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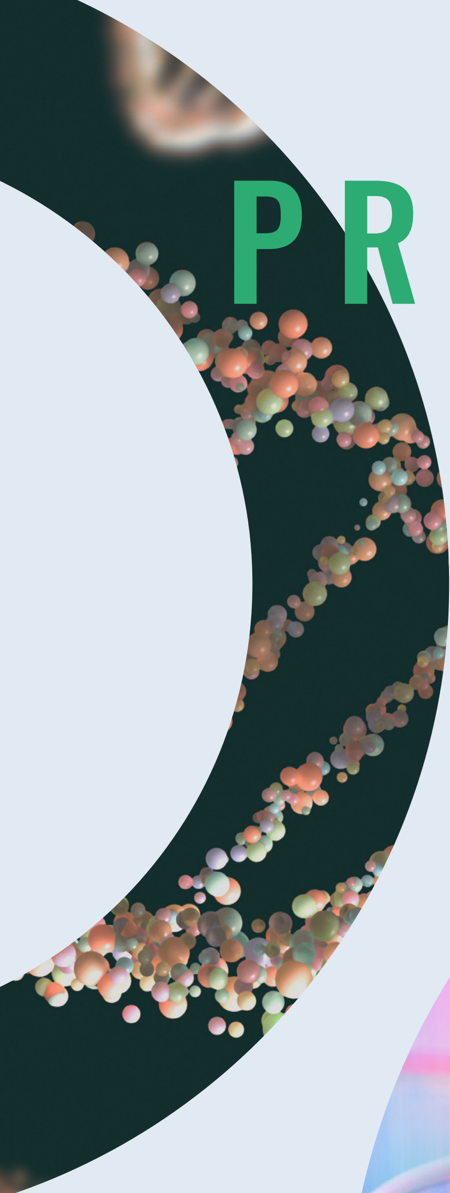

COMMENTARY PAPER

Genomic sequencing and laboratory equipment risks

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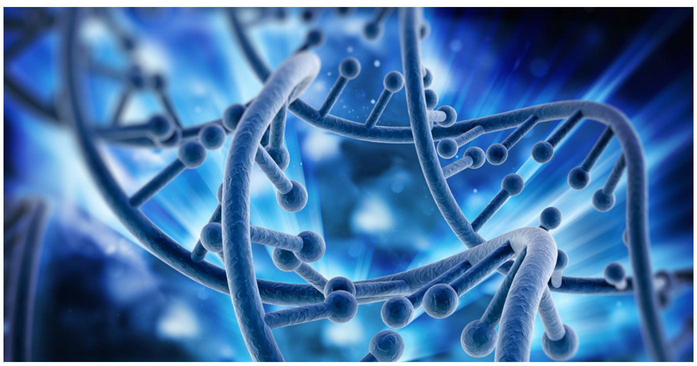
Genomic sequencing and laboratory equipment risks

According to the Centers for Disease Control (CDC), elevated levels of low-density lipoprotein cholesterol (LDL-C) – also known as “bad” cholesterol – raises a person’s risk of heart disease and stroke. In 1986, patients were introduced to a new way to lower LDL-C through the use of statins, a group of cholesterol-lowering medications that require daily dosing. Could daily dosing become a thing of the past? Genomic sequencing – followed by gene editing – introduces that possibility. Rather than manage the problem with drugs, elevated levels of LCL-C could be lowered for good with one injection.



The Muscular Dystrophy Association (MDA) explains that spinal muscular atrophy (SMA) is a genetic disease that affects the central nervous system, peripheral nervous system and voluntary muscle movement. SMA is a genetic condition that affects children and the number one genetic cause of infant mortality. Infants with SMA type 1, the most common form of the disease, have a life expectancy of two years. Today we are fortunate to have Zolgensma (onasemnogene abeparvovec-xioi), a lifesaving gene therapy treatment for SMA that corrects the problem in the illness-causing gene itself. The treatment is given as a one-time infusion.

In 2022, the United Kingdom became the first country to successfully cure Alyssa, a 13 year old girl who suffered from incurable T-cell acute lymphoblastic leukemia. Alyssa was first treated with chemotherapy and a bone marrow transplant starting in May 2021. However, the cancer came back and there were no further conventional treatment options. At that point Alyssa was enrolled in a clinical trial were she received genetically modified chimeric antigen receptor (CAR) T-cells – a type of immune system/white blood cell – from a healthy donor. The T-cells were edited with instructions to hunt and kill the cancerous T-cells without attacking each other. After a month Alyssa was in remission. After six months the cancer was undetectable.

Our genome

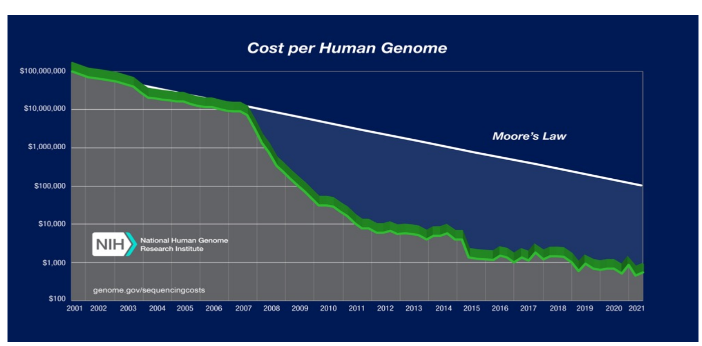
A genome is a comprehensive manual that contains instructions for the body to develop and operate. From the time you embark on that Olympic swim through the fallopian tubes towards the egg, to the person you are today. No different than following a recipe to make your favorite dish, each one of our cells contains a complete set of instructions needed to build and maintain our body throughout life. The genome promotes growth, guides organs to do their job and helps the body repair itself when ill or injured. These instructions are written on genetic material know as deoxyribonucleic acid or DNA. Interestingly, humans are 99.9% biologically identical, with only 0.1% of our DNA making us unique. Therefore, the more doctors learn about our individual genomes and how they work, we’ll benefit from more individualized healthcare.

What is genomic sequencing?

The first read/decoded human genome was accomplished in 2001. An astonishing feat that helped the research community start to decipher how we are built, what – from a homology/similarity of our genome's perspective – almost makes all of us identical twins, how “flaws” or mutations in our DNA cause certain ailments, and how we may respond to medicines. Genomic sequencing is therefore the action of decoding DNA, or more specifically – and as defined by the National Human Genome Research Institute (NHGRI) – “determining the order of the four chemical building blocks – called "bases" – that make up the DNA molecule.”

Genomic sequencing equipment and cost

On September 30, 2022, a manufacturer of life science technologies made headlines by showcasing their new line of DNA sequencers that would enable a genome to be sequenced for just $200. To put this number in perspective, at the turn of the millennium the cost to achieve the same feat topped $100 million. By 2015, the cost had dropped to $1,245. The cost of the sequencing hardware ranges from $985,000 to $1.25 million.



Types of laboratories

We typically imagine laboratories as clean, sophisticated and safe environments – and for the most part that perception is correct. While the Wuhan virology laboratory made headlines in 2020 as the potential source of the SARS-CoV-2 virus, laboratories are not featured all too often in the news.

Clinical and medical laboratories

During an annual physical, general practitioners (GPs) usually recommend a comprehensive wellness blood test. The blood test is sent to a clinical or medical laboratory that processes tests on specimens to quantify blood glucose, triglycerides and cholesterols. While clinical labs can perform DNA sequencing as well as other complex tests, they are best known for performing single patient diagnostic testing that is directly used for patient care.

Analytical and quality laboratories

In these laboratories, new products and materials are tested to ensure conformity to manufacturer specifications and the absence of impurities. Such labs are an essential part of the production and supply chain.

University laboratories/academic research

These laboratories focus on either scientific research or research in the humanities. Universities house research teaching labs where student demonstrations and experiments take place.

Research and development (R&D) laboratories

This category covers a broad spectrum of facilities with various risk qualifications and containment requirements. Biosafety laboratories, as discussed above, that house potentially harmful biological agents are also accounted for under this category, as well as laboratories with radioactive risks. Laboratories that experiment on seeds, crops, materials and life sciences research, would also be considered R&D labs.

National laboratories

The United States Department of Energy (DOE) funds research that is conducted in 17 national laboratories. Such research focuses on developing new energy technologies, projects such as the nation's nuclear weapons program, as well as the Human Genome Project, which resulted in our ability to now sequence anyone's genome.

Laboratory equipment

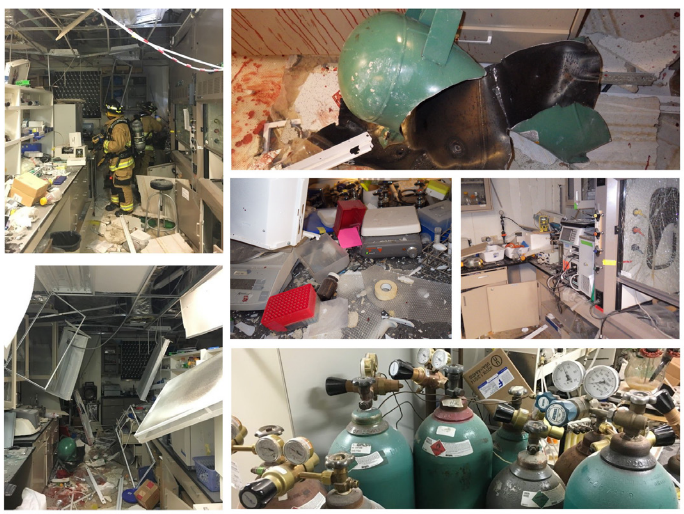
While genomic research is already impacting the fields of oncology, pharmacology, and rare, undiagnosed and infectious disease, the idea that cost effective personal genomics is within reach is a tremendous benefit to humanity. To achieve this feat, years of research took place in laboratories (or labs) around the globe. Labs that house life science research and development equipment, such as the first generation DNA sequencers that use electrophoresis instruments, the next generation sequencers (NGS) as well as the third generation nanospore sequencers. Labs of this type are also equipped with sophisticated and expensive hardware such as mass spectrometers, gas chromatographs, cold storage, ovens and incubators, high performance liquid chromatographs, spectrometers, particle, elemental and thermal analyzers as well as electrochemistry equipment.

Laboratory loss scenarios

While laboratories develop vaccines, they are not immune to disaster events. Some labs contain highly flammable chemicals, compressed flammable gases, hydrocarbons and high-temperature equipment. Labs also experience frequent turnover of users.

Failure of a high-pressure vessel

A laboratory explosion caused a postdoctoral researcher to lose an arm. The researcher was combining hydrogen, carbon dioxide and oxygen gases from high-pressure cylinders into a lower pressure tank when the incident occurred. According to Jyllian Kemsley from Chemical & Engineering News, "The researcher purchased a 49 liter steel gas tank, a digital pressure gauge not rated as intrinsically safe, a pressure-relief valve and fittings, and assembled them. The researcher added the gases to the portable tank, which was then connected to the bioreactor. The researcher used a mixture of 70% hydrogen, 25% oxygen and 5% carbon dioxide for the experiment." The explosion was caused by a spark from the digital pressure gauge that was not designed to be used with flammable gases.



Of particular interest, the week before the explosion, a similar set-up with a 3.8 liter tank resulted in a "small internal explosion" when the researcher pressed the 'off' button on the digital pressure gauge. The researcher also occasionally experienced static shocks when touching the tank, which was not grounded. The researcher reported the shocks and possibly the small explosion to the overseeing researcher, who advised them "not to worry about it."

Overheated equipment

A university lab housed in the agricultural building sustained fire damage. Investigators determined that the fire started as a result of equipment that had overheated.

Cooling system failure

The laboratory specialized in design and manufacturing of specialty chemicals for gasoline additives as well as printing industry solvents. An explosion occurred resulting in four deaths and injury to fourteen others. A report published by the U.S. Chemical Safety and Hazard Investigation Board detailed the cause of the accident. "The explosion occurred in a 2500-gallon batch reactor during production of methylcyclopentadienyl manganese tricarbonyl (MCMT). The reactor cooling system, which lacked backups, failed; this led to thermal runaway. Pressures rapidly reached 400 PSI, bursting the rupture disc, but the relief was insufficient to prevent the continued runaway reaction. Nearby witnesses described a jet engine-like sound as high pressure gases vented from the reactor. At the same time pressure increased in the reactor, temperatures also increased in the reactor until the solvent (diglyme) reached its decomposition temperature. The pressure and temperature continued to increase until the reactor violently ruptured and the MCMT exploded, destroying the reactor. Damage from the explosion was severe enough that 4 buildings in the immediate vicinity of the plant were condemned."

Fortis LifeSafety Management (LSM)

Laboratories are one of the few environments where four of the five classes of fire can occur either individually or in combination with one another.

- Class A: Ordinary materials, such as paper, wood, plastics, and cardboard
- Class B: Flammable and combustible liquids, as well as organic solvents
- Class C: Energized electrical equipment, such as appliances, burners, hot plates, power tools, and panel boxes
- Class D: Combustible metals, such as magnesium, lithium, sodium, calcium, and titanium

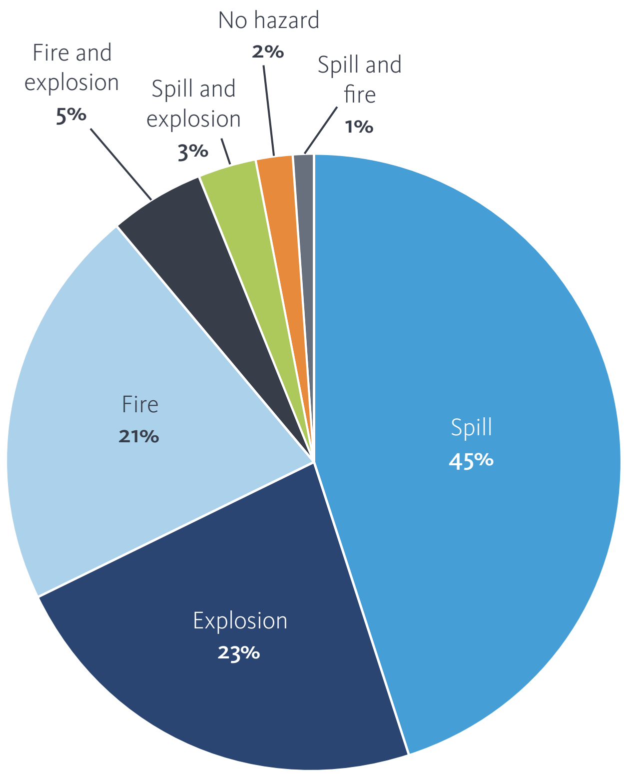
Flash fire from loss of cooling water

A university lab needed a plumber to repair a leaking faucet. The plumber asked if it was alright to shut off the water to the whole lab. Lab personnel gave their approval. However, the personnel did not know, or perhaps forgot, that another lab member had started a UV-photolysis of a solvent-containing reaction in a closed wooden box. The photolysis required constant cooling water flow to prevent the apparatus from over-heating. After a few minutes with no cooling water flow, the organic solvent ignited and burst into flames.

Laboratory incident statistics

The November 2018 issue of the journal Nature provided a statistical based critique of academic lab safety. The following is provided exactly as published:

- 25-38% of lab personnel surveyed have been involved in an accident or injury in the lab that was not reported to the supervisor or principal investigator.
- 27% of researchers stated that they never conducted any kind of risk assessment before performing laboratory work. Academic researchers were the least likely to assess risk, followed by industry and government.
- In one study of lab safety between 1966 and 1984, 81% of accidents occurred in teaching labs, 13% in research labs and 2% in fabrication rooms.
- Only 40% of researchers surveyed reported wearing PPE at all times when working.
- 25% of researchers had not been trained in the specific hazard with which they worked.
- Articles in chemistry journals seldom mention safety information on chemical reagents. One study looked at journal mentions of 11 hazardous compounds. These compounds were mentioned 107 times in journal articles but only one article provided cautionary information.
- In one profile of safety incidents at research labs, virtually identical incidents occurred at the same institutions within 10–15 years, resulting in the destruction or temporary closure of the buildings.



Property loss considerations

Losses in laboratories range from fires and explosions to leaks and spills, all of which can both harm lab researchers/students/clinical workers and shut down or delay production. Adverse weather, improper equipment installation, facility and equipment maintenance and equipment failures impact laboratories as well. Unfortunately, in many cases, lab personnel are the reason behind the loss.

While recovery from these losses is not much different than other commercial facilities, there is great urgency in restoring these facilities as quickly as possible. In some cases, patient tests will have to be rerouted to another lab that is not in close proximity to the medical center, and researchers may experience spoliation of ongoing experiments. Retaining experts that are fully versed in laboratory risk mitigation is critical to managing the recovery scope and the carrier's overall exposure.

About EFI Global

EFI Global, part of Sedgwick, is a well-established brand with an excellent reputation in the Americas, Africa, Asia-Pacific and Europe as a market leader in environmental consulting, engineering failure analysis and origin-and-cause investigations. Each year, EFI Global completes more than 45,000 projects worldwide for a wide range of clients, such as commercial, industrial, institutional, insurance, government, risk managers, public and private entities. EFI Global is one of the world's most respected emergency response firms, capable of providing practical solutions to the most complex problems. Our multidisciplinary team of first responders, project managers, engineers, geologists and scientists are selected for their technical proficiency and in-depth industry knowledge to aid clients in resolving technical problems. For more, see **efiglobal.com**.

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James Woolf has more than three decades of combined experience in the fire service and law enforcement — conducting over 1,100 origin and cause investigations. In his career, Mr. Woolf has served as a line firefighter and fire officer, fire investigator/inspector, fire service instructor, patrol officer, detective and chief of police. Mr. Woolf is also a U.S. Army veteran where he served as a legal specialist/sergeant and infantry paratrooper in the 82nd Airborne Division. For more information, contact **james.woolf@efiglobal.com**.

Michael Lilien, PE, CFEI - forensic engineer
As a forensic electrical engineer, Michael's range of engineering experience is wide and deep. He has worked as a forensic engineer, managing projects as varied as home and vehicle fires to product testing, evaluation and investigation. He has spent considerable time at electric utilities working in construction project management, field and distribution operations, standards writing and design review. His experience in manufacturing includes leading engineering teams with troubleshooting product and testing issues and product research, development and design. For more information, contact **michael.lilien@efiglobal.com**.

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