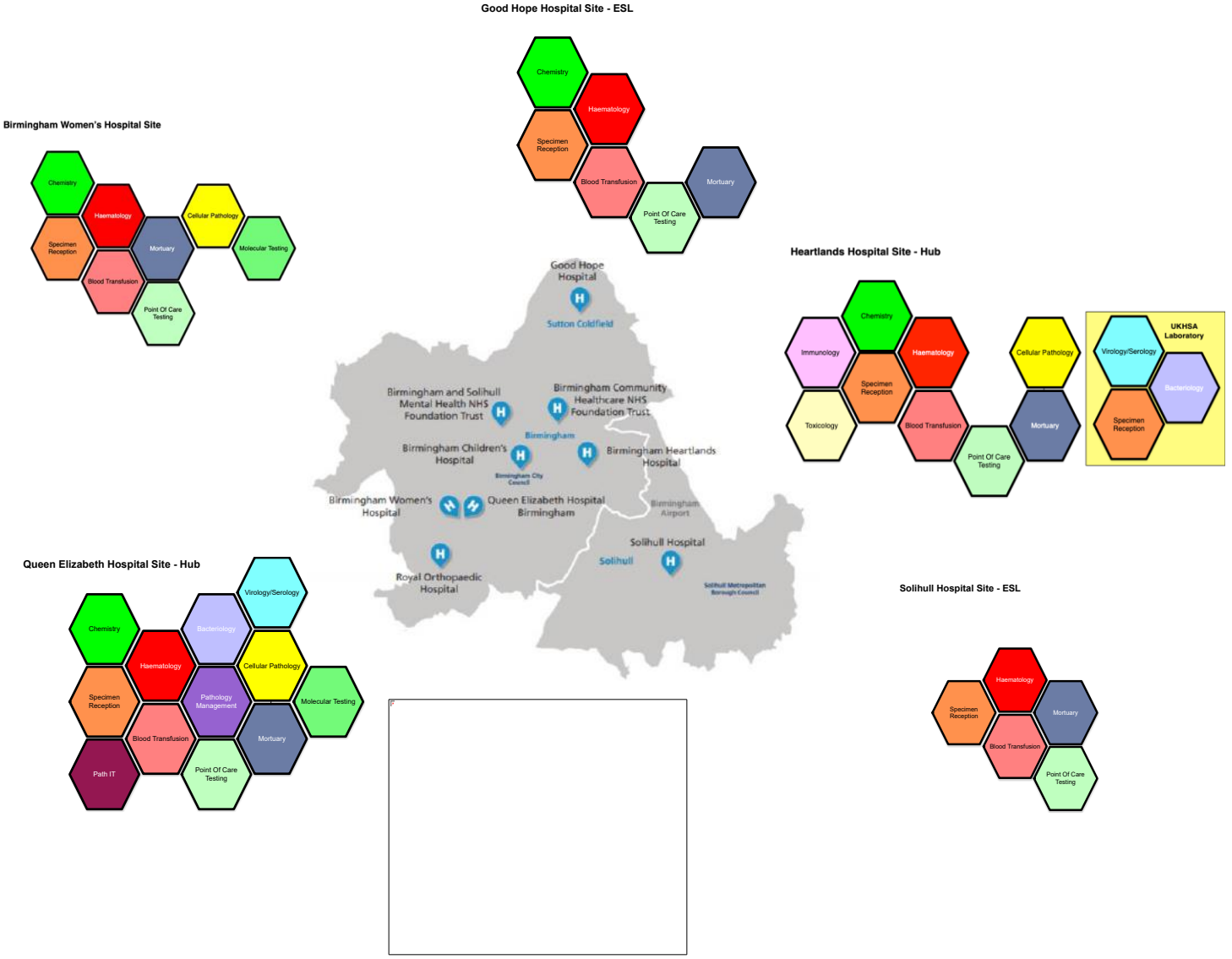
Challenges in Diagnostic Development and Translation

A View from NHS Laboratory Diagnostics

Pathology

Fig 1: Current Situation



Pathology

- Cellular Pathology – bits of people – not industrialised
- Microbiology/Virology – bits of bugs and viruses – semi-industrialised
- Biochemisty – everything is ultimately biochemistry - industrialised
- Haematology – blood cells and maths – industrialised
- RCPath – 18 Specialities

The Backbone of Clinical Decision-Making

- 70%+ of clinical decisions rely on lab diagnostics
- 1.1 billion tests performed annually across NHS labs
- Core to screening, prevention, acute & chronic care

The Scale

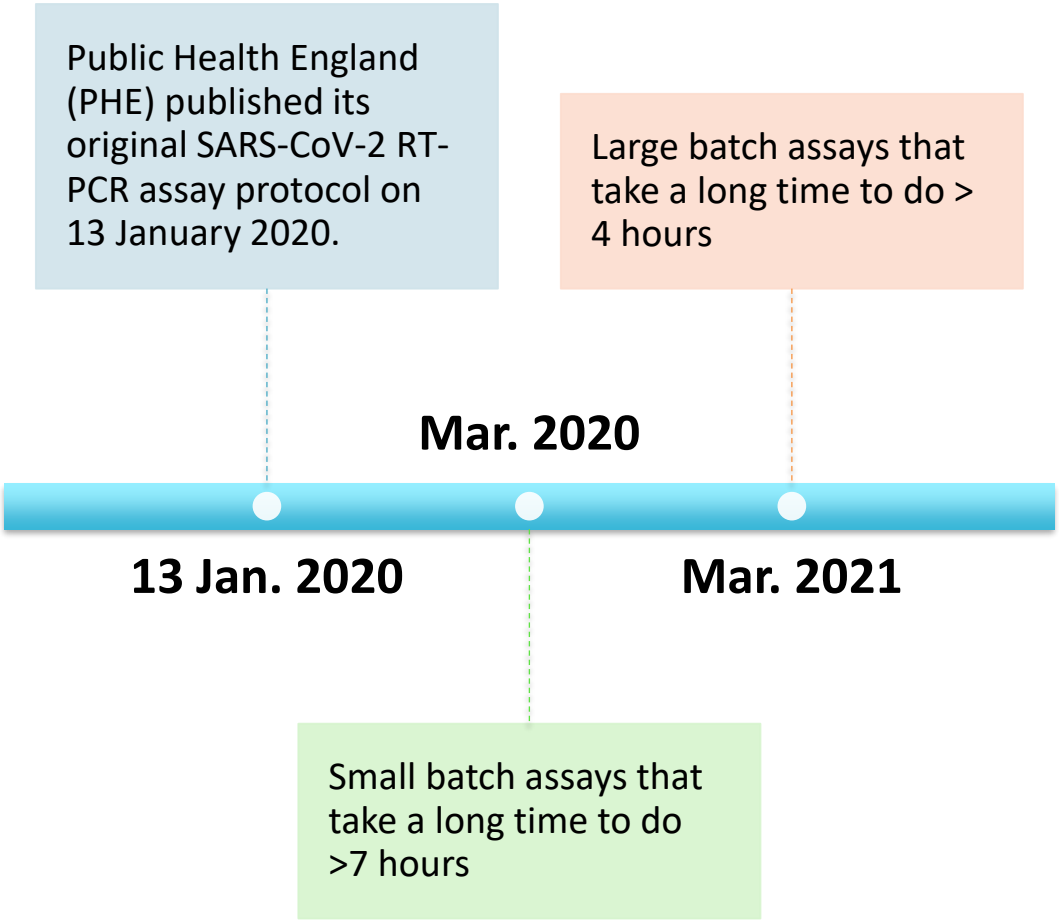
SPECIALTY	TOTAL TESTS/REQUESTS
Clinical Biochemistry	27,347,297
Haematology & Blood Bank	3,215,149
Microbiology	918,934
Immunology	329,757
Histopathology & Cytology (combined)	94,921
Total	**31,905,058**

Where Innovation Stalls

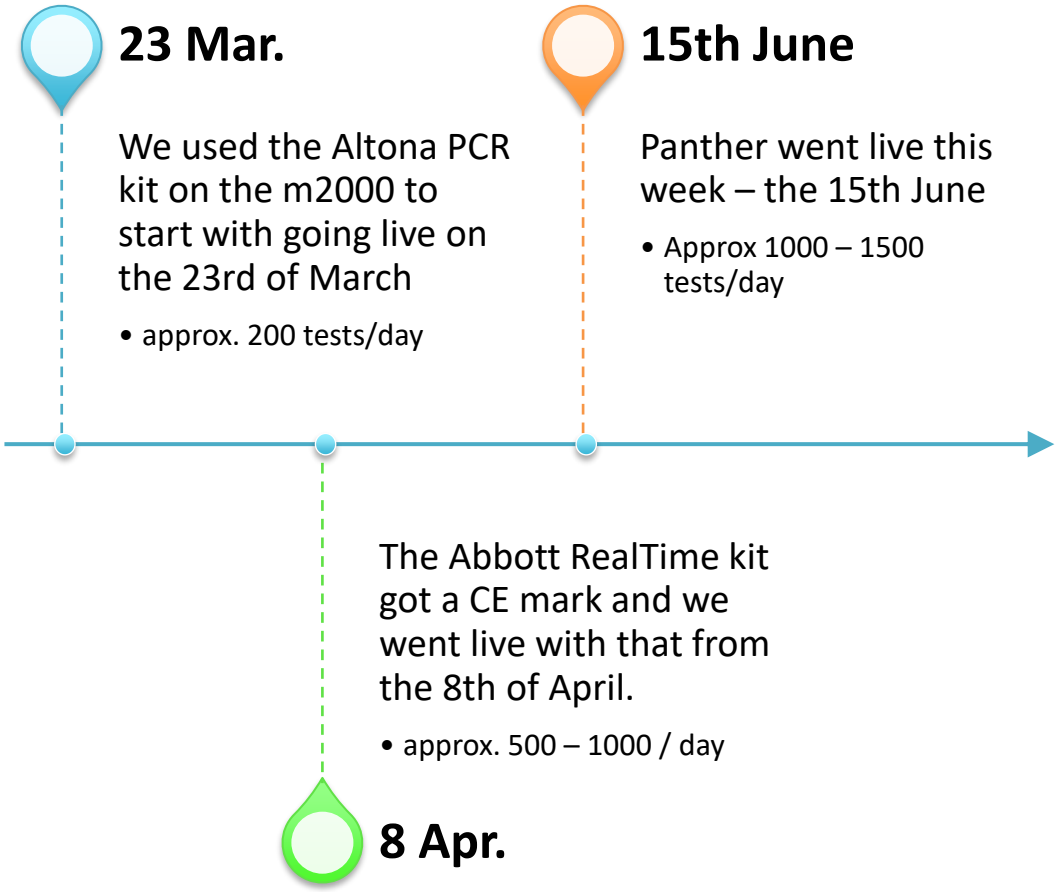
- Research & Discovery → Prototype → Evaluation → Commissioning
- Attrition points: cost-effectiveness, digital integration, clinical validation


Hood C
Hood B

Industrializing Sars-Cov-2 Testing



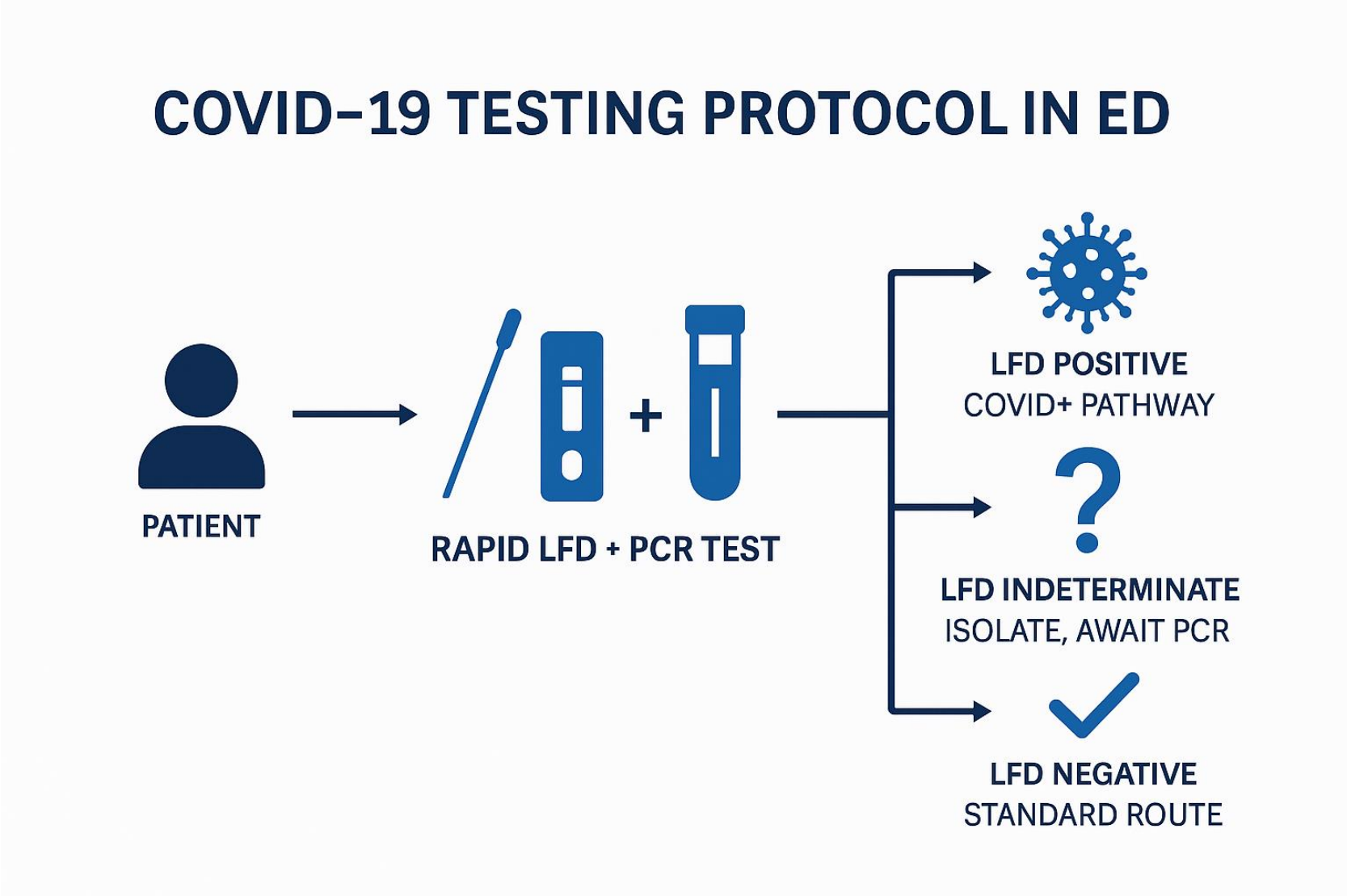
Pre-analytical Phase



Altona Diagnostics SARS-CoV-2 PCR Kit – Timeline Summary

Date	Event
10 Jan 2020	SARS-CoV-2 genome published (Wuhan-Hu-1 sequence via GISAID)
13 Jan 2020	WHO shares first PCR protocols (including PHE/Charité Berlin methods)
27 Jan 2020	**Altona begins in-house development** of a SARS-CoV-2 RT-PCR assay
7 Feb 2020	Prototype assay released to selected reference labs for internal testing
24 Feb 2020	**CE-IVD mark granted** for "RealStar® SARS-CoV-2 RT-PCR Kit 1.0"
March 2020	Commercial rollout across Europe, including NHS labs
Apr–Jun 2020	Kit validated by national reference labs (e.g. PHE Porton Down)

real-time RT-PCR – the ‘easy’ bit



Building Blocks of Service

- Right test
- Right time
- Right patient
- Right results
- In Time

Health + Add to myFT

Regulation and 'poor alignment' are stymying health innovation, says report

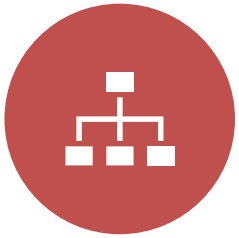
Author recommends breaking 'siloed' work practices to spur life sciences sector and improve care

Digital therapeutics, AI-driven diagnostics and genomic medicine had the potential to radically evolve NHS care, the report noted © Rui Vieira/PA

Laura Hughes in London

Published NOV 28 2024

Regulation Requirements



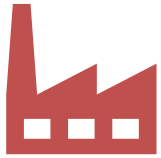
IVD DEFINITION AND CLASSIFICATION (HTTPS://ASSETS.PUBLISHING.SERVICE.GOV.UK/MEDIA/67863A313EF063B15DCA0F47/GUIDANCE_ON_THE_REGULATION_OF_IVD_MEDICAL_DEVICES_IN_GB.PDF)

CONFORMITY ASSESSMENT AND UKCA MARKING (CE MARKING)

MUST HAVE ROBUST POST MARKET SURVEILLANCE SYSTEMS AND REPORT SERIOUS INCIDENTS OR DEVICE DEFICIENCIES TO MHRA

ISO 15189 ACCREDITATION

2.7 Exemption for health institutions (commonly referred to as in-house manufacturing)



"Regulation 33 excludes from its scope devices 'manufactured and used only within the same health institution and on the premises of their manufacture or used on premises in the immediate vicinity without having been transferred to another legal entity.'"

"If the device is transferred to another legal entity, you will be considered a manufacturer, and the full regulations will Apply"

Capacity for Innovation

BAND 5 STAFF MAKE UP 60%+ OF DIAGNOSTIC TEAMS

SAMPLE-TO-RESULT DELAYS FROM STAFFING AND CAPACITY

INCREASING DEMAND

What Happens When Diagnostics Fail

VANITY FAIR

POLITICS HOLLYWOOD ROYALS STYLE CULTURE

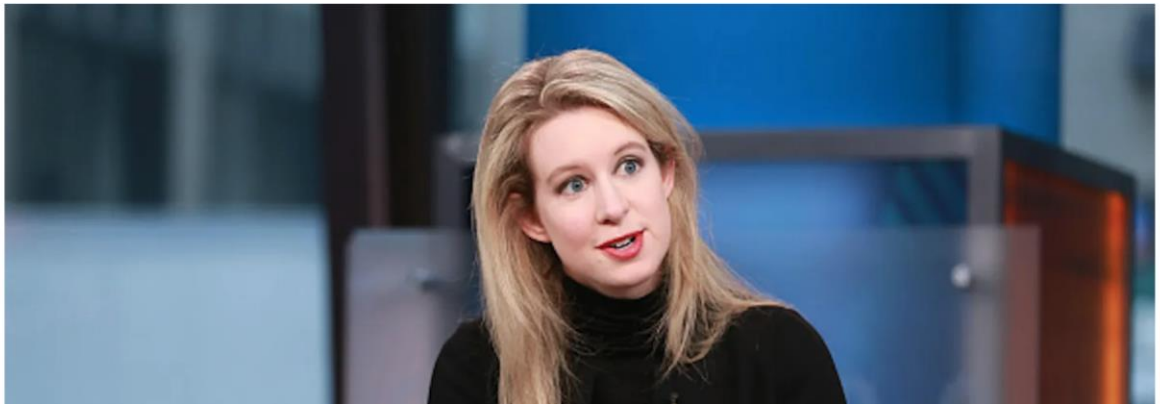
BLOOD UNICORN

Theranos Faces Yet Another Devastating Setback

The company is revising "tens of thousands" of inaccurate blood-test results.

BY MAYA KOSOFF

MAY 19, 2016



In April **2009**, Quest and NID agreed to pay **$302 million** to resolve both criminal and civil charges filed by the U.S. Department of Justice.
$40 million was a criminal fine for plea on a felony misbranding charge related to the PTH (parathyroid hormone) assay.
$262 million addressed False Claims Act allegations involving several assays, including the 25-OH-D (vitamin D) test, due to **inaccurate and unreliable results** between April 2002 and April 2006

THE UNITED STATES ATTORNEY'S OFFICE
EASTERN DISTRICT of NEW YORK
ARCHIVE

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NEWS

Quest Diagnostics Incorporated to Pay $302 Million to Resolve Allegations That a Subsidiary Sold Misbranded Test Kits

FOR IMMEDIATE RELEASE April 15, 2009

Quest Subsidiary, Nichols Institute Diagnostics, Pleads Guilty to Felony Misbranding

Quest Diagnostics Incorporated ("Quest") and its subsidiary, Nichols Institute Diagnostics ("NID"), have entered into a global settlement with the United States to resolve criminal and civil claims concerning various types of diagnostic test kits that NID manufactured, marketed and sold to laboratories throughout the country until 2006. The payment of $302 million will resolve these allegations and represents one of the largest recoveries ever in a case involving a medical device.

As part of the criminal resolution, NID pled guilty this morning before United States District Judge Sterling Johnson, Jr., at the U.S. Courthouse in Brooklyn, to a felony misbranding charge in violation of the Food, Drug, and Cosmetic Act, 21 U.S.C. §§ 301 et seq. The charge relates to NID's Nichols Advantage Chemiluminescence Intact Parathyroid Hormone Immunoassay (the "Advantage Intact PTH Assay"), a test that was used by laboratories throughout the country to measure parathyroid hormone ("PTH") levels in patients. As part of the plea, NID will pay a criminal fine of $40 million. Quest has also entered into a non-prosecution agreement with the United States under which it will be obligated to continue to cooperate with the government.

Still Sending Faxes in 2025?

LEGACY: EDIFACT, READ CODES

FUTURE: SNOMED CT, FHIR APIS

NPEX: 6M PAPER DOCS ELIMINATED, BUT PATCHY ROLLOUT

Beyond Analytical Validity

MUST PROVE: ACCURACY + COST-EFFECTIVENESS + WORKFLOW IMPACT

'INNOVATION WITHOUT IMPLEMENTATION IS JUST INVENTION.'

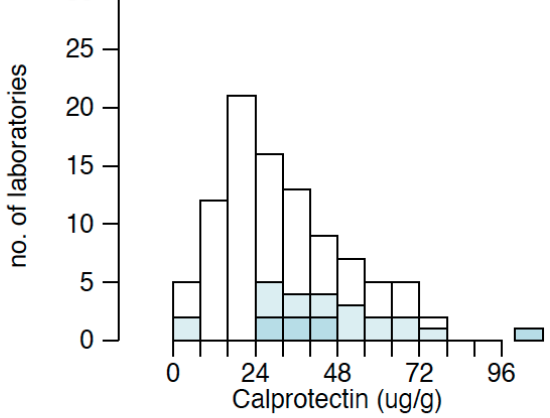
Faecal Calprotectin

- 1990s: Calprotectin identified as a biomarker of intestinal inflammation in research settings (e.g. Røseth et al. 1992, 1997).
- 2000–2001: The first CE-marked commercial ELISA kit released in Europe by Calpro AS.
- 2003–2005: Other companies enter the market:
- BÜHLMANN releases their Calprotectin ELISA and later rapid test formats.
- Phadia (now part of Thermo Fisher) also introduces a calprotectin assay.
- 2013 onward: NICE DG11 (2013) formally evaluates faecal calprotectin for distinguishing IBD vs IBS.

DG11

- Robust evidence is needed on the comparative performance of different faecal calprotectin tests, including the performance of POCTs compared with laboratory-based tests.

All methods [ALTM]	95	32.7	19.2	58.9
ELISA	42	29.1	19.7	67.7
Buhlmann [2BU]	7	50.6	11.3	22.4
Immundiagnostik (K6927) [2IK]	5	47.3	11.0	23.2
Thermo EliA Calpro 2 [2KO2]	22	18.4	9.2	50.1
Immunoturbidimetric	24	45.2	20.4	45.2
Buhlmann fCAL turbo [4BU]	7	38.8	11.6	30.0
Abbott Alinity	1	26.0		
Roche Cobas	3	71.7		
OC Sensor - Pledia [4EK]	12	42.6	17.4	41.0
Immunometric	27	25.4	9.1	35.9
Diasorin CLIA [9IN]	22	24.5	8.2	33.7



(ALTM)

Your Interpretation N
Mode N
Target N

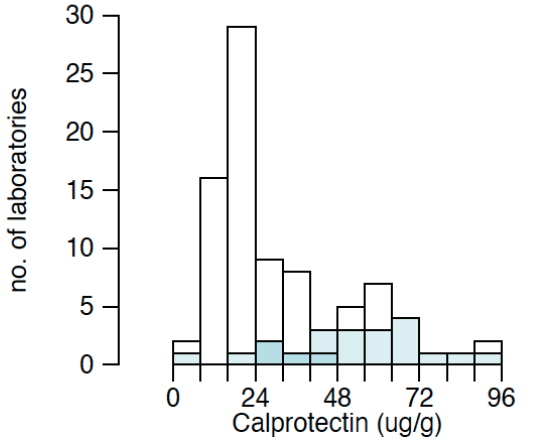
Standard Uncertainty 2.6

Your specimen:
%bias

Method mean 38.8
(Buhlmann fCAL turbo [4BU])

Specimen : 245B

	n	Mean	SD	CV(%)
All methods [ALTM]	86	30.0	21.1	70.3
ELISA	37	24.9	17.2	69.1
Buhlmann [2BU]	5	33.7	4.0	11.9
Thermo EliA Calpro 2 [2KO2]	20	17.5	6.6	37.8
Immunoturbidimetric	21	54.3	22.7	41.8
Buhlmann fCAL turbo [4BU]	4	30.9		
Roche Cobas	1	47.0		
OC Sensor - Pledia [4EK]	12	61.0	15.4	25.2
Immunometric	26	19.2	4.2	21.8
Diasorin CLIA [9IN]	21	18.7	2.4	12.8
Inova QUANTA Flash [9IF]	4	23.6		



Your result <20
Target value
()

Your Interpretation N
Mode N
Target N

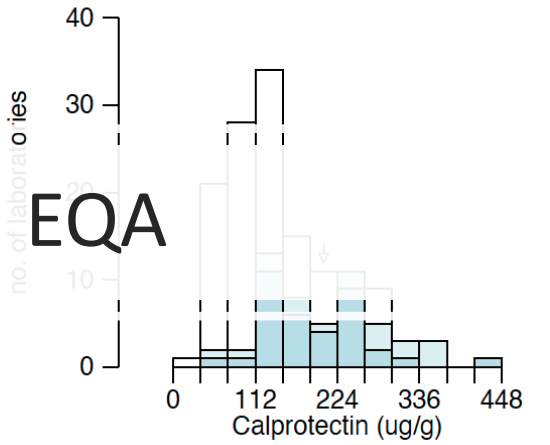
Standard Uncertainty

Your specimen:
%bias

Method mean 30.9
(Buhlmann fCAL turbo [4BU])

Specimen : 245C

	n	Mean	SD	CV(%)
All methods [ALTM]	135	145	78	54.1
ELISA	52	116	57	48.8
Buhlmann [2BU]	11	165	89	54.2
Immundiagnostik (K6927) [2IK]	5	182	29	15.9
Thermo EliA Calpro 2 [2KO2]	23	91.4	38.4	42.1
Immunoturbidimetric	53	202	82	40.3
Buhlmann fCAL turbo [4BU]	36	187	66	35.1
Abbott Alinity	5	176	42	23.8
Roche Cobas	16	190	76	39.7
OC Sensor - Pledia [4EK]	12	233	98	42.2
Immunometric	28	97.4	35.3	36.2
Diasorin CLIA [9IN]	22	94.1	34.2	36.3



EQA

Your result 219
Target value 145
(ALTM)

Your Interpretation P
Mode P
Target

Standard Uncertainty 8.9

Your specimen:
%bias +51.5

Method mean 187
(Buhlmann fCAL turbo [4BU])

Building Bridges, Not Silos

Workforce planning & automation

Pathology networks & digital hubs

Translational pipelines

Evidence frameworks

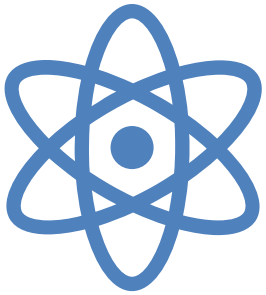
What Each Sector Can Do

ACADEMIA: ALIGN WITH NHS NEEDS, CO-DESIGN

INDUSTRY: EVIDENCE + INTEROPERABILITY FROM DAY 1

NHS LABS: ENABLE PILOTS, STAFF DEVELOPMENT, DIGITAL READINESS

Let’s Make Diagnostics Deliver



Ecosystem: labs, clinicians, patients, innovators

Where can we work together to shorten bench-to-bedside?