

June 2021

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Laboratory
News

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FOR ddPCR

98%

Specificity using
algorithm vs. 88%
for standard
droplet digital PCR

PAGE 6

Preanalytical Peril

The sample's
journey to the lab



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Subscriptions

AACC
900 Seventh St., NW, Suite 400
Washington, DC 20001
Phone: +1 202.857.0717 or +1 800.892.1400
Email: custserv@aacc.org

Editorial Correspondence

Bill Malone, Managing Editor
Phone: +1 202.835.8756 or +1 800.892.1400
Email: bmalone@aacc.org

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“One of the first goals when managing incoming calls is to direct calls away from staff such as clinical laboratory scientists, whose primary focus should be performing testing.”
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AACC Calls for Funding Boost to National Center for Health Statistics

As part of a coalition of associations, patient organizations, scientific societies, and research institutions, AACC is calling on Congress to appropriate at least \$200 million for the National Center for Health Statistics (NCHS) within the Centers for Disease Control and Prevention (CDC) for 2022. NCHS's base budget for the government's 2021 fiscal year is only \$25 million.

"The COVID-19 pandemic highlighted the troubling limitations of the nation's statistical system," the coalition's letter to Congress says. "While NCHS was successful in providing critical information to monitor the impacts of the pandemic, the need for major investments to expand on the scope, timeliness, quality, and useability of information was glaringly apparent."

The letter notes that during the pandemic, problems getting information on healthcare utilization both for COVID-19 and non-COVID-19 related care "confounded the response."

With increased funding, NCHS could develop partnerships with electronic health record vendors and providers to standardize and share data for monitoring healthcare at the national, state, and local levels, and could improve linkage and integration of the country's data collection systems.

Another goal: expand the use of machine learning and artificial intelligence (AI) to improve data collection and processing. AI could automate the coding of deaths of high public health interest such as those from emerging infectious diseases, which the agency currently has to code manually.



HHS: SEX DISCRIMINATION IN HEALTHCARE INCLUDES SEXUAL ORIENTATION, GENDER IDENTITY

The Department of Health and Human Services (HHS) announced that the Office for Civil Rights will interpret and enforce Section 1557 of the Affordable Care Act and Title IX's prohibitions on discrimination based on sex to include discrimination on the basis of sexual orientation or gender identity. This section of the law prohibits discrimination on the basis of race, color, national origin, sex, age, or disability in covered health programs or activities. HHS is making the update in light of the U.S. Supreme Court's decision in *Bostock v. Clayton County* and subsequent court decisions.

"The Supreme Court has made clear that people have a right not to be discriminated against on the basis of sex and receive equal treatment under the law, no matter their gender identity or sexual orientation. That's why today HHS announced it will act on related

reports of discrimination," said HHS Secretary Xavier Becerra.

In its announcement, HHS cited research showing that one quarter of LGBTQ people who faced discrimination postponed or avoided receiving needed medical care for fear of further discrimination.

The Supreme Court's June 15, 2020 decision held that the Civil Rights Act of 1964 prohibiting employment discrimination based on sex encompasses discrimination based on sexual orientation and gender identity. HHS also noted that it will comply with the Religious Freedom Restoration Act and all other legal requirements.

CMS AI CHALLENGE AWARDS \$1.23 MILLION FOR PREDICTING HEALTH OUTCOMES

The Centers for Medicare and Medicaid Services (CMS) has chosen ClosedLoop.ai as the \$1 million winner in the agency's artificial intelligence (AI) Health Outcomes Challenge. Healthcare

system Geisinger is the runner-up and will receive \$230,000. The competition, operated by the CMS Innovation Center in collaboration with the American Academy of Family Physicians and Arnold Ventures, began in 2019 with the goal of accelerating development of AI solutions for predicting patient health outcomes. From an initial group of more than 300 entries, the challenge progressed through several stages, and participants were narrowed down to the top 25 and then seven finalists before selecting the winners.

The contestants had to show that their software predicted unplanned hospital and skilled nursing facility admissions and adverse events, as well as identify beneficiaries at risk of mortality within 12 months. The finalists also had to tackle sources of bias in their solutions that could have the potential to affect health disparities. Finally, CMS also required them to demonstrate how they would be able to easily explain the predictions to clinicians.

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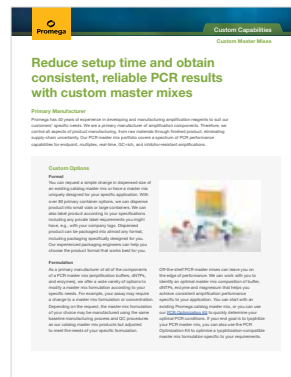
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Are You Wasting Money on Quality Control?

Laboratory errors lead to unnecessary follow-up testing and delayed or incorrect diagnoses, adding millions of dollars annually to healthcare budgets. The sole purpose of clinical laboratory quality control (QC) is to protect patients from unacceptable risk of harm from incorrect or medically unreliable results. If a laboratory's QC processes cannot detect unacceptable risk, then all the time, money, and effort put into them is wasted. Unfortunately, many laboratories may be performing QC that is not adding value.

Assessing a Medically Unreliable Result

What constitutes a medically unreliable result (MUR), and how much risk is unacceptable? An incorrect result is "a result that does not meet the requirements for its intended medical use; in the case of quantitative test procedures, a result with a failure of measurement that exceeds a limit based on medical utility" (1). This echoes advice from the Stockholm (2) and Milan (3) conferences that recommend the use of clinical limits as the best choice for allowable total error limits (TEa).

Monthly QC review should ensure that method performance is stable and that the number of MURs per year is acceptable. Daily QC should be able to detect a change in method accuracy or precision that would cause too many MURs to be reported. Of course, it is imperative that QC samples be commutable and mirror patient samples.

In a recent informal LinkedIn poll, I asked, "If a laboratory method fails, when should you see a QC reject flag (with 100 patients in each run)?" Forty-five percent chose either "when sigma drops to 1.65" or "when the error rate reaches 5%," which means the same thing. The rest of the votes were split evenly between "when sigma drops to 3.0" (equivalent to 0.1 MUR/failure) and "if one error is

reported." While there are a plethora of references on TEa limits in the literature, there is currently not a consensus standard for the maximum allowable number of lab errors.

The Clinical and Laboratory Standards Institute (CLSI) EP23-A document (1) states that "at the least, the ability of the QC procedures to detect medically allowable error should be evaluated." Through various studies on QC effectiveness (4, 5, 6) I have repeatedly found that approximately 30% of QC processes would never detect a simulated shift in the mean that caused 5% of patient results to fail the TEa limit. While I prefer QC processes that allow only one MUR per failure event, a 5% acceptable failure rate does represent popular practice.

Why QC Fails

I further explored why QC fails recently with Sanford Moos, QC auditor at Sherman Abrams Labs in Brooklyn, New York, who kindly sent me QC data to evaluate from three calcium QC samples. For the low level, because the chart mean was set at 1 standard deviation (SD) above the measured mean, the intended 1-5s rule that was recommended by QC software would reject a QC result if it was more than 6 SD above, or 4 SD below, the measured mean. With a negative bias and a sigma value of 7.0, the mean could shift -4 SD before the new sigma value would reach the defined acceptable risk level of 3.0 sigma. A shift of -4 SD would place the mean at exactly the assigned QC rule limit of -5 SD. Fifty percent of QC results would fall above the 1-5s line, and 50% would send reject flags; it would probably take two QC runs to detect failure of this method.

Level 2 contained a clerical error and could not be evaluated. Level 3 had a sigma value of only 3.2. A shift of +0.2 SD would make this method fail acceptable risk criteria. The recommended 1-5s rule would never detect this shift.



Zoe Brooks,
ART



After further discussion, Mr. Moos and I agreed on several reasons why QC could fail in laboratories:

- Focus on the cost, rather than the value, of quality control.
- Not enough evaluation of the ability of QC procedures to detect medically allowable error. Daily QC will effectively detect a significant shift from current performance only if mean and SD values on the QC chart represent current performance, and test frequency and QC rules or statistical limits have been verified to send a QC reject signal before an unacceptable number of MURs are reported.
- Lack of testing QC samples at clinically meaningful levels.
- Assumption that good proficiency testing (PT) equals acceptable quality, when in fact it would take a 20% error rate to trigger a failure of one sample in five, and a failure state could exist for months before PT would detect it.
- Setting of arbitrary or statistical, rather than clinical, limits for the acceptable number of MURs per year and per failure event.
- Failure to perform routine risk evaluation comparing the estimated risk to the acceptable risk criteria (e.g., the number and cost of error).
- Insufficient education on the basics of QC.
- Differences in QC practices and acceptable standards between labs.
- Belief that QC is merely a perfunctory task that does not affect patient care.
- Government allows/encourages labs to run only once a day.

In addition, laboratory accreditation inspectors do not necessarily enforce recommendations from CLSI, CLIA, or the Internal Organization for Standardization for QC.

What can labs do about this? First, laboratorians must decide whether they are willing to keep reporting bad results or if they are willing to change. It is important that laboratorians understand that better QC saves money and improves patient care. The good news is that software now exists to evaluate QC and quantify savings.

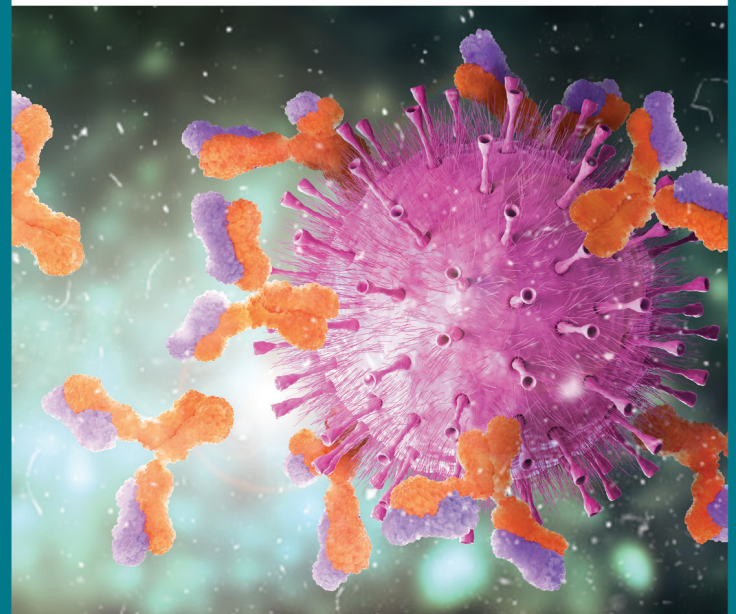
References

1. Clinical and Laboratory Standards Institute (CLSI). Laboratory quality control based on risk management, approved guideline. CLSI Document EP23-A. Wayne, Pa.: CLSI 2011.
2. Kallner A, et al. The 1999 Stockholm Consensus Conference on quality specifications in laboratory medicine. *Scand J Clin Lab Invest* 1999; 59: 475.
3. Brooks Z. Benchmarking laboratory quality. ResearchGate 2001.
4. Brooks Z. The business case for optimized quality control practice. ResearchGate 2012.
5. Brooks Z. Evaluation of quality Optimizer software to simplify application of CLSI EP 23-A, minimize patient risk, and reduce clinical cost. ResearchGate 2015.

Zoe Brooks, ART, is CEO, cofounder, and director of research and innovation at AWEsome Numbers, Inc.

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The Sample

Algorithm May Help Reduce Droplet Digital False Positives in Some Lung Cancer Patients

Correcting induced false-positive events and using a new data interpretation algorithm may make droplet digital PCR (ddPCR) more sensitive and accurate in patients with stage 4 non-small cell lung cancer (NSCLC) (Clin Chem 2021; doi:10.1093/clinchem/hvab040).

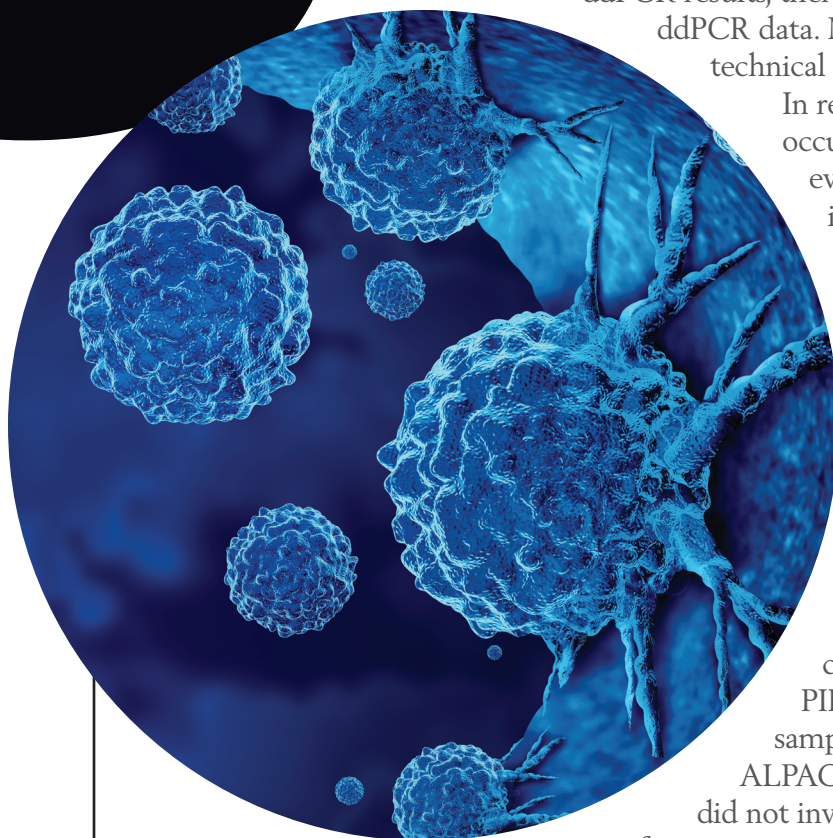
Often used to detect mutations in cancer patients' circulating cell-free (cf) DNA, ddPCR is highly sensitive and can detect variants with low variant allele frequencies. Based on water-oil emulsion droplet technology, ddPCR involves fractionating the sample into thousands of droplets and amplifying template molecules in each individual droplet.

Distinguishing a true positive from a false positive signal is a challenge with ddPCR. While optimum sensitivity and specificity rely on correct interpretation of ddPCR results, there is no standardized method for interpreting ddPCR data. Meanwhile, few studies have focused on technical artifacts that affect ddPCR results.

In response, researchers aimed to report the occurrence of polymerase-induced false-positive events (PIFs) and an input-dependent increase in PIFs in ddPCR experiments. The researchers developed a novel ddPCR data interpretation algorithm called "adaptive limit of blank (LoB) and PIFs: an automated correction algorithm" (ALPACA). The algorithm combines corrections for assay-specific error rates and technical artifacts.

The researchers determined false positive rates for six ddPCR assays at varying amounts of input DNA. This process revealed PIFs and other false positives. The researchers used an *in silico* correction algorithm plus ALPACA to remove PIFs and to apply an adaptive LoB to each sample. Afterwards, the researchers compared ALPACA's performance to a standard strategy that did not involve PIF correction, using a LoB of 3 and data from commercial reference DNA. The researchers conducted this comparison on cfDNA from healthy volunteers and a cohort of 209 patients with stage 4 NSCLC, as well as their molecularly profiled tumors.

Applying ALPACA reduced false-positive results in cfDNA of healthy volunteers and NSCLC patients, compared to the standard strategy. For healthy volunteers, specificity was 98% using ALPACA, versus 88% for the standard method. For stage 4 NSCLC patients, specificity was 99%, versus 93% using the standard method. Using ALPACA did not markedly affect sensitivity in commercial reference DNA or patient cfDNA.



PRECONCEPTION THYROTROPIN SCREENING RESULTS ASSOCIATED WITH ADVERSE OUTCOMES

A recent paper makes a case for preconception thyrotropin screening (JAMA Network Open 2021;4(4):e215723. doi:10.1001/jamanetworkopen.2021.5723).

Maternal thyroid function—especially during early gestation—is important for the best pregnancy outcomes. Previous research suggests an early, narrow window for diagnosing and treating thyroid maladies. Although medical guidelines recommend screening for thyroid dysfunction during pregnancy, little research has examined preconception screening.

In a population-based cohort study of approximately 5.8 million Chinese women ages 20 to 49, researchers studied associations between preconception thyrotropin levels and preterm birth (PTB), small size for gestational age (SGA), birth defects, and perinatal infant death. The mothers gave blood after at least 8 hours of fasting prior to preconception exams conducted within 6 months before pregnancy. The women also had exams in early pregnancy and following adverse outcomes.

The researchers established a population-specific reference range that established the 2.5th, 50th, and 97.5th percentiles for thyrotropin levels as 0.37 mIU/L, 1.66 mIU/L, and 4.88 mIU/L, respectively.

The women's median thyrotropin level was 1.60 mIU/L. Cumulative incidences for adverse pregnancy outcomes were 6.56% for PTB, 7.21% for SGA, 0.02% for birth defects, and 0.33% for perinatal infant death. Compared with a reference group with thyrotropin range concentrations ranging from 0.37-2.49 mIU/L, both low (less than 0.10 mIU/L to 0.36 mIU/L) and high (4.88 to 10.00 mIU/L) maternal preconception thyrotropin levels were associated with higher risk of PTB, SGA, and perinatal infant death. The researchers found J-shaped associations—indicating lowest incidence in the

middle ranges and peaks in the upper and lower ranges—between preconception thyrotropin levels and PTB and perinatal infant death.

Based on these findings, the researchers suggest that an optimal preconception thyrotropin level is between 0.37 mIU/L and 2.50 mIU/L.

The researchers note some study limitations. These include not testing thyroid autoantibodies, which are associated with a higher risk of PTB, not following up on offspring's intellectual and cognitive function, and stratifying patients according to iodine status.

PANCREATIC STONE PROTEIN TESTING MAY HELP PREDICT SEPSIS

Serial pancreatic stone protein (PSP) increases in the days preceding the onset of signs involved in clinical diagnosis of sepsis, according to recent research (Crit Care 2021;25:151).

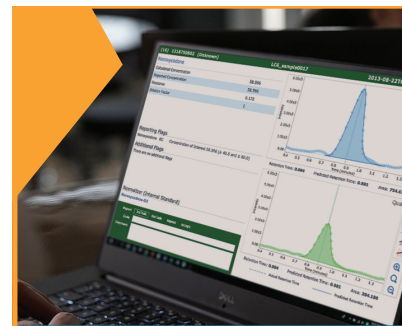
Biomarkers may help identify subclinical signs of sepsis, leading to earlier recognition and management of sepsis and better outcomes. Researchers conducted an observational clinical study to explore how well serial measurements of C-reactive protein (CRP), procalcitonin (PCT), and pancreatic stone protein (PSP) would spot sepsis in 234 patients at risk of nosocomial sepsis in 14 intensive care units (ICUs) in France, Switzerland, Italy, and the United Kingdom.

Via receiver operating characteristic (ROC) analysis, the researchers assessed these biomarkers' performance as sepsis biomarkers by examining the association of clinical diagnoses with the trajectories of PSP, CRP, and PCT during the 3 days preceding diagnosis. In the absence of an unambiguous definition of sepsis and highly accurate diagnostic tools, an expert committee determined the presence or absence of sepsis on any given day of an ICU stay.

Fifty-three patients developed nosocomial sepsis after a median of 6

days. The diagnostic accuracy of PSP, CRP, and PCT were similar. Sepsis diagnosis was associated with an increase in all biomarkers' value over the 3 days preceding this. However, PSP started to increase 5 days before the clinical diagnosis of sepsis, compared to 3 days prior for PCT, and 2 days prior for CRP. The area under the ROC curve at the time of clinical sepsis was similar for all markers (PSP, 0.75; CRP, 0.77; and PCT, 0.75).

While the diagnostic accuracy of PSP, CRP, and PCT for sepsis were similar, the rise in PSP before the others justifies further evaluation of it as a serially measured biomarker for managing critically ill patients.



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Forensic scientists join together to create an open-access drug characterization and tracking database that can benefit laboratories across the nation.





New Drugs of Abuse

NPS Discovery and the Hunt for

BY FRANCES SCOTT, PHD

Both healthcare professionals and the public have been bombarded with news reports about the opioid crisis. However, the opioid crisis is just the latest in a more than decade-long trend of emerging drugs that are chemically similar to well-known drugs, but that may behave very differently inside the body and are difficult for laboratories to identify and classify using existing technologies (see sidebar, *A Century of NPS in the United States*, page 10).

The most recent wave of novel psychoactive substances (NPS) emerged in the 2000s. As law enforcement and laboratories found and

identified new members of drug classes such as cathinones and cannabinoids in drug seizures, the Drug Enforcement Administration (DEA) provided temporary scheduling, making these drugs illegal. In response, manufacturers—often located overseas—simply switched to producing other compounds. The constantly shifting landscape affected forensic laboratories at all levels, as criminalists and toxicologists struggled to identify unknown substances and their effects in people. In addition, no one system existed to share this information efficiently.

Experts at the Center for Forensic Science Research and Education (CFSRE) in Pennsylvania tackled this problem with the ingenuity laboratories are known for. Alex Krotulski, PhD; Amanda Mohr, associate director; Melissa Fogarty, laboratory manager; and Barry Logan, PhD, executive director, thought they could develop new information and rapidly disseminate it, shortening the lifecycle of some of these dangerous drugs.

Beginning in 2015, CFSRE began work on four National Institute of Justice (NIJ)-funded projects aimed at developing new methods to find NPS as quickly as possible. The result: NPS Discovery, an open-access database that today allows laboratories to rapidly share information on these drugs as soon as they are found.

WHY ARE EMERGING DRUGS HARD TO IDENTIFY?

Identifying NPS is challenging: You cannot find what you are not looking for. For example, a laboratory cannot identify an unknown peak in a chromatogram as a particular drug

without a standard reference material, and test results cannot be confirmed without a validated method. Even if a lab suspects the presence of an NPS—through ambiguous assay development or intelligence on drug use in the area—it cannot easily add the drug to its existing test methods, especially if a standard for that drug does not yet exist. The relatively short “use lives” of many NPS is also a barrier. In response to changing legislation, new drugs can appear and then disappear again within months (Figure 1, online only).

Another challenge is the highly geographic nature of drug-use trends. For example, phencyclidine (commonly referred to as PCP) is largely remembered as the drug of choice for California biker gangs in the 1960s but is now so infrequently seen that many labs may not even routinely test for it. However, according to Peter Stout, PhD, chief executive officer for the Houston Forensic Science Center in Texas, PCP was the second-most-prevalent drug seen in their driving under the influence of drugs (DUID) samples from 2014 to 2019.

With the often short-lived fads for one NPS or another, geographical disparities may be heightened, meaning information must be shared nationally in order to benefit criminalists and toxicologists attempting to identify new drugs on their turf.

SOLVING THE PROBLEM WITH NEW TECHNOLOGY AND INFORMATION SHARING

In 2015, as part of an NIJ-funded study to identify NPS in blood, urine, and oral fluid samples from attendees of electronic dance music festivals (1), Krotulski, Mohr, Fogarty, and Logan developed a method for an instrument that forensic laboratories were just starting to use for drug testing: The liquid chromatography quadrupole time-of-flight mass spectrometer (LC-QTOF-MS). LC-QTOF-MS can capture a wide range of components and gives highly accurate results.

The team developed a rapid LC-QTOF-MS method that required only 15 minutes of analysis time—critical for labs with burgeoning drug caseloads. The testing setup also allowed for more exploration of samples to find emerging NPS

A Century of NPS in the United States

Changing drug structure to avoid drug laws is not new – and many emerging drugs aren’t really new either.

1920s and 1930s: Opium derivatives

- 1925: International Opium Convention bans heroin
- Dibenzoylmorphine and acetylpropionylmorphine surface as legal alternatives to heroin
- 1930: Congress passes a broad “class law” banning a variety of opiates

1960s and 1970s: LSD and PCP derivatives

- Hallucinogens and dissociative drugs
- 2,5-dimethoxy-4-methylamphetamine (DOM) and ALD-52 marketed as legal analogs/alternatives to LSD/PCP
- Class law approach from 1930s is not used; each drug is banned by name, individually

1980s and 1990s: Grab bag

- Fentanyl alternatives (opioid analgesics)
 - Alphamethylfentanyl and 1-methyl-4-phenyl-4-propionoxypiperidine (MPPP)
 - In the 90s, batches of MPPP also contained MPTP which caused Parkinson’s disease-like symptoms in users
- Piperazines (stimulants)
 - Benzylpiperazine (BZP) and trifluoromethylphenylpiperazine (TFMPP)
 - By 2003, piperazines were in nearly every suspected Ecstasy (MDMA) tablet received in Kentucky
- Amphetamines/cathinones (stimulants/empathogens)
 - Methcathinone was present in the 90s before re-emerging during the mid-2010s cathinone wave

Early 2000s: Phenethylamines and tryptamines

- Stimulants and empathogens
- Popularized by Alexander Shulgin’s books *PiHKAL* and *TiHKAL*

Late 2000s to present: Synthetic cannabinoids and cathinones

- Synthetic cannabinoids
 - Effects similar to marijuana (tetrahydrocannabinol)
 - Marketed as “legal pot,” “Spice,” “K2”
- Synthetic cathinones
 - Marketed as “research chemicals,” “bath salts,” “plant food”
 - Terms chosen deliberately to avoid prosecution under the Federal Analogue Act, which stipulates that a chemical cannot be treated as a Schedule I drug unless it’s “intended for human consumption”

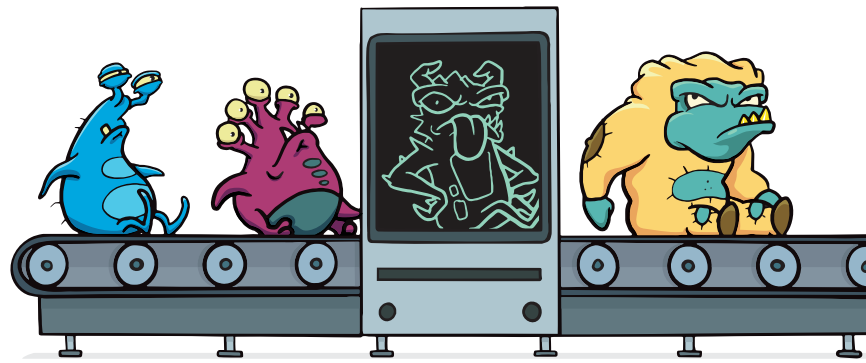
2013 to present: Fentanyl analogs and “new” opioids

- Often mixed with heroin
- Many times the analgesic activity of heroin
- Led to skyrocketing overdose cases

stimulants and hallucinogens, as well as their metabolites.

In 2017, the research team greatly expanded their efforts. Through a graduate research fellowship, Krotulski broadened the scope of the previously developed LC-QTOF-MS method to include more drugs and proposed

sample-mining on existing toxicology samples from the forensic toxicology reference laboratory NMS Labs, which has a relationship with CFSRE, to gain further knowledge of drug trends (2). By retesting extracts from NMS Labs using an expanded scope of testing (e.g., sample-mining), the CFSRE



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1. Cybulski R, Bateman A, Bourassa L, Bryan A, Beail B, Matsumoto J, Cookson B, Fang FC. Clinical impact of a Multiplex Gastrointestinal PCR Panel in Patients with Acute Gastroenteritis. 2018. Clinical Infectious Diseases, ciy357, <https://doi.org/10.1093/cid/ciy357>.
2. Axelrad JE, Freedberg DE, Whittier S, Greendyke W, Lebowitz B, Green DA. Impact of Gastrointestinal Panel Implementation on Healthcare Utilization and Outcomes. J of Clin. Microbiology. 2019; 27;57(3). e01775-18.



Sharing information from multiple sources is **vital** in forensic toxicology.

team discovered NPS that were not initially targeted in the samples. The team reanalyzed these samples and used data mining for others, combing through previously acquired data files for newly identified NPS.

The CFSRE team members also wanted to expand their testing for synthetic cannabinoids, which would require a different method from synthetic cathinones and other NPS. The researchers ultimately developed and validated a new nontargeted 7-minute method for synthetic cannabinoids (3). Using this method, they retested authentic case samples from NMS Labs using the more sensitive LC-QTOF-MS instrumentation, and developed a workflow to re-process data from broad screening tests performed by NMS Labs using slightly older, less sensitive instrumentation (LC-TOF-MS) and a new, more extensive database containing all NPS discovered by the team with the previous efforts, and focusing on fentanyl and other novel opioids (4).

The outcomes of these research efforts have been far-reaching. The CFSRE team developed and validated the most comprehensive and sophisticated methodologies and workflows in the United States for the characterization of NPS in forensic samples. They have also built an extensive mass spectral database laboratories can use for comparative purposes in crime labs and medical examiner's offices. All reports and information generated through these efforts are freely available on NPS Discovery.

THE NEED FOR INFORMATION SHARING

Sharing information from multiple sources is vital in forensic toxicology: Trends seen in postmortem cases may not align with clinical overdose cases. Stout noted the curious patterns of methamphetamine in Houston, where a third of all seized drug samples contain methamphetamine, but methamphetamine is not often seen in the city's DUIDs. "It is really difficult to

tell from the perspective of lab results why that is. It could be differences in interdiction," Stout said. "It could be drivers on meth[amphetamine] are not easily spotted. Seems unlikely that all that meth[amphetamine] is just passing through [without being used by residents]."

To acquire data from as many sources as possible, the CFSRE team sought out other collaborations. One, funded by the Centers for Disease Control and Prevention through the Organized Crime Drug Enforcement Task Force, brought samples of drugs from seizures by Customs and Border Protection to be analyzed using the methods developed by the CFSRE team. This added to the body of timely knowledge about NPS in the U.S.

With a mountain of data and new information before them, Krotulski, Mohr, Fogarty, and Logan realized they had to get this information out to those who need it—forensic scientists, of course, but also clinicians and clinical laboratorians who might be faced with apparent overdoses from unknown drugs, law enforcement officers seeing increased or unusual adverse effects from drugs, and policymakers and legislators struggling to keep up with legislating these emerging drugs. This is the true value of NPS Discovery as a resource.

DEVELOPING NPS DISCOVERY AS A NATIONAL DATA-SHARING TOOL

Beginning in 2018, the CFSRE researchers produced monographs (Figure 2, online only) for each newly discovered drug, as well as trend reports (Figure 3, online only) showing the positivity and prevalence of all NPS identified over the previous quarter.

Then in 2019, CFSRE began issuing public health alerts to inform clinicians and emergency room personnel, as well as law enforcement officers, forensic scientists, and other interested parties, about NPS adverse intoxications, mass overdoses, and fatalities.

These alerts describe the clinical effects of new drugs and may include recommendations for clinicians, public health officials, forensic laboratory personnel, and medical examiners and coroners. These rapid communications may not reflect all knowledge of a new drug, but quickly alert practitioners in cases of extreme danger.

The most comprehensive task for the CFSRE team was setting up the NPS Discovery website (www.npsdiscovery.org). The website contains the monographs, trend reports, and public alerts, as well as the NPS Dashboard, also launched in 2019. The Dashboard is an interactive tool that brings together the information from NIJ-funded work and other efforts in this area (Figure 6, online). With the Dashboard, users can examine data related to a class of drugs or a particular drug, determine prevalence and emergence over time, as well as see information on geographical distribution, type of case, and demographics of the subject.

Although NPS have been demonstrably on the rise for over 10 years, they remain a small percentage of casework. Marijuana, methamphetamine, cocaine, heroin, and fentanyl remained the top five most encountered drugs in the 2019 National Forensic Laboratory Information System report, accounting for nearly 75% of all drug reports nationwide (5).

The database results are also limited by the service area of NMS Labs. As most of the toxicology samples come from NMS Labs, they are necessarily restricted to those labs that send them samples. Crime labs with the resources to perform their own investigations are not included. However, NMS Labs does receive toxicology samples from almost every state.

The data are only qualitative, and only one analysis has been performed due to the necessity of retesting left-over sample extracts. NPS Discovery is a starting place for labs seeking to identify an unknown, not a source for

confirmation, which each lab will still have to do in accordance with its own policies. In addition, isomer pairs are usually not distinguished from each other, so the unknown may only be identifiable as one of two (or more) possibilities.

NPS DISCOVERY IN ACTION

The impact of the NPS Discovery products has been extensive (see sidebar below). Recently, for example, the CFSRE team alerted stakeholders to the first appearance of novel opioids isotonitazene and bromphine in toxicology samples in the U.S.

NPS Discovery first reported on isotonitazene in November 2019. When the DEA temporarily placed it on the Schedule I list in December 2020, it referenced that CFSRE publication (6). After bromphine was first reported by NPS Discovery in June 2020 the DEA public alert published in August 2020 again referenced CFSRE work (7).

The NPS Discovery team continues to expand the scope of their efforts. CFSRE has collaborated with medical examiner and coroner offices to run casework for NPS when those offices were unable to get testing elsewhere.

The team has also created clinical partnerships with hospitals in New York City, Boston, Salt Lake City, and other areas to detect NPS in samples from patients who have survived overdoses. They have also partnered with the Philadelphia Department of Public Health on testing to help inform the department and the general public of what is present and prevalent in the city so that the department may tailor its efforts.

“Our laboratory is now positioned as a national leader in NPS testing and reporting, which in turn has allowed for vast knowledge transfer from our laboratory to others leading to action and interpretation not previously available,” Krotulski said. The forensic science community, and many other stakeholders, continue to reap the benefits. ■

Frances Scott, PhD, is a physical scientist in the Office of Investigative and Forensic Sciences in the National Institute of Justice.

+EMAIL: Frances.Scott@ojp.usdoj.gov

REFERENCES

1. Alex J. Krotulski et al. Monitoring changes in the novel psychoactive substance (NPS) market through enhanced

identification of emerging drugs and their metabolites in biological samples. Final report to the National Institute of Justice, grant number 2015-IJ-CX-K012, June 2018, NCJ 251787. <https://www.ncjrs.gov/pdffiles1/nij/grants/251787.pdf> (Accessed March 2021).

2. Alex J. Krotulski. A more timely process for identifying and analyzing trends in emerging novel psychoactive substances in the United States. Final report to the National Institute of Justice, grant number 2017-R2-CX-002, October 2020, NCJ 255599. <https://www.ncjrs.gov/pdffiles1/nij/grants/255599.pdf> (Accessed March 2021).
3. Alex J. Krotulski, Amanda L.A. Mohr, and Barry K. Logan. Retrospective identification of synthetic cannabinoids in forensic toxicology casework using archived high resolution mass spectrometry data. Final report to the National Institute of Justice, grant number 2017-R2-CX-0021, November 2020, NCJ 255669. <https://www.ncjrs.gov/pdffiles1/nij/grants/255668.pdf> (Accessed March 2021).
4. Amanda LA Mohr, Judith Rodriguez Salas, and Barry K Logan. Toxicological time travel: retrospective datamining of analytical time-of-flight mass spectrometry data for evaluating the rise and fall of novel opioid and fentanyl analog use in the United States. Final report to the National Institute of Justice, grant number 2017-DN-BX-0169, December 2020, NCJ 255883. <https://www.ncjrs.gov/pdffiles1/nij/grants/255883.pdf> (Accessed March 2021).
5. U.S. Drug Enforcement Administration, Diversion Control Division. National Forensic Laboratory Information System: NFLISDrug 2019 Annual Report. <https://www.nflis.dea diversion.usdoj.gov/DesktopModules/ReportDownloads/Reports/NFLIS-Drug-AR2019.pdf> (Accessed March 2021).
6. U.S. Drug Enforcement Administration, Diversion Control Division. Schedules of controlled substances: Temporary placement of isotonitazene in schedule I, 21 CFR Part 1308, Docket no. DEA-631. Federal Register 2020; 85 (118).
7. U.S. Drug Enforcement Administration, Diversion Control Division. Bromphine (chemical name:1-(1-(1-(4-bromophenyl)ethyl)piperidin-4-yl)-1,3-dihydro-2H-benzimidazol-2-one), Public Alert, August 2020. https://www.dea diversion.usdoj.gov/drug_chem_info/bromphine.pdf (Accessed March 2021).

NPS Discovery in Action

- First reports of 90 new drugs in the United States
- 10 public health alerts issued
- 2.5 years of NPS trend data
- The New Jersey Drug Monitoring Initiative used the NPS Discovery isotonitazene information for a public alert to law enforcement and other stakeholders on their extensive email distribution list.
- The World Health Organization (WHO) routinely references these publications in their Critical Review Reports.
- The European Monitoring Centre for Drugs and Drug Addiction also publishes Initial Reports, similar to the WHO Critical Review Reports, referencing the NPS Discovery publications.
 - The usual pattern is that NPS are first seen in Europe before coming to America, so the timeliness of the Center for Forensic Science Research and Education work is clear, as they are producing alerts and journal articles that are timely and relevant to the European population.

Beyond

SARS

As coronavirus testing demand begins to decline in the U.S., labs look ahead to how they might repurpose the extra equipment they acquired when the pandemic was at its peak.

BY KAREN BLUM



COVID-19 Testing

When the COVID-19 pandemic first surged in spring 2020, hospital emergency rooms and intensive care units weren't the only medical facilities that were overloaded. Clinical laboratories across the U.S. ramped up to purchase additional diagnostic testing equipment and adjust staff schedules to operate longer hours. Now, as SARS-CoV-2 testing demand is declining, laboratory directors in some areas of the nation have a

little breathing room—and a chance to think about how they can repurpose their extra platforms going forward.

During the first wave, just as hospitals faced shortages of personal protective equipment, ventilators, and other necessary supplies, laboratories found themselves scrambling for reagents, pipette tips, and other testing equipment, in addition to having to juggle their short staffs to match their clients' increased demands.

Elizabeth Palavecino, MD, director of clinical microbiology at Wake Forest Baptist Medical Center, in Winston-Salem, North Carolina, says she was lucky to have already had several different testing systems available, and just had to purchase one new one.

“If you didn’t have those instruments at the beginning [of the pandemic], it was almost impossible to get new instruments to start testing or increase your capacity,” she said.

Her lab started testing with its existing equipment, at one point using five different platforms from different vendors—a bit of a nightmare for competency testing and quality control. “We usually have one platform for one particular test, like flu, but in this case, because we couldn’t get enough reagent from any one vendor, we had to have different ones,” she said.

Then, one major company couldn’t keep up with the demand for pipettes specific to its high-throughput testing platform, forcing Palavecino and col-

leagues to start sending their samples out to a reference lab because they didn’t have the capacity to do all the testing that they needed in-house. “That was a big letdown,” she said.

Now, in the U.S. at least, it appears there’s light at the end of the tunnel. From mid-January to early March, SARS-CoV-2 testing declined about 26% nationwide.

leagues to start sending their samples out to a reference lab because they didn’t have the capacity to do all the testing that they needed in-house. “That was a big letdown,” she said.

The Children’s Hospital of Philadelphia, which performs a large amount of laboratory-developed, real-time polymerase chain reaction (PCR) testing, purchased an extra thermal cycler on top of the four they owned to keep up with testing volumes, said Rebecca Harris, MD, director of the infectious disease diagnostics laboratory. They also acquired an expansion for their rapid molecular testing platform to double its capacity, and one high-throughput automated PCR instrument to double capacity for that type of testing.

“We were better off than a lot of labs, because we were mainly relying on lab-developed tests as our main testing options, but we definitely had

to restrict use of the rapid molecular test for most of the initial portion of the pandemic,” she said. “We have a lot better capacity for that now.” Peter Perrotta, MD, chair of pathology services at West Virginia University (WVU) and director of pathology services for the WVU Health System, in Morgantown, helped establish and is CLIA director of the WVU Rapid Development Laboratory. The state-supported effort is a collaboration between his clinical laboratory team, WVU virologists and engineers, and Marshall University bioinformaticists. For this lab, the group purchased open platforms that would enable the development of COVID-19-related tests—both those that are molecular and PCR-based, and those that are protein- or enzyme-linked immunosorbent assay-based for antibody testing. During the COVID-19 peak, the lab hired three new people as well and staggered work shifts to adjust to the 24/7 schedule.

SHIFTING TO OTHER PATHOGENS

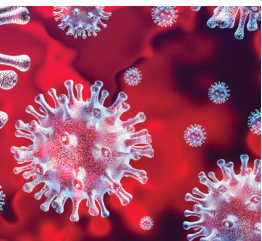
Now, in the U.S. at least, it appears there’s light at the end of the tunnel. From mid-January to early March, SARS-CoV-2 testing declined about 26% nationwide, from an average of more than 2 million tests per day to about 1.5 million tests per day, according to data from The COVID Tracking Project, a volunteer effort launched by *The Atlantic*. (The project stopped collecting new data as of March 7.)

“The instrumentation and additional testing capacity we had to have was and remains an insurance policy” to handle high volumes of SARS-CoV-2 testing, Harris said. “But we are definitely thinking about ways we could put the additional testing capacity that we’ve already purchased to our advantage in the future.”

A clear-cut use in her laboratory could be maintaining some type of targeted viral respiratory panel, such as for influenza A and B, respiratory syncytial virus (RSV), and SARS-CoV-2, on an automated platform, she said. “Before the pandemic, our capacity for rapid molecular testing was really quite limited, and rapid flu testing in the lab was restricted to the emergency department,” said Harris. They also performed laboratory-developed flu/RSV tests with a 12-hour turnaround time, which was “pretty logistically challenging” to maintain in prepandemic times. Now, they could decrease turnaround times to 2 to 5 hours, she said.

Her laboratory also will assess if there is any high-volume testing they could convert to molecular methods with the extra equipment. “In our lab, that might be something like our MRSA, VRE, or group B strep screenings that we currently do by culture alone,” Harris said. “There might be other lab-developed molecular tests that we want to move to an automated platform if we think there’s a real clinical benefit in the improvement in turnaround time. And we will be looking at our send-out menu to see if there is anything that would be easy for us to now bring in-house, if there’s an FDA-approved method on a platform we have in the lab that would reduce costs, as well as if there is any other outreach testing that we should pursue now that we have this capacity.”

COVID-19 testing needs should continue to drop as more people become vaccinated, Palavecino said. Prior to the pandemic, her group had been thinking about purchasing equipment to do testing for group A *Streptococcus* to rule out pharyngitis in children. The automated real-time reverse transcription PCR system used by her lab could be repurposed to process additional tests like these. “If we get to a point where we have instruments available to do the testing, we may start using those instruments for other pathogens,” she said. Her lab had already previously used its antigen testing equipment for flu and RSV, so that, too, can resume more as COVID-19 recedes, she said.



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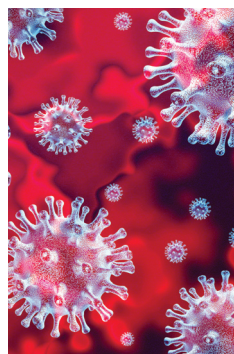
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“I really stopped believing that I could accurately predict what’s going to happen during the pandemic, but I try to err on the side of being overprepared.”

—Rebecca Harris, MD

TACKLING EMERGING PANDEMIC-RELATED NEEDS

Some laboratory equipment already is being repurposed. One piece of equipment Perrotta’s group purchased for molecular testing has been adapted for library preparation for SARS-CoV-2 sequencing. They’re now sequencing 200 to 400 samples a week to help epidemiologists track the entry and spread of SARS-CoV-2 variants across the state of West Virginia. They also are developing other molecular- and protein-based assays that are variant-specific. In addition, his team has developed quantitative and neutralization tests to characterize antibody responses.

“Our idea now is that we are going to be in emerging infections, a laboratory that will augment our state’s capability to respond to infectious diseases and other public health emergencies,” Perrotta said. Researchers are using equipment for some vaccine trials and other projects, many of which are coordinated by the WVU Clinical and Translational Science Institute, he added.

OVERPREPARING FOR THE FUTURE

Repurposing could happen for larger-scale laboratories, too. Quest Diagnostics performed and reported approximately 40 million molecular SARS-CoV-2 tests since March 2020, requiring the purchase of significant additional molecular equipment, said Barbara Feringa, MPH, executive director for the company’s women’s and reproductive health division.

Now, the company is planning to repurpose these upgraded platforms for women’s healthcare testing, such as for human papillomavirus, chlamydia, and gonorrhea and trichomonas, among other sexually transmitted infections. They also are considering consolidating additional molecular testing for other infectious diseases onto molecular platforms used for SARS-CoV-2 testing, Feringa said. Additional platforms used for viral load testing can be redeployed across regional labs to reduce turnaround times on tests for HIV and hepatitis C, said Jim Davis, the company’s executive vice president of general diagnostics.

The way things are going, laboratorians should have at least through 2021 to determine their future plans, our interviewees said.

“I think we’re going to have a certain level of COVID-19 testing that goes on for at least a year, through the next fall and winter, but hopefully we don’t see another spike,” Perrotta said.

Harris added, “I really stopped believing that I could accurately predict what’s going to happen during the pandemic, but I try to err on the side of being overprepared. I’m setting my own expectation that the lab may need to maintain high-volume testing into 2022. If it dies down sooner than that, I will be pleasantly surprised.” ■

Karen Blum is a freelance medical and science writer who lives in Owings Mills, Maryland.

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Sample Delivery to the Clinical Lab:

Neither Heat, Nor Snow, Nor Gravitational Force

BY CHRISTINA C. PIERRE, PHD, DABCC AND JOE WIENCEK, PHD, DABCC, FAACC



Evidence shows that a sample's journey to the lab can be perilous, making this preanalytical step ripe for improvement.



Chiseled in gray granite over the entrance to the New York City Post Office on 8th Avenue are the words, “Neither snow nor rain nor heat nor gloom of night stays these couriers from the swift completion of their appointed rounds.” This unofficial motto for the United States Postal Service truly symbolizes the importance of high-fidelity delivery systems. For the clinical laboratory, timeliness and deliberate care in the delivery of patient samples are similarly essential to providing accurate test results for patient care.

Clinical samples may originate from catchment areas hundreds of kilometers away to within the same walls of the healthcare institution. A fundamental understanding of external and internal sample transport can equip the modern laboratorian for mitigating preanalytical error in this important area of the total testing process.

EXTERNAL SAMPLE TRANSPORT

Worldwide, healthcare institutions continue to expand their outreach programs. As a result, higher volumes of laboratory samples routinely travel from offsite clinics to centralized, core clinical laboratories for testing. External sample transport involves many individual steps before samples reach the laboratory for analysis (Figure 1). Along the way, a sample's journey passes through two critical phases, beginning with staff at the offsite physician office or outpatient clinic collecting the patient sample, processing it, and placing it inside or outside of the clinic for courier pickup, depending on the facilities' hours of operation. After a clinic closes, samples are routinely placed inside an outdoor courier lockbox for off-hours access.

The second critical phase begins with the courier picking up the sample, and placing it in one of various cooler caddies within their transport vehicle, contingent on sample storage requirements. This is the longest part of the sample's journey. Couriers often travel vast distances in their routes and may visit multiple pickup sites before

finally reaching the destination clinical laboratory. Samples that reach this destination are then sorted into two categories—to be analyzed onsite or to be shipped using similar transport steps to an offsite reference laboratory.

Climate Zones

Climate zones are a major determinate of the protections biological samples will require for appropriate external sample transport. According to the International Energy Conservation Code (IECC), funded by the U.S. Department of Energy, Office of Energy Efficiency and Renewable Energy, the United States consists of several distinct climate zones (Figure 2). Each zone presents unique challenges for laboratorians to consider when optimizing their institution's sample transport roadmap.

For example, on June 20, 2017, Phoenix, Arizona (hot-dry zone) recorded ambient air temperatures just under 50°C, which grounded flights within the region. At the other extreme, on January 28, 2019, Minnesota (cold-very cold zone) experienced its coldest ambient air temperature (-56°C) in more than two decades—the Arctic polar vortex of 2019. A reference lab within this region notified institutions across the U.S. that samples should not be shipped to its facility during this time and posted an alert on their website test catalog. Although these cases represent extremes, the laboratory service needs to consider both the average and extremes to develop a robust external sample transport program that minimizes preanalytical variables.

Courier Lockbox

Courier lockboxes are an often-overlooked step in the preanalytical phase of laboratory testing (1). These insulated lockboxes come in various shapes and sizes to accommodate different clinical sample types and volumes and are commonly made of thin, high-impact polystyrene or 20–24 gauge cold-rolled steel. For outdoor courier lockboxes, there are no universally acceptable standards or

guidelines that provide recommendations on 1) sample storage time limits; 2) lockbox material and insulation; 3) lockbox location; or 4) maintenance of lockbox temperatures during seasonal extremes. This absence of guidelines is highlighted in a recent study that shows instructions for lockboxes are inconsistent between a selection of academic, private, and reference labs (1).

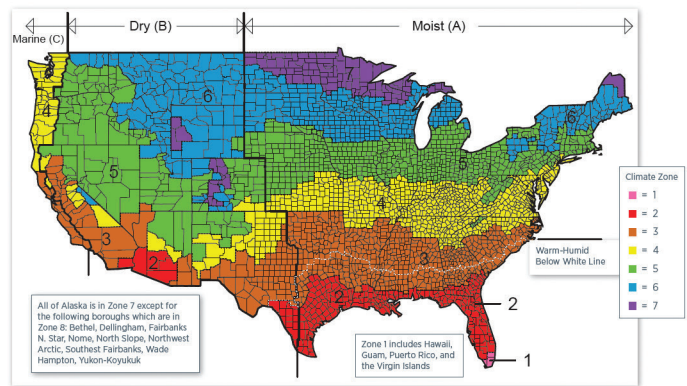
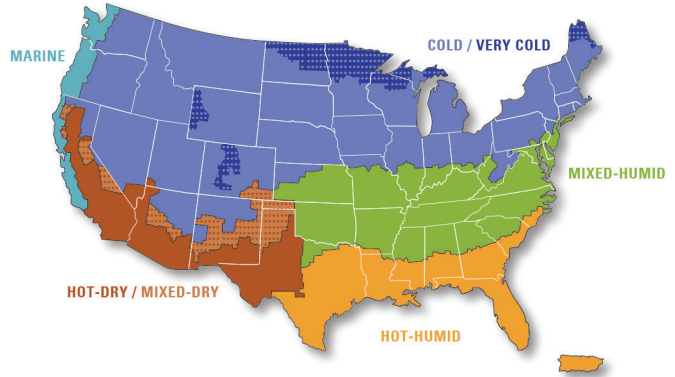
Based on our experience and recent publications, samples inside outdoor lockboxes exposed to ambient seasonal temperatures are a significance source of preanalytic error. Recent studies demonstrate that centrifuged and uncentrifuged lithium heparin samples stored in outdoor lockboxes with and without ice packs showed significant changes (1). These changes were apparent within 1 hour in summer temperatures in Charlottesville, Virginia. Real-time, continuous temperature monitoring revealed that lockboxes with ice packs had a mean temperature of 22.3°C (range: 16.5–22.3°C) whereas lockboxes without ice packs had a mean temperature of 42.6°C (range: 34.4–46.9°C).

In a similar study, outdoor courier lockboxes were monitored during four seasons in the southern region of the U.S. Inside steel, insulated lockboxes with no ice packs, the ambient outdoor temperatures demonstrated wide fluctuations over three days in spring (range: 7.0-25.2°C) and fall (range: 2.2-22.8°C) (2).

Courier Transport

Planes, trains, and automobiles are the most common transport vehicles used in external sample transport. Clinical

F2 Map of the United States Depicting the Various Climate Zones



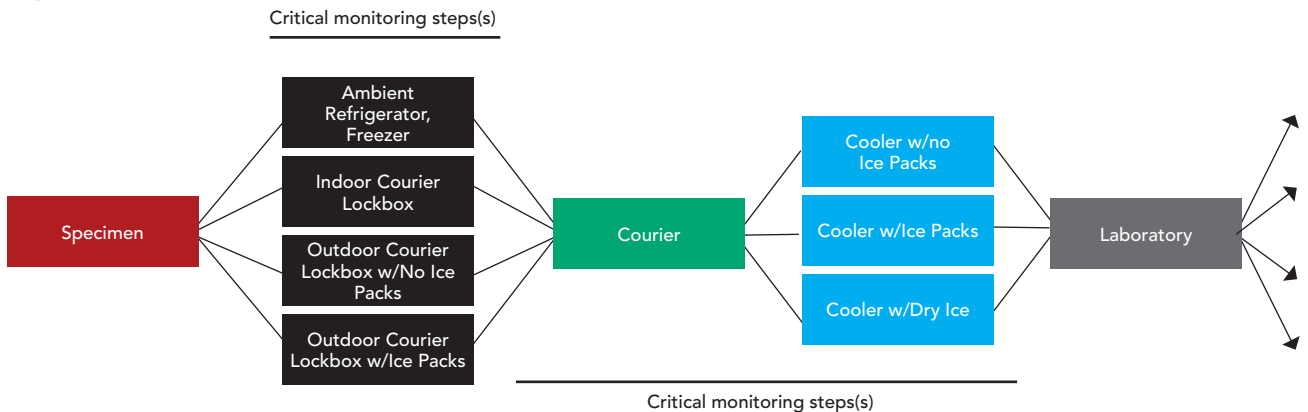
Climate Zones courtesy of U.S. Department of Energy

laboratorians must fully understand each to optimize acceptable transport conditions. For example, samples boarding and deboarding planes encounter potentially unique conditions. Pallets of samples sitting on a tarmac waiting to be loaded onto or offloaded from a plane can be exposed to the extreme heat that is absorbed by dark asphalt. Similarly, samples being transported by train or automobile may be affected by exposure to sun through windows, air conditioners, heaters, and seasonal

ambient temperatures. In addition, storage containers in any of these steps can be specific to institution or courier service, which introduces another level of variability.

Agitation or shock forces are an underappreciated problem and ripe for monitoring in external sample transport. Agitation can mix blood cells, cellular debris, fibrin, and potentially other sample contents that are separated or partially separated during the centrifugation process. One recent

F1 External Transport Sample Journey



study—performed in association with a reagent formulation change—showed that samples analyzed directly after courier transport yielded falsely increased vitamin D concentrations (3).

To demonstrate that courier transport and agitation were the culprit, hundreds of samples in question were held upright overnight and retested. The same specimens were then intentionally mixed and reanalyzed. After deliberate inversion, samples showed comparable results to those being analyzed directly after courier transport, whereas results generated when held overnight decreased (3).

Integrated External Sample Transport System

Integrated sample transport systems are a possible solution to for standardizing external sample transportation. Researchers in Padova, Italy, used a system with secondary and tertiary transport containers that could be monitored and tracked in various stages of delivery. Over several years of their study, the authors were able to establish standard operating procedures and characterize courier routes associated with their offsite collection centers.

Through these efforts, they increased the number of overall courier trips with acceptable temperatures and reduced both unacceptable temperatures and excessive transport times defined institutionally as $< 20^{\circ}\text{C}$, $> 25^{\circ}\text{C}$, and > 3 h, respectively (4). This group also demonstrated the feasibility of a state-of-the-art, temperature-controlled delivery system, akin to a small refrigerator (5).

Internal Sample Transport

Pneumatic tube systems are an integral feature of most healthcare institutions and enable safe and efficient transport of clinical samples for

centralized testing. A schematic drawing of a basic pneumatic tube system is depicted in Figure 3. These systems use a network of pipelines to transport capsules, also known as carriers, from one point to another.

Capsules are sent and received at ports known as stations. Stations are strategically located throughout the healthcare institution to facilitate transport between sites with the highest sample traffic. Often, capsules do not travel a straight path from one station to another; in fact, pneumatic tube systems are frequently complex and branched. An apparatus known as a diverter enables carriers to change direction. Diverters can be likened to railroad switches that enable trains to switch from one track to another.

What drives the capsules through this network of tubes? As the name “pneumatic” suggests, a blower generates changes in air pressure that move capsules through the system. In contrast to inert materials, clinical samples are sensitive to changes in air pressure and shock forces (e.g., 3-dimensional or 3-axis acceleration) experienced inside the system. The effect of these forces on sample integrity and the accuracy of downstream analyses is well documented. Pneumatic tube

transport can introduce bias in the measurement of several chemistry analytes, blood gas measurements, and hemostasis and platelet studies. In the arena of blood banking, pneumatic tube transport has deleterious effects on the integrity of blood products.

To date, no clinical laboratory regulatory body has outlined requirements to measure or mitigate the impact of pneumatic tube transport on the accuracy of downstream testing. A limited discussion of the effect of pneumatic tube transport on blood gas measurements and specimen hemolysis follows below and is meant to provide a framework for some of the considerations around this issue.

Can Blood Gas Specimens Be Tubed?

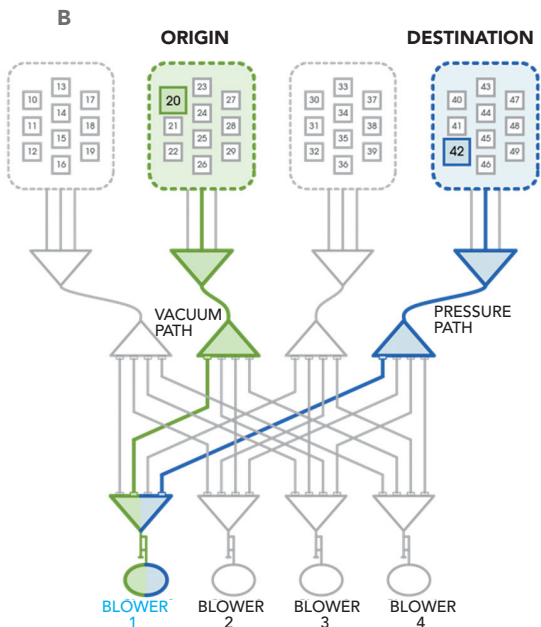
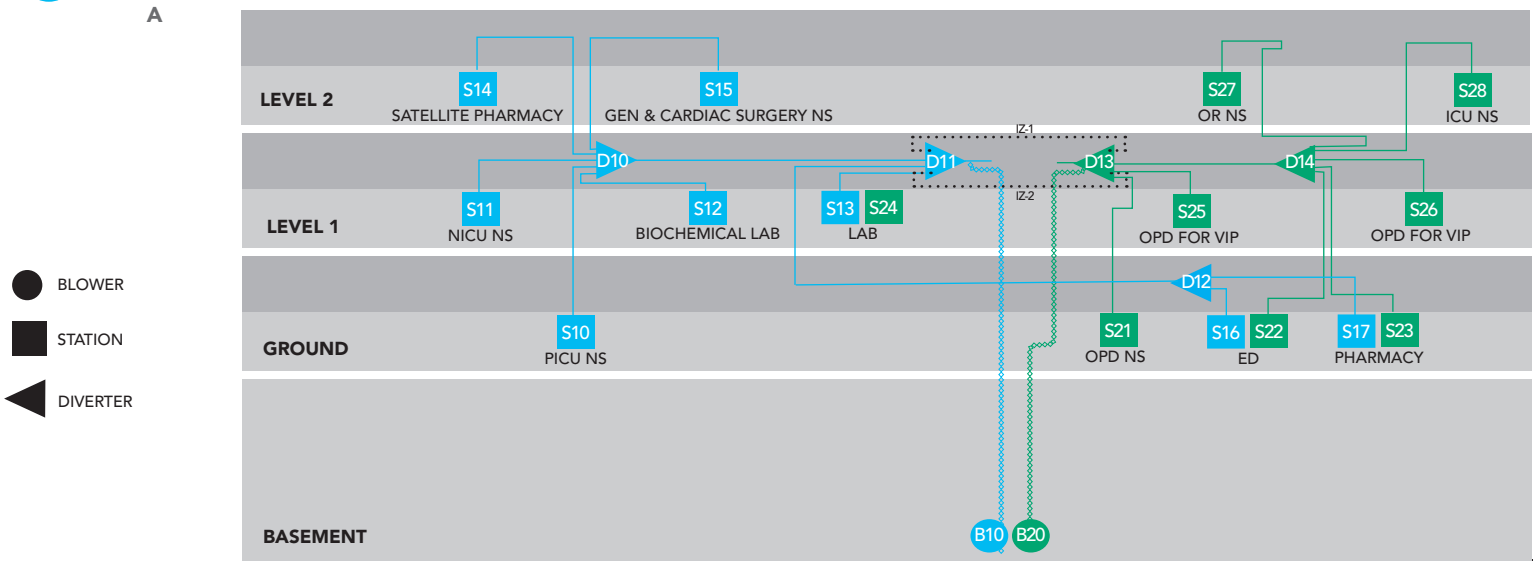
In the clinical laboratory, one of the most widely studied challenges associated with pneumatic tube systems is the transport of samples destined for blood gas analyses. For example, in blood samples with a partial pressure of oxygen (pO_2) lower than atmospheric pO_2 (approximately 159 mmHg at sea level), oxygen from air bubbles can diffuse into the sample resulting in falsely increased oxygen, while oxygen can diffuse from hyper-oxygenated samples into air bubbles.

Most blood gas analyzer manufacturers recommend purging air from samples and capping syringes with a rubber stopper to minimize air contamination. Furthermore, the College of American Pathologists requires laboratories to implement procedures to prevent ambient air contamination of samples for blood gas testing and document suspected erroneous results. However, the vigorous shaking that can occur as specimens are whisked through the pneumatic tube system can generate



Oxygen from air bubbles can diffuse into the sample, resulting in falsely increased oxygen.

F3 Sample pneumatic tube system schematic. A) Illustrates a simple two-zone system of a four-level building with tubes (interzone pipes) connecting the zones, which are color-coded in blue and green. B) Illustrates a hypothetical capsule path from one station to another. This figure was graciously provided and published with the permission of Pevco™.



air bubbles and enhance diffusion between air bubbles and the sample.

Positive and negative air pressure changes that occur as capsules travel through the tube system may also affect blood gas analytes. Several studies have investigated this issue with varying conclusions as to whether pneumatic tube transport introduces clinically significant biases in blood gas results. This variability likely reflects differences in tube system characteristics, including distance traveled by the

sample, route, number of diversions, air pressure, and magnitude and number of accelerations (6).

One study observed a mean bias of 8.0 mmHg in pO₂ in arterial blood gas samples that were tubed compared to those walked to the laboratory for analysis but determined that this difference was neither clinically nor statistically significant (7). A mean bias of 0.94 mmHg was observed for partial pressure of carbon dioxide (pCO₂) in arterial blood gas samples in the same study.

In contrast, another study found a statistically significant mean bias of 3.16 kPa (approximately 24 mmHg) in arterial pO₂ between specimens analyzed at the point of care compared to those transported via pneumatic tube system for analysis (8). Transport of samples in pressure-sealed containers resulted in a reduced mean bias that was determined to be statistically insignificant. Interestingly, there was no correlation between transport time, which ranged from approximately 7 to 42 minutes, and the magnitude of the differences observed (7).

These contrasting studies are two of many that support the need for clinical laboratories to empirically determine the effect of pneumatic tube system transport on specimens destined for blood gas measurements.

Air Bubbles Caused By Pneumatic Tube Transport Induce Hemolysis

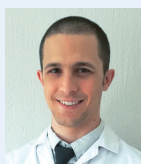
Another effect of pneumatic tube transport on blood samples is the induction of hemolysis. Mullins et al. measured the magnitude and temporal pattern of 3-axis acceleration by sending a bubble-wrapped smartphone with kinetic sensing applications through the pneumatic tube system (6). The experiment showed that the magnitude of forces experienced by tubed samples was at least 8 x g in contrast with hand delivered samples, which did not experience forces in excess of 2 x g. Samples transported through routes with longer transport times and larger acceleration forces had more hemolysis—as measured by hemolysis index and increased concentrations of lactate dehydrogenase (LDH)—compared to those transported by hand or through a shorter route with smaller acceleration forces. Number of forces experienced positively correlated with the degree of hemolysis and LDH elevation.

This study also hinted that air bubble formation during transport may contribute to sample hemolysis through hydrodynamic stress. In a follow-up study (9), the same group showed that artificial generation of bubbles in samples using a gentle air stream induced hemolysis, with accompanying increases in LDH and potassium.

 Nova Biomedical's Educational Webinar Series Presents:

Comparing the Accuracy of POC Creatinine/eGFR vs. Measured GFR for Evaluating Kidney Disease

Chronic kidney disease is rising rapidly in low- and middle-income countries due to limited resources and is associated with high morbidity and mortality. Serum creatinine and estimation of glomerular filtration rate (eGFR) are critical diagnostic tools for kidney disease, yet access to centralized laboratory services remains limited in primary care resource-limited settings. In this webinar, Dr. Currin discusses the results of a large, 670 patient study in a rural South African population evaluating point-of-care (POC) technologies for serum creatinine/eGFR measurement and comparing their performance to a gold standard measurement using iohexol measured GFR (mGFR).



Primary Presenter

Sean Currin, MD,
Department of Chemical Pathology,
University of Witwatersrand and National Health Laboratory Service
Charlotte Maxeke Johannesburg Academic Hospital, Johannesburg, South Africa

A Point-of-Care Creatinine and eGFR Meter for Kidney Function Monitoring

This presentation will describe the handheld POC device, StatSensor Creatinine, that was shown to be more accurate than the laboratory creatinine assay when both were compared to patients' true measured GFR. It will describe areas where the device has been shown to be effective in identifying patients with CKD and AKI, particularly in screening programs. Dr. Begos will share Nova Biomedical's commitment to a close relationship with researchers, clinicians, and government health agencies to improve care for patients with kidney disease worldwide.



Presenter

Dennis Begos, MD, FACS, FACRS
Associate Medical Director,
Medical and Scientific Affairs,
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T1 Practical Recommendations for External and Internal Sample Transport

Sample Transport Recommendations
External

- Recognize challenges of climate zones
- Outline institution-specific sample transport roadmaps
- Develop and implement standard operating procedures
- Monitor temperature, time, location, and shock/acceleration forces

Internal

- Study the schematic of the institution's pneumatic tube system
- Validate the pneumatic tube system with appropriate experiments
- Prioritize validation studies for blood gas analytes and analytes impacted by hemolysis

Importantly, this study showed that the production of air bubbles in a specimen is sufficient to induce hemolysis and lead to false changes in analytes affected by hemolysis, even in the absence of acceleration forces. Hemolysis was reduced by complete filling of blood collection tubes to minimize air space present in the tubes (and consequently, the potential for bubble formation), further supporting the relationship between air bubble induction and sample hemolysis.

Validation of Hospital Pneumatic Tube Systems

Given the variability of effects on blood samples between and even within hospitals, it has become increasingly evident that each institution should validate its pneumatic tube system for blood transport. Farnsworth et al. outlined parameters for such a validation, including the need to examine different routes, measure intraday and interday variability (elapsed time, area under the curve, number and magnitude of accelerations), and determine whether transport induces clinically significant changes in analytes (10).

Another study focused largely on comparing four commercially available 3-axis accelerometers for use in monitoring hospital pneumatic tube systems (11). This study demonstrated differences in performance between accelerometers with respect to the maximum force the devices were capable of measuring and the failure

rate of the devices. There are currently no regulatory requirements to validate the performance of pneumatic tube systems, and harmonization and minimum performance characteristics of 3-axis accelerometers are also lacking. Given these limitations, the authors of the study recommend using a single device for all validation studies.

QUALITY MANAGEMENT RECOMMENDATIONS FOR SAMPLE TRANSPORT

With the largest proportion of errors in clinical laboratory testing attributed to the preanalytical phase, mitigating the negative impacts of sample transport represents an opportunity to improve the quality and accuracy of laboratory testing. The first, and perhaps most important, step of implementing meaningful interventions is the ability to identify and quantify the effects of various transport modalities. Table 1 outlines several recommendations for the assessment and measurement of the effects of both external and internal transport on samples. Once identified, laboratory leaders can implement appropriate mitigation strategies and monitor them for effectiveness. ■

Christina C. Pierre, PhD, DABCC, is a clinical chemist at Penn Medicine Lancaster General Hospital in Lancaster, Pennsylvania.

+ E-MAIL: christina.pierre@penntestmed.upenn.edu

Joe Wiencek, PhD, DABCC, FAACC, is an assistant professor at Vanderbilt University School of Medicine and medical director of the core clinical chemistry laboratory at Vanderbilt University Medical Center in Nashville, Tennessee.

+EMAIL: joe.wiencek@vumc.org

REFERENCES

1. Dibbern ME, Pierre CC, Wiencek J. Outdoor courier lockboxes in summer are a significant source of preanalytical error. (In press.)
2. Wiencek J, Nichols JH. Impact of ambient seasonal temperature on specimens stored in courier lock-boxes. *J Appl Lab Med* 2018;2:973–6.
3. Hernandez JA, Stanford JE, Savoie CV, et al. Spuriously elevated 25-Hydroxyvitamin D in lithium heparin plasma samples transported by courier. *J Appl Lab Med* 2018;2:809–811.
4. Zaninotto M, Tasinato A, Padoan A, et al. An integrated system for monitoring the quality of sample transportation. *Clin Biochem* 2012;45:688–90.
5. Zaninotto M, Tasinato A, Vecchiato G, et al. Performance specifications in extra-analytical phase of laboratory testing: Sample handling and transportation. *Clin Biochem* 2017;50:574–8.
6. Mullins GR, Harrison JH, Bruns DE. Smartphone monitoring of pneumatic tube system-induced sample hemolysis. *Clin Chim Acta* 2016: 462:1–5.
7. Carabini LM, Nuriel J, Diaz Milan R, et al. The clinical significance of patient specimen transport modality: Pneumatic tube system impact on blood gas analytes. *Respir Care* 2016;61:1311–5.
8. Collinson PO, John CM, Gaze DC, et al. Changes in blood gas samples produced by a pneumatic tube system. *J Clin Pathol* 2002;55:105–7.
9. Mullins GR, Bruns DE. Air bubbles and hemolysis of blood samples during transport by pneumatic tube systems. *Clin Chim Acta* 2017: 473:9–13.
10. Farnsworth CW, Webber DM, Krekeler JA, et al. Parameters for validating a hospital pneumatic tube system. *Clin Chem* 2019;65:694–702.
11. Franks CE, Krekeler JA, Gronowski, et al. A comparison of four 3-axis accelerometers for monitoring hospital pneumatic tube systems. *J Appl Lab Med* 2020;5:1345–50.

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FDA Issues Pooling and Serial Testing Amendment for Certain SARS-CoV-2 Tests

The Food and Drug Administration (FDA) has established a pathway to make it easier for certain molecular SARS-CoV-2 tests with emergency use authorizations (EUA) to gain additional authorization for use with pooled specimens from asymptomatic individuals as part of a serial testing program. To obtain authorization for this additional indication, test developers must submit a complete notification and meet required validation data as set forth in a letter that FDA issued on April 20. Once a test's EUA is amended, the test may then be used with pooled anterior nasal specimens from individuals without known or suspected COVID-19 when such individuals are tested as part of a program that includes testing at regular intervals (e.g., at least once per week). The number of specimens that can be pooled (up to three, up to five, or up to 10) and the type of pooling that can be done with a test (media pooling or swab pooling) depends on the specific indication for which a manufacturer applies.

Once FDA confirms that the required documentation for a test has been submitted, the agency will add the test to a list on the agency's website called, "Exhibit 1 of the Pooling and Serial Testing Amendment." However, the agency notes that a test's addition to Exhibit 1 does not necessarily mean that FDA has reviewed the underlying validation data or confirmed that the test is appropriately validated.



FDA AUTHORIZES HIGH-THROUGHPUT SYSTEM FOR THERMO FISHER SARS-COV-2 TEST

Thermo Fisher Scientific has received emergency use authorization (EUA) from the Food and Drug Administration for the Thermo Fisher Scientific Amplitude Solution with the TaqPath COVID-19 High-Throughput Combo kit. The Amplitude Solution is designed to enable clinical and public health laboratories to expand polymerase chain reaction (PCR) testing and process up to 8,000 samples in a single day even with limited personnel. It combines Thermo Fisher's extraction and real-time PCR instruments with liquid handling products from Tecan Group, and comes with a secured supply of kits, reagents, and other consumables to meet SARS-CoV-2 testing needs. The modular system also uses a high-throughput version of

Thermo Fisher's Applied Biosystems TaqPath COVID-19 Combo kit (which received an EUA in March 2020) to process samples in four steps with minimal hands-on time and laboratory space requirements. Additionally, the kit's multigene target design and updated interpretive software could help labs detect SARS-CoV-2 variants.

CE MARK GIVEN TO ADVANCED BIOLOGICAL LABORATORIES SARS-COV-2 VARIANTS TEST

Advanced Biological Laboratories has earned the CE mark for its UltraGene SARS-CoV-2 Triplex assay. This test uses real-time reverse transcription polymerase chain reaction (PCR) to identify SARS-CoV-2 RNA, detect the presence of SARS-CoV-2 variants, and distinguish between the main circulating SARS-CoV-2 variants of lineages

B.1.1.7, B.1.351, and P.1. Designed for use with upper respiratory specimens, the UltraGene SARS-CoV-2 Triplex assay is available in a two-wells-per-sample format. The first well includes primer and probe sets designed to detect RNA from the SARS-CoV-2 nucleocapsid (*N*) and envelope (*E*) genes, as well as an extraction, reverse transcription, and PCR amplification positive control. The second well includes primer and probe sets designed to detect RNA from the *N* gene, as well as genomic variations in the spike (*S*) and *ORF1ab* genes, enabling identification of the aforementioned SARS-CoV-2 variants. Validated on the UltraGene qPCR 48 and Applied Biosystems QuantStudio 5 instruments, the test works on platforms equipped with FAM, HEX, Cy 5, and ROX and fluorescent channels and is available in two models for two distinct workflows.

GENOMSYS EARNS CE MARK FOR GENOMIC PROCESSING DATA SOFTWARE

The CE mark has been granted to GenomSys for its MPEG-G Codec Suite, a collection of software tools designed to process genomic data so that it's compliant with the ISO/IEC-23092 genomic data standard (MPEG-G). The MPEG-G Codec Suite includes source code examples, a comprehensive user manual, and additional software to transcode from and to legacy formats (to preserve past investments) and to integrate functionalities into existing applications and pipelines. With these tools, laboratories can transform their legacy formatted files into MPEG-G and leverage the accompanying efficiencies and high-security level that comes with this widely interoperable data standard. In addition to providing benefits related to data protection, MPEG-G can enable cost savings for organizations handling large volumes of genomic data by significantly reducing the size of whole-exome sequencing files. MPEG-G also can shorten the time needed to process genomic data by more than 89% since it does not require any preprocessing steps during analysis.

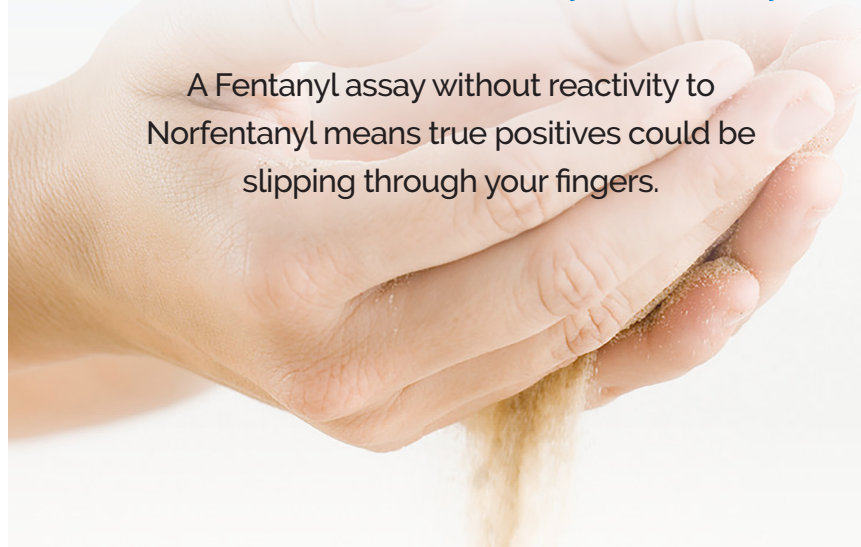
CE MARK GRANTED TO CURIOSITY DIAGNOSTICS FOR RAPID POC MRSA TEST

The ultrafast PCR|ONE system, developed by Curiosity Diagnostics (a wholly owned special purpose vehicle of Scope Fluidics), has received the CE mark for the diagnosis of methicillin-resistant *Staphylococcus aureus* (MRSA). Consisting of an analyzer and disposable cartridges, the PCR|ONE platform is a standalone system that detects up to 20 pathogens and genetic targets in a single run of the instrument at the point of care. It uses proprietary infrared amplification technology to perform 40 cycles of real-time polymerase chain reaction (PCR) in 7 minutes, enabling the system to identify bacteria and viruses on a molecular level in 15 minutes. It also performs each PCR in triplicate in order to maximize accuracy. For the drug-sensitive form of *Staphylococcus aureus*, the system demonstrates 96.8% sensitivity and 97.1% specificity, while for MRSA, the system demonstrates 95% sensitivity and 100% specificity.

BINX HEALTH GETS CLIA WAIVER FOR POC CHLAMYDIA/GONORRHEA TEST

The Food and Drug Administration (FDA) has granted a CLIA waiver to Binx Health for the IO CT/NG assay, which detects *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in female vaginal swabs and male urine specimens. Using a single-use, assay-specific cartridge, the binx IO platform combines ultra-rapid polymerase chain reaction amplification with Binx Health's proprietary electrochemical detection technology to produce results in approximately 30 minutes. Studies have evaluated the IO CT/NG assay in females 16 years and older and in males 17 years and older and have demonstrated that its performance is comparable to tests performed in a CLIA certified laboratory that meets the requirements for high or moderate complexity testing. With this CLIA waiver, the IO CT/NG assay can now be performed in point-of-care settings such as physician offices, community-based clinics, urgent care settings, and outpatient healthcare facilities.

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Industry Playbook

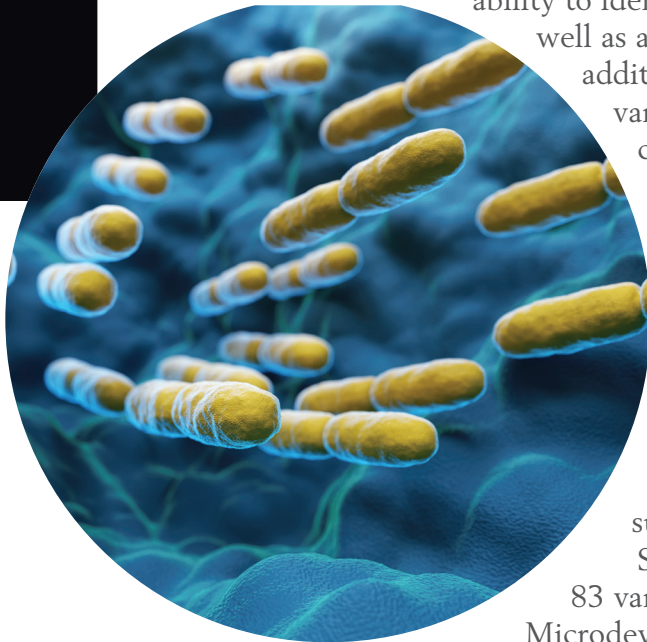
CARB-X Awards Companies With Over \$3 Million to Further Research

To advance detection and treatment of sepsis, Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator (CARB-X), a global nonprofit dedicated to antibacterial research and development, is teaming up with Baebies to fund development of a rapid diagnostic platform for neonatal sepsis. CARB-X is granting Baebies an initial \$3.9 million for the project.

With research showing that sepsis kills nearly 1.4 million children each year, the partners aim to detect early signs of bacterial infection in newborns. The Baebies platform will analyze a small blood sample for infection using digital microfluidics technology. If an infection is found, the platform will have the ability to identify within about 15 minutes which pathogen is causing it, as well as any antibiotic sensitivity that could interfere with treatment. In addition, the platform will be able to measure expression levels of various genes from 125µL of whole blood to detect different causes of inflammatory responses.

In a separate initiative, CARB-X is providing up to \$3.6 million to Novel Microdevices for a rapid molecular test to diagnose sexually transmitted bacterial infections. Novel Microdevices' recently developed Novel Dx system provides healthcare professionals with an easily accessible point-of-care diagnostic that can produce testing results in just 25 minutes. Patients would add a disposable cartridge containing either a vaginal swab or urine sample to the 4-pound, portable device to analyze the genetic sequence of cells to identify infections such as *Chlamydia trachomatis* and *Neisseria gonorrhoeae*.

Since the launch of CARB-X in 2016, the company has granted 83 various awards of over \$3 million. Both Baebies and Novel Microdevices have the potential to receive additional funding if specific milestones are met.



COMPANIES LAUNCH SARS-COV-2 POOLED TESTING FOR SCHOOLS

Dascena Labs and Concentric by Ginkgo are partnering to offer low-cost pooled testing for students and staff in K-12 schools. The companies will combine Dascena Labs' efforts in polymerase chain reaction (PCR) testing with Concentric's expertise in pooled testing to ensure safe learning environments as schools begin to reopen.

Dascena, a company that focuses on developing machine learning algorithms for early disease detection, launched Dascena Labs specifically to

aid in SARS-CoV-2 testing. The subsidiary offers PCR testing to patients through its sample collection sites across the U.S. Since its launch in late 2020, Dascena Labs has processed more than 720,000 patient samples. Similarly, Concentric by Ginkgo is the biosecurity and public health effort formed by Ginkgo Bioworks to offer affordable pooled testing in several states across the U.S.

The companies plan to offer services to all schools in the country. According to the partners, each school that registers for pooled testing will be mailed all necessary materials needed for testing, scanning, and shipping back. Each classroom will be

able to test up to 25 samples at once, with results returned in 48 hours.

SANFORD HEALTH TEAMS WITH CONGENICA FOR RAPID RARE DISEASE DETECTION

Sanford Health and Congenica are joining forces on a genetic testing program focused on providing better outcomes for patients suffering from rare diseases.

Congenica will offer its Congenica Express platform for rapid and accurate whole genome analysis in just minutes. Through automation and artificial intelligence, Congenica Express works to identify, classify,



and analyze genetic variants that have previously been identified in disorders, which according to the company is 75% of variants. The platform also has the ability to add new genetic information to the existing knowledge base for future automation.

Research shows that more than 300 million individuals are living with a rare disease, with half that population being children. On average, it can take roughly 5 years from the time a patient first sees a healthcare professional about a mysterious symptom to the time an accurate diagnosis is processed. Through their partnership, Sanford Health and Congenica aim to reduce this turnaround time from years to weeks. By partnering with Sanford Health, United Kingdom-based Congenica will also have the opportunity to expand its global network and offer services in the U.S.

HOLOGIC ACQUIRES MOBIDIAG STARTUP FOR \$795 MILLION

Hologic and Mobidiag have signed an agreement under which Hologic will acquire the private startup company for approximately \$795 million. Through the acquisition, Hologic will expand commercialization of Mobidiag products and services across the U.S.

Mobidiag, a biotechnology company that specializes in molecular diagnostic solutions, will allow Hologic to gain access to its collection of polymerase chain reaction (PCR)-based tests and platforms for acute

care conditions such as gastrointestinal infections, antimicrobial resistance management, healthcare associated infections, respiratory infections, and sepsis. Mobidiag's platforms offer rapid turnaround times of 2 hours maximum through automated test analysis. The company's Novodiag platform combines real-time PCR and microarray abilities to identify multiple pathogens in a single sample. In a statement, Hologic says it will invest in further assay development to advance use of the Novodiag platform.

"Acquiring Mobidiag will further strengthen our international and diagnostics businesses by enabling us to expand into the large, fast-growing acute care adjacency with a near-patient testing solution that offers ease of use, multiplex capability, and rapid turnaround time," said Jan Verstreken, group president, international at Hologic.

DIASORIN, LUMINEX SIGN \$1.8 BILLION ACQUISITION DEAL

After a unanimous approval from the company's board of directors, DiaSorin announced acquisition of Luminex Corporation for \$37 per share or a total of roughly \$1.8 billion in an all-cash transaction.

Luminex specializes in development, manufacture, and commercialization of biological testing products and has a rapidly growing portfolio of multiplexing technology. According to the companies, the

acquisition will allow DiaSorin to gain access to Luminex's molecular diagnostics multiplexing technology to complement its existing products. The deal also aims to establish opportunities for future partnerships in the life sciences industry, expand DiaSorin's network in the U.S. while also broadening international access to Luminex's technology, and generate high values for shareholders.

"Together, DiaSorin and Luminex will provide a unique offer to laboratories, researchers, clinicians, and patients worldwide, matching our extensive solutions in immunodiagnosics and molecular diagnostics with Luminex's outstanding expertise in multiplexing technology and recognized leadership in life science applications. We look forward to having DiaSorin and Luminex employees working together for an exciting new journey," said Carlo Rosa, CEO of DiaSorin.

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Ask The Expert

How Should Clinical Laboratories Manage Incoming Calls?



EXPERT

By David Shiembob, MBA, C(ASCP)^{CM}

Who generally calls the lab, and what answers are they looking for?

A: In my experience, calls coming into the lab largely involve questions about turnaround times (TATs), specimen requirements, and test selection. These callers consist of ordering physicians, nurses, staff at ambulatory clinics and other

medical laboratory locations, and outreach clients.

Which lab staff should handle incoming calls from clinicians or clients?

A general principle for operating an efficient laboratory is to have all team members functioning at the top of their abilities. With this in mind, one of the first goals when managing incoming calls is to direct calls away from staff such as clinical laboratory scientists, whose primary focus should be performing testing. Not only is it inefficient to have clinical laboratory scientists handle TAT calls, but these distractions can result in testing errors. By ensuring the correct staff handle calls, labs can increase efficiency and improve the quality of patient care.

Designating entry-level staff to handle incoming phone calls is a great first step toward achieving optimal productivity. However, in a smaller laboratory, these individuals are sometimes the same staff who receive and process specimens, and excessive interruptions for them also can lead to testing errors. A dedicated client services group is therefore the ideal solution, and call volumes can often justify these positions, especially if the laboratory handles a significant amount of outside testing.

What tools are available to help manage calls?

An effective phone tree is an important tool for triaging calls to the most appropriate staff. A typical call flow would be three to four rings each at client services, then specimen receiving, and lastly at a testing section. I know clients who have even changed their testing section phone extensions to redirect callers who were in the habit of contacting them directly.

Understanding the source and subject of incoming calls allows for more proactive solutions. Logging call information is a key first step. A powerful but complex solution is to implement customer relationship management (CRM) software. The sky is the limit (both in capabilities and cost) with these

types of solutions, which allow for sophisticated reporting and for client services, lab management, and sales teams to share information. CRMs are most appropriate for laboratories that serve a large number of outside clients. If a CRM isn't feasible, it may be easier to implement a paper- or spreadsheet-based log, but compiling the data into a usable format is time-consuming. Another simple but limited solution for counting and categorizing calls is to ask lab staff to place a small item like a bead into labeled bins whenever they take a call. These containers can be categorized by call topic or client type. Although not as sophisticated, this method places a low burden on staff while providing some basic statistics on call frequency.

How can the lab reduce the number of incoming calls?

Look upstream to understand why your laboratory is receiving so many calls. Requests for specimen and test information can be reduced by implementing an online laboratory test directory (LTD). Ensure that all callers are aware of the LTD and refer them to it for questions related to specimen requirements. Also, communicate TAT information in as many places as possible. In addition to the LTD, TAT information can be built into test names in the ordering system and included in the initial message of the laboratory call tree.

If a disproportionate number of calls relate to a particular issue or come from a specific group (as can be determined with call logging), targeted education may be helpful. Creating a laboratory formulary is another valuable initiative that can reduce call volume. A laboratory formulary results in a simplified list of tests in the ordering system, which can make ordering easier for clinicians, while also eliminating confusion and questions related to esoteric reference tests.

David Shiembob, MBA, C(ASCP)^{CM}, is the supervisor of consultative services at ARUP Laboratories in Salt Lake City.
+EMAIL: David.Shiembob@aruplab.com

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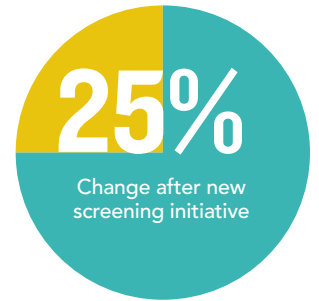
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Making a Difference in the Health of Populations Worldwide

Clinical laboratories demonstrate how combining collaboration and innovation breaks down barriers to better health. **BY KIMBERLY SCOTT**

As clinical laboratories continue to focus on adding value beyond individual test results, their role in improving the health of populations has become critically important. Whether detecting gestational diabetes early enough to prevent complications or using less invasive means of detecting colorectal cancer, laboratory testing is essential to population health.

Below, we highlight four initiatives involving clinical laboratories that have made a difference in the health of specific populations in various parts of the world. These initiatives have been recognized by AACC, in conjunction with Abbott and other leading healthcare organizations, through the UNIVANTS of Healthcare Excellence Awards. The awards recognize interdisciplinary teams around the globe that have achieved measurable, innovative impacts within healthcare systems.

Over the past two years, *Clinical Laboratory News* has been profiling initiatives recognized through the UNIVANTS program, including three population health initiatives highlighted in the December 2020 special supplement: Kidney Check: The Next Generation of Surveillance for Hypertension, Diabetes



and Chronic Kidney Disease; Early Diagnosis and Improved Management of Patients with Diabetes Through Strategic and Automated Test Algorithms via Primary Care; and Novel Collaborative Approach Among Public and Private Sectors for Streamlined SARS-CoV-2 Testing Toward Optimized Patient Outcomes During the COVID-19 Pandemic.

EARLY DETECTION AND MANAGEMENT OF GESTATIONAL DIABETES MELLITUS

Prevalence of gestational diabetes mellitus (GDM) is increasing worldwide, mainly driven by increases in obesity, older age of pregnant women, and higher prevalence of sedentary lifestyles. GDM has direct associations to adverse outcomes in mothers, their babies, and pregnancy-related complications. Short-term complications of GDM include pregnancy-induced hypertensive disorders, premature labor, shoulder dystocia, caesarean section, and low or high birthweight. Long-term complications include risk of developing glucose disorders, cardiovascular disease, and increased likelihood of cancer.

In 2006, the Hospital Clinic San Carlos in Madrid, Spain, defined a new pathway for diagnosis of GDM in pregnant women. The central laboratory helped coordinate obstetrician consultation and blood draws, as well as all related testing and follow-up. Women were screened between weeks 24 and 28 of pregnancy with a two-step process. First, they were screened using the O'Sullivan test, and if the glycemia

10.6% to 35.5%
Increase in the percentage of pregnant women diagnosed with GDM

24 days to 4 days
Reduction in time from first visit for GDM screening to final diagnosis

Hospital Clinic San Carlos, Madrid



value was higher than 140 mg/dL, the patient underwent a 100g oral glucose overload, using the Carpenter-Coustan criteria for the diagnosis of GDM.

"The clinical laboratory coordinating the diagnostic process was fundamental for improvement both at the care level and in terms of patient satisfaction," said Maria Jose Torrejon, MD, head of the Hormones and Metabolism Laboratory at San Carlos. "The number of medical appointments was reduced, and the time for the final diagnosis of GDM was reduced from 24 to 4 days. Further, 96% of pregnant patients served by the hospital had GDM screening carried out before week 28."

The expedited testing procedures meant that fewer patients were lost to follow-up, and more at-risk patients were identified that were previously missed. The hospital implemented the one-step International Association of Diabetes and Pregnancy Study Groups (IADPSG) recommendations for GDM screening and used the approach to detect and treat more pregnant women with GDM, including those with low hyperglycemia.

As a result of the screening initiative, diagnosis of GDM increased from 10.6% to 35.5%, resulting in targeted treatment and reduction in GDM-related complications for mothers and their newborns. Overall direct cost savings of 15,000 euros per 100

women were achieved, corresponding to an annual savings of 250,000 euros. Although the team expected—and observed—an increase in pregnant women diagnosed with GDM, overall healthcare costs were reduced due to fewer complications: gestational hypertension problems (-14.6%); premature births (-10.9%); Caesarian sections (-6.5%) and admissions to the NICU (-24.4%).

"Without global consensus or standardized guidelines for diagnosis and treatment of GDM, there are differences of opinions with respect to how and whom to treat," said Nuria Garcia de la Torre, MD, a consultant endocrinologist. "With the expansive research performed at our site, however, driving positive outcomes for our patients, we know our process works, enabling us to give high quality care."

This highly scalable GDM screening initiative was recognized by the UNIVANTS of Healthcare Excellence program with distinction.

ENHANCED IDENTIFICATION FOR HCV AND HIV IN THE ED

Hepatitis C virus (HCV) and human immunodeficiency virus (HIV) are underdiagnosed and untreated chronic diseases with growing health concerns. Globally, an estimated 71 million people have HCV and 38 million have HIV2, representing major

public health burdens. The World Health Organization estimates that 21% of HIV-positive individuals are unaware of their status. Thus, identifying individuals with unknown disease while successfully enabling treatment is essential for disease containment and prevention. Linkage to care is especially complicated in high risk and underserved populations who utilize emergency care services as their primary healthcare option.

An integrated clinical care team at the University of Alabama-Birmingham (UAB) Hospital sought to change this paradigm by enhancing identification and care for patients with undetected HCV and HIV. In partnership with the emergency department (ED), infectious disease physicians, linkage coordinators, information technology, and the clinical laboratory, the team developed and implemented an opt-out screening program within the ED coupled with disease-specific linkage-to-care services. The HIV screening program was implemented in 2011, and the HCV screening program was implemented in 2013.

Active education and physician-level endorsement led to an increased uptake in population screening, resulting in a 61% increase in the number of patients with newly identified HCV infections linked to HCV treatment and care, and 100% of acutely infected HIV and 84% of chronically infected individuals linked to care. Dedicated care coordinators enhanced patient engagement and ensured sustained linkage to care with routine consultation and subsequent confirmation, as appropriate. In addition, 99 known HCV positive individuals previously identified by HCV antibody testing were re-engaged to care. This care coordination and improved access to HCV providers led to a 91% reduction in the average days between testing and initial medical appointments, enabling rapid treatment and reduced overall healthcare costs.

“Early diagnosis is critical for linking someone with care shortly after their diagnosis, while it’s still fresh in their mind,” said Joel Rodgers, clinical research administration manager in emergency medicine at the UAB. “If someone tests positive for HIV at the screening level in the ED, we perform a rapid confirmatory test. If that comes

back positive, the ED physician gives the patient a packet of information and has a conversation with the person. A linkage coordinator follows up to schedule an appointment. We do the same for HCV, although there is no rapid test to confirm.”

Given that ED visits are costly and can lead to other high-cost services, the screening initiative resulted in a 76% reduction in healthcare costs when primary care appointments were used in lieu of emergency department visits (\$1,067 versus \$13,898 per visit).

Since implementing the initiative in Birmingham, the university has expanded it to two other hospitals within the system, Rodgers noted. The HCV/HIV screening initiative was recognized by the UNIVANTS of Healthcare Excellence program with distinction.

USE OF FIT TO SCREEN FOR SIGNIFICANT BOWEL DISEASE

Recognizing that patients presenting to general practitioners (GPs) with new bowel symptoms can be difficult to assess, as symptoms are poor predictors of pathology, the National Health Service (NHS) in Tayside, Scotland, in 2015 implemented a new screening initiative for significant bowel disease.

In Scotland, colonoscopies are not standard screening exams but are used to diagnose patients who present with new bowel symptoms. During the pilot for the screening initiative, at least 35% of patients were referred for colonoscopies after presenting with bowel symptoms, but colorectal cancer was identified in only 2 of 4,000 patients screened, and inflammatory bowel disease was identified in 5%.

Clinicians believed there had to be a better way to investigate these patients than simply referring them for colonoscopies and thus introduced fecal immunochemical tests (FIT) to quantify fecal hemoglobin (fHb), which then determines whether patients should be referred for a colonoscopy. Tayside now uses FIT to screen for significant bowel disease, along with clinical history and other blood tests. The FIT test is sent home with patients, who collect their own samples and returns them to the lab. Results are typically returned in less than 24 hours, allowing GPs to quickly refer patients who have a high fHb.

In practice, this translates to

2,349/195

Newly diagnosed HCV/HIV infections in patients seen in the emergency department

91%



Reduction in average days between testing and initial medical appointments

University of Alabama-Birmingham Hospital

approximately one-third of patients who present to their GP with new bowel symptoms who in the past would have been referred for a colonoscopy now being screened with FIT. In Tayside, that means almost 1,400 patients each year do not have to be referred for invasive testing. Patients with a very high fHb have a greater than 50% risk of SBD and are referred for urgent colonoscopy. Since the initiative began, referrals for colonoscopies have dropped by 15%.

“For an individual patient, the impact is extremely significant,” said Judith Strachan, BSc, FRCPath, a consultant clinical scientist with NHS Tayside. “First, a negative FIT test in the absence of other worrying signs and symptoms means that they are highly unlikely to have significant bowel disease. This means that they do not need an invasive and unpleasant colonoscopy and can be reassured that they do not have significant disease, thus reducing anxiety and a wait for further tests. For patients with ongoing symptoms, advice and safety netting is available with repeat FIT testing if necessary. For patients with elevated FIT results, they may well be ‘fast tracked’ to more investigations, thus leading to a quicker diagnosis of significant bowel disease.”

In the first year since introducing FIT as a standard test available to GPs, referrals in NHS Tayside from primary care via the Colorectal Pathway fell 9%, and referrals to gastroenterology fell 24%. Overall reduction in referrals was 15%.

70,000

Number of people in Mexico who have become more aware of the complications and risks of HCV

221

Number of people confirmed to have active HCV infections

Biomédica de Referencia and Mexican Foundation for Liver Health

The FIT work led by NHS Tayside has made a significant contribution to patient care, Strachan said. Due to Tayside's pioneering work, FIT testing in primary care is now universally available in NHS Scotland. The service was in place before the COVID-19 pandemic, but its value to diagnostic services has been greatly emphasized during the recovery phase, Strachan said. The FIT initiative was recognized by the UNIVANTS of Healthcare Excellence program with distinction.

SCREENING FOR UNDETECTED HEPATITIS C

Left untreated, patients with chronic hepatitis C (HCV) can develop cirrhosis or liver cancer. To improve the identification and treatment of patients

with HCV, Biomédica de Referencia, a clinical laboratory and imaging company in Mexico City, in 2007 partnered with the Mexican Foundation for Liver Health (FundHepa) to develop a screening program for HCV. An integrated care team formed to overcome key barriers for HCV identification and treatment, such as lack of public awareness, cost of testing, access to education, follow-up, and treatment.

The team led comprehensive media campaigns to raise disease awareness, collaborated with partners to make HCV screening available free of charge, and developed treatment strategies that linked all HCV-positive patients to relevant education and care.

The program has had significant, and enduring, success. Between 2007 and 2019, there was an eight-fold increase in the number of patients screened for HCV—1,170 people in 2007 to 9,372 people in 2019. To date, more than 70,000 individuals in Mexico have become more aware of the complications and risks of HCV. Further, 367 people with detectable anti-HCV antibodies (0.5%) have been identified by the program. Among those, 221 were confirmed to have active HCV infection. Identification of these individuals enables rapid treatment, prevents disease progression, and reduces healthcare costs. Success of the program has led to 29 additional companies and six clinical laboratories across Mexico joining the initiative with a collective goal of improving public health in Mexico.

While the initiative started as a social responsibility project coordinated by a committee of 10% of Biomédica de Referencia's employees, the campaign now involves almost half of the organization's workers, something of which the chief executive officer and clinical director of Biomédica de Referencia is proud.

"Too often medicine is reactive," says CEO Clara Corona de Lau. "Our care initiative has proactively identified hundreds of patients who need care, who have benefited from treatment, and who ultimately helped reduce the spread of this deadly disease. Our entire staff takes great pride in supporting HCV elimination and favorably impacting public health."

Given that the average cost of treatment for late-stage complications of HCV infection is more than three times higher than the cost of treatment in the early stages of the disease, the screening initiative also has significant cost savings implications.

"Discovering HCV-positive patients in the early stages of the disease truly increases the chance of better outcomes and reduces downstream treatment costs substantially," said David Kershenovich, MD, PhD, hepatologist and Director of the National Institute of Health Science and Nutrition Salvador Zubiran.

EARLY INTERVENTION IS KEY

Detecting diseases and chronic conditions early enough to have a significant effect on patient outcomes is essential to improving the health of populations. Early detection is a core element in all four of the initiatives highlighted. These interdisciplinary initiatives have made measurable positive impacts on targeted populations while at the same time contributing to cost savings, as treatment in the early stages of a disease almost always costs less than treatment in more advanced stages.

These are just a few of the projects in which clinical laboratories are playing a critical role in transforming healthcare delivery. To learn about other initiatives recognized through the UNIVANTS of Healthcare Excellence program, go to www.univantshce.com. ■

Kimberly Scott is a freelance writer who lives in Lewes, Delaware.

+EMAIL: kmscott2@verizon.net

UNIVANTS 2020 Teams Recognized In This Issue

Identification and Care for Patients with Undetected HCV and/or HIV via Opt-Out ED Screening with Active Education and Linkage to Care | University of Alabama Birmingham Hospital | Lauren Walter, Sonya Heath, Joel Rodgers, Adrienne Moore, Kelly Ross Davis

Use of Fecal Immunochemical Tests Unlocks the Door to Efficient and Effective Investigation of Patients with New Bowel Symptoms | NHS Tayside | Judith Strachan, Ian Kennedy, Andrew Cowie, Craig Mowat, Lynne Taylor

Improving Population Health through Screening for Hepatitis C to Enable Treatment for Undetected Viral Infections | Biomédica de Referencia | Clara Corona de Lau, Dana Lau Corona, Evelin Nájera López, Emma Alicia Arana Grimaldo, María Concepción Gutiérrez Ruiz

Early Detection and Management of Gestational Diabetes Mellitus for Improved Outcomes of Mothers and their Babies | Hospital Clínico San Carlos | María José Torrejón, M. Cruz Cárdenas, Miguel Ángel Herráiz Martínez, Alfonso L. Calle-Pascual, Nuria García de la Torre Lobo