Optimizing Diagnostic Testing with Quality Controls, Temperature and Humidity Monitoring

Jessica Van Allen
Lead Technical Support Manager, ZeptoMetrix

Cindy Gisler
Global Product Manager, Traceable

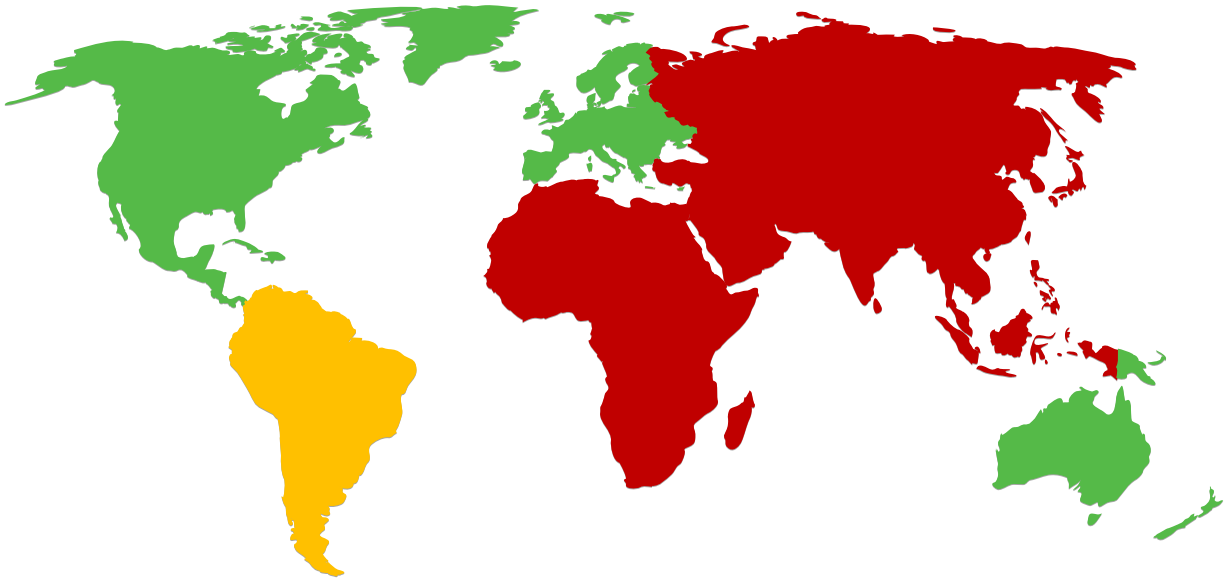
Learning Objectives

- Assess the critical role of quality controls
- Identify attributes of effective quality controls
- Evaluate quality control solutions for clinical laboratories
- Applying knowledge of certified measurement and monitoring instruments

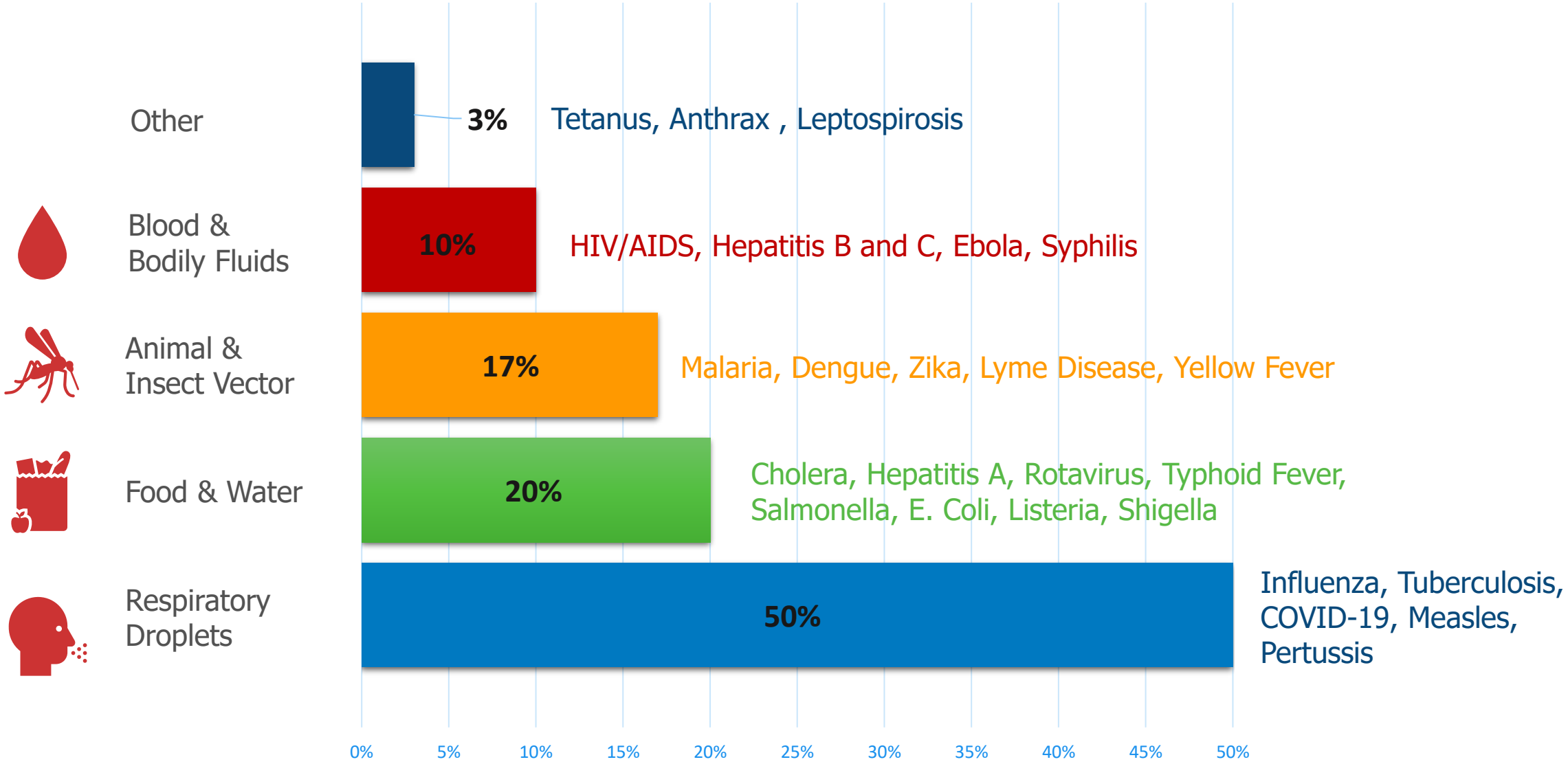
Infectious Diseases and the Importance of Quality Controls in Diagnostic Testing

Worldwide Disease Cases

Continent	Infectious Diseases (Millions)	Foodborne Diseases (Millions)	Waterborne Diseases (Millions)	Total Cases (Millions)
Africa	300	150	200	650
Asia	500	250	300	1,050
Europe	50	60	20	130
North America	80	48	10	138
South America	120	80	40	240
Oceania	30	12	5	47
Global Total	1,080	600	575	2,255



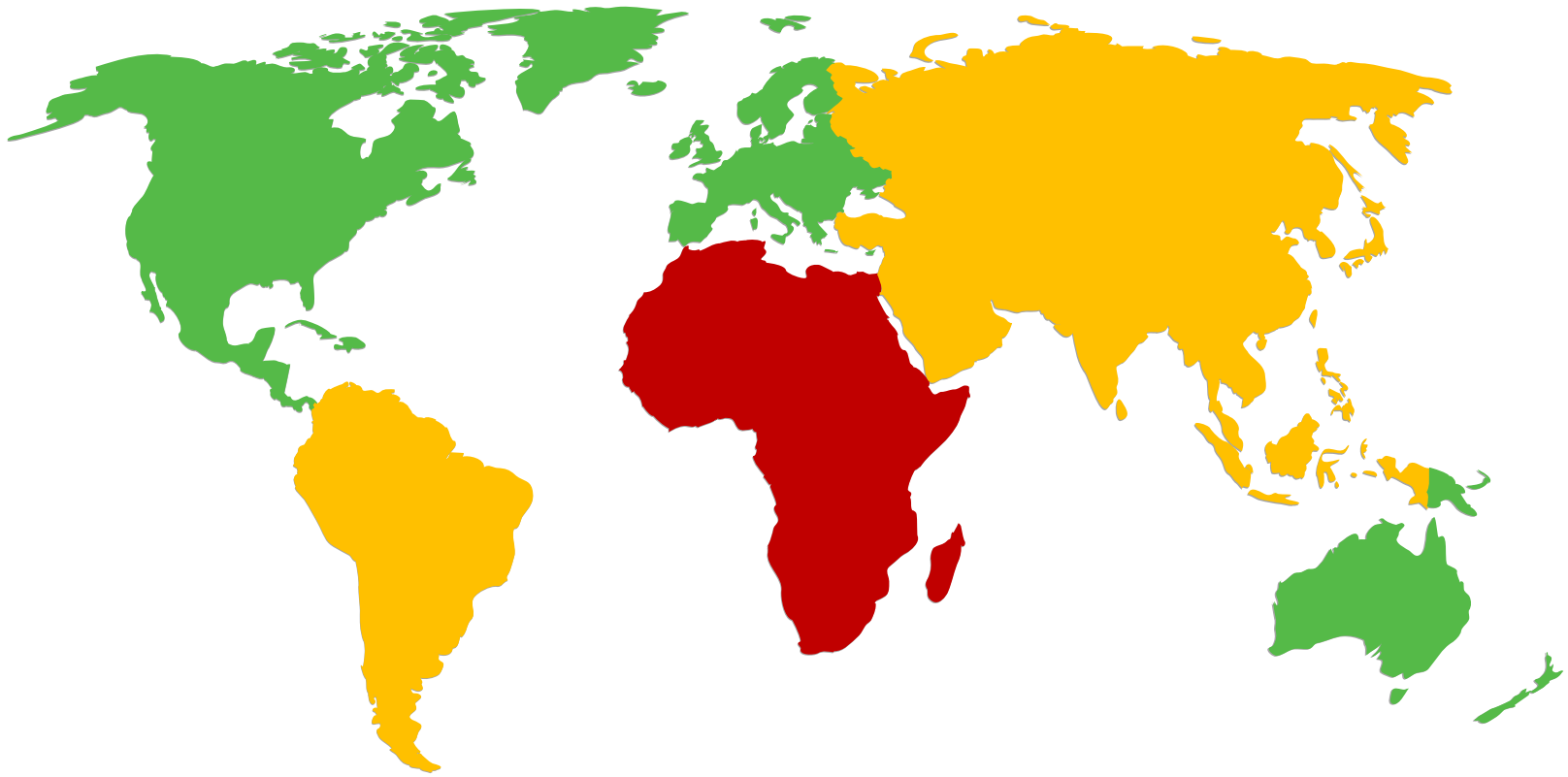
Disease Transmission



Estimated Deaths by Respiratory Diseases

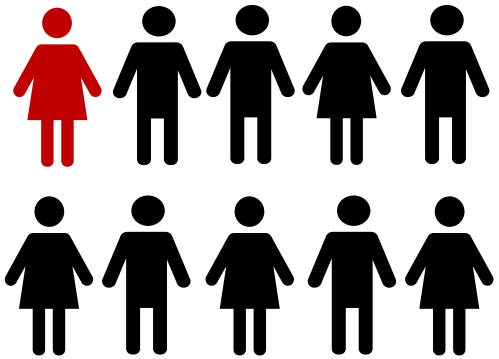
Disease	2019 Deaths	2020 Deaths	2021 Deaths	2022 Deaths	2023 Deaths (Estimated)
COVID-19	N/A	1.8M+	3.5M+	2.3M+	1.2M+
Influenza	22,000 (US)	~700 (US)	~5,000 (US)	~12,000 (US)	~15,000 (US)
Pneumonia (Bacterial & Viral)	2.5M	2.6M	2.5M	2.4M	2.4M
Tuberculosis (TB)	1.4M	1.5M	1.6M	1.6M	1.5M
Measles	207,500	140,000	150,000	160,000	170,000
Pertussis	160,700	~150,000	~155,000	~160,000	~160,000
RSV	100,000	120,000	130,000	140,000	150,000
Meningococcal Disease	50,000	40,000	45,000	50,000	50,000

Worldwide Foodborne Illness & Death (WHO)



~420,000 deaths

1:10

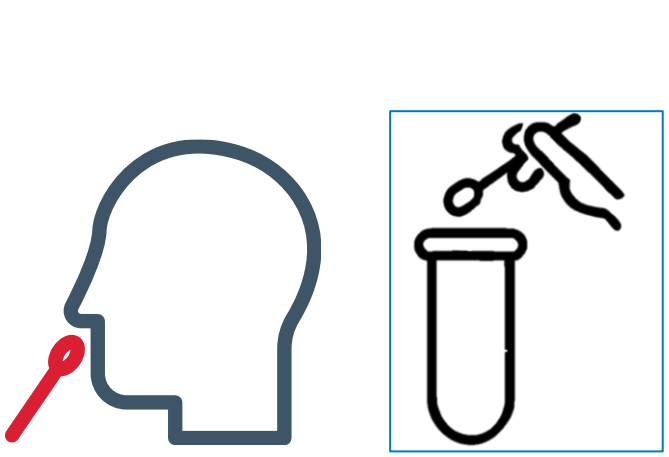


~600 million
foodborne illnesses

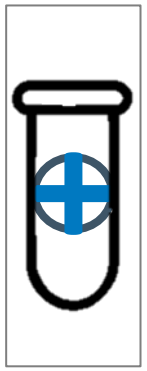
Food & Waterborne Illness & Deaths Worldwide

Disease	2019 Deaths	2020 Deaths	2021 Deaths	2022 Deaths	2023 Deaths (Estimated)
Diarrheal Diseases	1.5M	1.4M	1.4M	1.3M	1.3M
Cholera	95,000	90,000	90,000	100,000	100,000
Typhoid & Paratyphoid	80,000	75,000	75,000	70,000	70,000
Hepatitis A	7,000	7,000	7,000	7,000	7,000
Shigellosis	200,000	190,000	190,000	180,000	180,000
E. coli Infections	265,000	250,000	250,000	240,000	240,000
Norovirus	50,000	45,000	45,000	40,000	40,000
Campylobacteriosis	37,600	35,000	35,000	33,000	33,000
Listeriosis	5,000	5,000	5,000	5,000	5,000
Hepatitis E	44,000	42,000	42,000	41,000	41,000

Diagnostic Testing Workflow

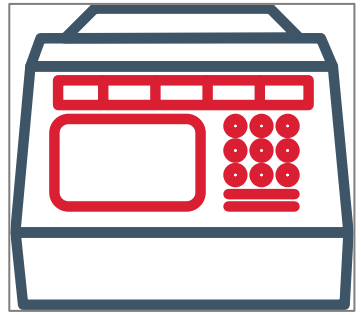


Sample Collection



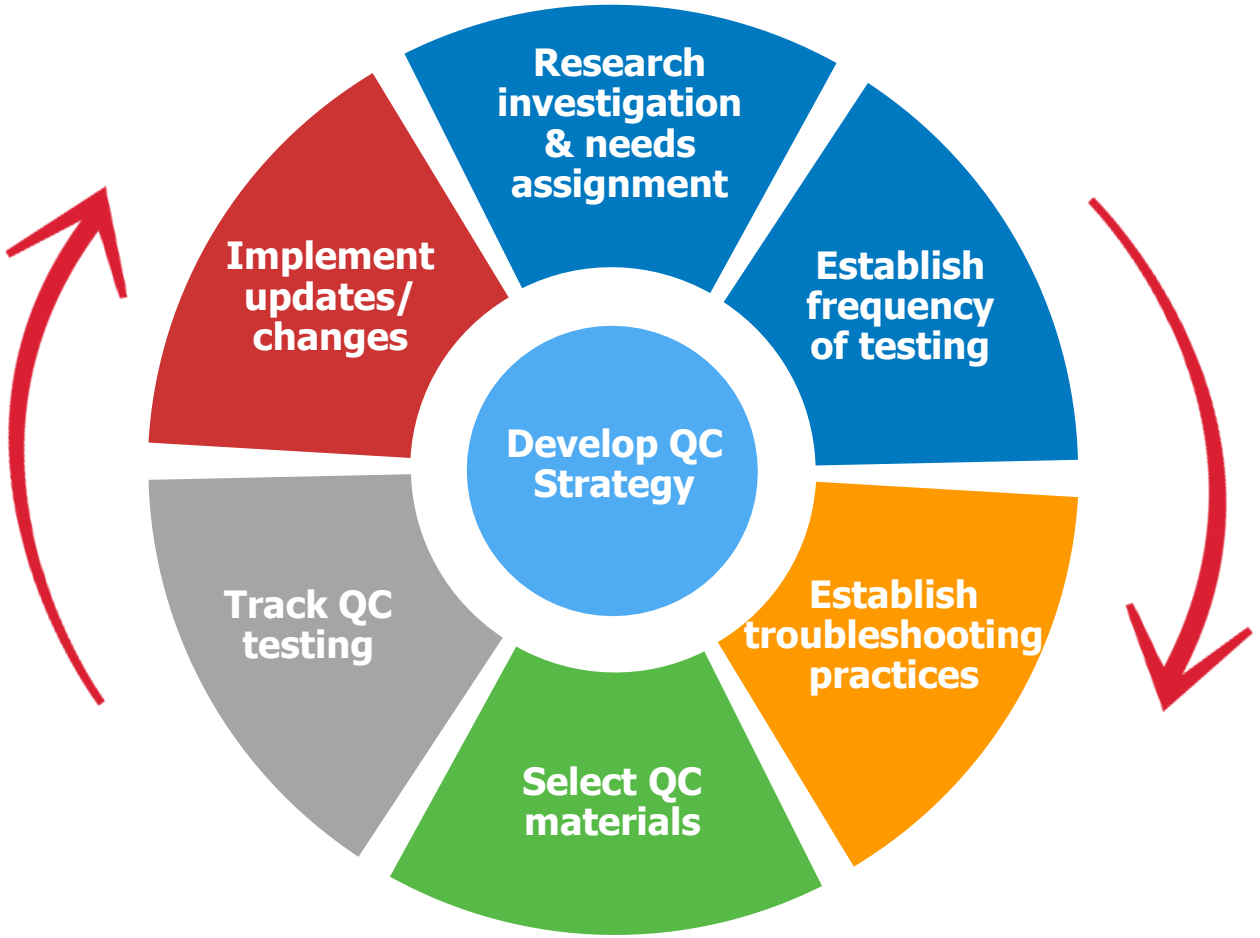
Controls

Sample Processing



Testing

Understanding the role of QC in a Quality Management System



Why do we need a QMS?

The cost of poor quality is more than the cost of quality management!

Laboratory errors occur due to…

- Lack of understanding/training
- Inadequate attention to detail
- Time pressures
- Poor sample control
- Lack of quality control & assessment
- Poor workload management
- Non-validated tests
- Poor results Verification

Types of Controls

Control Types	Description	Purpose
Positive Control	Contains a known amount of the target analyte or nucleic acid.	Confirms that the test detects the target correctly and the assay components are functioning as intended.
Negative Control	Lacks the target analyte or nucleic acid (may include a non-target sample).	Ensures no contamination or non-specific amplification occurs during the test.
Internal Control	Added to each test sample, typically a non-target nucleic acid.	Monitors the entire workflow, including sample extraction, amplification, and detection steps.
External Control	An independent control run alongside patient samples.	Verifies assay performance but does not interact with the patient samples directly.
No Template Control (NTC)	Contains all assay components except the nucleic acid template.	Detects contamination in reagents or workflow steps.
Reference Standards	Well-characterized materials that mimic patient samples (e.g., synthetic or extracted DNA/RNA).	Used for calibration, validation, and proficiency testing of assays.

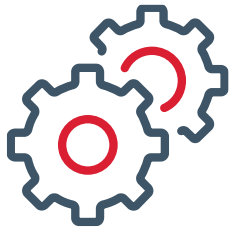
Use of Controls

Aspect	Internal Control	External Control	Positive Control	Negative Control
Integration in Workflow	Included in the same tube/reaction as the sample	Run separately alongside patient samples	Run as a separate reaction	Run as a separate reaction
Purpose	Monitors process consistency and inhibitors	Verifies overall assay performance	Confirms test detects the target correctly	Ensures no contamination or false positives
Example	Non-target synthetic RNA/DNA	Prepared reference material	Sample with known target DNA/RNA	Sample without target DNA/RNA

Why External Quality Run Controls?

- Globally millions of people are tested for infectious disease
- Fast & Accurate testing reduces illness & deaths
- Accurate and precise tests are necessary to confirm correct results
  - Eliminate false positive or false negative reports
  - Improve patient care and maximize confidence in patient test results

Clinical Outcomes



Operational Outcomes

Financial Outcomes

Innovation

Routine Quality Control – ISO 15189

MEDICAL LABORATORIES – REQUIREMENTS FOR QUALITY AND COMPETENCE

7.3.7.2 Internal quality control (IQC)

The laboratory shall have an IQC procedure for monitoring the ongoing validity of examination results, according to specified criteria, that verifies the attainment of the intended quality and ensures validity pertinent to clinical decision making.

1. The intended clinical application of the examination should be considered, as the performance specifications for the same measurand can differ in different clinical settings.
2. The procedure should also allow for the detection of either lot-to-lot reagent or calibrator variation, or both, of the examination method. To enable this, the laboratory procedure should avoid lot change in IQC material on the same day/run as either lot-to-lot reagent or calibrator change, or both.
3. The use of third-party IQC material should be considered, either as an alternative to, or in addition to, control material supplied by the reagent or instrument manufacturer.

Why Third-Party External Quality Run Controls?

- Laboratory quality control is intended to detect, reduce, and correct deficiencies in a laboratory's internal analytical processes before patient results are released, thereby improving the quality of the reported results.
- Independent unbiased assessment of performance
- ISO recommended (15189:2012)

Best Practices in QC Materials

Features to consider

- Independent of manufacturer (third party)
- Independent of analyzer internal controls
- Preferably can be used on multiple platforms/independent of platform
- Contains useful combination of organisms of interest
- Ease of use
- Safety

Comparison of different commonly used QC options

- “Home Brew” – created in lab from patient samples
- Kit/Manufacturer Internal controls – on board controls and/or sold by assay manufacturer with test kit
- Third Party External controls
- Proficiency Testing/External Quality Assessment Samples (PT/EQAS)
  - Not really a “control”

How Does Your QC Compare?

	Home Brew	Internal / Kit Controls	3rd Party External Controls
Independent of assay	✅	❌	✅
Storage	❌	?	✅
Ease of use	❌	✅	✅
Full Process	✅	?	✅
Safety	❌	✅	✅
Cross Platform Capabilities	✅	❌	✅

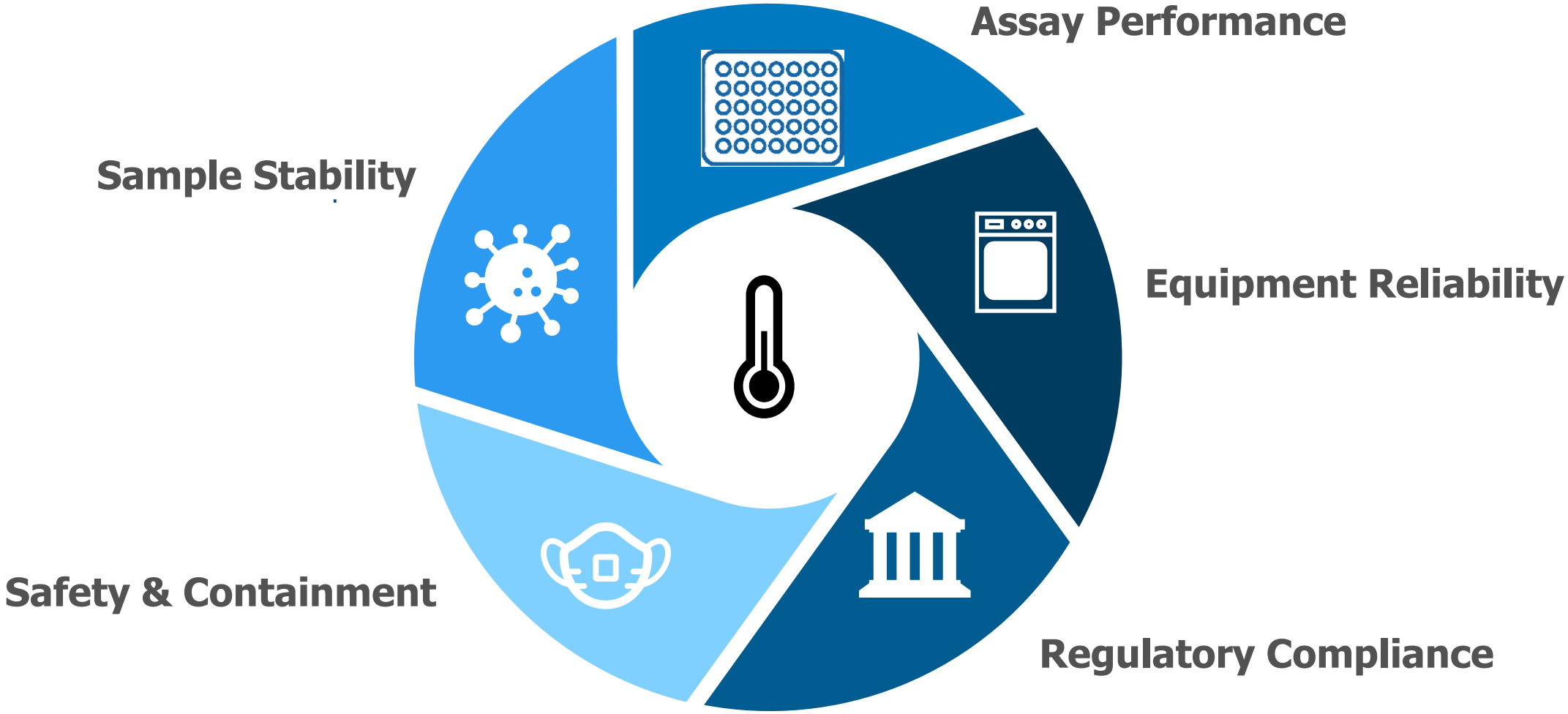
Quality Control Manufacturer Comparisons

Company	Storage Temperature	Format	Attribute	Product	Properties	Shipping
ZeptoMetrix	2 to 8 °C	Liquid	Ready to Use	Intact Inactivated Organism	Qualitative or Quantitative	Gel Pack
Bio-Rad (Exact)	−20 °C	Liquid	Requires Thaw	Inactivated Whole Organism and Synthetic RNA	Qualitative or Quantitative	Dry Ice
LGC Clinical Diagnostics	2 to 8 °C	Liquid	Ready to Use	Recombinant	Qualitative or Quantitative	Gel Pack
Microbiologics	2 to 25 °C	Pellet/Swab	Requires Hydration	Inactivated Whole Organism	Qualitative	Gel Pack
Maine Molecular	−25 to 8 °C	Frozen/Liquid	Requires Thaw/ Ready to Use	Synthetic RNA/DNA	Qualitative	Dry Ice
Qnostics	−80 to −20 °C	Frozen	Requires Thaw	Inactivated Whole Organism	Quantitative	Dry Ice

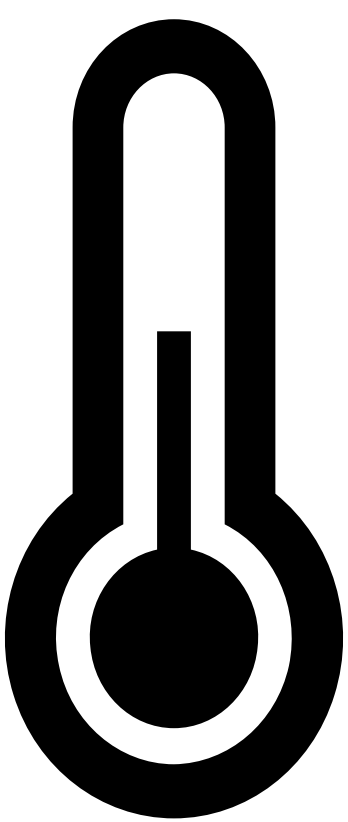
Importance of Monitoring Temperature & Humidity in Diagnostic Testing

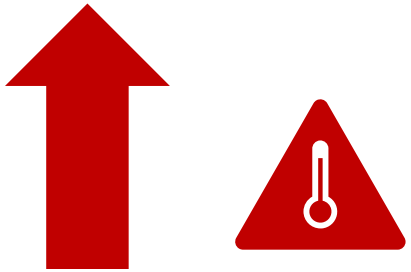
Critical Temperatures

Importance of Temperature & Humidity Monitoring



Temperature & Sample Stability





~100 °C denaturing proteins, chemical degradation, boiling

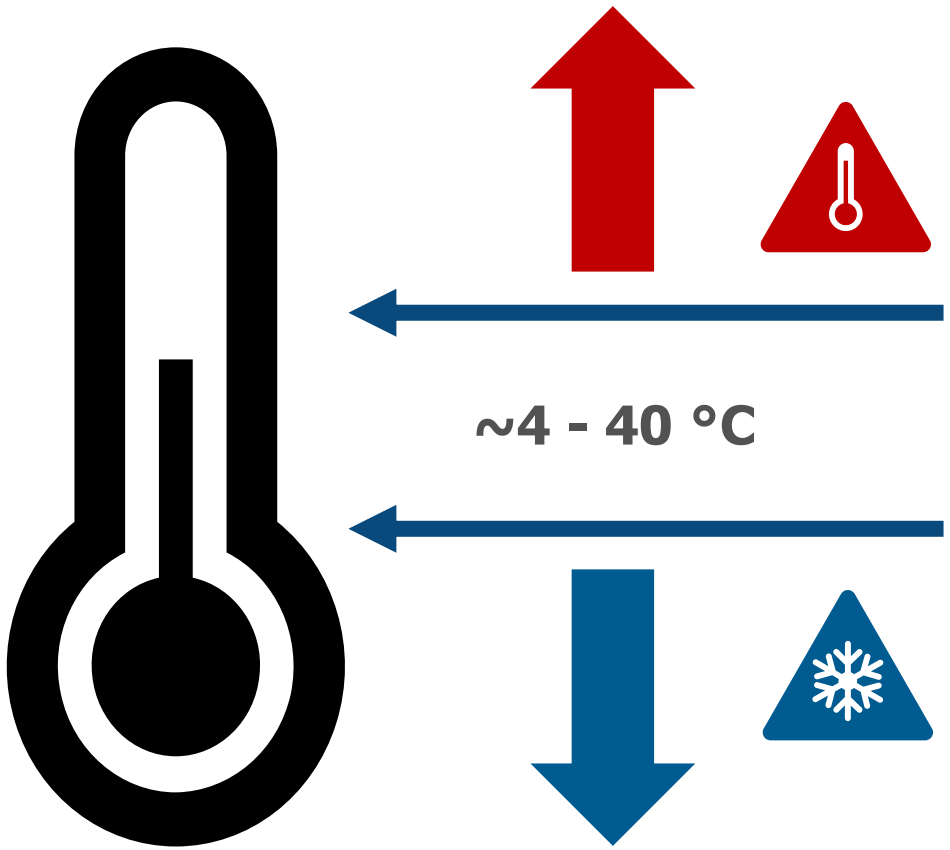
~>40-45 °C Cell Death, VOA

~4 - 40 °C ***'Goldilocks' temperature***

~<5 °C Cell Death

<-20 °C Freezing/Rupture

Sample Stability



Living Plant / Animal Cells	Living Molds, Bacteria & Viruses	DNA / RNA	Chemicals
❌	?	❌	❌
?	?	Denatures	?
✅	✅	✅	?
✅	✅	✅	✅
❌	❌	✅	✅
❌	?	✅	✅

Temperature, Time and Pathogens

Pathogen	Min Temp (°C)	Max Temp (°C)	Duration of Survival	Notes
Mycobacterium tuberculosis (TB)	~0°C	65°C	Months at low temps, minutes at max	Resistant in cool, moist environments; heat kills above 60°C in minutes.
Hepatitis B Virus (HBV)	~4°C	~60°C	Weeks at 4°C, minutes at 60°C	Stable at room temperature for up to 7 days; inactivated by boiling.
Neisseria meningitidis (Meningitis)	~10°C	37°C	Days at low temps, hours at 37°C	Does not survive well outside the host; heat and UV-sensitive.
Measles Virus	~4°C	56°C	Hours at room temp, minutes at 56°C	Highly sensitive to heat, UV, and disinfectants.
Bordetella pertussis (Whooping Cough)	~10°C	37°C	Days at low temps, hours at 37°C	Survives better in moist conditions; sensitive to drying and heat.
Vibrio cholerae (Cholera)	~10°C	55°C	Weeks at 10°C, minutes at 55°C	Survives in water; inactivated by boiling and chlorination.
Salmonella spp. (Typhoid)	~7°C	55°C	Weeks at 7°C, minutes at 55°C	Survives in frozen conditions; killed by heat above 55°C.
Hepatitis A Virus (HAV)	-20°C	85°C	Months at -20°C, minutes at 85°C	Survives freezing; heat kills effectively.
Shigella spp.	~4°C	60°C	Days at low temps, minutes at 60°C	Heat-sensitive; thrives in cool, moist environments.
Escherichia coli (E. coli)	~7°C	70°C	Weeks at 7°C, minutes at 70°C	Survives refrigeration; killed by thorough cooking.
Norovirus	-20°C	65°C	Months at -20°C, minutes at 65°C	Freezing does not kill the virus; heat inactivates it.
Campylobacter spp.	~4°C	55°C	Weeks at 4°C, minutes at 55°C	Does not grow below 30°C or above 45°C; heat-sensitive.
Listeria monocytogenes	~-1°C	74°C	Months at low temps, minutes at 74°C	Survives freezing and grows at refrigeration temperatures.
Hepatitis E Virus (HEV)	~4°C	~60°C	Weeks at low temps, minutes at 60°C	Stable in cold environments; heat-sensitive.
Influenza Virus	~0°C	56°C	Weeks at low temps, minutes at 56°C	Stable in cold and moist conditions; heat and UV-sensitive.
Respiratory Syncytial Virus (RSV)	~4°C	37°C	Days at low temps, hours at 37°C	Does not survive well in the environment; heat-sensitive.
Corynebacterium diphtheriae (Diphtheria)	~4°C	55°C	Weeks at low temps, minutes at 55°C	Survives in dried environments; inactivated by heat.
Plasmodium spp. (Malaria)	~15°C	40°C	Weeks in cool water, hours at max temp	Temperature-dependent lifecycle; cannot survive freezing or high heat.

Thaw/Freezer Cycle Dangers

Biological Samples

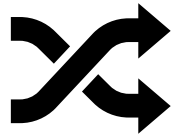
Ice crystal formation

Cell rupture

RNA & DNA changes

Deactivation, Denaturation or Agglutination

Structural Disintegration & Osmotic Shock



Contamination

Microbial & Pathogenic Samples

Loss of Viability

Changes in Microbial Load

Changes in Microbial Community

Pathogenicity Changes

Biohazard

Mitigation Strategies

Proper Freezing

- Cryoprotectants
- Rapid Freezing (LN)
- Processing with cold techniques

Minimize Thaw/Freeze

- Aliquots
- Controlled Rapid Thaw
  - Water baths

Proper Storage

- Correct Temperature
- Humidity Controls

Monitoring

- Onsite Alarms
  - Alert excursions (audible/visible)
- Data loggers (documents excursions)
  - Time
  - Frequency
  - Duration
- Cloud Connected Systems
  - Constant monitoring
  - Local & Remote alerts for excursions
  - Audible/Visual/Electronic

Comparing Common Temperature Measurement Technologies

	Digital Thermometer	Liquid-in-Glass Thermometer	IR Thermometer	Thermistor	Cryogenic Temperature Probe
Description	Electronic with a digital display	Alcohol/mercury-filled glass tube	Non-contact infrared radiation	Resistance-based ceramic/polymer	Probes for cryogenic applications
Uses	General lab equipment	Backup thermometer	Spot-check equipment surfaces	General lab refrigerators/freezers	Cryogenic tanks and freezers
Accuracy Range	±0.5 °C to ±1.0 °C	±1.0 °C to ±2.0 °C	±1.0 °C to ±2.0 °C	±0.2 °C to ±0.5 °C	±0.1 °C
Pros	Affordable, easy to use, quick readings	Simple, low-cost, no batteries	Non-contact, fast measurement	Cost-effective, sensitive	Highly accurate for cryogenics
Cons	Recalibration or replacement. Can have limited ranges.	Fragile, hazardous, Inconvenient for frequent checks	Cannot measure internal temps. Surface only. Sensitive to environment	Fragile in extreme environments. Limited range	More Expensive, requires skilled use & expert calibration

Selecting the Best Probe for Your Temperature Application

REFRIGERATOR/FREEZER

NO

YES

EXTREME TEMPERATURES

NO

YES

Bottle Probe

- Sealed, nontoxic
- Temperature-buffered
- Eliminates rapid changes when refrigerator door is opened

Vaccine Bottle Probe

- Smaller bottle
- Reacts faster than standard bottle probe

Stainless Steel Probe

- Fast response
- Readings update quickly
- Works through ports (ultra-low freezers, ovens, incubators, etc.)
- Not available yet

Bullet Probe

- Small size
- Use in air or liquids

Choosing Temperature Monitors (CDC, WHO, FDA)

Devices must adhere to the standards of organizations such as:
- ISO 15189: For medical laboratories.
- ISO 17025: For calibration and testing labs.
- FDA 21 CFR Part 11: For electronic records in diagnostic labs.

Accuracy

- ±0.5 °C or better
- High-precision requirements

Range

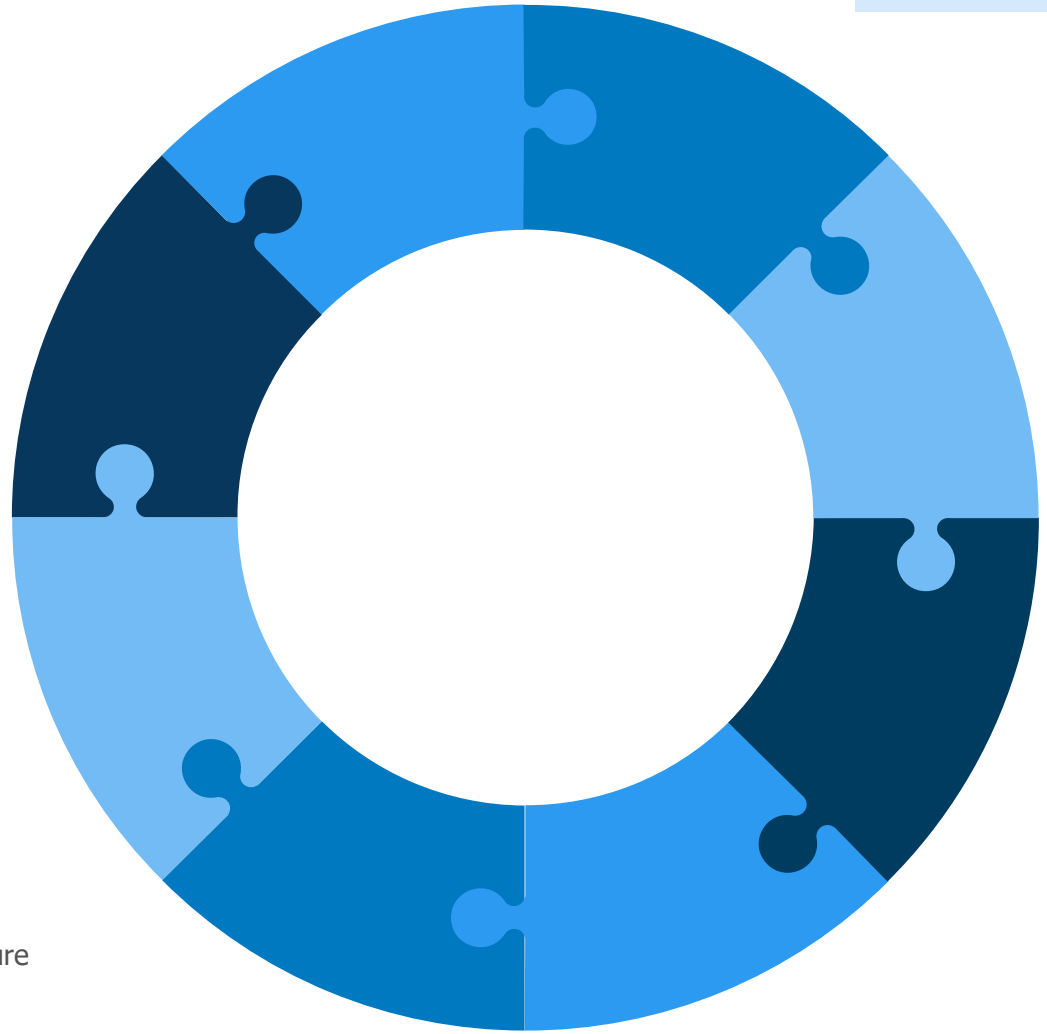
- Typical laboratories: -50 °C to 60 °C.
- Specialized equipment: -80 °C for freezers to +150 °C for incubators.

Resolution

- Minimum 0.1 °C for precise readings

Response Time

- Fast response to detect rapid temperature changes, typically <10 seconds



Data Logging

- Capacity for minimum of 30 days of readings with timestamps
- Programmable logging intervals <30 minutes

Alarm System

- Alerts & Alarms audible/visible/data Memory for recording alarms & events
- Alerts for exceeding thresholds

Calibration

- Certificate of Calibration
- Detachable and or smart probes

Power Supply

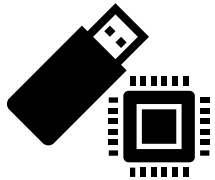
- Battery operated or battery backup
- Low battery indicator

Choosing the Right Datalogger

Type	USB Data Loggers	Standalone Data Loggers	Wireless Data Loggers	Cloud-Connected Data Loggers	Multi-Channel Data Loggers	Cryogenic Data Loggers	Disposable Data Loggers	Integrated System Loggers
Features	Plug directly into a computer for data retrieval	Self-contained units with internal memory and an LCD display	Use Wi-Fi, Bluetooth, or RF for real-time monitoring	Transmit data directly to cloud storage for global access	Measure multiple parameters (e.g, temp, humidity) simultaneously	Specifically designed for ultra-low and cryogenic storage applications	Single-use devices for short-term applications (e.g, shipping)	Part of larger systems (e.g, refrigerators, freezers) with built-in logging functionality
Pros	Affordable, easy to use, portable	Simple setup, no external connections needed	Real-time data, remote access, configurable alerts	Highly scalable, remote monitoring from anywhere	Versatile, ideal for complex monitoring requirements	Operate reliably in extreme conditions	Cost-effective for one-time use, easy to deploy	Seamless integration, no extra devices needed
Cons	Manual data retrieval; no real time alerts	Limited by storage capacity; must retrieve data manually	Dependent on network stability; higher initial cost	Requires internet connection; subscription fees may apply	More expensive, requires advanced setup	Limited use outside cryogenics; high cost	Cannot be reused; limited features and storage capacity	May lack portability; tied to specific equipment

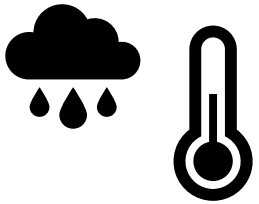
Key Features of Dataloggers

Data Storage Capacity

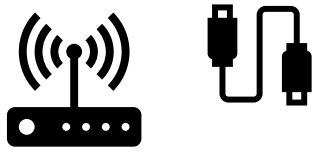


Measurement Parameters

DL most often paired with Temperature, Humidity etc.



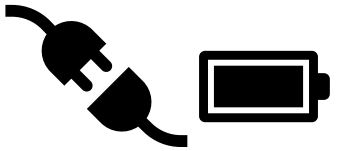
Connectivity



Regulatory Compliance

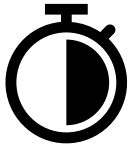
User Interfaces

Power Source

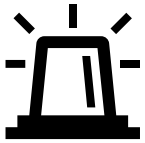


Durability

Sampling Rates



Alarms & Alerts



Dataloggers are Ideal for These Locations and Uses

IF YOU ARE

- Reference Lab
- Blood Bank/Biobank
- Hospital/Clinical Lab
- Acute Care/Physician's office

IF YOU PURCHASE THESE

- Refrigerators and Freezers
- LN_2 Dewars and Cryo Storage
- Cryogenic Storage
- Incubators and Ovens
- Reagents

Humidity Considerations

Humidity Change Dangers

Biological Samples

Dehydration or Hydration Swelling

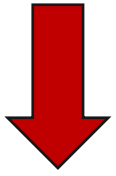
Cell rupture

DNA / RNA Hydrolysis or Degradation

Deactivation, Denaturation or Agglutination

Structural Disintegration & Osmotic Shock

Microbial & Pathogenic Samples



Loss of Viability & Load

Sporulation & Dormancy

Changes in Microbial Community

Pathogenicity Changes

Transmission Risks

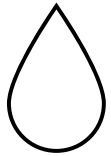
Water dependent bacteria, encapsulated viruses, & fungi thrive at high humidity (ex. *Chlorea, Influenza)*

Spore producing microorganisms, Aerolized pathogens, nonenveloped viruses can thrive in low humidity (ex. *Clostridium, Bacillus, Norovirus, Rhinovirus)*

Humidity and Pathogens

Pathogen	Sensitivity to Humidity	Optimal Humidity Level (%)	Environmental Preferences
Norovirus	Low sensitivity	30-70%	Stable across varying humidity; survives well in dry environments.
Influenza Virus	High sensitivity	40-60%	Thrives in humid environments but survives longer in dry, cold air.
Mycobacterium tuberculosis (TB)	Low sensitivity	40-60%	Survives better in dry, cool, and moist environments; desiccation-resistant.
Hepatitis A Virus (HAV)	Low sensitivity	40-70%	Relatively stable under low humidity but prefers moist conditions.
Hepatitis B Virus (HBV)	Low sensitivity	40-70%	Stable at low humidity but survives better in moist conditions.
Hepatitis E Virus (HEV)	Low sensitivity	40-70%	Stable in moist and low humidity environments.
Listeria monocytogenes	Low sensitivity	40-80%	Survives well across varying humidity; grows in refrigeration.
Salmonella spp. (Typhoid)	Moderate sensitivity	40-80%	Thrives in moist environments; survives longer in dry conditions than some pathogens.
Measles Virus	High sensitivity	50-80%	Highly sensitive to low humidity; survives better in moist air.
Respiratory Syncytial Virus (RSV)	High sensitivity	50-80%	Requires moist conditions; unstable in low humidity.
Escherichia coli (E. coli)	Moderate sensitivity	50-85%	Stable in moist conditions; survives drying moderately well.
Corynebacterium diphtheriae (Diphtheria)	Moderate sensitivity	50-85%	Survives better in moist air but can tolerate drying to some extent.
Bordetella pertussis (Whooping Cough)	High sensitivity	60-85%	Thrives in moist conditions; does not survive well when dried.
Vibrio cholerae (Cholera)	High sensitivity	60-90%	Prefers high humidity; survives in moist aquatic environments.
Shigella spp.	High sensitivity	60-90%	Thrives in moist environments; sensitive to drying.
Campylobacter spp.	High sensitivity	60-90%	Thrives in moist conditions; does not survive well when dried.
Plasmodium spp. (Malaria)	High sensitivity	70-100%	Requires humid environments for mosquito vectors to thrive.
Neisseria meningitidis (Meningitis)	High sensitivity	70-90%	Requires moist environments for survival; dries out quickly.

Mitigation Strategies



Humidity Controls

- Protectants
- Rapid Freezing (LN)
- Desiccants

Minimize Thaw/Freeze

Proper Storage

- Correct Temperature
- Humidity Controls

Monitoring (Humidity, Temperature, CO2)

- Onsite Alarms
- Data loggers (documents excursions)
  - Time
  - Frequency
  - Duration
- Cloud Connected Systems
  - Constant monitoring
  - Local & Remote alerts for excursions
  - Audible/Visual/Electronic

Features of Humidity Monitors

Devices must adhere to the standards of organizations such as:
- ISO 15189: For medical laboratories.
- ISO 17025: For calibration and testing labs.
- ISO 14644: For clean room monitoring
- FDA 21 CFR Part 11 & Part 820: For electronic records in diagnostic labs.

Accuracy

- ±2-3% RH (Relative Humidity) for most lab applications.
- ±1% RH for highly controlled environment (e.g., cleanrooms).

Range

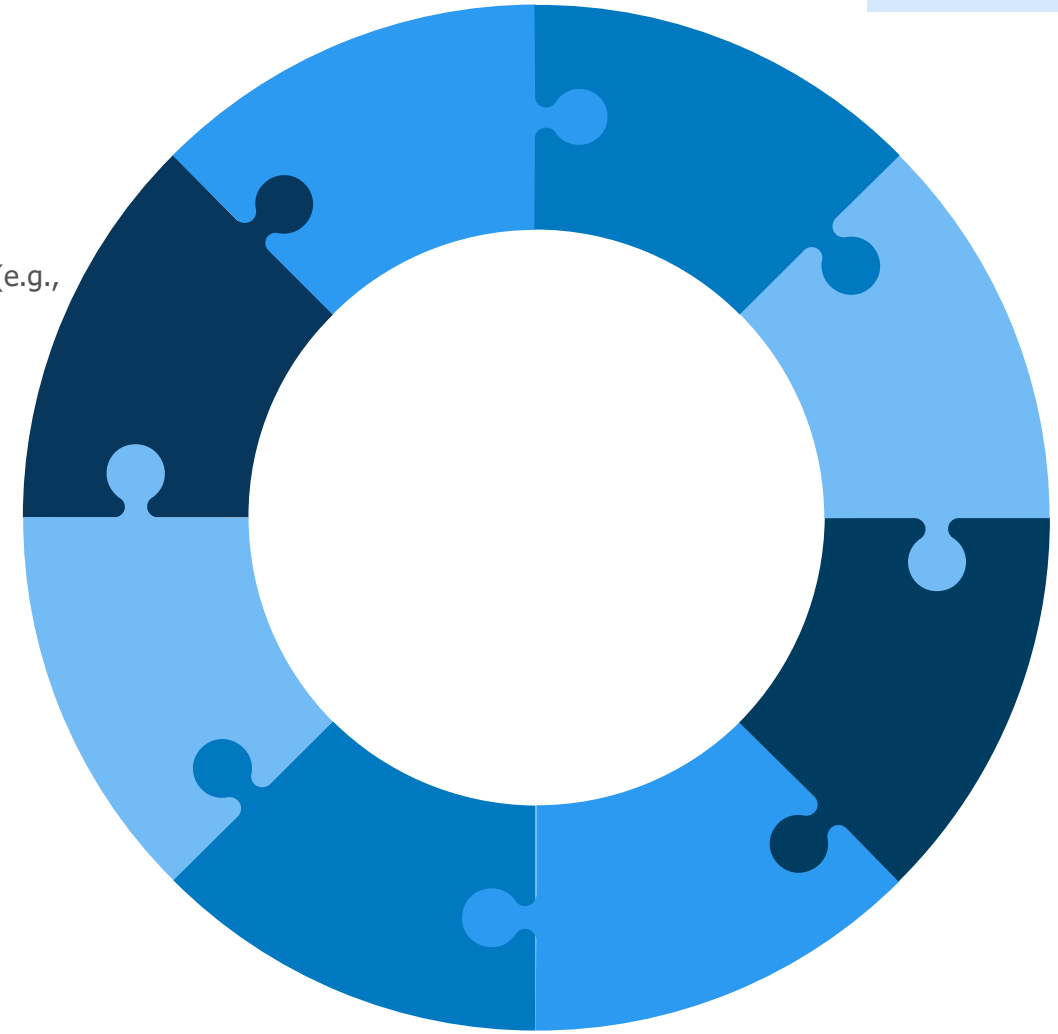
- Typical laboratories: 0% to 100% RH

Resolution

- Minimum 1% RH

Response Time

- Fast response to detect rapid changes within 10-30 seconds for accurate monitoring



Data Logging

- Capacity for minimum of 30 days of readings with timestamps

Alarm System

- Alerts & Alarms audible/visible/data Memory for recording alarms & events
- Alerts for exceeding RH thresholds (e.g., >60% in storage areas)

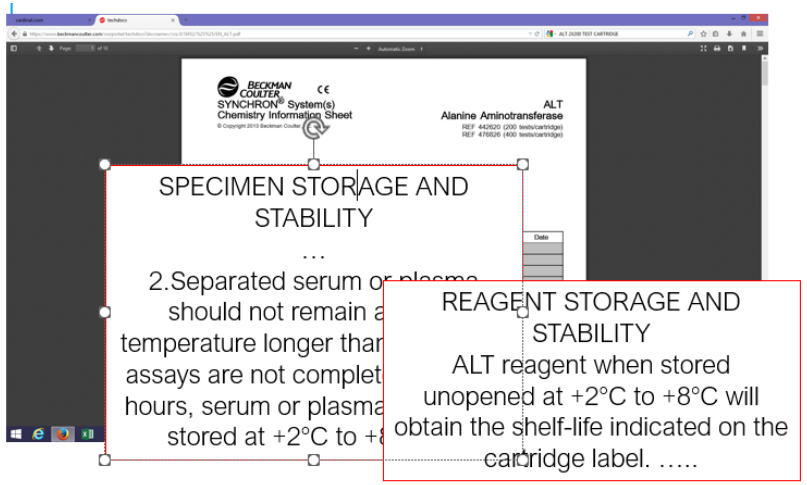
Calibration

- Certificate of Calibration

Power Supply

- Battery operated or battery backup
- Low battery indicator

No Matter What You Are Storing, Make Sure You Are Monitoring

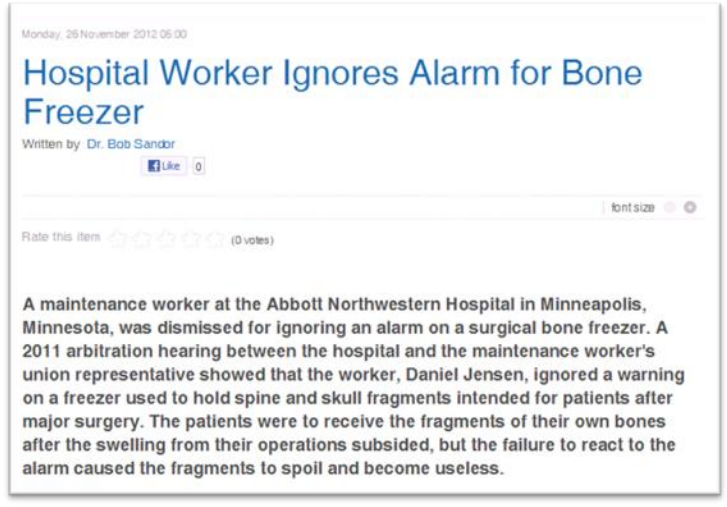


"Our future family ... is gone': Parents in two cities grieve their lost embryos

The freezer failure

The malfunction occurred when temperatures unexpectedly fluctuated in the liquid nitrogen storage tank where the eggs and embryos were stored, University Hospitals said. An investigation revealed that the remote alarm system on the tank, designed to alert an employee to changes such as temperature swings was off.

"We don't know when the remote alarm was turned off, but it remained off through that weekend, so an alert wasn't sent to our employee as the tank temperature began to rise on Saturday night, when the lab isn't staffed,".



THANK YOU