

## Lab on a chip: ORNL's top commercialization success

(As published in The Oak Ridger's Historically Speaking column December 8, 2021)

Carolyn Krause introduced Mike Paulus at a recent Friends of ORNL virtual monthly meeting. She was editor of the ORNL Review for 25 years and had personal knowledge of some of the top 10 inventions from Oak Ridge National Laboratory that have become commercialization successes. You see, she wrote about them in the Review! She also has written up the talk and included it here in Historically Speaking. Enjoy the talk!

\*\*\*

In 1987 Mike Paulus visited Mike Ramsey in his lab at Oak Ridge National Laboratory. Ramsey showed him a microscope slide on which tiny scratches were etched, creating channels through which fluids could be pushed by an electric potential. He later called this microfabricated fluidic device for performing chemical separations faster by using smaller samples the "lab on a chip."

"I thought that it was the silliest thing I had ever seen and that it wouldn't amount to anything," said Paulus, director of technology transfer at ORNL, to Friends of ORNL at its monthly virtual meeting. In his talk to FORNL on his ranking of the top ten ORNL technology commercialization successes, he said the lab on a chip finished first.

Invented by Ramsey and Stephen Jacobson, the miniature device was first patented in 1995 and licensed to Caliper Life Sciences, a company Ramsey co-founded. It later evolved into the LabChip® GXII Touch HT protein characterization system, which is manufactured by PerkinElmer. The device is used by scientists involved in gene editing, drug discovery and other biochemical separations research.

"So, the lab on a chip embodied in the LabChip GX Touch is the biggest hit ORNL has ever had," Paulus said, noting that the invention was first marketed as the Agilent 2100 Bioanalyzer in 1999 by Agilent, Caliper's strategic partner. PerkinElmer acquired Caliper in 2011 for \$600 million.

The 10 ORNL inventions Paulus listed as leading commercialization successes, including a second one co-invented by Ramsey, were made after 1985 because "that's when the lab was given the authority to license patented ORNL technologies to companies and receive royalties," he said. Since 1985 when the lab's new technology transfer office of ORNL started tracking the commercial success of its licensees, ORNL has entered 847 patent and copyright licenses.

Paulus said that he ranked the top ten commercialization successes based on royalties received from the companies to which patented ORNL inventions were licensed. "Royalties are paid as a percentage of product sales – a good proxy for economic impact," he added. "The ten inventions accounted for more than \$30 million in payments to ORNL and for 45% of the \$65 million paid to the lab, yet they represent only 1.2% of all the licenses we have executed.

"The top ten licenses were recognized with ten R&D 100 awards in nine cases, and one other picked up two of these awards. The licenses included 200 U.S. and international patents. The ones that made a big splash have large patent portfolios."

Paulson noted that ORNL began engaging in technology transfer in the first half of the 1980s when these key national technology transfer laws were enacted: Stevenson-Wydler Technology Innovation Act of 1980, Bayh-Dole Act of 1980, and Federal Technology Transfer Act of 1986. The latter law had the most impact on ORNL because it enabled national laboratories to enter into cooperative research and development agreements (CRADAs) and to negotiate licenses to companies for patented inventions made at the labs.

On September 5, 1985, ORNL entered its first patent license under the new framework with Cummins Engine Company. Cummins licensed an ORNL-patented family of high-temperature nickel-iron aluminide alloys for use in large diesel engines and turbochargers. The first instance of technology transfer occurred two years earlier; the patent rights to the INOR-8 (Hastelloy N) alloy developed at ORNL for molten salt

## Lab on a chip: ORNL's top commercialization success

(As published in The Oak Ridger's Historically Speaking column December 8, 2021)

reactors under Bill Manly were transferred in 1983 to Cabot Corp. where Manly moved to become its senior vice president.

"Most of the commercial successes we've had are the result of long investment and deep expertise at ORNL because of support from ongoing Department of Energy programs," Paulus said.

### Other commercialization successes

The ORNL invention finishing second in Paulus' ranking is the integrated wireless temperature measurement system for semiconductor process monitoring. The partner for inventors Bob Lauf, Don Bible and Carl Sohns, who conceived the device in a bar during a technical meeting, was SensArray in Santa Clara, Calif. It launched the SensArray integrated wafer wireless temperature metrology system in 2004.

SensArray was acquired by KLA Tencor in 2007; in 2021 KLA Corporation joined the Fortune 500 with \$6 billion in annual revenue. "This wireless monitoring of wafer temperature based on an ORNL patent," Paulus said, "is still a significant part of process control for the semiconductor industry."

Finishing third in Paulus' ranking is the invention by George Wei, Terry Tiegs and Paul Becher of silicon carbide whisker-reinforced ceramic composites for cutting tools. "These composites are good for cutting tool applications," Paulus said. "The whiskers are like rebar and they provide cracking and breaking resistance."

Licensed in 1986 to Advanced Composite Materials Corp. as ORNL's second patent license, cutting tools made of the ORNL composite were first sold in 1987 and later distributed by Greenleaf Tooling Solutions in the United States and Sandvik AG in Sweden. The Silar® silicon carbide whiskers technology for reinforcing aluminum oxide is claimed to make the hardest cutting tool outside of diamond, and the business was purchased in 2017 for \$7 million by Haydale of the United Kingdom.

Ranked fourth is Ramsey's co-invention of a hand-held mass spectrometry system with Bill Whitten. It was licensed in 2012 to 908 Devices, a \$150 million initial public offering co-founded by Ramsey. The IPO, which closed in December 2020, has a market cap of \$914 million.

Paulus said the invention is a miniature ion trap mass analyzer, a combination of a mass spectrometer and microfluidic device that has been reduced from a bulky desktop system to a handheld system. It determines the identity and quantity of the sample's various ions based on when they are rejected over time by an electric potential.

The ORNL invention finishing second in Paulus' ranking was a high-temperature superconducting material made by the rolling-assisted biaxial textured substrate (RABiTS) technology developed by Amit Goyal and Parans Paranthaman. Further developed by ORNL in a CRADA with American Superconductor (AMSC), the patented technology was licensed to AMSC in 2000 and to its competitor SuperPower in 2007. The products launched were the SuperPower REBCO 2G HTS high-temperature superconducting wire introduced in 2009 and the AMSC Amperium wire introduced in 2010. Furukawa Electric acquired SuperPower for \$65 million in 2012.

"Because these superconducting power lines must be cooled to liquid nitrogen temperatures to have zero resistance, it only makes economic sense to install these lines where you have the most densely populated infrastructure or to replace above-ground cables you don't have room for," Paulus said. "We are still waiting for superconducting power lines to take off."

Thin-film, solid-state battery technology invented at ORNL in the 1990s was ranked sixth by Paulus. Invented by John Bates, Nancy Dudney and Bernd Neudecker, the technology was further developed through CRADAs the lab had with Eveready, Teledyne and Cymbet. The technology was licensed to

## Lab on a chip: ORNL's top commercialization success

(As published in The Oak Ridger's Historically Speaking column December 8, 2021)

FrontEdge Technology, Cymbet, Infinite Power Solutions and STMicroelectronics, all of which launched solid-state micro lithium ion batteries. These thin-film batteries are longer-lasting, more robust and safer than lithium ion batteries used today that have liquid electrolytes.

None of the battery companies have had more than \$10 million in sales, Paulus said. One was purchased by Apple Computer, Paulus noted, adding that "it was a strategic acquisition that did not find its way to the marketplace."

Paulus ranked seventh a bio-succinic acid process developed by ORNL's Nhuan Nghiem and Brian Davison, in collaboration with scientists at DOE's Argonne National Laboratory and the National Renewable Energy Laboratory. The project goal was to replace petroleum-derived chemicals with substances made by bacteria for producing plastics.

The bio-derived product was first launched by Applied CarboChemicals in a \$30 million demonstration plant built in France and operated from 2010 to 2014. Applied CarboChemicals merged with Diversified Natural Products in 2003 and formed JV BioAmber in 2008. However, seven years later the ORNL-ANL-NREL process for making bio-succinic acid became obsolete when BioAmber switched to a cheaper yeast-based technology and built a production plant in Canada.

The eighth-ranked commercialization success is LandScan, a global population database with a one-kilometer resolution that combines census data with satellite imagery and other information. It is used to estimate how many people are present during the day or at night in a region affected by a disaster. Other uses include urban planning and research on urban dynamics.

The patented database, licensed in 2005 and updated annually, was developed at ORNL by Budhu Bhaduri, Phillip Coleman, Edward Bright, Amy Rose and Marie Urban. East View Geospatial was the exclusive distributor from 2012 to 2021 when LandScan was transitioned to an open-source license for academic use

A content-based image retrieval system for improving semiconductor yield is the ninth ranked success. Known as TrueADC, this ORNL-invented automated image retrieval system can do the work of 60 human operators.

"This robust image processing capability is a precursor of today's artificial intelligence technology," Paulus said. "TrueADC finds anomalies in semiconductors and compares their shapes and features to those in similar anomalies in a database." The identified flaws are connected by software to specific process failures that are corrected.

This invention by Ken Tobin, Regina Ferrell, Tom Karnowski, Shaun Gleason and Hamed Sari-Sarraf was licensed in 2004 to August Technology Corp. After two mergers, the ORNL technology became owned in 2019 by Onto Innovation, a company headquartered in Massachusetts that has a market cap of \$4.3 billion.

Paulus' tenth ranked success is what he calls "open port sampling interfaces for mass spectrometry," invented by Gary Van Berkel and Vilmos Kertesz. Each surface sampling probe uses a solvent to pick up a small sample of a material. The sample is ionized and injected into a mass spectrometer for analysis of the sample's content. After years of interaction between the inventors and the SCIEX company through a CRADA, SCIEX launched the ORNL invention in 2020 as SCIEX Echo MS.

The lessons Paulus and his colleagues have learned from ORNL's commercial successes are that companies typically do not have significant sales for ten years after the ORNL technologies are licensed; collaboration is key as indicated by the facts that five of the licensees were supported by CRADAs and two of the licensees were companies founded by a former ORNL employee (Mike Ramsey); most of the

## Lab on a chip: ORNL's top commercialization success

(As published in The Oak Ridger's Historically Speaking column December 8, 2021)

top ten licensees have large U.S. and international patent portfolios and winning R&D 100 awards is a good predictor of success.

### **ORNL's first four decades**

As for the technologies developed at ORNL during its first four decades (1943-83), Paulus said that "knowledge exchange transmitted lab technologies" to industry rather than patent licenses. He gave many examples that emerged from ORNL's nuclear roots.

In 1946 the first medical radioisotope made from a reactor was shipped from ORNL. In the 1960s more than 100,000 shipments of radioisotopes were made annually from Oak Ridge. Today as a result of research at ORNL, more than 40 million nuclear medicine procedures using radioisotopes from various commercial and national lab suppliers are performed annually.

In 1947 the plutonium uranium reduction extraction (PUREX) method was developed at ORNL to separate plutonium from nuclear reactors' spent uranium fuel rods. PUREX became the basis for the French breeder reactors used to generate power. Today ORNL's CSSX process is deployed at a \$1.6 billion waste processing facility at Savannah River National Laboratory.

Advanced alloys that withstand high temperatures and are still commercially available today were developed at ORNL with industrial partners. They include Hastelloy N for molten salt reactors, P91 steel for fast breeder reactors, Grade 91 ferritic alloy for fossil fuel plants and aluminum alloys for use in automotive technologies.

ORNL researchers demonstrated that centrifuges, based on the gas centrifuges used to separate uranium isotopes, could purify polio and other vaccines to minimize side effects. Today ORNL engineers are working on improving centrifuge technology.

The pressurized water reactor (PWR) conceived at ORNL is the basis for PWRs used in U.S. submarines and aircraft carriers and two-thirds of the world's nuclear power plants. ORNL designed, built, and operated 13 research reactors and established a school to train future nuclear engineers. In 2020 ORNL released the Virtual Environment for Reactor Applications (VERA) computer code to guide the design of safer, more efficient nuclear reactors for power plants.

In the 1960s, ORNL researchers formed ORTEC to commercialize nuclear detectors and instrumentation. In the 1980s, ORTEC sold its positron emission tomography (PET) business to entrepreneurs who created CTI, which Siemens purchased in 2005 for \$1 billion. Today in the United States, two million PET scans are performed annually to help physicians determine if their patients have cancer, heart disease or brain disorders.

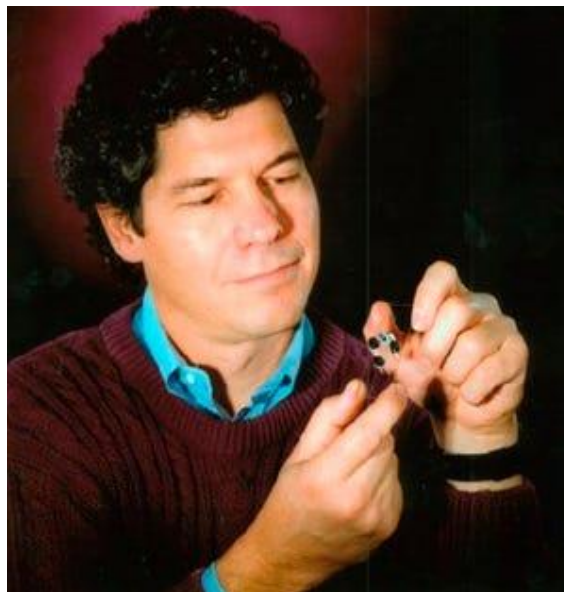
Through knowledge exchange and technology transfer involving patent licenses, ORNL has made practical contributions in the past 75 years that have improved life in our nation and world.

## Lab on a chip: ORNL's top commercialization success

(As published in The Oak Ridger's Historically Speaking column December 8, 2021)



Mike Ramsey, who invented the lab on a chip in the 1990s at ORNL, is the Minnie N. Goldby Distinguished Professor of Chemistry at the University of North Carolina at Chapel Hill. It recently honored him as Inventor of the Year in 2020. He is the scientific founder of other companies, including 908 Devices, which recently developed a handheld tool (shown here) to help first responders quickly detect chemical, explosive, drug, and hazmat threats.



Mike Ramsey with an early lab on a chip



## Lab on a chip: ORNL's top commercialization success

(As published in The Oak Ridger's Historically Speaking column December 8, 2021)



The evolution of the lab on a chip to the LabChip GX Touch devices made by PerkinElmer for medical and research uses



Mike Paulus gives a virtual lecture to Friends of ORNL on the lab's Top 10 technology commercialization successes