Growth Direct System

Kompendiale QC-Mikrobiologie 4.0

automatisch, schnell & papierlos

Rapidmicro biosystems

Your host for today

Field Application Scientist

Rapid Micro Biosystems
B.Sc. Biopharma process engineering

- 17 Jahre Erfahrung in der Pharmazeutischen Industrie in verschiedenen Positionen
- Seit 2022 bei Rapid Micro Biosystems tätig
- Verantwortlich für globale Prozess- und Implementierungsberatung, Geräte Demonstrationen, Pre- und Post Sales Support, Regulatorische Fragen

Overview

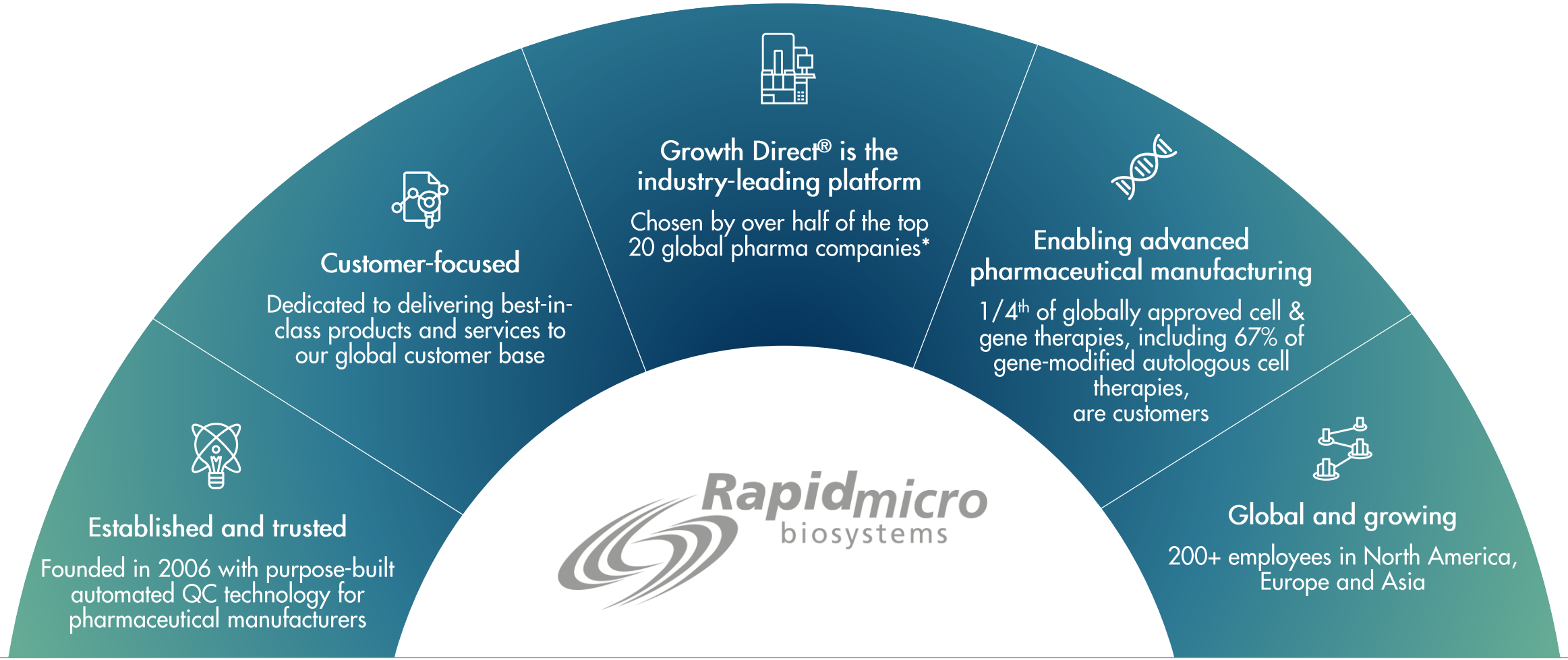
- Herausforderungen und Grenzen der traditionellen Mikrobiologie
- Disrupting the Status Quo:

  Digitalisierung und Atomatisierung des Auszählens mit dem

  Growth Direct System
- Konkrete Belege und Beispiele:

  Die Vorteile und Verbesserungen durch die Einführung des

  Growth Direct Systems



Rapid Micro Biosystems is creating the future of rapid, secure quality control automation to enable advanced pharmaceutical manufacturing

* By revenue

The only fully automated, high-throughput and secure QC solution

Broad application suite & easy sample collection

High capacity, high throughput walk-away testing

Fully automated handling & traceability of samples

Rapid detection & enumeration

Robust security & data integrity

>75
MANUFACTURING SITES

Our top-tier customer base includes the majority of top 20 global pharma*

125+
cumulative instruments placed

3M+
cumulative consumables sold

>45%
customers with multi-site deployments

>55%
customers with multiple systems

CUSTOMER SEGMENTS WITH ESTABLISHED USE

- Biologics
- Cell & Gene Therapy/ CAR-T
- CDMO
- Small Molecules
- 503B Compounders
- Personal Care Products

GEOGRAPHIES WITH SOLD INSTRUMENTS

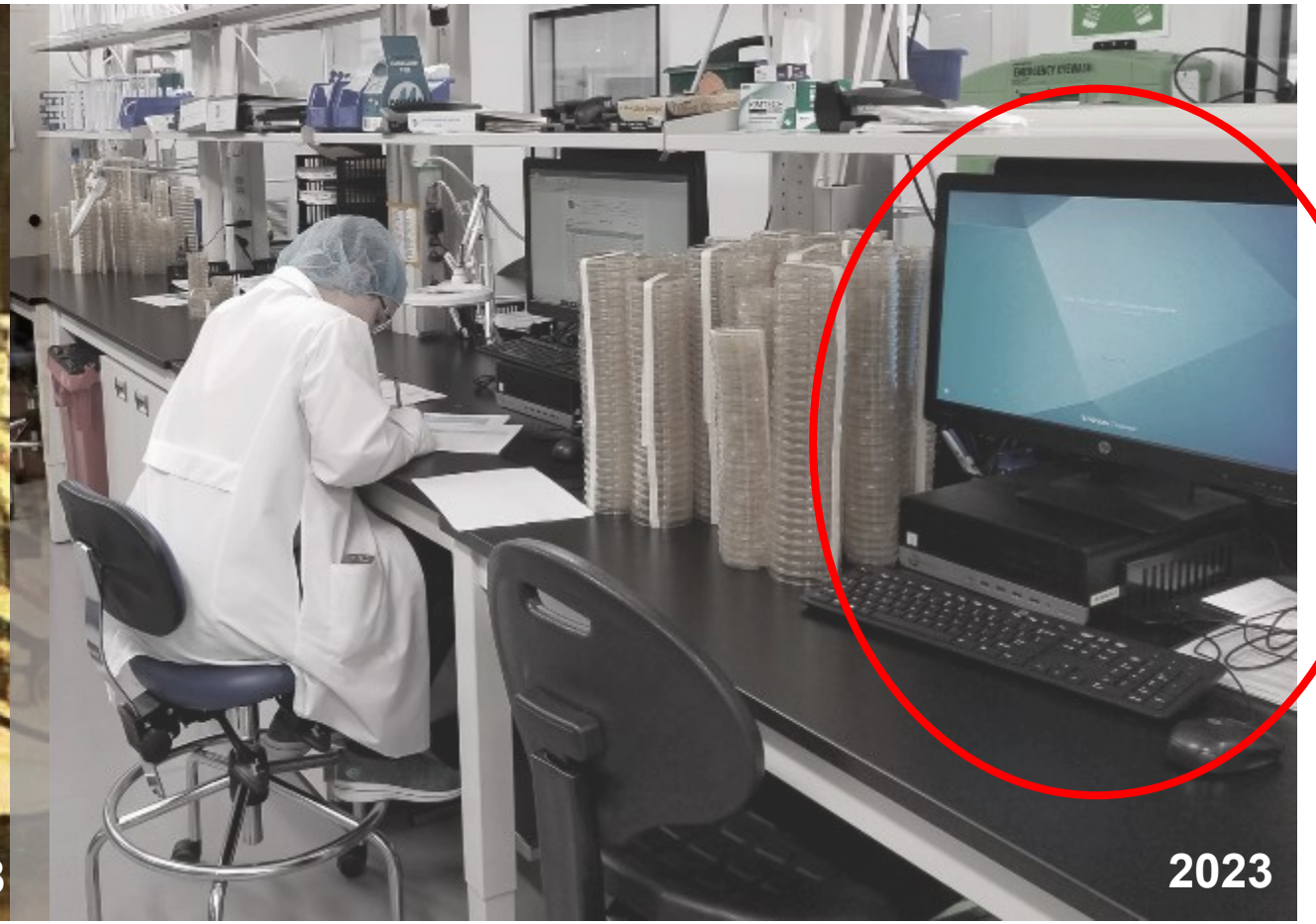
* By revenue

- Herausforderungen und

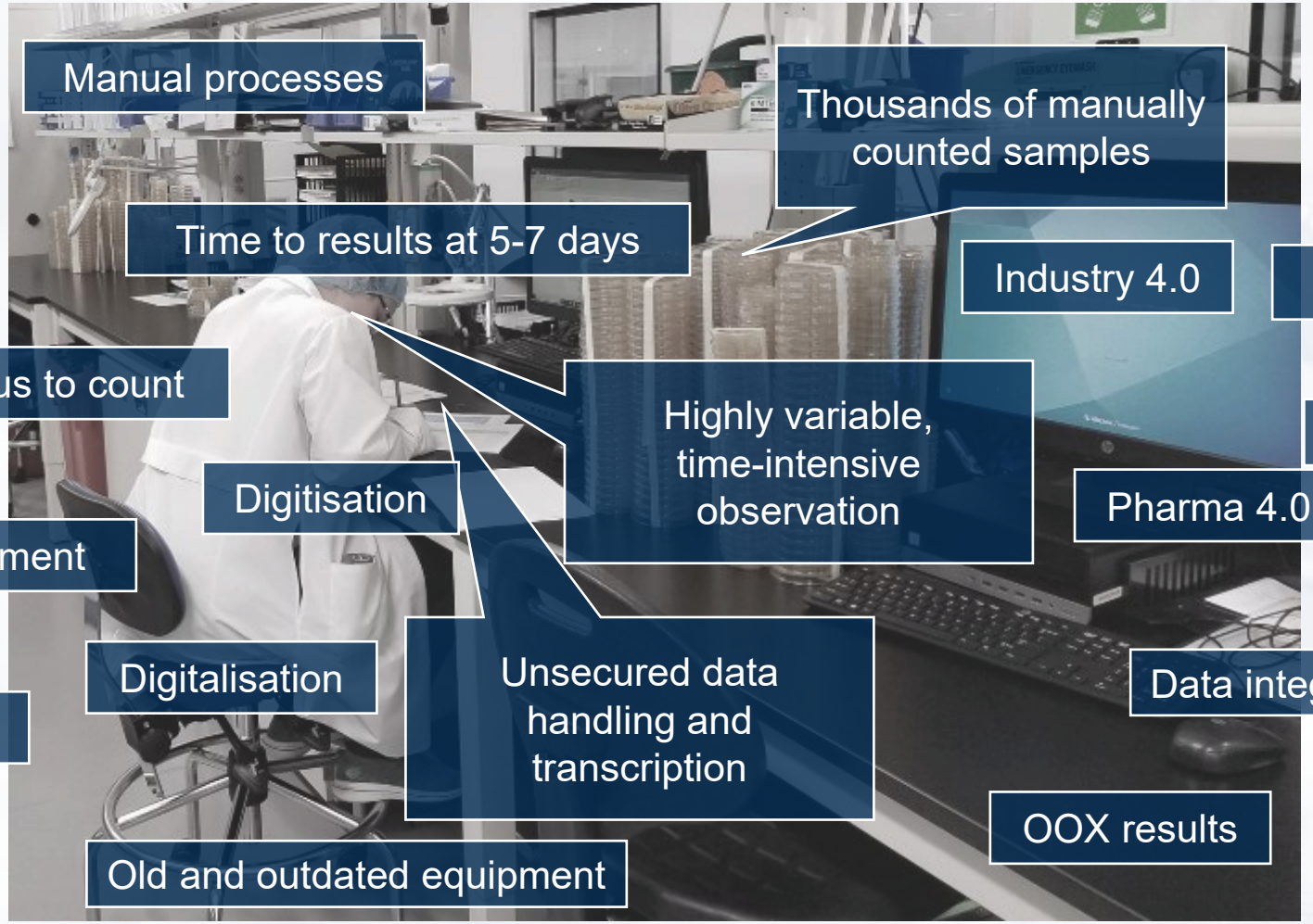
  Grenzen der traditionellen

  Mikrobiologie

The Microbial Quality Control Lab of the 2020's: Spot the differences



Challenges of modern Microbiologists



Disrupting the Status Quo:

Digitalisierung und

Atomatisierung des Auszählens

mit dem Growth Direct System

Rapidmicro biosystems

Growth Direct® System – Overview

The Growth Direct® System consists of 3 elements: rapid agar cassettes, automated incubators, and advanced robotics/image analysis

- Two incubators with 660-sample total capacity
- Proprietary colony detection and enumeration vision algorithm
- Fully automated robotic sample handling
- LIMS integration for paperless reporting
- High-resolution optical station with sample imaging every four hours
- Complete sample security and full compliance with data integrity requirements

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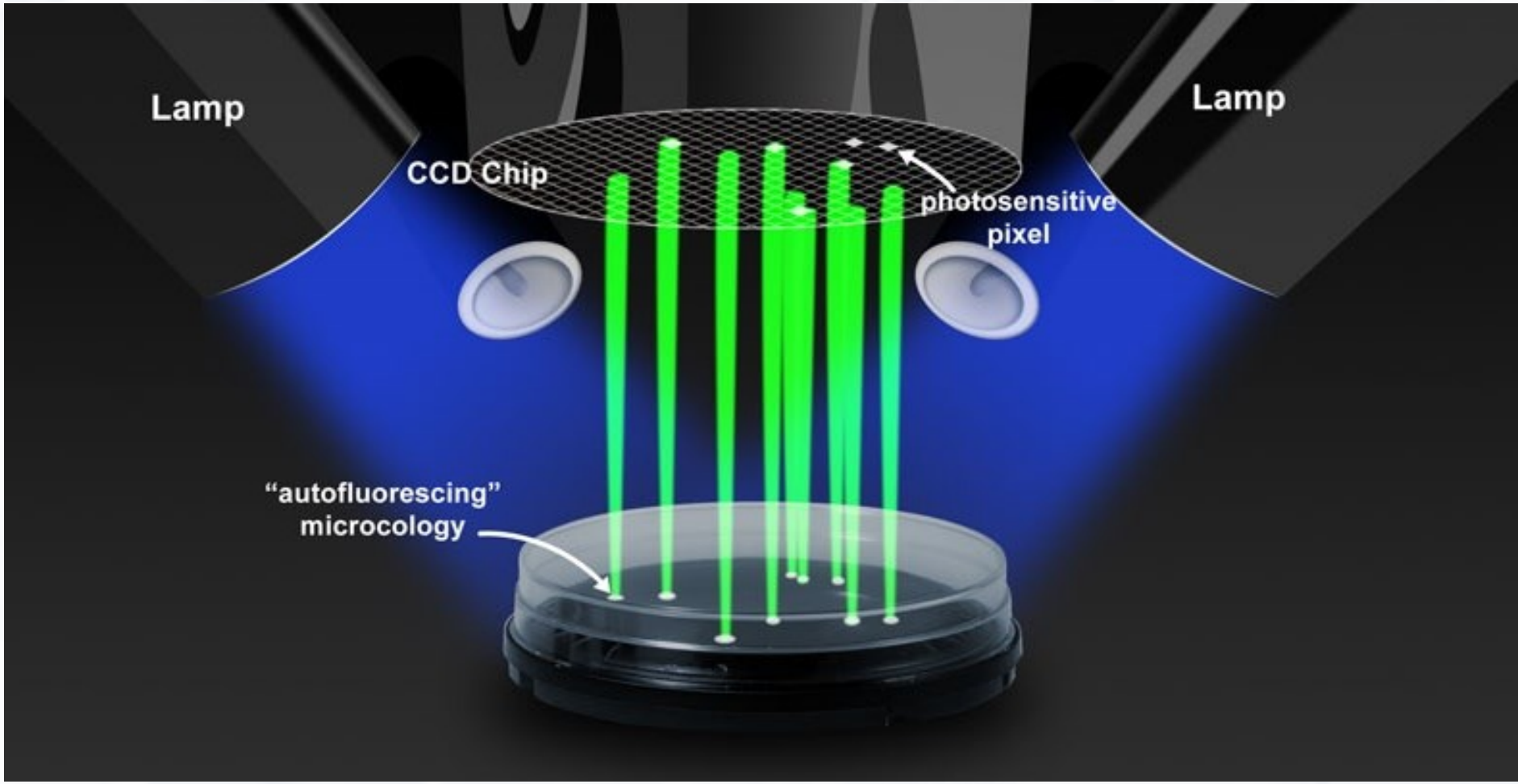
Growth Direct® System - Technology

HOW IT WORKS

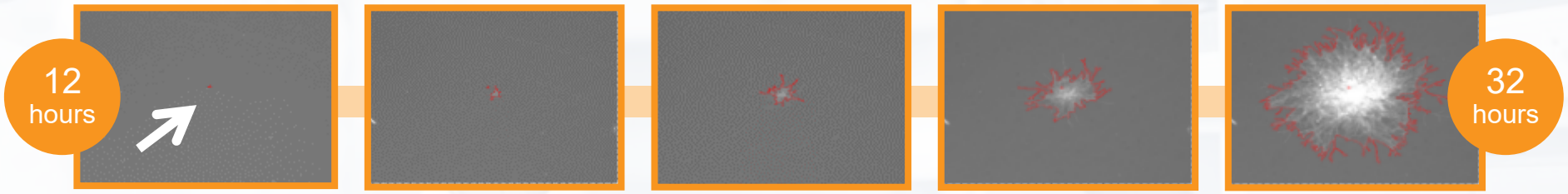
Patented technology uses a blue light that causes micro-colonies to auto fluorescence, captured on a CCD chip.



Growth Direct® System – Technology

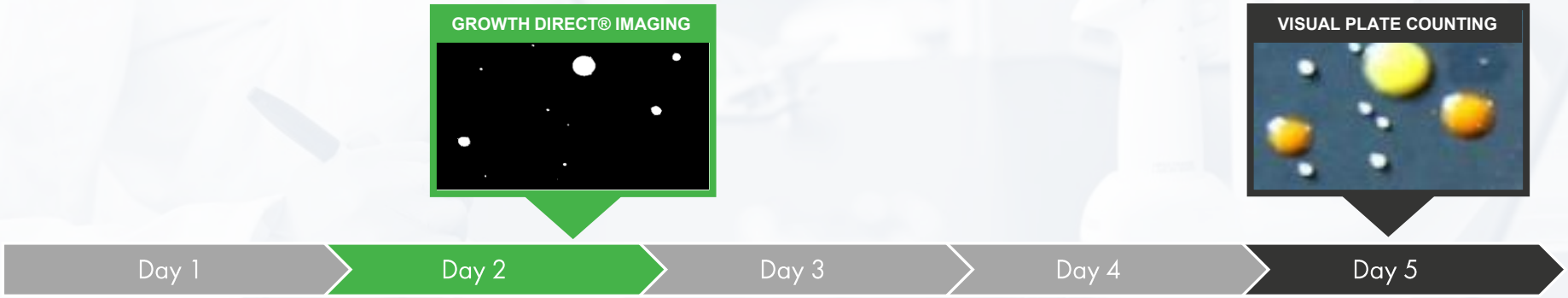
Growth Direct® counts colonies (in CFU) in half the time.

Powerful software starts to detect colonies within hours, enabling real-time enumeration of organisms.

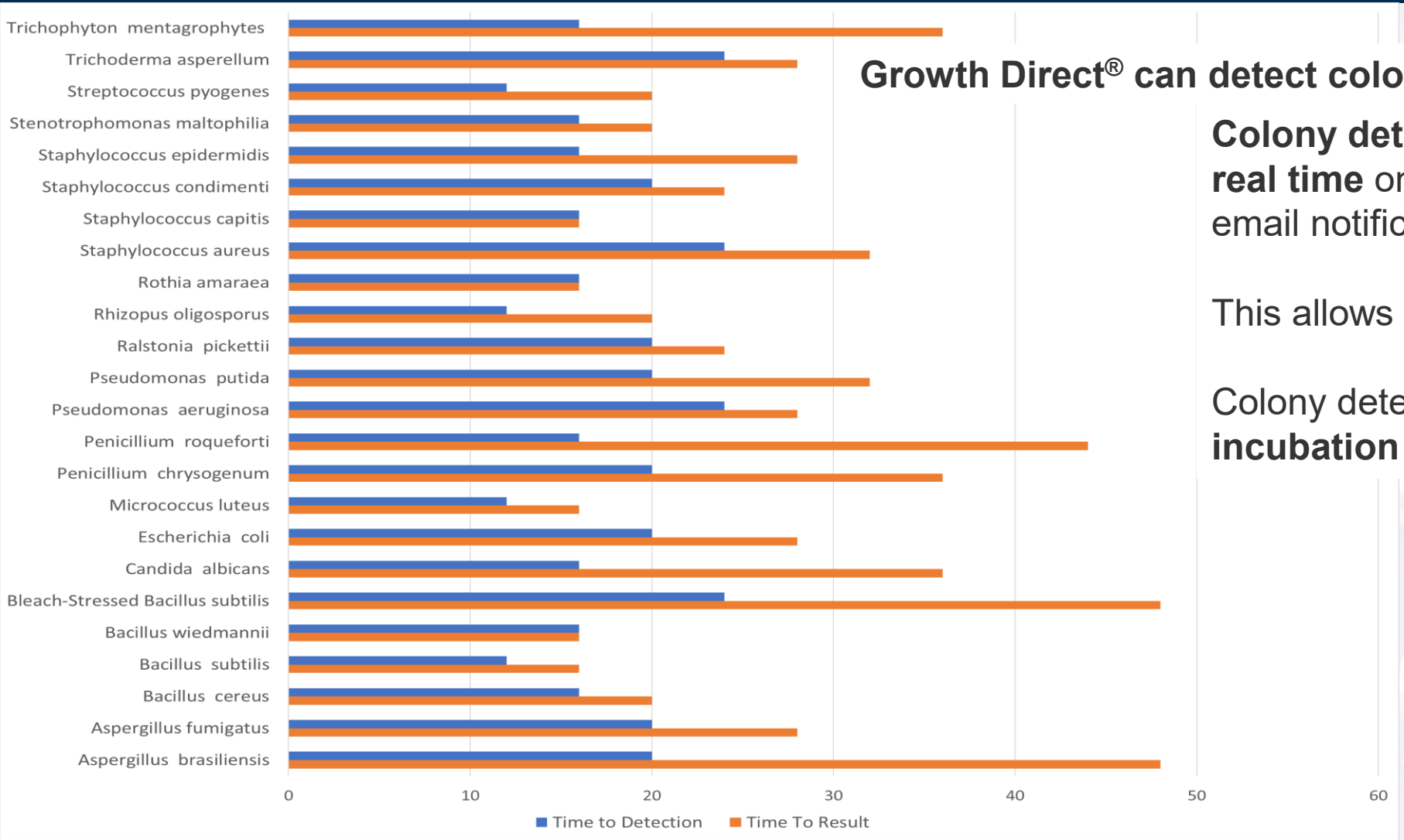


An A. brasiliensis Microcolony in CHO cells

Growth Direct® counts the same colonies in half the time of the traditional method.



Time to detection and result improvement



Growth Direct® can detect colonies in <24 hours for EM

Colony detection is highlighted in real time on screen, accompanied by email notifications.

This allows **faster reaction time.**

Colony detection TTR is **generic for incubation temperature.**

Growth Direct® System – Lab automation

Growth Direct® reduces risks by eliminating 85% of manual steps.

Growth Direct® Rapid Automated Method automates the entire testing process, enabling expert QC lab staff to focus on higher value job functions.

- Fewer manual tasks
- Fewer human errors
- Fewer regulatory issues
- Fewer validation requirements

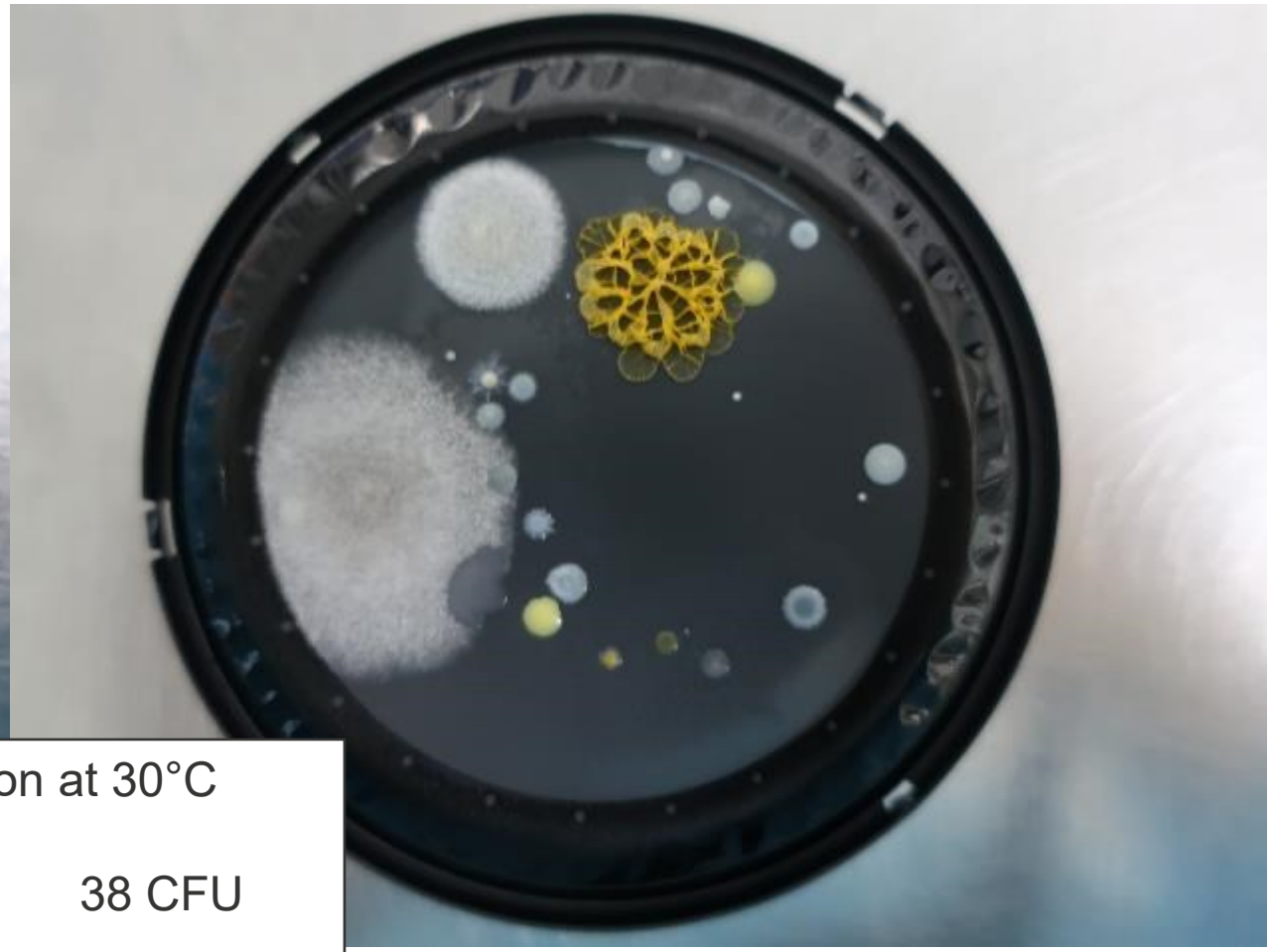
Validation rationale & regulatory compliance

Growth Direct technology validation is considered as an “automated compendial” method

Complies with

- USP <1223>
  Validation of alternative microbiological methods
- EP 5.1.6.
  Alternative methods for control of microbiological quality
- PDA TR No.33
  Evaluation, Validation and Implementation of Alternative and Rapid Microbiological Methods
- JP 4.05 & G4-6-170
  Microbiological Examination of Non-Sterile Products & Rapid Microbial Methods

Real life example Environmental monitoring – Active air sample



5 day incubation at 30°C

GD count	38 CFU
Operator 1	25 CFU
Operator 2	26 CFU
Operator 3	25 CFU

Real life example Environmental monitoring – Active air sample

→ Colonies merging

→ Colonies are overgrown by Mould

→ GD algorithm and 4 hour interval capturing growth on the cassette

“GD does not find or count more colonies, it is counting what is and was always there”

Real world sample

Cassette 21484

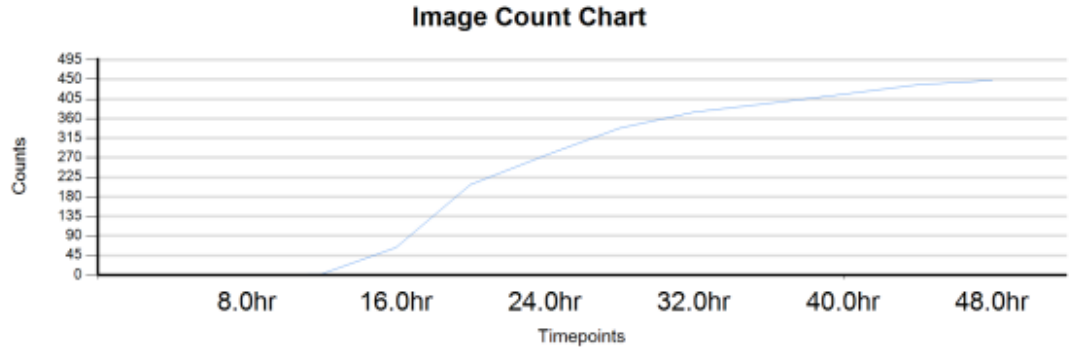
Personal monitoring - Hand

Cassette mapping	Serial Number	Location	Final Growth Direct Count [CFU]	Example for…
21484	E0005C1YY	Hand	448	Merging colonies and Counting range

Incubation time: 48h
Incubation temperature: 32.5°C
Media: TSA

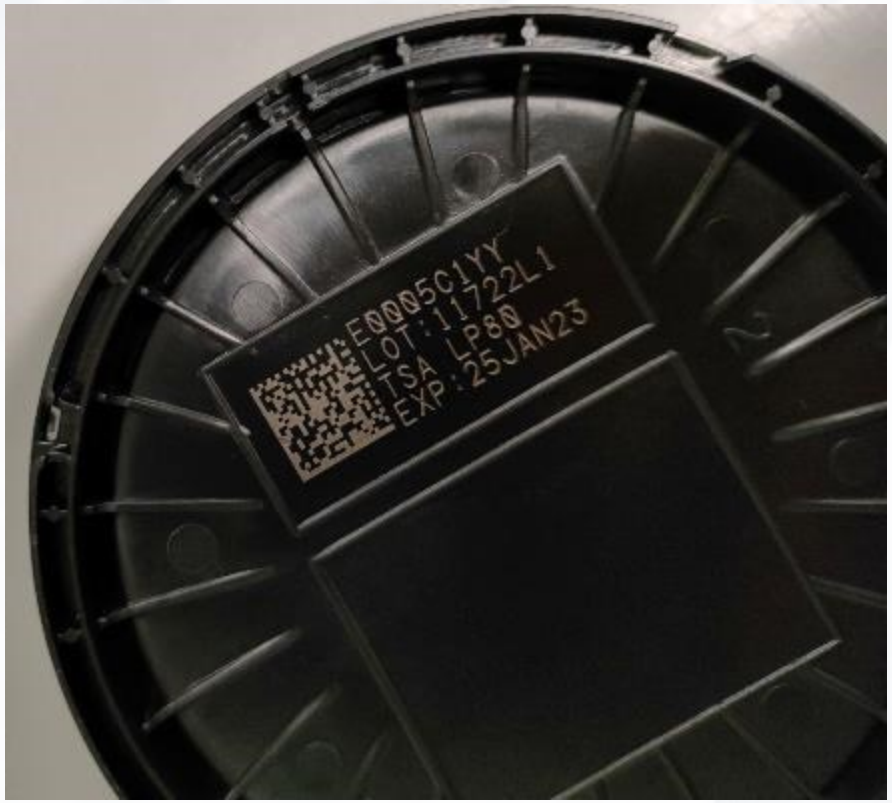
Test Report_Hand

First micobial detection after 12h



Timepoint	Actual	Expected	Count	Dilution
1 (4.0hr)	11/07/2022 17:46:22	11/07/2022 17:44:00	0	0
2 (8.0hr)	11/07/2022 21:48:30	11/07/2022 21:46:20	0	0
3 (12.0hr)	11/08/2022 01:48:57	11/08/2022 01:46:40	2	2
4 (16.0hr)	11/08/2022 05:49:24	11/08/2022 05:47:00	63	63
5 (20.0hr)	11/08/2022 09:49:32	11/08/2022 09:47:20	208	208
6 (24.0hr)	11/08/2022 13:49:59	11/08/2022 13:47:40	275	275
7 (28.0hr)	11/08/2022 17:50:22	11/08/2022 17:48:00	338	338
8 (32.0hr)	11/08/2022 21:50:43	11/08/2022 21:48:20	375	375
9 (36.0hr)	11/09/2022 01:51:04	11/09/2022 01:48:40	395	395
10 (40.0hr)	11/09/2022 05:51:10	11/09/2022 05:49:00	416	416
11 (44.0hr)	11/09/2022 09:51:45	11/09/2022 09:49:20	438	438
12 (48.0hr)	11/09/2022 13:51:49	11/09/2022 13:49:40	448	448

Cassette mapping	Serial Number	Location	Final Growth Direct Count [CFU]	Example for…
21484	E0005C1YY	Hand	448	Merging colonies and Counting range



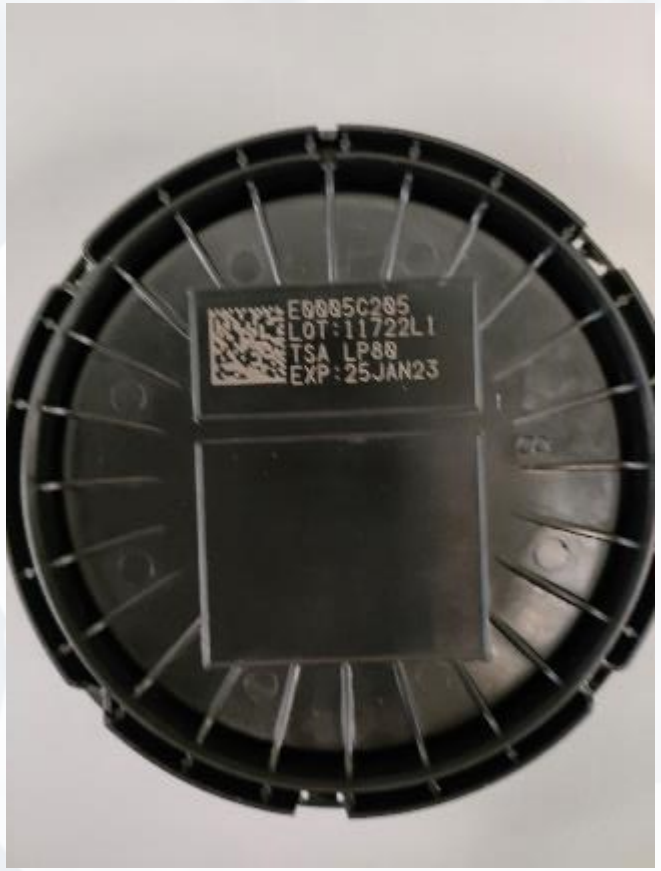
Real world sample

Cassette 21503

Surface sample- Small freezer top

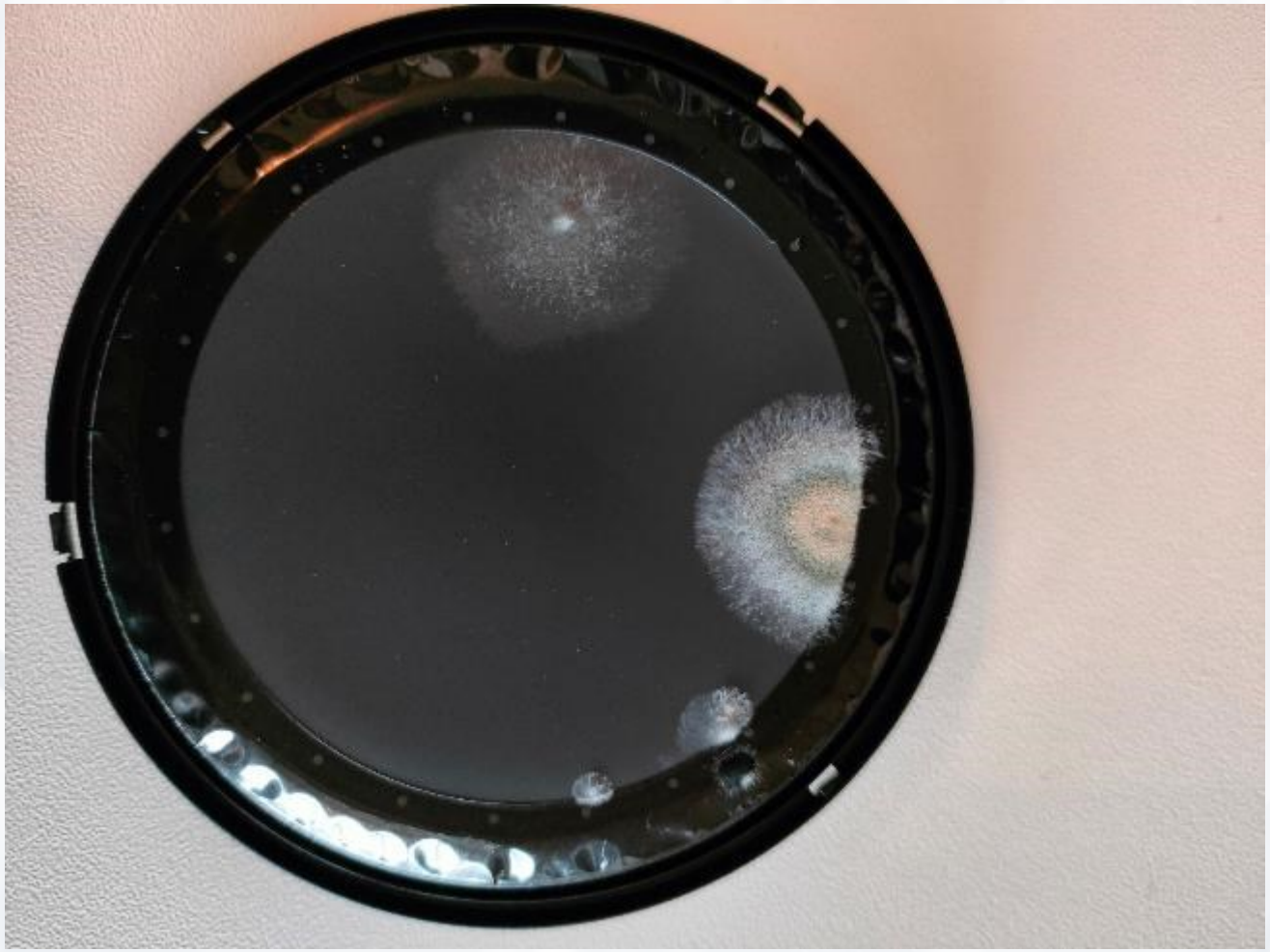
Cassette mapping	Cassette serial Number	Sample location	Final Growth Direct Count [CFU]	Example for…
Sample 9 21503	E0005C205	Small freezer top	4	Mold

Incubation time: 48h
Incubation temperature: 32.5°C
Media: TSA



Cassette mapping	Cassette serial Number	Sample location	Final Growth Direct Count [CFU]	Example for…
Sample 9 21503	E0005C205	Small freezer top	4	Mold

Incubation time: 120h
Incubation temperature:
32.5°C for 48h
22°C for 72h
Media: TSA



Konkrete Belege und Beispiele:

Die Vorteile und Verbesserungen

durch die Einführung des

Growth Direct Systems

Rapidmicro biosystems

Customer on-site Feasibility study – Executive summary

Test	Description	Test media	Incubation time & temperature	Result Accuracy GD vs. manual count	Comment
Accuracy Test 1 ✓	50 CFU target inoculation 6 replicates 5 ATCC strains 4 inhouse isolates	ET80-HT TSA containing neutralizers Filtration membrane on top EM membrane	48 h 32.5°C	Min: 95% Max: 133% Overall: 107%	• MO detection after 16h • Final result after < 48h
Accuracy Test 2 ✓	300 CFU target inoculation 6 replicates 5 ATCC strains 4 inhouse isolates			Min: 97% Max: 171% Overall: 117%	• Maximum count of 2282 CFU • GD counts all MO
Method Suitability Test 3 real sample ✓	20 different buffer samples – unknown CFU 1 mL/0.1 mL sample	ET80-HT TSA containing neutralizers Filtration membrane on top EM membrane Bioburden TSA	48 h 32.5°C	Min: 98% Max: 111% Overall: 100%	• GD counts MO on plate, not visible to operator • GD ensures patient safety • Real life test with 20 different media samples
EM Test 4 ✓	20 Active air samples 20 Passive air samples 20 Surface samples	ET80-HT TSA containing neutralizers	3 days 30°C	Min: 100% Max: 156% Overall: 117%	• MO detection after 16h • Final results after < 72h • GD counts all colonies and MO on plates
			6 days 30°C	Min: 90% Max: 398% Overall: 148%	

Case 1: Biopharma industry leader received Form 483 observation at Biopharma site that had not instituted dual read

OVERVIEW

Biopharma industry leader received 483 that Growth Direct® (GD) would have prevented.

Company context:

- Top 20 pharma company
- Biopharmaceutical production site
- Site that received 483 for Product Bioburden testing
- Site did not receive any remarks and observations for using GD for Environmental Monitoring

During 2022 FDA inspection, site received 483 observation for data integrity.

IMPACT

Form 483 excerpt:

> On July 29, 2022, while observing a microbiologist in the Quality Control Lab performing read-outs of bioburden plates post-incubation, the analyst read and recorded the results on pink paper log sheets. A second analyst was not present to verify the accuracy of these data. The analyst confirmed that secondary verification is not required for microbiological sample read-outs. Microbiological sample read-outs should be verified by a second analyst.

Company risked significant potential costs from 483:

- Costly **investigation** and **corrective actions** (e.g., capital investments, training, dual read); for companies with major 483s[1], these can **total $10M+**
- **Damage to reputation** and potential **increased regulatory scrutiny** across rest of portfolio
- Potential **loss of customers and market cap** decline (e.g., ~$1B+ for one CDMO)

Note: Amounts in illustration are estimated based on industry specifics publicly available. [1]For Form 483s with 8-12 observations, not uncommon to cost $10-50M to resolve.

Case 2: Biopharma industry leader received Form 483 observation at cell therapy site that had instituted dual reads

OVERVIEW

Biopharma industry leader received 483 that Growth Direct® (GD) would have prevented.

Company context:

- Top 20 pharma company
- CAR-T cell therapy manufacturing site
- Site that received 483 does not use GD

During 2020 FDA inspection, site received 483 observation for data integrity, despite already performing dual reads.

IMPACT

Form 483 excerpt:

> 6. Deviations from written test procedures are not justified to assure compliance with established specifications and standards.
>
> On 10/07/2020 in the Environmental Monitoring Laboratory Rm (b) (4) we randomly selected and inspected EM plates that had been enumerated, counts verified by a second verifier, and results recorded in LIMS earlier the same day. We observed (b) (4) of the inspected EM plates showed discrepant enumeration results. The observed discrepancies were confirmed by the firm's management.

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Case 3: In single water contamination event, Growth Direct® System could save company 6 manufacturing days

OVERVIEW

Top 20 Global Pharma company uses Growth Direct® (GD) at therapeutic protein manufacturing site.

company context:

- Top 20 global pharmaceutical company
- Site produces therapeutic proteins
- Site is center of excellence that tests innovative manufacturing and quality solutions

This site initially adopted GD for use in their water testing lab:

- One system for water testing at one site
- 3 systems total used at this site, for water, bioburden and EM

Success at this site led to this companies' global adoption of GD
currently 11 systems at 8 sites.

OPERATIONAL VALUE

In a single incident, the Growth Direct® System has the potential to pay for itself multiple times over.

Potentially damaging excursion at site occurred during manufacturing pause	vs.	If site had been manufacturing, GD would have mitigated negative impact
! Action limit excursion identified by GD within 24 hrs vs. 7 days with traditional method		✓ 6 days of manufacturing potentially saved
! Entire water system sanitized immediately		✓ Assuming production value of $200-800k/day, GD could have saved company ~$1-5M in value in just one incident

Note: Illustration based on real world data provided by company including projected savings using company's own internal cost estimates.

Growth Direct capabilities

- **Superior Data integrity** and **paperless workflow** with connection to any LIMS
- Alert-based **remediation** possible **within 12 hours**
- **Automated compendial method** reduce **errors** and **manual intervention** to a **minimum**
- Readiness for **productivity increase** and **digitalization**
- **Risk mitigation on audits** from FDA and regulatory organizations
- **Competitiveness**, Digitalization and Pharma 4.0 fulfilled
- **Counting 24/7 for 365 days**, continuous loading of the system on every working day
- **Mould detection**, fulfilling GMP Annex 1 requirements for all grades
- Opportunity for **method disruption**, (global) method **harmonization** and **standardization**
- Addressing **staff turnover** and skills shortage with automation
- **Supporting investigations**, **deviations** and **CAPA‘s** with automated, rapid enumeration
- **Documented validation and automated**, repetitive and objective counting


Fragen?


Dann besuchen
Sie mich am
Stand 37!
Rapidmicro
biosystems

Dankeschön!

Johannes Oberdörfer

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