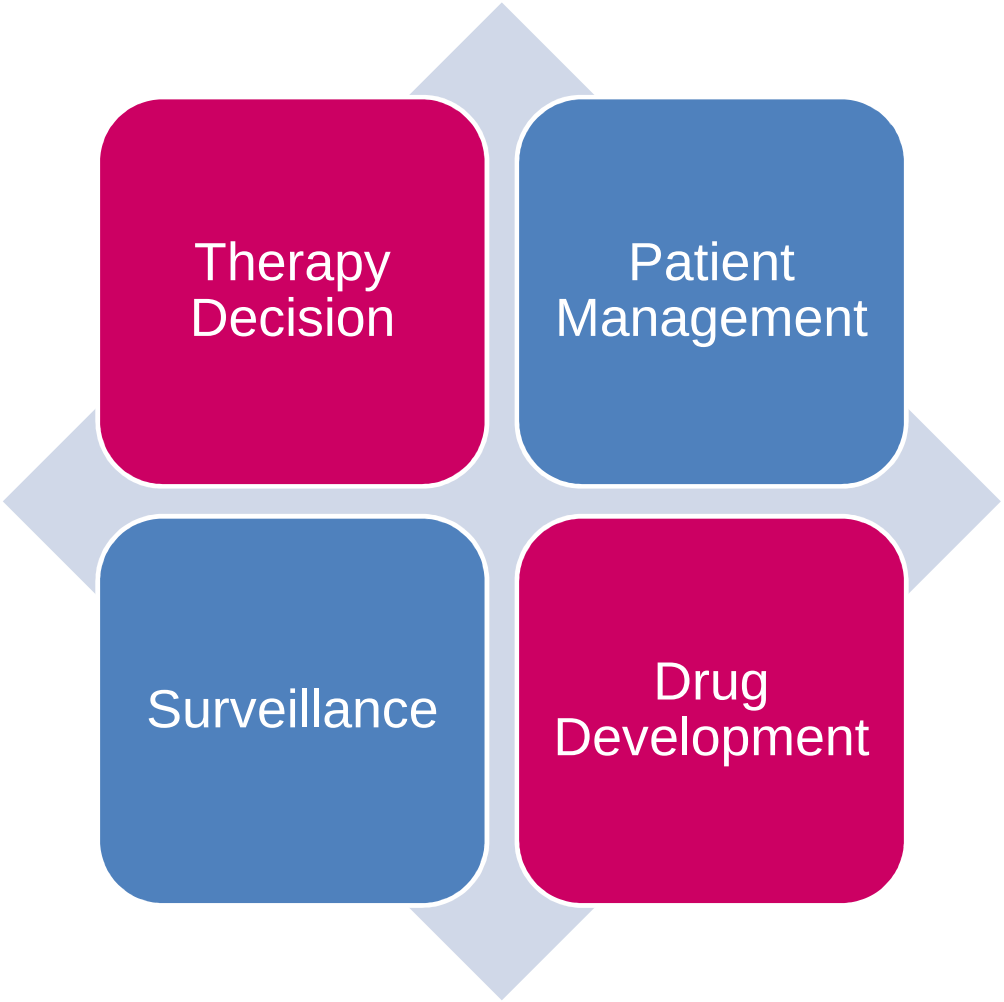
NEW YORK – SpeeDx and QuantuMDx on Thursday announced a collaboration with the Foundation for Innovative New Diagnostics (FIND) to assess the feasibility of porting SpeeDx sexually transmitted infection tests to the QuantuMDx point-of-care testing device.

FIND is funding the project with an undisclosed amount.

Specifically, SpeeDx will use its proprietary PlexPCR technology to develop multiplex tests for common STIs, including gonorrhea and *Mycoplasma genitalium*, to be run on the QuantuMDx Q-POC device.

https://www.finddx.org/amr/companion-dx-gono/

Rapid Diagnostics targeting AMR



Drug Diagnostics Partnering
A Chance to Tackle AMR?