APAS® TECHNOLOGY PRESENTED TO PHARMA INDUSTRY LEADERS

Technical presentation completed to subject matter experts from BioPhorum

Adelaide, Australia, 14 September 2022: Australian medical technology company LBT Innovations Limited (ASX: LBT) (**LBT** or the **Company**), a leader in medical technology automation using artificial intelligence, is pleased to announce the presentation of the Company's new APAS® Pharma technology to BioPhorum, a membership organisation including representatives from leading pharmaceutical and biotech companies from around the world.

Key Points:

- **APAS® Pharma presented to industry leaders and subject matter experts from the pharmaceutical industry**
- **Webinar delivered to BioPhorum's Alternative and Rapid Microbiology Methods working group**
- **Performance data from APAS® Pharma presented following successful proof-of-concept**

LBT has presented the Company's new APAS® Pharma technology to industry leaders and subject matter experts from the pharmaceutical industry as part of BioPhorum's Alternative and Rapid Microbiology Methods working group. The working group consists of over 40 members, representing leading pharmaceutical and biotech companies from around the world.

This is the first time the Company has presented broadly to pharma industry partners regarding the APAS® platform being a potential solution to address bottlenecks in Microbial Quality Control (**MQC**) testing. Global regulators require MQC testing to occur in the manufacturing of pharmaceutical products. Current testing methods are performed using manual processes, that require strict data integrity and traceability that lead to potential errors resulting in increasing regulatory oversight.

The new APAS® Pharma growth detection analysis module, utilises the existing APAS® Independence instrument hardware and performance characteristics. The platform remains the only regulatory cleared product for autonomous and automated culture plate reading for clinical applications. Performance data of the new APAS® Pharma analysis module is now released following the successful proof-of-concept project completed with a multinational pharmaceutical company.

LBT CEO and Managing Director, Brent Barnes said:

"Our mission is to bring digital microbiology to all labs. Our platform APAS® technology has the potential to become the gold standard for digital culture plate automation for clinical microbiology. Following recent commercial success, we see a tremendous opportunity for the APAS® platform to be expanded into new verticals. The proof-of-concept data demonstrate the technology works, and we are ideally positioned to work with new partners to help them automate and streamline their current workflows.

I'd like to thank BioPhorum for inviting us to participate in this event."

As LBT expand into this new market segment, the Company will increase its participation in industry events such as these, including attending key industry conferences in the United States in coming months. The Company is also continuing to engage with industry partners on future product development for this new application.

About BioPhorum

A business-to-business membership organization, BioPhorum consists of 10 phorums leading more than 90 industry-changing initiatives with the help of 6,000 active subject matter experts. Established in 2008, BioPhorum brings leaders and subject matter experts together from across the biopharmaceutical and device industry to collaborate on challenges in existing and emerging topics that affect the whole industry including change notification, cybersecurity, extractables and leachables, forecast and demand planning, knowledge management, single-use systems, and sterile filtration.

Approved for release by the Chair of the LBT Board.

– ENDS –

About LBT Innovations

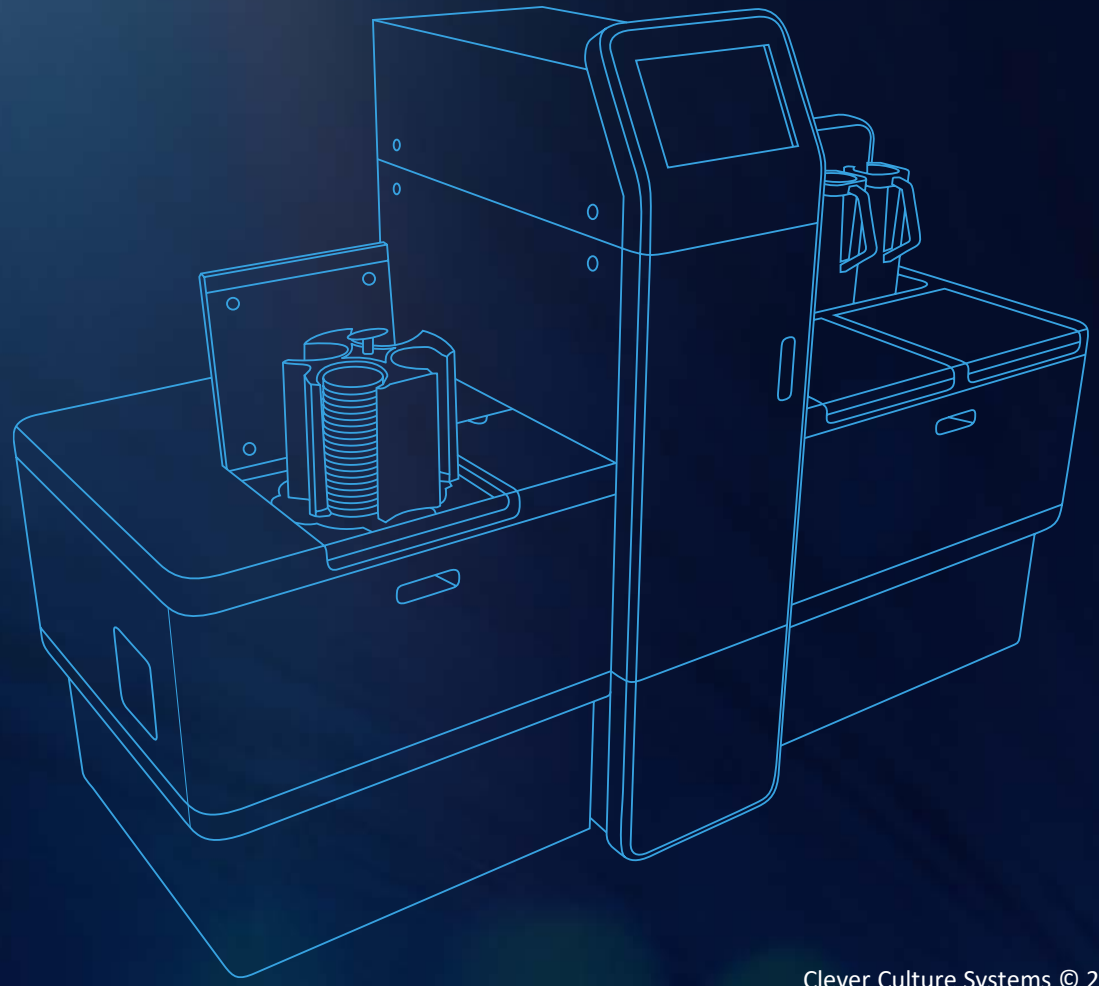
LBT Innovations (LBT) improves patient outcomes by making healthcare more efficient. Based in Adelaide, South Australia, the Company has a history of developing world leading products in microbiology automation. Its first product, MicroStreak®, was a global first in the automation of culture plate specimen processing. The Company's second product, the Automated Plate Assessment System (APAS® Independence) uses LBT's intelligent imaging and machine learning software to automate the imaging, analysis and interpretation of culture plates following incubation. The technology remains the only US FDA-cleared artificial intelligence technology for automated culture plate reading and is being commercialised through LBT's wholly owned subsidiary Clever Culture Systems AG (CCS). Channel partners for the sale and distribution of the APAS® Independence are in place for the United States (Thermo Fisher Scientific, Inc; Exclusive Distributor) and selected countries in Europe (Beckman Coulter, Inc; Marketing Agent).

INVESTOR ENQUIRIES

LBT Innovations
Brent Barnes Chief Executive Officer & Managing Director Tel: +61 8 8227 1555 E: info@lbtinnovations.com

APAS INDEPENDENCE

Automated microbiology culture plate reading – Realising the potential of AI
BioPhorum Presentation



Clever Culture Systems
September 2022

CLEVER CULTURE SYSTEMS

LBT INNOVATIONS

Clever Culture Systems

APAS INDEPENDENCE

Intelligent imaging and machine learning systems for microbiology culture plate reading

Rhys Hill
Research Director &
APAS Inventor

Steven Giglio
Scientific Director

Jack Brown
Corporate Development
Director

CLEVER CULTURE SYSTEMS

LBT INNOVATIONS

APAS INDEPENDENCE

Automation for industrial microbiology

CLEVER CULTURE SYSTEMS

LBT INNOVATIONS

Culture plate reading - What is the problem?

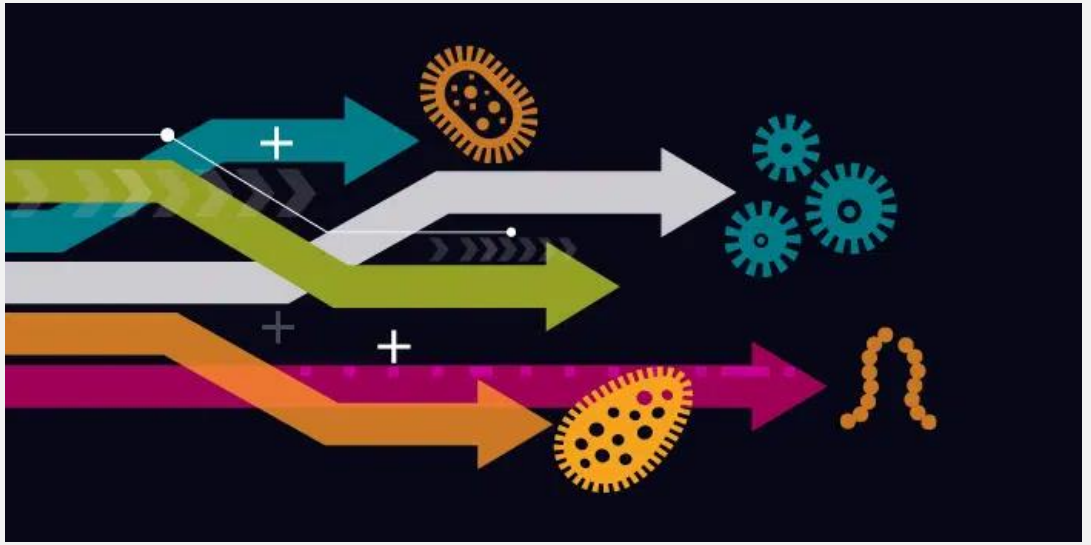
Traditional methods reliability *"has always been limited by the abilities of the human observer and data recorder"*[1]

Benefits of modern microbial methods

- Improved data integrity through automation
  - Eliminates subjectivity of analyst evaluation
  - Direct integration into LIMS
- Cost and time savings
  - Removes secondary plate reading
  - Reduces hands on time for plate reading

Considerations

- Understand technology limitations
- Assess process risks



1. A Systematic Approach for the Evaluation, Validation and Implementation of Automated Colony Counting Systems. Sven Deutschmann, Bill Carpenter, Caroline Duignan, et al. PDA Journal of Pharmaceutical Science and Technology March 2022

Introducing APAS® Independence

High-throughput system (200 plates/hr), automatically reads and reports plates showing no microbial growth

Cutting edge AI technology
Consistent – reads the plate the same every time

Easy Integration
Simple plug and play technology

Demonstrated Performance
Higher quality and consistency of results

Affordable Automation
Multiple hardware solutions, suitable for any lab

Improved Data Integrity
Data trails and audit reports available

Workflow driven automation

APAS INDEPENDENCE

Ensures quality and data integrity of the culture plate reading workflow

Minimal change to existing process

– Automated validation of no growth plates; Review required for plates with growth

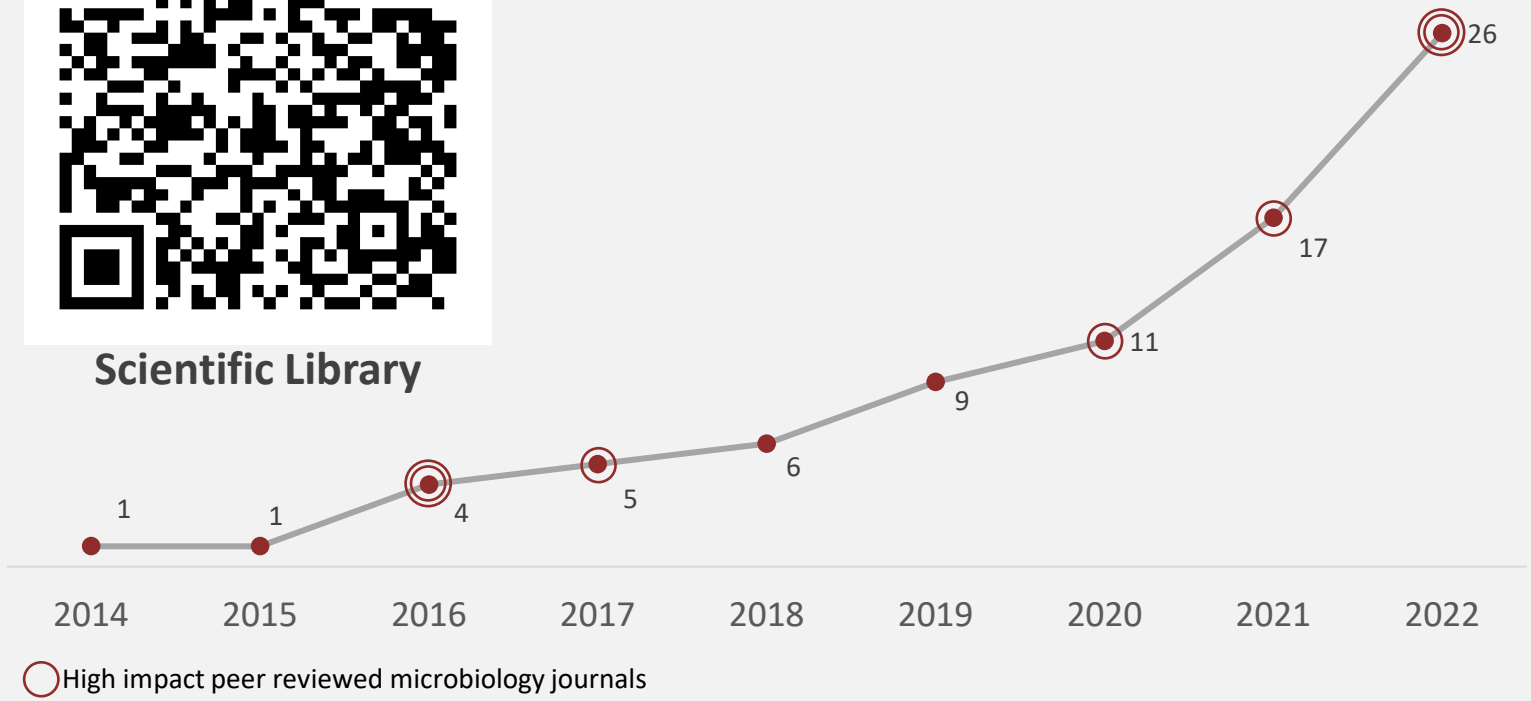
– Performance demonstrated in successful proof-of-concept with pharmaceutical partner

Peer-Reviewed Performance

APAS INDEPENDENCE

Validated in >25 clinical publications and evaluations

Scientific Library



Regulatory cleared for clinical applications

FDA CLEARED

CE

UKCA

Australian Government
Department of Health
Therapeutic Goods Administration

APAS INDEPENDENCE

Artificial Intelligence - Theory

CLEVER CULTURE SYSTEMS

LBT INNOVATIONS

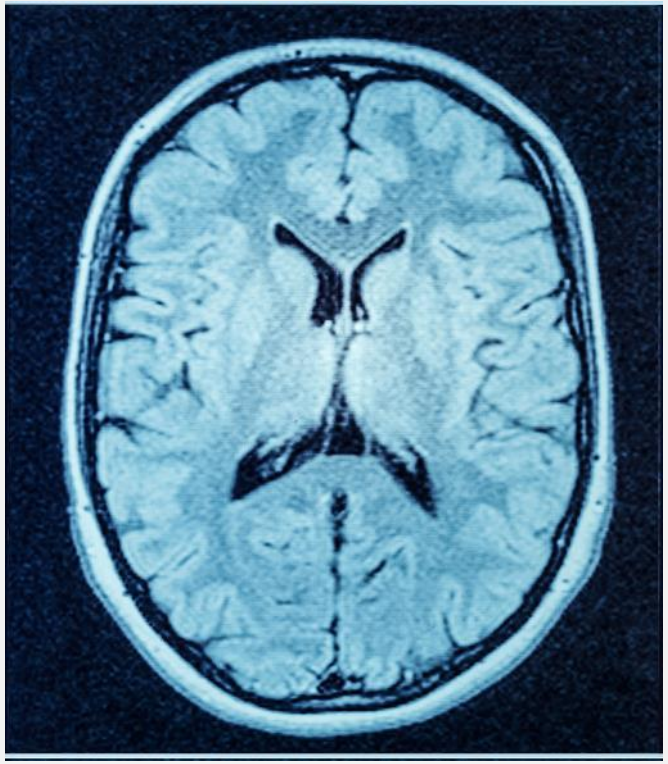
What is Artificial Intelligence?

APAS INDEPENDENCE

- Artificial Intelligence (AI) is a field of computer science and psychology
  - Intended to replicate human intelligence in a machine
  - Field began properly in the 1950s
  - Some early wins - Chess
  - Turns out humans are very capable

- Has always been a strong link between AI and biology
  - Strong influence from psychology and neuroscience in AI research
  - Neural networks mimic brain structure in software
  - Brain is very complex – ~100 billion neurons
  - No one really know how neurons work

- For visual processing, the eye itself appears significant



Limitations

APAS INDEPENDENCE

AI is currently not actually intelligent!!

- AI does not provide original thoughts, cannot be creative
- Machine Learning (ML) is a way to achieve AI
  - AI viewed to be too hard to program explicitly
- ML is mostly a giant statistical framework
  - Intended to replicate an existing complicated decision-making process
  - Various ML models just have increasingly complex ways of doing this
- Any apparent intelligence comes from the input data or from the programmers
- Importantly, software created via ML is repeatable, but not necessarily predictable
- For many problems it can be a huge time-saver, so…

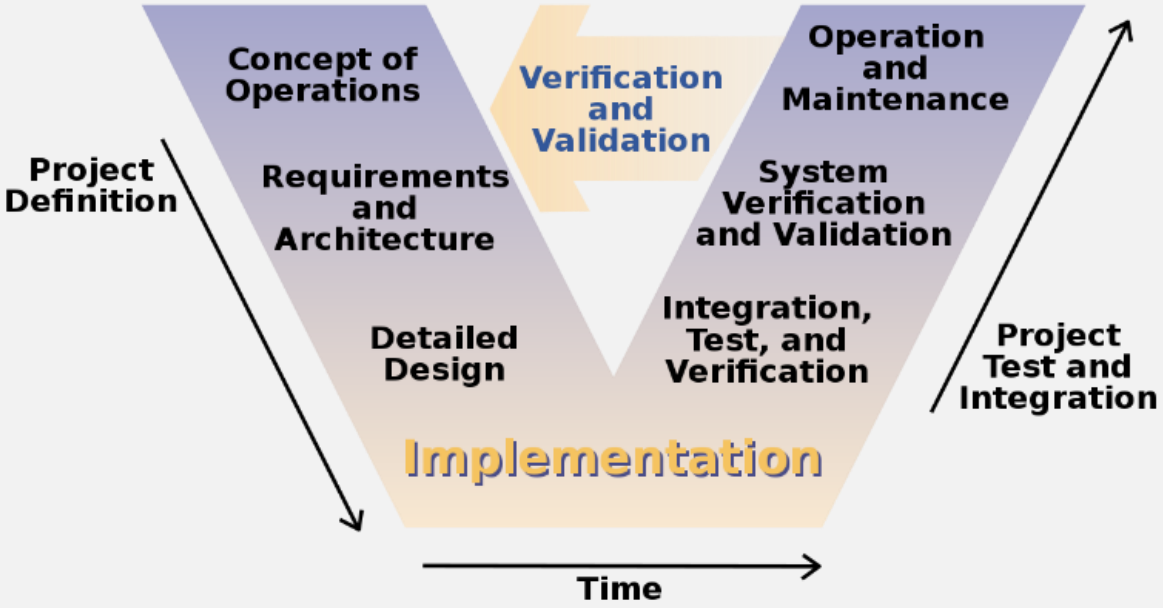
2001 Space Odyssey: HAL Sentient Supercomputer

Verification and Validation

APAS INDEPENDENCE

The best way to know if an AI system works is to test it

- If an AI systems works on one image, it may not work on another similar one
  - Need to test with very large datasets for statistical rigour
- Regulators have a view on what should be tested
- Since the system can't be understood, hard to make short-cuts
  - Traditional image analysis can make some assumptions
  - Can be used to narrow testing scope
- Important to define the true scope of the problem
  - Different organisms
  - Different media
  - Possible contaminants
  - Sources of interference



Quality by Design

APAS INDEPENDENCE

Ensuring Robustness: Limit external influences and check every image

Uniform lighting

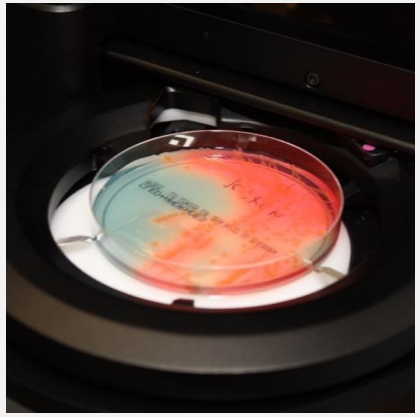
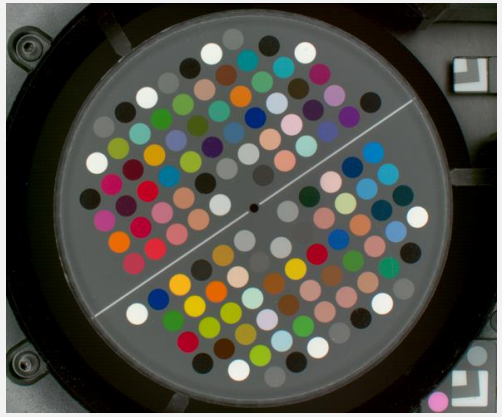
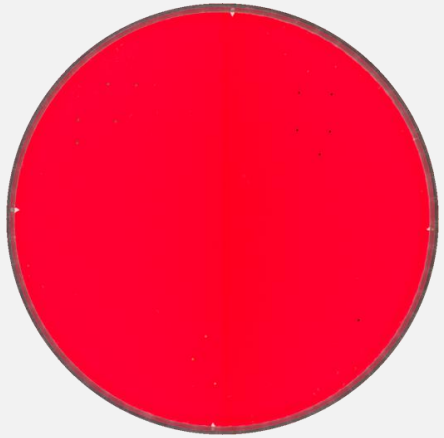


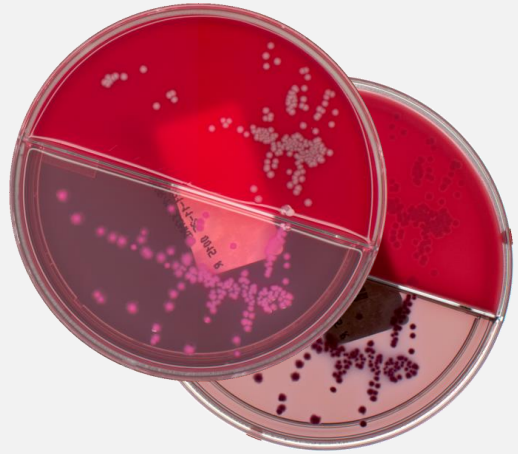
Plate handling to minimise interference



Daily and per image colour check



System check

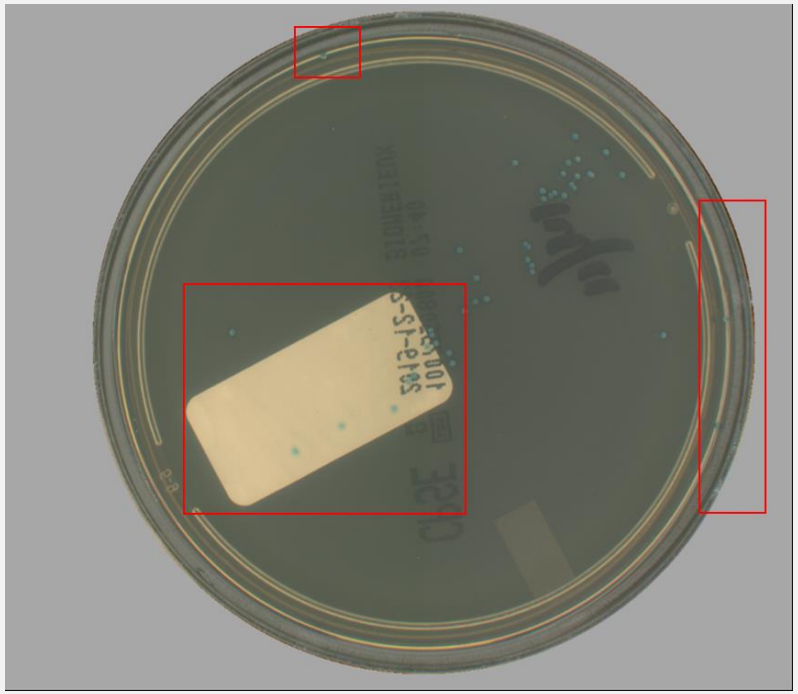


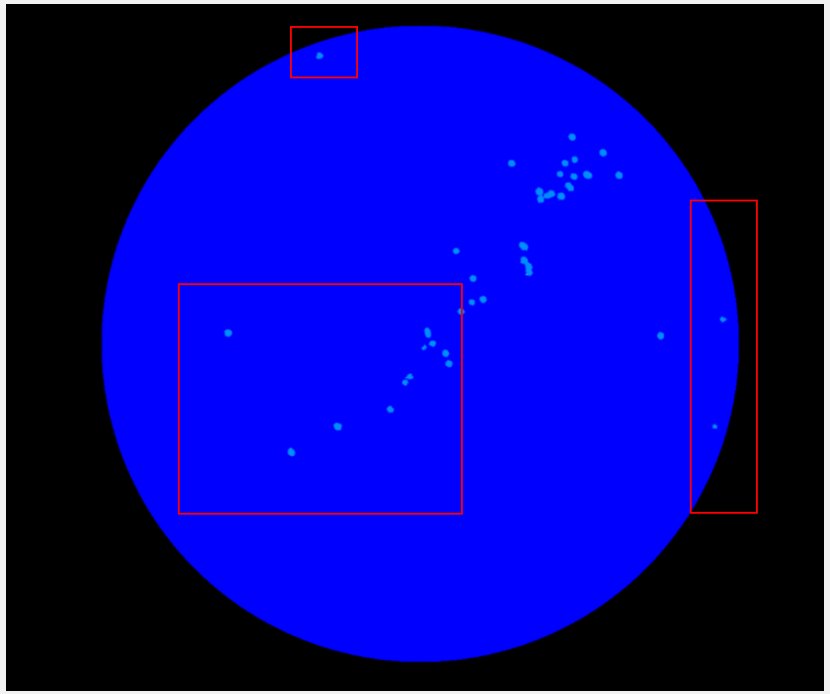
Result: High-quality reproducible images

Accurate growth detection across the plate

APAS INDEPENDENCE

APAS® is able to accurately identify colonies at plate edges and those obscured by labels and other plate markings





Micro-Ai-logist: Algorithm development

- Daily interaction with development team is the key
  - Cross functional communication is challenging, sometimes confronting
- Microbiology and AI work closely to solve issues, multiple touchpoints
  - Engineers
  - Regulatory
  - Software development
- Simple microbiology concepts may drive significant amounts of detailed assessment and work
  - Challenge assumptions
  - Revisit the requirement/use of the algorithm
  - Re-develop algorithm
  - Re-test algorithm (pilot)
  - Formal performance testing ➔ Pass/Fail

APAS INDEPENDENCE

Artificial Intelligence in practice for the microbiology laboratory

CLEVER CULTURE SYSTEMS

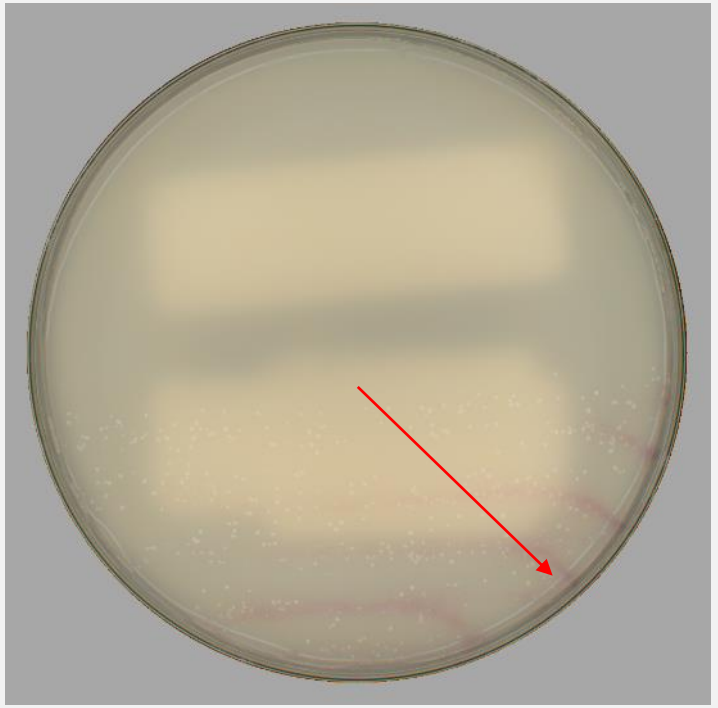
LBT INNOVATIONS

Overcoming limitations

APAS INDEPENDENCE

AI Generalisation with real-world data

- Using a single source of data will produce a limited model
  - Different results from lab-to-lab, not a global result
  - Introduces risk, less confidence in algorithm output
  - System may not match published results
- Uses broad real-world and analytical datasets
  - Broad range of inputs to generalise the model
  - Performance in new laboratories can be better predicted and performance measured
  - Regulatory burden passed
- Interferences play a large part in the establishment of specificity parameters
  - Streaking, agar scratches, matrix debris, labels etc.



Inoculum effect

How we test performance

- Core software follows standard software development processes
  - IEC 62304
  - Software V&V
- AI Verification: Analytical testing program
- AI Validation is based on real-world use
  - Clinical applications: include a formal clinical study performed against a panel of human readers establishing truth state
  - Pharma module requires validation in-situ by user
    - Hard to obtain examples of sterility plates outside of an actual manufacturing facility

APAS Analytical Testing – AI verification

Focussed on details of performance:

- Linearity
- Range-of-assay
- Limit-of-detection (LoD)
- Repeatability & Reproducibility
- Precision

LoD defined as minimum detection sizes and minimum detection of colonies on a plate

APAS® Performance – MRSA screening

TABLE 1 Comparison of the APAS Independence digital assignment to manual interpretation of BD BBL CHROMagar MRSA II and BD BBL CHROMagar Staph aureus

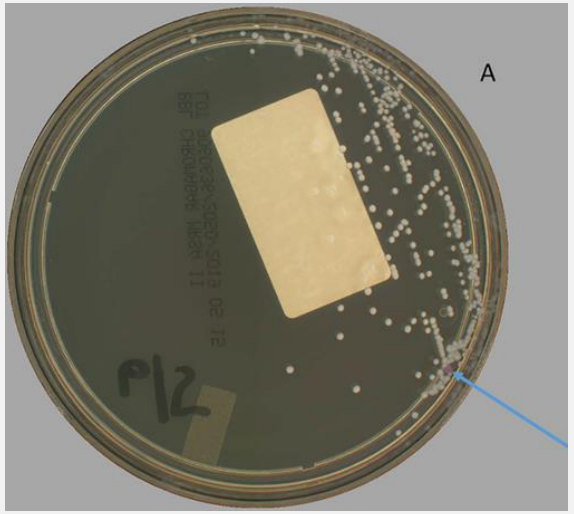
Medium	No. of specimens[a]					Value (% [95% CI])[b]			
	Tested	APAS+ MN+	APAS− MN−	APAS+ MN−	APAS− MN+	PPA	NPA	PPV	NPV
CHROMagar MRSA II	5,913	236	5,525	152	0	100 (96–100)	97.3 (97–97.5)	60.8 (59.3–62.3)	100 (96–100)
CHROMagar Staph aureus	744	133	585	20	6[c]	95.7 (92.7–98.7)	96.7 (94.5–98.9)	86.9 (80.7–93.1)	99 (92–100)

TABLE 2 Discordant resolution by category

Strain	No. of specimens with:[a]					
	Pink inoculum[b]	Positive manual read and negative APAS results	Pink colonies	False-positive manual read and negative APAS results	True positive missed by manual read	Agar issues
MRSA	85	0	44	0	5	18
S. aureus	10	5	5	1	5	0

Gammel et al., (2021). JCM. Comparison of an Automated Plate Assessment System (APAS Independence) and Artificial Intelligence (AI) to Manual Plate Reading of Methicillin-Resistant and Methicillin-Susceptible Staphylococcus aureus CHROMagar Surveillance Cultures

- 5 False negatives by manual reads, where system detected MRSA
- Example human miss below, APAS system positive



APAS® Performance – Urine screening

APAS multi-site clinical trial completed for *de novo* FDA regulatory clearance

- Three sites (2 US, 1 AU)
- 99.0% sensitivity across three sites
- False negatives resulted from:
  - Colonies less than 0.5mm in size – not clinically significant for reporting
  - Dust contamination – inherent challenge of media and application

Table 2. Summary of APAS performance with urine cultures across three centers

	Total cases	True positive	True negative	False positive	False negative	% Sensitivity (95% CI)	% Specificity (95% CI)
Site 1	5,634	4,144	1,490	270	41	99.0 (98.7–99.3)	81.9 (79.8–83.8)
Site 2	1,769	1,256	513	75	15	98.8 (98.0–99.3)	85.4 (82.1–88.2)
Site 3	1,821	1,184	637	63	13	98.9 (98.1–99.4)	90.1 (87.5–99.2)
Pooled	9,224	6,584	2,640	408	69	99.0 (98.7–99.2)	84.5 (83.1–85.9)

Glasson, et al., (2017) ALM. Multicentre Evaluation of an Image Analysis Device (APAS): Comparison Between Digital Image and Traditional Plate Reading Using Urine Cultures.

APAS INDEPENDENCE

APAS PHARMA

CLEVER CULTURE SYSTEMS

LBT INNOVATIONS

Variability in user reads

APAS INDEPENDENCE

Clinical Evaluation: Observations on variations in manual reading of cultures

AMERICAN SOCIETY FOR MICROBIOLOGY | Journal of Clinical Microbiology

"Variation in colony morphology occur, even when experienced microbiologists apply defined rules"

"A counting error of 6.6% has been reported by others."

"Findings reinforce view that growth enumeration is not always accurate and that the manual assessment of colony numbers provides only an estimate of colony growth."

"Within the panels, there was 94.5% (28,565/30,231) agreement for the level of growth from blood agar, with 1,666 readings that differed from the consensus."

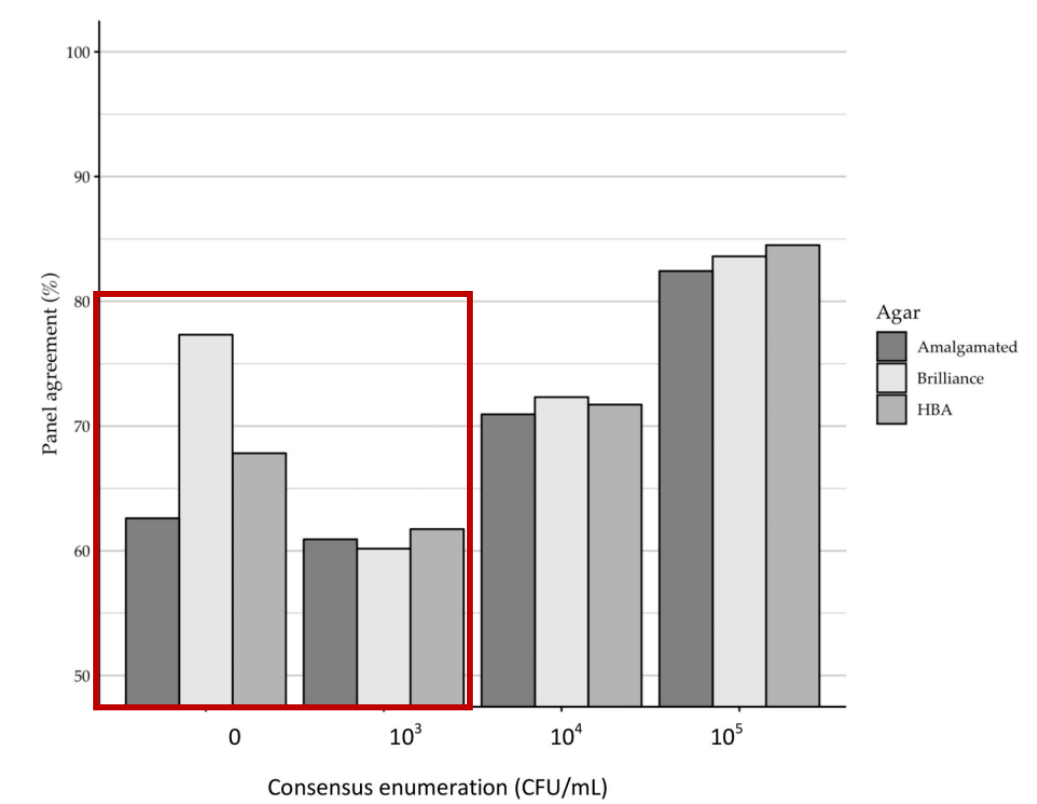
Glasson, et al., 2016. Observations on Variations in Manual Reading of Cultures.

Variability in user reads

Clinical Evaluation: APAS Screening for Urine cultures

Total agreement between all microbiologists for enumeration

- 69.6% of samples on HBA (334/480)
- 72.9% on Brilliance UTI agar (350/480).
- Observed microbiologist agreement on enumeration was lowest at colony growth of 0 – 10^3 CFU



Microbiologist panel agreement percentages by level of enumeration of each of two agars separately and for the amalgamated sample enumeration.

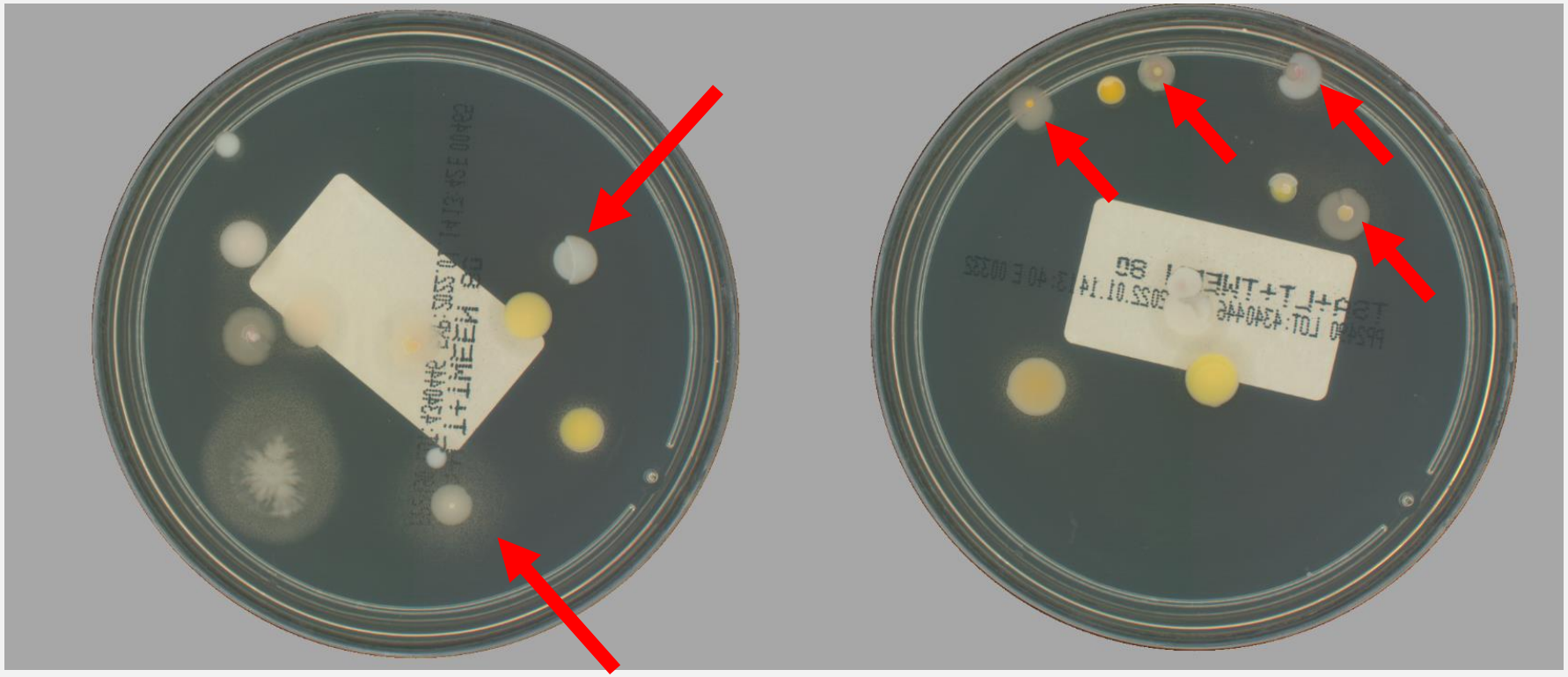
https://cleverculturesystems.com/clinical-evaluation-of-the-apas-independence/

Variability in user reads – colony counts

- Colony counts are ‘accurate’ in between 25-250 cfu/plate : estimate V TNTC
- **Ready for The Count? Back-To-Basics Review Of Microbial Colony Counting – Tim Sandle Review**
  - 3 Pharma labs
  - Study of operator variability using black and white beads in agars, various sizes
  - Misreading of some plates by up to 50%
  - Smaller colonies had higher error rates
  - Larger colonies counted more consistently, but influenced by position on the plate
  - Consistent across each lab

https://www.researchgate.net/publication/339416178_Ready_for_The_Count_Back-To-Basics_Review_Of_Microbial_Colony_Counting

Complex presentations result in inconsistent counting



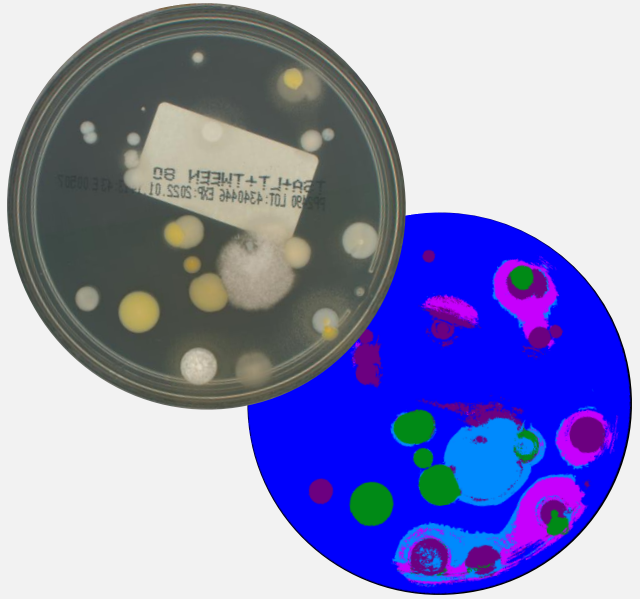
APAS Pharma Overview

APAS INDEPENDENCE

APAS analysis module for the reading of settle plates

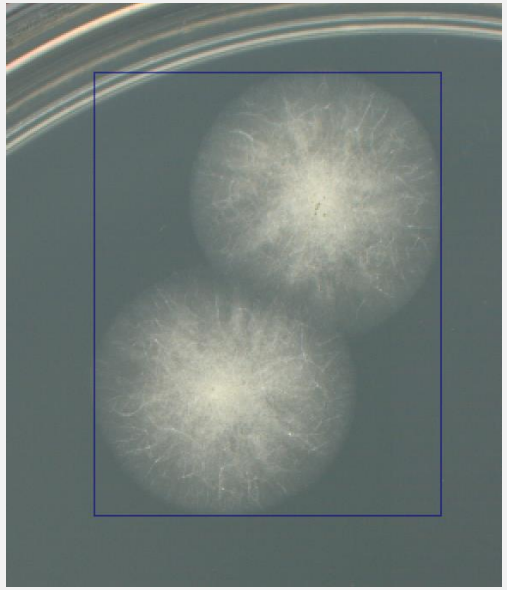
APAS PHARMA

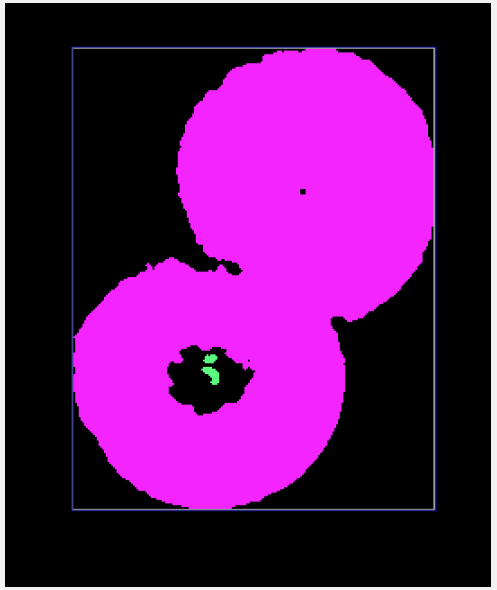
- Successful proof-of-concept analysis module developed
  - Developed using standard 90mm Tryptone Soy Agar culture media
  - Development completed in partnership with leading pharmaceutical company
  - **100% growth detection**
  - Linearity >0.9 for bacterial count



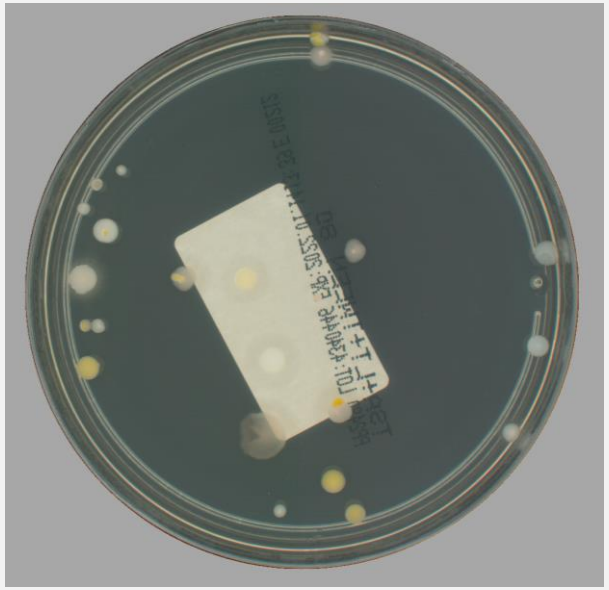
Example settle plate, showing APAS® growth detection

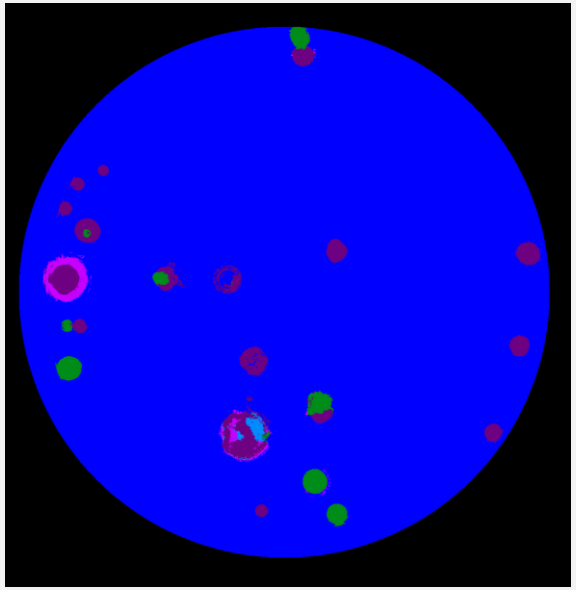
APAS Pharma - Examples





Fungal growth detected and automatically flagged for review



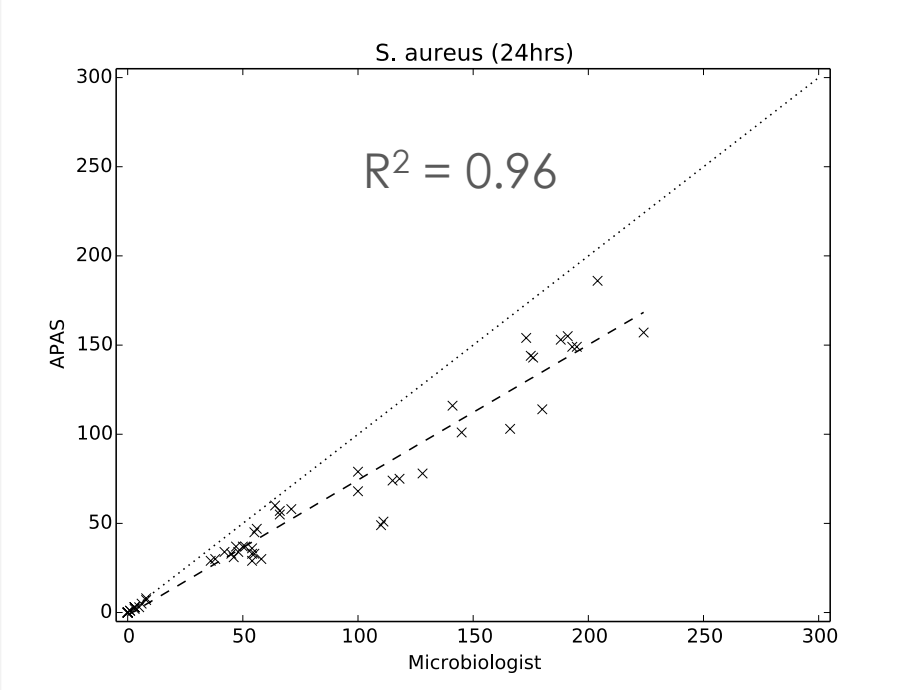


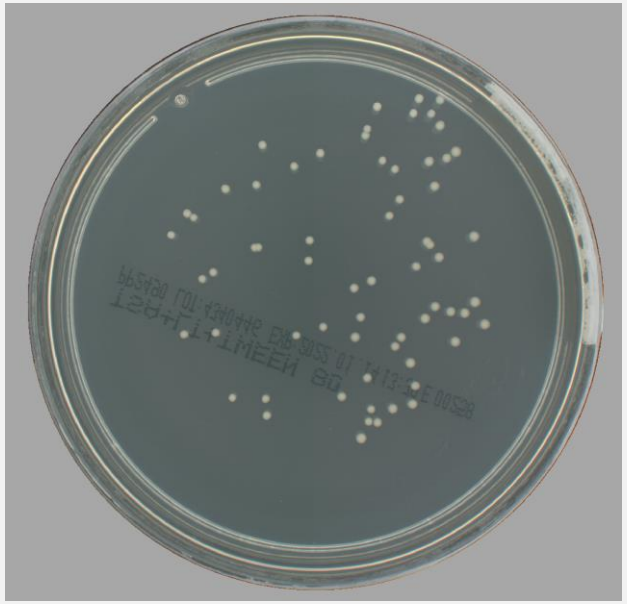
Classification based on similar morphologies

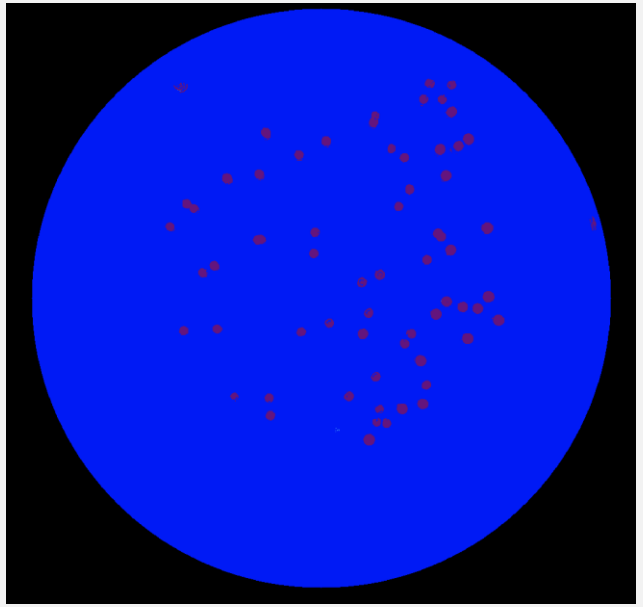
No false negative plates occurred in the APAS system (NPV = 100%)

APAS Pharma – Proven performance

Demonstrated colony counting linearity – *S. aureus*



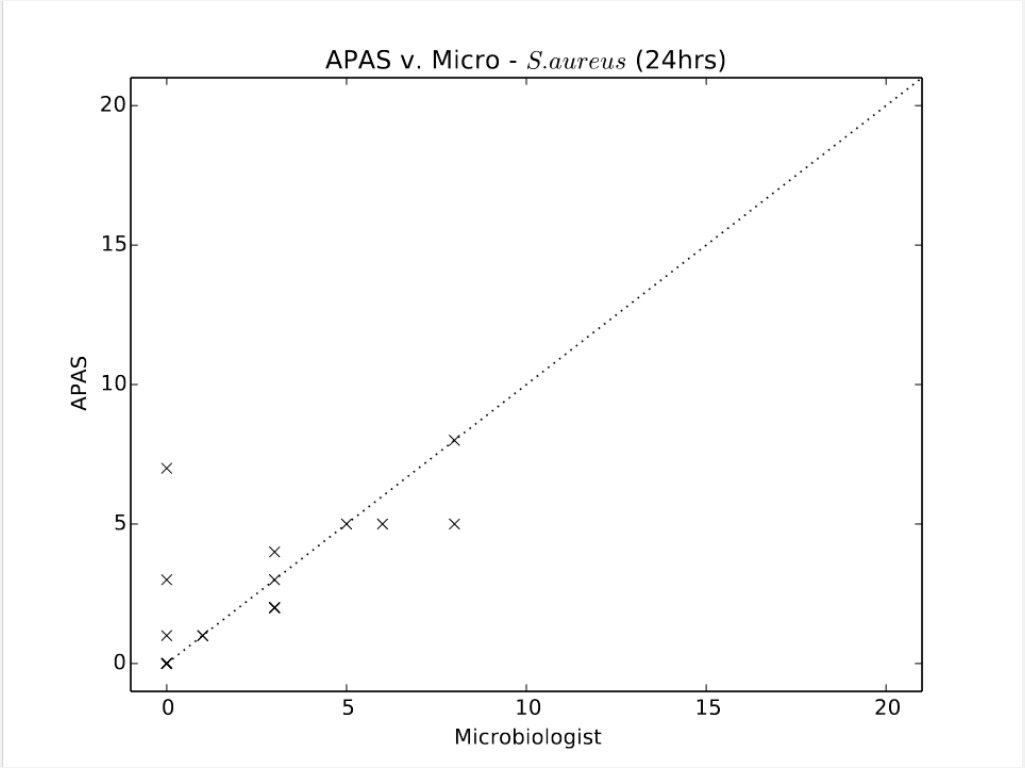




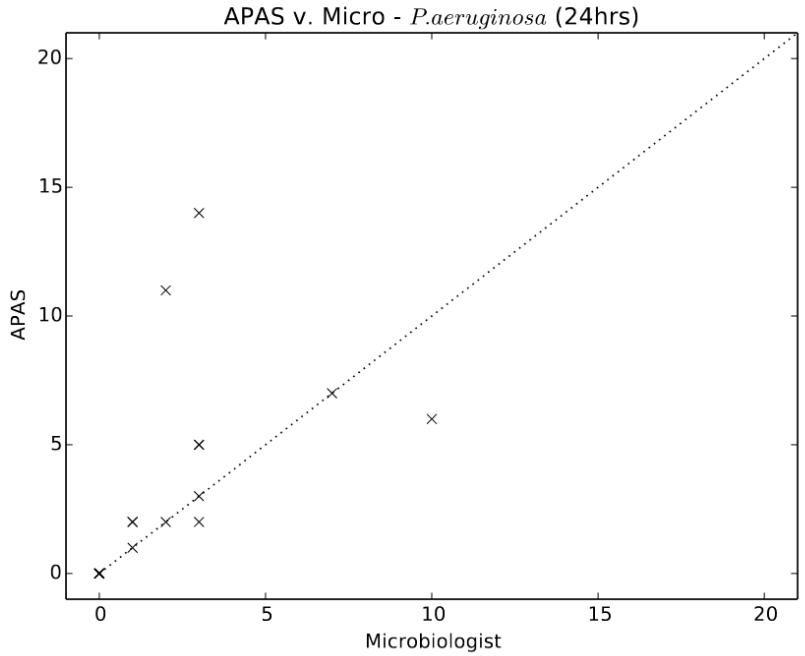
No False Negatives

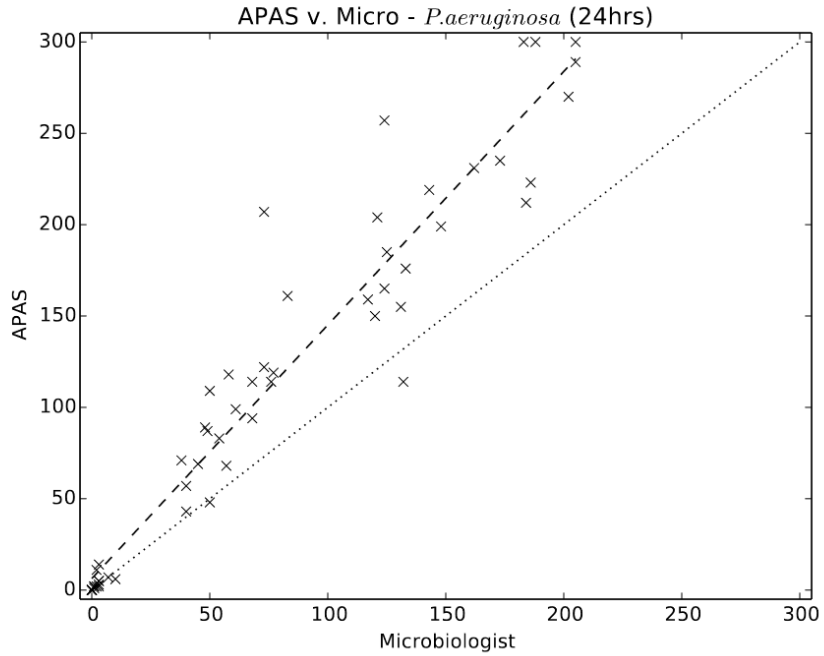
APAS Pharma – Proven performance (Cont.)

Organism	APAS v. Human
Aspergillus brasiliensis (NCPF 2275)	0.71
Pseudomonas aeruginosa (NCTC 12924)	0.90
Staphylococcus aureus (NCTC 10788)	0.96



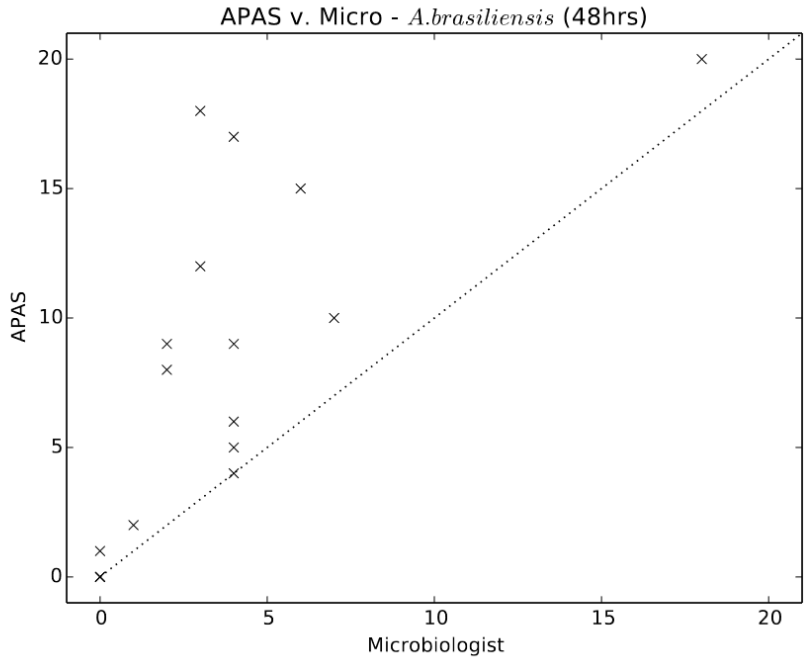
Ps. Aeruginosa

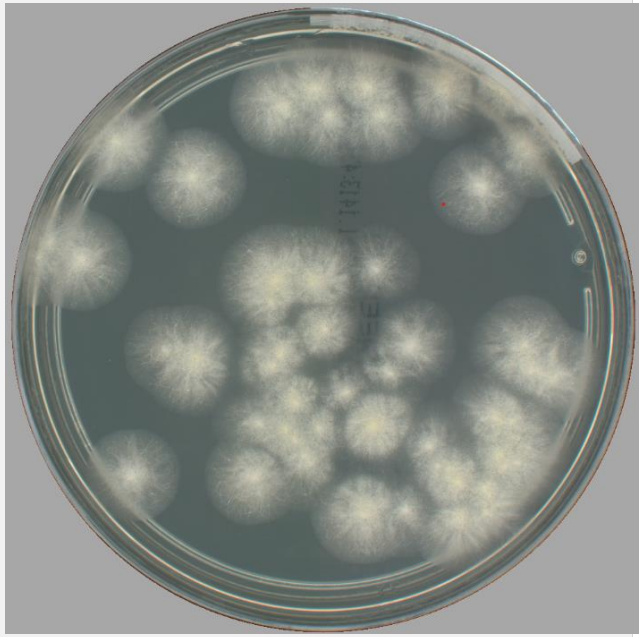


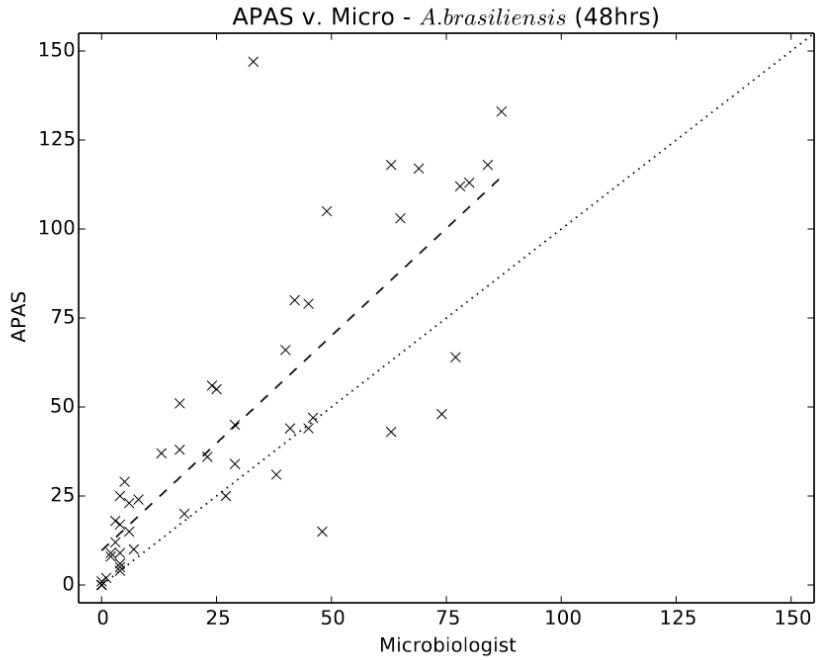


Counting variability due to different colony sizes exhibited

A. brasiliensis – general overcounting







Counting variability due to different colony sizes exhibited, complex shapes

APAS INDEPENDENCE

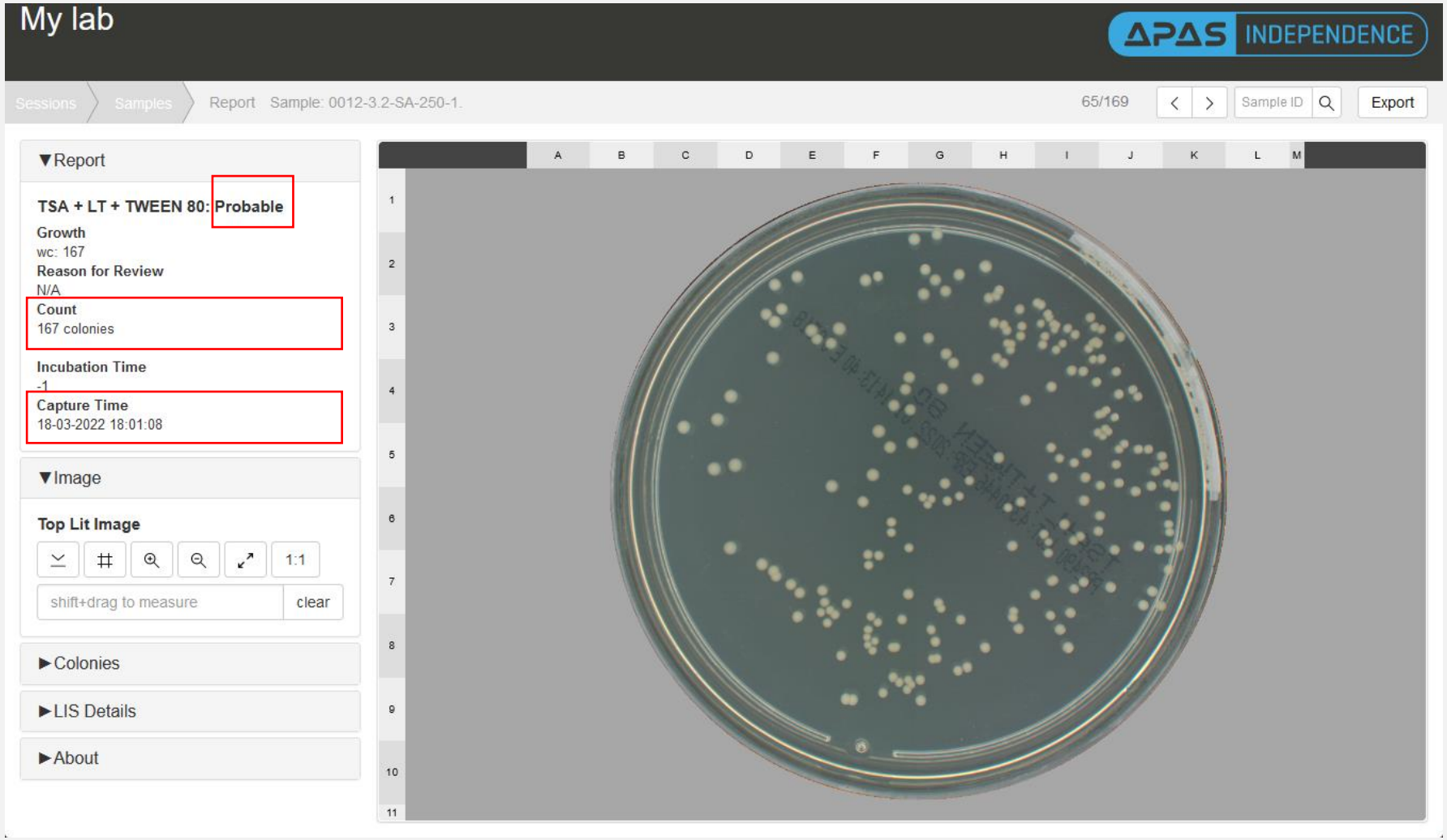
APAS PHARMA

Laboratory integration

CLEVER CULTURE SYSTEMS

LBT INNOVATIONS

LIMS Integration: Reduced user touch time to report



Increased traceability
Digital record of results / images for review

QC proportion in-built
Configurable percentage of plates selected randomly for review

LIMS integration
Eliminates human transcription errors

LIMS Data
All information on this screen transmitted to LIMS

Reduces human subjectivity
Consistent counting algorithms, with flags at agreed action limits

CFR 21 Part 11 Compliance
Audit and data reports available

Prioritised Screening – Sorting into APAS output stacks

APAS Result	Action	Report
No growth	Plate sent to negative stack*	No growth
Fungi present	Plate sent to review stack	Fungi detected, review required
< {Action limit} colonies present (Action limit determined by plate origin)	Plate sent to doubtful stack	{N} colonies detected, either no action required (after validation), or microbiologist confirmation required.
≥ {Action limit} colonies present (Action limit determined by plate origin)	Plate sent to probable stack	Greater than {N} colonies detected, microbiologist confirmation required.

Notes:

- “Stacks” can be combined, except negative stack
- Interaction with LIMS and receiving e.g. ‘clean room type’ can drive reporting and stack segregation

Automation that gets the most out of your laboratory

APAS INDEPENDENCE

Successful proof of concept completed

Demonstrated performance: High throughput, highly accurate automated device to segregate plates with no growth

- No changes were made to the core system for this work

Linearity studies demonstrated acceptable results

>0.9 for bacterial counts

Fungi identified, and flagged for operator review

Configurable action limits to drive plate sorting when growth present

Dedicated efforts will be needed to establish accuracy at action limits cut offs

APAS can flag all growths for review, so trained staff can (re)count if needed

Ongoing development

Improvements to colony counting performance

Technology to be extended to additional applications (Finger Dab and Contact Plates)

Questions