The History of CROs: Including CRO Snapshots

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Note: This chapter was prepared by the author based on both his personal knowledge of the preclinical Contract Research Organization industry referred to as CRO throughout this chapter and from information provided by a number of other professionals who are currently employed at or had previously been employed at the various organizations discussed in this chapter (contributors are listed at the end of the chapter). The information presented focuses mainly on CROs in North America where it is estimated that around 100 different CROs have existed over time, but many of these have either terminated operations or have been acquired by other organizations, primarily larger CROs. In addition, with the passing of so many key players from those organizations over time, it was almost impossible to gather information for many CROs. Furthermore, some larger CROs declined the opportunity of sharing the requested historical information about their organizations due to confidential issues which the author found to be disappointing. Nevertheless, the author believes that in the absence of any previously published history of the CRO industry, the information presented in this chapter is useful and portrays a meaningful history of this industry. While the author acknowledges that there may be gaps and errors in some of the information presented, this should not be unexpected in the absence of any previously written history and the availability of professionals who lived the history.

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Appendix I presents a genealogy chart of toxicology CROs – historical, name changes, mergers, and other organizational changes. It will most likely be out of date by the time this volume is published.

Introduction

The Contract Research Industry is an integral part of the toxicology community and has been for almost 100 years. In many ways, the growth of this industry has mirrored the growth of toxicology in the twentieth century as toxicology was not developed as a pure science but rather one that grew out of other sciences such as pharmacology, physiology, anatomy, and biochemistry. Indeed, many have described toxicology as “pharmacology, but at higher doses,” and this has not been an unfair characterization. CROs have served multiple functions over the years beyond that of just conducting contracted toxicology studies. They have served as a primary source in the development of new and novel technical procedures involving all commonly used research animal models, they have been at the forefront in testing better animal housing and caging advancements, they have been leaders in the introduction of more efficient and scientifically improved technical procedures, and they have served as a significant training ground for the development and training of a vast number of toxicologists who later went on to hold senior leadership positions in the industrial, governmental, and regulatory sectors of the toxicology industry.

The first recognized CRO that was not considered an extension of a chemical or pharmaceutical organization was most likely Food and Drug Research Laboratory (FDRL) which was formed in 1926. This was followed by the Illinois Institute of Technology Research Institute (IITRI) in 1936, Southern Research Institute (SRI) in 1941, Hazleton Laboratories and SRI International in 1946, and Lovelace Biomedical in 1947. During those early years, there were no standard toxicology testing study designs, no published regulatory requirements for toxicology testing, and no associations or societies that represented toxicology and where the toxicologists of the day could convene to share ideas and concerns. Indeed toxicology was not even recognized as a true scientific discipline. There were only a few independent CROs in operation as a significant amount of toxicology testing at that time was performed at either company laboratories such as Dow, DuPont, and Eastman Kodak or at university laboratories such as Kettering of the University of Cincinnati, the
University of Miami (Florida), New York University, Rutgers University (in association with Esso Research), and the Carnegie Mellon Institute Chemical Hygiene Laboratory (in association with Union Carbide). Toxicology at that time was mostly descriptive in nature with little knowledge or interest in mechanisms. Study designs, laboratory techniques, and the interpretation of study results differed among the various laboratories that were conducting the toxicology testing. Studies were generally conducted according to the inclinations of the investigator, and pathological evaluations were almost never performed.

During the 1960s, several key events occurred which stimulated greater dialogue and discussion involving the role and future of toxicology. The first key event was the worldwide reported incidence of babies being born with a condition by the name of phocomelia, which manifested itself as shortened, absent, or flipper-like limbs. This was first reported in 1961 and was traced back to women who had been prescribed and taken the drug thalidomide for morning sickness during their first trimester of pregnancy, while the incidence of phocomelia was less in the United States than in Europe due to the resistance of FDA scientist Dr. Frances Kelsey, who refused to grant approval for thalidomide use in the United States. This event though helped lead to profound changes in FDA approval procedures by the passage of the Kefauver-Harris Drug Amendment Act in 1962. This Act tightened restrictions surrounding the surveillance and approval process for drugs to be marketed and sold in the United States. This act required that drug manufacturers prove that a drug was both safe and effective before it could be marketed. The other key event that occurred during the same year was the publication of Rachel Carson’s book, *Silent Spring*, which alerted the public to the detrimental effects on the environment of the widespread and indiscriminate use of pesticides. This in turn led to discussions in Congress about the need for implementing a national environmental policy, culminating with the creation of the Environmental Protection Agency in December of 1970.

The 1960s represented a major turning point in the history of toxicology, as a significant emphasis was now being placed on drug and environmental safety, resulting in the critical need for toxicologists trained in both applied and regulatory toxicology. It also resulted in the need for a significant increased capacity for conducting toxicology studies to support drug and environmental safety, leading to the creation of new CROs to meet that demand. These new CROs included such companies as Gulf South Research Institute, Litton Bionetics,
Bio/dynamics, International Research and Development Corporation (IRDC), and Bio-Research Laboratories (in Canada), in the early 1960s, and Calvert Laboratories and Centre International de Toxicologie (CIT) in France in the late 1960s.

During the 1970s, several significant governmental organizations were created to monitor and foster a greater control over issues associated with worker safety with the passage of the Occupational Safety and Health Act in December of 1970, which led to the creation of NIOSH (National Institute for Occupational Safety and Health). In addition with the passage of this act, Issues associated with the rising use of pesticide products led to the creation of the Environmental Protection Agency (EPA) in December of 1970. In 1972, the administration of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) that was first established in 1947 was moved from the authority of the Department of Agriculture to the newly created EPA, where a new emphasis was placed on the preservation of human health and protection of the environment by strengthening the registration process by shifting the burden of proof to the chemical manufacturer, enforcing compliance against banned products, and creating a regulatory framework that was missing from the original law. The primary objectives of the original act were to register pesticides distributed in interstate commerce with the Department of Agriculture and to protect farmers by requiring accurate labeling of pesticide contents, which enabled farmers to make informed choices regarding the product’s effectiveness. However, concerns regarding the toxic effects of pesticide and residues on applicators, non-target species, and the environment resulted in significant changes in the 1972 revision. In 1976, the Toxic Substance Control Act (TSCA) became law which required industry reporting, record keeping, and testing of chemicals substances in commerce. In 1978, the National Toxicology Program (NTP) was established as part of the National Institute of Environmental Health (NIEHS) whose mission resulted from congressional concerns about the health effects of chemical agents in the environment, especially as it related to carcinogenic concerns. A significant number of long-term chronic toxicity/carcinogenicity studies were contracted to select CROs that met the room and housing requirements of NTP (with, e.g., facilities designed as clean-dirty facilities), these included Southern Research Institute, Midwest Research Institute (founded in 1944), and Battelle Memorial Institute (founded in 1929). The impact of these new initiatives, which required an increased number of toxicology studies to be conducted, resulted in a significant increase in the number of new CROs to
meet that demand. These new CROs included MB Research Labs, Stillmeadow, TPS, WIL Research, Springborn, Borriston Laboratories, and Argus Research Laboratories. However, this decade also saw the closing of several CROs, such as Cannon Laboratories, as a result of the introduction of Good Laboratory Practices (GLPs) into the industry by the FDA and as a result of poor and/or dishonest practices in some existing CROs and in some in-house company laboratories, leading some organizations to opt out of the industry due to the significant effort and cost to become GLP compliant.

The CRO landscape remained fairly constant during the 1980s and 1990s although several new CROs were created during this time to meet the increasing need of outsourced toxicology testing as the larger pharmaceutical companies began to downsize their in-house testing capabilities along with the rapid rise of the biotech industry. These included Sinclair Research, R.O.W. Sciences, Sierra Biomedical, and ITR (Canada). Portending the future of acquisitions in the industry, Hazleton Laboratories became the largest CRO in the world during that time through a series of acquisitions, buying the Tobacco Research Council Laboratories in Harrogate, England in 1974, Affenzucht Munster in Munster, Germany in 1980, the Institut Merieux site in Lyon, France in 1981, RALTECH (owned byRalston Purina) in Madison, Wisconsin in 1982, and Litton Bionetics in Rockville and Gaithersburg, Maryland, in 1985.

A new and aggressive player joined the CRO industry when Charles River Laboratories (CRL) entered the preclinical CRO field with the acquisition of Sierra Biomedical in 1999. Formed in 1947 as a rodent breeding company, CRL changed the landscape of the industry with a bold and aggressive acquisition strategy over the next 20 years, including the purchase of Argus Research and Pathology Associates in 2001; Springborn Laboratories in 2002; ClinTrials BioResearch (CTBR) in 2004; Argenta, BioFocus, and ChanTest Laboratories in 2014; WIL Research in 2016; MPI Research in 2018; and CiToxLab in 2019 – making CRL the world’s largest preclinical CRO. In 2019, LabCorp (parent company of Covance) and Envigo executed a merger between Huntington Life Sciences and Harland Laboratories in 2015 and entered into an agreement whereby Covance purchased Envigo’s preclinical capabilities while Envigo purchased Covance’s research animal model capabilities.

As the CRO industry enters into the third decade of this century, there is no reason to expect that the level of acquisitions will slow as larger organizations look to increase their portfolios and profitability in the face of a continuing bullish outsourcing demand of toxicology and related services and since the cost and timing of building new CROs remain both expensive and difficult.
The Early Years

Food Drug Research Laboratories

The first recognized private CRO was Food Drug Research Laboratories (FDRL), created in 1926 by Philip Hawk and Bernard Oser as Food Research Laboratories in Philadelphia, Pennsylvania. Oser, a biochemist by training, received his doctorate from Fordham University and worked at FDRL for 47 years. He served in numerous senior scientist and management roles, culminating in his serving as president from 1957 to 1970 and then as chairman until 1973. He was a founding member of the Institute of Food Technologies and in the 1950s he was a significant voice in alerting the food industry of the need for toxicological studies and safety evaluations on food additives. He also served as the chairman of the First Gordon Conference on Toxicology and Safety Evaluation in 1956, which brought together many of the scientists who later formed the Society of Toxicology and served on the editorial board of *Toxicology and Applied Pharmacology*. In the mid-1930s, the company changed its name to Food Drug Research Laboratories with Kenneth Morgaridge joining the organization as vice president in the late 1930s. In 1956, the company relocated to Maspeth, New York, and set up operations in an old dance hall. Noted toxicologists there at that time included Harold Schwartz and Steve Carson. In the early 1970s, the company again relocated, this time to East Orange, New Jersey, where the corporate headquarters were located and clinical studies were conducted, and Waverly, New York, where approximately 60 people were employed and rodent, dog, and nonhuman primate studies were conducted and where the FDRL Wistar rat strain was developed. Noted toxicologists at the Waverly site included Mike Gallo, Kent Stevens, Peter Becci, Tom Re, John Babish, and Richard Parent. In the early 1990s, the company was renamed Liberty Laboratories, which refocused its activities almost completely on feline breeding and sales.

Lakeside Laboratories

Lakeside Laboratories was established in 1925 and was part of the ethical drug division of Colgate Palmolive Company. It was headquartered in Milwaukee, Wisconsin very close to Lake Michigan and that is how it got its name. In a
sense it was not a true CRO, since it belonged to a pharmaceutical company. However, it did conduct some contract work for other companies. The vivarium consisted of about ten animal rooms in which specialty work such as placental transfer, metabolism (using various radiolabeled compounds), and PK studies was conducted. The group was headed by Jim Tom Hill who was supported by Patricia Frank, Claude Judd, and Norm Jefferson. In 1975, it was purchased by Merrill Dow National, and shortly afterward the facility was closed.

**Illinois Institute of Technology Research Institute**

The Illinois Institute of Technology Research Institute (IITRI) was established in 1936. It was originally founded as the Armour Research Foundation by the Armour Institute of Technology (a doctorate-granting university whose name was later changed to the Illinois Institute of Technology), and in 1963 the organization changed its name to IITRI. Based in Chicago, Illinois, the facility consisted of 50 animal rooms which included both standard vivarium space and specialized facilities for containment at BSL-2 and BSL-3 levels. In addition, over the past 40 years, IITRI has been a premier provider of inhalation toxicology services. David McCormick has had a long-standing career there as a toxicologist and company leader. It was the first CRO to develop and validate murine models for the identification of immunotoxic agents as part of a tripartite program performed in collaboration with NIEHS and the Medical College of Virginia, and it was the largest provider of preclinical pharmacology and toxicology drug development services for the National Cancer Institute over the past 20 years. It has extensive experience in bioelectromagnetics and conducted programs for NIEHS and NTP to evaluate the possible carcinogenicity of magnetic fields and radiofrequency fields emitted by cell phones and other wireless devices. Noted toxicologists at IITRI included David McCormick and Nabil Hatoum.

**Chemical Hygiene Fellowship (Bushy Run Research Center)**

The Chemical Hygiene Fellowship was established in November of 1937 under a contract between the Mellon Institute and the Carbide and Carbon Chemical Company (Union Carbide). Its beginning was modest, with a staff of
two and two rooms totaling 500 square feet at the Mellon Institute in Pittsburgh, Pennsylvania, that is now part of the Pittsburgh Medical School. Over the next 22 years, the laboratory grew to a staff of 25 and approximately 11,000 square feet of space. In 1959, the laboratory moved to a 30,000 square foot building in Murrysville, Pennsylvania, about 15 miles east of Pittsburgh, which had originally been used as a radiation laboratory as part of the Manhattan Project, and by 1976 had grown to a staff of 110 with 65,000 square feet of space. This building was located on 230 acres on what was called the Bushy Run Campus. Up until 1980, the laboratory was managed by Mellon Institute, but in 1980 Union Carbide assumed the duties of managing the laboratory, and the name was changed to the Bushy Run Research Center (BRRC). Most studies were conducted to support Union Carbide chemicals. Henry Smyth served as the first director of the laboratory and held that position for 30 years, passing away in 1957 on the actual day of the laboratory’s 50th anniversary. He was followed by Charles Carpenter and then Carol Weil. The laboratory was especially known for its expertise in inhalation and dermal carcinogenesis studies which would be consistent with their mission of testing chemical compounds development by Union Carbide. BRRC was the first laboratory to adopt rigid specifications for standardized toxicity testing, especially for range-finding studies, and other laboratories soon followed their lead. BRRC was also the first laboratory to test chemicals for skin penetration as previously this route of administration had generally been ignored. They were also one of the first laboratories that placed a significant emphasis on collecting clinical and anatomical pathology data on the kidney and liver as an important measurement of toxicity. Noted toxicologists at BRRC included Henry Smyth, Carol Weil, Shayne Gad, Ray Yang, Daryl Dodd, and Steve Frantz. In 1998, the laboratory was closed.

Southern Research Institute

Southern Research Institute (SRI) was established in 1941 as a nonprofit organization to foster research and technology development as an economic engine for Birmingham, Alabama, and the Southern United States. Thomas W. Martin, an attorney and president of the Alabama Power Company, was the primary founder. Martin, with the cooperation of other business leaders in Birmingham, established SRI to help make the city a major research center in the South and to develop the South’s agricultural, mineral, and forest
resources. In the early years, biological research was not a focus area for the laboratory. The first director of SRI was Wilbur Lazier, an organic chemist who previously worked at DuPont and who had an important role in the development of nylon and other polymers. Research into oncology became a major part of SRI in 1974 when Howard Skipper became president. Skipper was a veteran of the US Army’s Chemical Warfare Service and had an established reputation as a researcher in the field of oncology. Toxicology at SRI began in earnest in 1976 with the establishment of a contract with what would ultimately become the National Toxicology Program (NTP). Paul Denine became the head of the new preclinical pharmacology and toxicology division in 1978, and he was followed by J. David Prejean who held that position for over 10 years. SRI had sites in Birmingham and in Fredrick, Maryland. The Fredrick site opened in 1990 and primarily conducted infectious disease studies in 19 animal rooms and 43,000 square feet of space. The Birmingham site supported numerous other capabilities unrelated to biological testing, such as engineering and environmental research. For toxicology testing, the Birmingham site consisted of 54 animal rooms and approximately 63,000 square feet of space, including several BSL-3 rooms. While noted mostly for conducting programs for governmental agencies such as NTP, NCI, and NIDA, SRI is also a full-service provider for drug development services, with a strong experience in testing biologics, especially vaccines, oncolytic viral vectors, and gene therapy vectors. Noted toxicologists at SRI include Paul Bushdid, Alan Stokes, Tina Rogers, David Serota, John Page, Charles Lindamood, and Charles Hebert, with Eric Morinello and Vince Torti receiving their initial CRO training at SRI.

Hazleton Laboratories

Hazleton Laboratories was established in 1946 by Lloyd Hazleton who previously had been on the faculty of both Georgetown Medical School and George Washington University Medical School. He received his doctorate in pharmacology from the University of Washington and established Hazleton Laboratories outside of Vienna, Virginia, on the grounds of an old schoolhouse. Hazleton was well respected within the toxicology community and was known for his philosophy of mentoring and training young toxicologists, receiving the Society of Toxicology’s Education Award in 1982 in
recognition of his company’s training of numerous young toxicologists that went on to successful careers in other organizations. At its zenith, the Vienna campus was on 90 acres of prime real estate and consisted of around 80 animal rooms that housed rodents, rabbits, dogs, and nonhuman primates. Lloyd Hazleton sold the company in 1970 to TRW Corporation who renamed it TRW Science Center. In 1972, TRW Corporation sold the company to Environmental Sciences Corporation, headed by Donald Nielsen and Kirby Cramer, who returned the Hazleton name. In 1976, Hazleton opened a new, state-of-the-art, rodent facility in Reston, Virginia, that had over 60 animal rooms. Through a series of acquisitions and through organic growth, Hazleton, in 1982, had become the world’s largest independent biological testing laboratory in the world. These acquisitions included the Tobacco Research Council Laboratories in Harrogate, England, in 1974; Affenzucht Munster in Munster, Germany, in 1980; the Institut Merieux site in Lyon, France, in 1981; and RALTECH in Madison, Wisconsin, in 1982. In 1985, Hazleton purchased Litton Bionetics in Rockville and Kensington, Maryland. In 1987, the company was sold to Corning, Inc. and renamed Corning Hazleton, and in 1996 Corning, Inc. spun off its toxicology testing segment as an independent company which was subsequently named Covance, Inc. In 2010, Covance, Inc. announced that it was closing the Vienna site and several years later the buildings were demolished and the site sold for real estate development. Noted toxicologists at the Hazleton Vienna site include Lloyd Hazleton, Cliff Jessup, Gene Paynter, Bill Knapp, Robert Weir, Bob Scala, James Gargus, Bill Olsen, Bill Coate, Fred Reno, Tom Mulligan, Dan Dalgard, Ray Cox, Sandra Morseth, Sidney Green, David Brusick, Steve Haworth, and Brian Myhr. Among those who received their initial training in toxicology at Hazleton were Geoffrey Hogan, Robert Kapp, Vince Piccirillo, David Serota, Gary Wolfe, Debra Pence, Joy Cavagnaro, Merrill Osheroff, Alan Hoberman, Vicki Markiewicz, Jan Trutter, and Tracey Zoetis.

**SRI International**

SRI International was established in 1946 by a group at Stanford University as an independent, nonprofit, non-endowed corporation chartered by the State of California and was originally named Stanford Research Institute. It formally separated from Stanford University in 1970 and became knowns as SRI
International in 1977. Gordon Newell created the toxicology group at SRI International in the early 1950s. Newell received his doctorate in biochemistry from the University of Wisconsin and was at SRI International for over 25 years. The main facility was located in Menlo Park, California, but there were several additional satellite facilities including Plymouth, Michigan, and Harrisonburg, Virginia. The Menlo Park facility included 40 buildings encompassing over 1.3 million square feet of space on a 63-acre site. The Bioscience Division included approximately 250,000 square feet of animal areas, laboratory space, and support areas. SRI International was one of the pioneers of genetic toxicology testing, inventing the pKM101 plasmid in Ames strains and in vivo unscheduled DNA syntheses tests and validating the Ames test, the repeat-dose micronucleus test, the mouse lymphoma test, and the in vitro and in vivo unscheduled DNA tests. Noted toxicologists at SRI International included Gordon Newell, Robert Baldwin, Rick Becker, Jon Reid, Jon Mirsalis, James MacGregor, Karen Steinmetz, Hanna Ng, Gordon Pryor, and Carol Green.

Lovelace Biomedical

Lovelace Biomedical was established in 1947 by William “Randy” Lovelace II, a Harvard trained surgeon, as a needed specialty medicine clinical and nonprofit medical foundation in Albuquerque, New Mexico. Originally known as the Lovelace Foundation for Medical Education and Research, over the years the organization’s research operations expanded in size and scope that was parallel with the advances of the medical and healthcare industries. Initially funded predominantly by government contracts to execute cutting-edge projects related to public health, Lovelace Biomedical is known as a place of medical firsts. With a strong tie to the aviation community during its earliest days, in the period between 1950 and 1970, Lovelace Biomedical became known as the nation’s premier center for aviation and space medicine research and, in 1959, under contract with NASA, tested 32 candidate pilots which culminated in the selection of the first 7 Mercury astronauts. In 1964, Randy Lovelace was appointed Director of Space Medicine for NASA. During the period from 1962 through 1993, Lovelace Biomedical entered into a cooperative agreement with the Atomic Energy Commission in the areas of toxicology, with an emphasis in inhalation toxicology. During the 1980s the company changed its name to the
Inhalation Toxicology Research Institute. They were the first organization to demonstrate that cigarette smoking caused cancer in laboratory animals. They developed many innovative measurement devices in the area of aerosol sciences, including the Lovelace multi-jet impactor, the Lovelace nebulizer for delivery of fine particles, and Lovelace particle separator, and a parallel plate diffusion battery measuring particle size in aerosols. In 1996, the company became privatized under the leadership of Robert Rubin as the not for profit Lovelace Respiratory Research Institute and over the next 20 years sponsored research that combined basic science in the areas of respiratory disease, contract sciences in toxicology, infectious diseases, and medical countermeasures. In 2016, under the leadership of Jacob McDonald, the organization again changed its name to Lovelace Biomedical with a strong focus and emphasis on commercial toxicology testing. The company is still based in Albuquerque and sits on 100 acres of land with 300,000 square feet of laboratory space and 80 animal rooms. Noted toxicologists that have worked there include Roger McClellan, Joe Mauderly, Charles Hobbs, Steve Belinsky, Janet Benson, Rogene Henderson, Ron Wolf, Matt Campen, Chet Leach, and Jacob McDonald.

Charles River

Chares River was founded in 1947 as Charles River Breeding Laboratories when Henry Foster purchased one thousand rat cages from a Virginia farm and set up a one-man laboratory in Boston, Massachusetts, that overlooked the Charles River. Over the next 50 years, Charles River Breeding Laboratories became one of the world’s largest breeders of quality laboratory animals for basic and applied research. In 1955, the company’s headquarters was relocated to Wilmington, Massachusetts, and began the commercial production of pathogen-free rodents by using the industry’s first barrier-type production building. In 1956, the first Caesarean Originated Barrier Sustained (COBS®) rodents were introduced and became the new industry standard for animal production. In 1966, the company became international with the opening of a new animal production facility in France, and in 1981 it instituted the first commercial comprehensive genetic monitoring program. Virus antibody-free (VAF/Plus®) animals were introduced in 1984, and during the same year the company was purchased by Bausch & Lomb with the Foster Family still running the company. In 1988, Charles River entered the field of transgenic services with the arrival of
the first transgenic mice for breeding. In 1992, Charles River began to expand its services by entering the specialty services area with the purchase of Specific Pathogen Antigen Free Avian Services (specializing in the production of eggs and poultry and serologic diagnostic services) and the 1996 purchase of Endosafe, Inc., a manufacturer of Limulus Amebocyte Lysate products and services. In 1997, James Foster bought the company back from Bausch & Lomb, and in 1998, the company expanded its portfolio by entering the biopharmaceutical services industry. Over the next 20 years, an aggressive acquisition strategy made Charles River the largest company of its type in the world. These acquisitions included Sierra Biomedical in 1999; Primedica in 2001; Inveresk Research in 2004; Piedmont Research Center in 2009; Accugenix in 2012; Argenta, BioFocus, and ChanTest in 2014; Celsis International and Oncotest GmgH in 2015; WIL Research and Agilux Laboratories in 2016; MPI Research in 2018; and CiToxLab in 2019. These sites were in addition to a 412,000 square foot laboratory facility in Shrewsbury, Massachusetts, that Charles River opened in 2007, closed in 2010, and reopened in 2016 (with 80,000 square feet of vivarium space).

The Middle Years

Industrial Biotest

Industrial Biotest (IBT) was founded in 1953 by Joseph Calandra who was a professor of pathology and biochemistry at Northwestern University. The facilities were located at a site in Northbrook, Illinois, and had up to 350 employees employed there. In 1966, it was sold to Nalco Holding Company. During the early 1970s, it was the largest preclinical CRO in the world and conducted more than one third of all contracted toxicology testing in the United States. In the mid-1970s, IBT was accused of conducting fraudulent and tainted toxicology testing and was investigated by both FDA and EPA staff, leading to many reported studies being rejected by regulatory agencies and the expensive re-testing of many compounds. Three senior executives of IBT were tried and convicted by a jury of conducting and submitting fraudulent studies and in the cover-up of those activities, and in 1978 IBT closed. Much of the negative events identified at IBT led to the promulgation of the Good Laboratory Practices (GLP) in 1976.
Woodard Research

Woodard Research was founded in 1956 by Geoffrey Woodard and his wife Marie Woodard. Geoffrey Woodard was a former FDA pharmacologist and who also taught at George Washington University. The facility was located in Herndon, Virginia, with approximately 100,000 square feet of space spread among various research buildings. Woodard Research conducted studies in rodents, rabbits, dogs, cats, nonhuman primates, quail, ducks, and fish, along with farm animals such as cattle and pigs. Along with the Geoffrey Woodard, other noted toxicologists that worked there include Robert Belilies and William Scott. In 1972, the laboratory closed.

Gulf South Research Institute

Gulf South Research Institute (GSRI) was established in the early 1960s in New Iberia, Louisiana, at an old naval base by the Louisiana Partnership for Technology. GSRI was located on a 118-acre site which included 440,000 square feet of vivarium space. Most of the work conducted there was related to a significant nonhuman primate colony population that was involved in viral studies, but there were also approximately ten rooms that were used to conduct carcinogenicity studies for the NTP. In addition, there was also the capability for conducting both acute and inhalation studies. Jim Clinton was the corporate director of GSRI and Richard Parent also worked there for several years. GSRI closed in 1984 and the site was taken over by the University of Louisiana at Lafayette, renamed the New Iberia Research Center with its role was redefined as a nonhuman primate center to provide nonhuman primates to support contract research. In 1990, it expanded its mission to provide preclinical safety testing services.

Bio/Dynamics

Bio/dynamics was founded in 1961 by two faulty members from Rutgers University Bureau of Biologic Research, Thomas Russell, a biochemist, and John McCoy, a pathologist (one of the founders of the Society of Toxicologic Pathologists). The first facility was housed in rented space in a veterinary
clinic in Edison, New Jersey. In 1963, the 55-acre Mettler farm in East Millstone, New Jersey, was purchased as the new site for Bio/dynamics, and Thomas Russell left Rutgers to devote his full attention to building the company. By 1964, the staff had grown to 12 employees. The farmhouse became the company headquarters office, the milk house a small animal laboratory/necropsy area, and the dairy barn a dog kennel. Getting to work in the morning occasionally involved traffic jams of cattle being herded down Mettler Lane with grazing on the lawn outside of the headquarters building. In 1973, the company was acquired by IMS International, a market research organization serving the international pharmaceutical industry. At that time, the staff had grown to approximately 100 employees with 9 buildings on site. In 1978, IMS International purchased Life Science Research (LSR), a UK-based contract toxicology laboratory and the two laboratories became the Life Sciences Division of IMS International. In 1976, a state-of-the-art inhalation facility was constructed and by 1980, there were approximately 300 employees with 15 buildings on site. In 1983, Thomas Russell left the company to pursue other ventures and Geoffrey Hogan became the President of Bio/dynamics. In 1987, Applied Bioscience International (APBI) was formed when IMS International divested itself of its life science division. Over the next several years, continued mergers and acquisitions produced a family of companies that included CANTAB, ENVIRON International Corporation, Environmental Testing and Certification Corporation (ECT), Landis International, and Pharmaco Dynamics Research, a clinical organization. In 1993, Pharmaco LSR was formed by the union of three APBI-owned companies, Bio/dynamics, LSR, and Pharmaco. At that time Bio/dynamics had 340 employees and 18 buildings on site. In 1995, Huntington International Holdings purchased APBI’s two toxicology companies (Bio/dynamics and LSR), and these companies were united with the Huntington International Holdings facility in Cambridge, England, to become Huntington Life Sciences (HLS). The group was originally led by Christopher Cliffe who was followed by Brian Cass in 1999, both being former executives of the Hazleton Laboratories site in Harrogate, England. Michael Caulfield, who began his career as an archivist at Bio/dynamics in 1985, became general manager of the HLS site in East Millstone. In 2014, HLS acquired Harlan Laboratories, a major supplier of rodents for biological testing and owner of several CROs in Europe, including the former SafePharm Laboratories in England and RCC Laboratories in Switzerland. Two divisions were established, Rodent Models and Services (RMS) and Contract Research Services (CRS), with Bio/dynamics becoming
Princeton CRS. In 2015, the company was re-branded as Envigo, and the East Millstone site had 350 employees and 95 animal rooms in facilities consisting of almost 200,000 square feet. In 2019, Envigo and LabCorp (the parent company of Covance, Inc.) entered into an agreement by which LabCorp purchased Envigo’s contract research service business, while Envigo purchased LabCorp’s animal research models and service business. Noted toxicologists that have worked there included Andrew Sivak, William Strauss, Ted King, Jerry Smith, William Rinehart, Sylvie Gosselin, Geoffrey Hogan, Carol Auletta, Gary Hoffman, Cathy Kelly, Robert Parker, Rosemary Mandella, John Atkinson, Debra Barrett, Diann Blanset, Dan Cerven, David Compton, Ira Daly, Paul Newton, George Rusch, Jim Killen, Lee Grotz, Oscar Moreno, John Mitchell, Robert Sabol, Raymond Schroeder, William Tierney, and Deborah Novicki.

**Litton Bionetics, Inc.**

Bionetics Research Laboratories was founded in 1961, with a small toxicology facility in Falls Church, Virginia, and a larger facility in Kensington, Maryland. During these early years, most of the toxicology work conducted there was under government contracts, especially for the National Cancer Institute, involving cancer bioassays in rodents for dyes that were being used as food additives. Ross Hart served as Director of Toxicology during those times. In 1968, the company was purchased by Litton Industries and changed its name to Litton Bionetics, Inc. In the early 1970s, a new, state-of-the-art facility was built in Rockville, Maryland (approximately 100,000 square feet of space), and all toxicology units and analytical chemistry were consolidated in this facility, along with a section of the facility designed to conduct inhalation studies. It was also at the Rockville facility that Robert Gallo housed his animals that were used in his research program that identified the retrovirus that was the cause of AIDS. Genetic and molecular toxicology functions remained at the Kensington site. Following the retirement of Ross Hart in the early 1970s, Robert Weir became Director of Toxicology and in 1972; Litton Bionetics was awarded the first government contract to manage and operate the Frederick Cancer Research Laboratory in Frederick, Maryland. In 1973, the first commercial genetic toxicology testing facility in the United States was opened in the Kensington facility under the leadership of David Brusick, and a second
site opened in Veenendal, The Netherlands, in 1980 under the direction of Fred Hoorn. In 1985, Hazleton Laboratories purchased the toxicology testing business of Litton Bionetics (Rockville and Kensington sites), and at that time there were approximately 200 employees at both sites. Noted mammalian toxicologists at Litton Bionetics included Robert Weir, John Keller, Les Goldsmith, Robet Belilies, Ron Filler, and Michael Moore. Noted genetic toxicologists include David Brusick, Brian Myhr, James Ivett, Robert Young, Hema Murli, Maria Cifone, Michael Cimono, Devara Jaganath, Tim Lawlor, and Steve Haworth.

International Research and Development Corporation

International Research and Development Corporation (IRDC) was founded in 1962 by Francis Wazeter, who had a doctorate in pharmacology and had formerly worked at the FDA. The facility was located in Mattawan, Michigan, and began its existence with approximately 140,000 square feet of space and 140 animal rooms. At its zenith, it consisted of over 300,000 square feet of space containing approximately 240 animal rooms and with over 400 employees. It serviced a full range of clients representing the pharmaceutical, chemical, cosmetic, and food industries both domestically and internationally, with 75% of its business associated with human and animal health products, 10% of its business associated with both petrochemicals/agrichecmicals and food and consumer products, and 5% of its business associated with medical devices. For several years, it also owned a clinical research company called IRAD that was in Florida. In the early 1990s, at the time that Francis Wazeter selected his son, Francis Wazeter, Jr., to run IRDC, the company fell on financial troubles. In 1990, a skin care products company in California, Carme, Inc., was acquired and financed mostly with bank debt. This acquisition proved to be a disastrous endeavor, and the company fell into bankruptcy and went into receivership in September 1995. The bankruptcy was the result of unethical business practices including a serious accounting fraud at the skin care products unit. In November 1995, the residual assets of IRDC were purchased by an investing group led by William Parfet to create a private company called MPI Research. Noted toxicologists at IRDC included Edwin Goldenthal, Cliff Jessup, James Schardein, Ray York, Dean Rodwell, Gerald Shafer, Malcolm Blair, Eric Spicer, James Laveglia, and Richard Slauter.
Bio-Research Laboratories (Canada)

Bio-Research Laboratories was founded in 1965 by Clifford Chappel, a former medical director at Wyeth Pharmaceuticals. It was originally located in a mini laboratory housed at MacDonald College in Montreal, Canada, and later moved to Pointe Claire in Montreal. It offered clinical patch testing, preclinical drug development, and aquatic toxicology services. It was here that the “great bacon study” was conducted where large amounts of bacon were fried daily and fed to animal test subjects to ascertain the effects of nitrosamines. In 1976, the company was purchased by Canada Development Corporation (CDC) as part of a strategy to build a Canadian owned healthcare company with other members of the group including Connaught Laboratories, Nordic Pharma, and Raylo – this new company was named Connlab. With the advent of Good Laboratory Practices (GLPs) making the Pointe Claire facility unacceptable for conducting studies, CDC in 1977 purchased the former Smith, Kline & French site in Senneville, Montreal, which consisted of 30 acres and a laboratory building. A new vivarium was added in 1978, there were 83 employees, and F. Fried was appointed president. In 1978, Fried retired and Michael Ankcorn was appointed president and CEO. In 1984, CDC decided to spin off Connlab as a public company which was renamed CDC Life Sciences. In 1985, a new, purpose-built 60,000 square foot building to support additional toxicology work was opened. In 1989, CDC Life Sciences was subject to a successful hostile takeover by Institut Merieux of France who put the toxicology divisions up for sale. The uncertainty and insecurity of this action resulted in both the loss of a significant amount of business and the departure of many senior leaders and technical staff. However, during this same time, the expertise of conducting infusion toxicology was developed and the site became a center for excellence of this technology. In 1991, Institut Merieux sold the company to CAI Capital who in turn sold the company to ClinTrials in 1997, renaming the company CTBR. In 2001, the CTBR/ClinTrials group was sold to Inveresk Research in Scotland and renamed CTBR/Inveresk, and an additional new vivarium facility was opened. In 2004, CTBR/Inveresk was sold to Charles River, at that time CTBR had over 1600 employees and approximately 350 animal rooms.

There were at least two other CROs named BioResearch – one in Philadelphia (started and managed by Karl Gabriel) and the other in Cambridge, MA, operated by Frederick Homburger and specializing in hamster studies.
Ricera

Ricera began as Diamond Shamrock in 1967 with the merger of Shamrock Oil and Diamond Alkali Chemical, a maker of heavy chemicals. The original president was William Bricker. Some year later, they went into a joint venture with Showa Denko and became SDS Biotech. They were then purchased by Fermeta, an Italian company, and changed the name to Ricera in 1986; Ricera was the Italian word for research. In 2007, Ricera became Concord Biosciences. The facility was in Concord Township near Painesville, Ohio, and consisted of 110,000 square feet and 20 animal rooms. Noted toxicologists who worked there include James Killeen, James Laveglia, Larry Powers, William Ford, and Darren Warren.

Calvert Laboratories

Calvert Laboratories was founded in 1969 as Pharmakon Laboratories in Scranton, Pennsylvania, by Richard Matthews who was a pharmacologist who had previously worked at Upjohn and Union Carbide. Matthews had an entrepreneurial spirit who saw the vision of the upcoming boom in biotechnology. Pharmakon Laboratories initially offered classic in vivo pharmacology studies. In 1980, the company moved to Waverly, Pennsylvania, and over the next ten years the company introduced additional testing services that included acute toxicology, cytogenetics and genetic toxicology, immunology, pharmacokinetics, and full-service general toxicology. In 1990, the company was purchased by the biotechnology company DNX (Princeton, NJ), which a few years later purchased the Hazleton site in Lyon, France, with the resulting company calling itself Pharmakon Research International. In 1996, Pharmakon merged with Bioclin, a clinical CRO to form a new publicly held company called Chrysalis, which was subdivided into nonclinical and clinical portions in the United States and Europe, which now covered a complete range of preclinical and clinical (phases I–IV) studies. In 1998, a large pharmaceutical company discontinued the development of a potential major cardiovascular drug, and as the clinical arm of Chrysalis I had been scaling up and incurring substantial expenses to conduct this project, the clinical part of Chrysalis found itself in bankruptcy. The nonclinical portion of Chrysalis remained solvent, but these events led to the purchase of Chrysalis by Phoenix International Life Sciences (PILS), which
was based in Montreal, Canada. However, PILS soon found itself in bankruptcy after the very same large pharmaceutical company that sank the clinical arm of Chrysalis cancelled the performance of a large bioanalytical program in support of a phase III study. This in turn led to MDS of Toronto, Canada, to acquire PILS in 1999. The many assets of PILS were dissected and sold, spun off as independent units, or absorbed within MDS. A small company in Cary, North Carolina, composed of former pharmaceutical executives and consultants to the pharmaceutical industry in general called Calvert Holdings acquired Chrysalis in 2000 and changed its name to Calvert Preclinical Services. The executive chairman of the board and majority owner of Calvert Preclinical Services was Russell McLauchlan, formerly of Lederle. In 2002, Calvert Preclinical Services changed its name to Calvert Laboratories. The services offered by Pharmakon-Chrysalis-Phoenix-MDS-Calvert remained the same: acute through chronic toxicology studies, carcinogenicity studies, DART studies, discovery and safety pharmacology studies, pharmacokinetics and ADME studies, and immunology studies at the Waverly facility that included approximately 40,000 square feet and 40 animal rooms. It became the first CRO to offer GLP contract services in safety pharmacology and immunology. Noted toxicologists at Pharmakon-Chrysalis-Calvert include Robert Naismith, Charles B. Spainhour, Joan Chapdelaine, Vincent Ciofalo, Roger Toothaker, Leon Stankowski, Juan SanSebastian, Michal Virat, Francois Verdier, and Bernard Regnier.

**Experimental Pathology Laboratories**

Experimental Pathology Laboratories (EPL) was founded in 1971 by John (Jack) Ferrell and William Busey, two pathologists who had previously worked at Hazleton Laboratories in Vienna, Virginia. Early pioneers in the profession of toxicologic pathology, they recognized the need for independent contract pathology services in the coming years and created a small business consisting of two pathologists, three technicians, and one secretary in Herndon, Virginia. Over the years, EPL has grown to be one of the largest leading independent pathology companies in the world, with sites in several states and in Europe. EPL has two main laboratories, one site in Sterling, Virginia, where the corporate headquarters are located, and one site in Research Triangle Park, North Carolina. The Sterling site occupies over 28,000 square feet of space which includes 8600 square feet of space dedicated for histological processing. This
The site includes complete facilities for the histologic processing and microscopic evaluation of mammalian and aquatic animal tissues, and it was designed specifically with attention placed on the orderly and effective flow of work and employee safety. The site in Research Triangle Park comprises approximately 43,000 square feet of space, and it is where EPL manages the NTP Archives and NTP Frozen Tissue Bank to store pathology materials, frozen specimens, and data from government-sponsored toxicity and carcinogenicity studies. EPL also manages the NIEHS Data and Specimen Repository at this site. EPL was instrumental in designing and developing a pathology peer review system for verifying the pathology data generated by the National Cancer Institute’s Carcinogenesis Program, later called the National Toxicology Program. This system of pathology peer review is widely used by pharmaceutical companies and toxicology laboratories to resolve difficult pathology issues when the data are to be submitted to regulatory agencies. After John Ferrell and William Busey retired in 1998, Jerry Hardisty became President of EPL, and following Hardisty’s retirement in 2015, Kathleen Funk became EPL President. Noted pathologists at EPL include John Ferrell, William Busey, Jerry Hardisty, Robert Maronpot, Paul Snyder, Kathleen Funk, Gerald Long, Peter Mann, Thomas Steinbach, and Paul Snyder.

MB Research Laboratories

MB Research Laboratories was founded in 1972 by Oscar Moreno and Terry Bannon in Spinnerstown, Pennsylvania. The original site consisted of 14,000 square feet of space and 12 animal rooms, with the mission of the company to provide rapid, accurate, and reproducible acute toxicity assays. While still fulfilling that role, MB Research Laboratories has been at the forefront in the development of alternative assays since 1989. The validation of alternatives has been supported by numerous governmental and industry grants. Today, MB Research Laboratories offers GLP in vitro and ex vivo alternatives for cytotoxicity, dermal irritation, ocular irritation, dermal sensitization, and dermal corrosivity studies while continuing to provide expertise in in vivo acute animal assays. Noted toxicologists at MB Research Laboratories include Oscar Moreno, Daniel Cerven, George DeGeorge, Albert Gilotti, Edward Yurknow, Dee Kim Tessler, John Mitchell, and Bennett Varsho.
Pacific BioLabs

Pacific BioLabs was founded in 1972 as Northview Biosciences in Northbrook, Illinois, by Martin Spalding, a chemist at the Murine Company (a maker of eye drops) that was acquired by Abbott Laboratories in 1970. In 1982, Northview Biolabs acquired E.S. Unilabs in Berkeley, California, a small contract laboratory that offered microbiology and small science services with a staff of 18, and reincorporated in California as Northview Pacific Laboratories, Inc. At the request of large client that was a contract sterilizer, Northview Biolabs opened in new facility in 1991 in Spartanburg, South Carolina. All of these business units were part of Northview Biosciences, Inc. (NVB), which served as a corporate holding company. In 2006, SGS acquired NVB and the facilities in Illinois (offering analytical chemistry and microbiology services for pharmaceutical companies) and South Carolina (offering medical device microbiology services), but not the California site. At that time, the Illinois site had 21,000 square feet of space and 90 employees, while the South Carolina site had 10,000 square feet of space and 13 employees. In 2006 Northview Pacific Laboratories, Inc. (now located in Hercules, California) was renamed Pacific BioLabs, Inc. The facility consists of 34,000 square feet of space with 29 animal rooms and 90 employees and offers analytical chemistry, bioanalysis, microbiology, and toxicology services. Noted toxicologists at Pacific BioLabs include Timothy Doherty, Dennis Chapman, Michael Yakes, and Gurpreet Ratra.

Utah Biomedical Toxicology Laboratories

Utah Biomedical Toxicology Laboratories (UTBL) was founded around 1973. Originally funded by NIH money to serve as a center for pursing artificial heart replacement research, it was purchased by the Sorenson family of Salt Lake City and led by James Sorenson. The facility was in Salt Lake City, Utah in the University of Utah Research Park. The laboratory contained approximately 20,000 square feet of space with 20 animal rooms, including 3 surgical suites with observation decks. Studies were conducted in rodents, rabbits, dogs, pigs, sheep, cattle, and horses. The laboratory specialized in surgical studies and medical device biocompatibility studies, and it was one of a few laboratories at that time conducting biocompatibility studies for medical devices. Noted toxicologists at UTBL include Randy White, Jerry Nelson, Russell Eyre, Steve Beck, Wayne Ball, and William Ford. In 1986, the company was divided into
two groups, toxicology and medical, and sold to HeartPort who closed the toxicology group. In 1992, HeartPort was purchased by a large pharmaceutical company, and the facility was taken over by the University of Utah in 1994.

**Stillmeadow, Inc.**

Stillmeadow, Inc. was founded in 1975 in Sugar Land Texas by Robert Sabol, who had a degree in animal sciences from Delaware Valley College and had previously served as a laboratory manager at Bio/dynamics. The original location consisted of 600 square feet of space and reached 5000 square feet of space by 1990 when it moved to its current location and expended to 50,000 square feet in 1995. In 1997, it acquired ENSR’s bio-monitoring laboratory and added a 10,000 square aquatic toxicology laboratory. In 2008, it added an additional 15,000 square foot building. Stillmeadow conducts mammalian toxicology studies but is especially known in the industry as one of the few CROs that conducts aquatic, entomology, and environmental toxicology studies. Noted toxicologists at Stillmeadow, Inc. included Vince Murphy, Kenneth Washburn, Jan Kuhn, Mark Holbert, Warner Phelps, Andres Doig, and Cole Younger.

**Toxicology Pathology Services, Inc.**

Toxicology Pathology Services, Inc. (TPS) was founded in 1976 by James Botta, an Auburn University-trained veterinarian. The laboratory, located in Mount Vernon, Indiana, consisted of 90,000 square feet of space with 44 animal rooms. In 1989, TPS was acquired by BASi, and in 2018, BASi was acquired by Seventh Wave. Noted toxicologists at TPS included James Botta, Gina Gratz, and Phillip Downing.

**WIL Research**

WIL Research was founded in 1976 as Welcome Independent Laboratories in Cincinnati, Ohio, by G. Bruce Briggs, a veterinary toxicologist and Ralph Hodgdon, a business administrator. Prior to establishing WIL Research, Briggs had held senior leadership roles at Pfizer; Smith, Kline & French, and Hill Top
Research. The original site in Cincinnati comprised 24,000 square feet of space with approximately 30 animal rooms. In 1978, WIL Research was acquired by Great Lakes Chemical Corporation and in 1980 WIL Research acquired the Hess and Clark Research Farm in Ashland, Ohio from Rhone Poulenc. During 1982–1983, the operations in Cincinnati were all transitioned to the Ashland site which was located on 40 acres comprising 7 research buildings and approximately 70,000 square feet of space. Currently this site occupies 300,000 square feet of laboratory space. WIL Research was the first CRO to develop, validate, install, and market an electronic data capture system for in-life and post-life toxicology measurements, including developmental and reproductive studies, statistics, and report generation. It was also the first CRO to install and operate BioClean animal rooms for conducting chronic toxicity studies in rodents. Noted toxicologists at WIL research included Bruce Briggs, James Laveglia, Dean Rodwell, Mark Nemec, Chris Chengelis, and Dale Mayhew.

**Springborn Institute for Bioresearch**

Springborn Institute for Bioresearch was founded in 1976 by Robert Springborn, a chemist who had previously been at Monsanto and W. R. Grace. The 26-acre site in Spencerville, Ohio, had previously been a veterinary research business created in 1965 called Bio-Tox Labs, which had been purchased by Diamond Shamrock in 1969 to perform large animal research. At the time of the Springborn purchase, the site encompassed 27,000 square feet of space with 18 animal rooms. In 2001, the organization changed its name to Springborn Life Sciences, and in 2002, Springborn Life Sciences was purchased by Charles River. Currently the site contains 117,000 square feet of laboratory space and approximately 250 employees. Noted toxicologists at Springborn included Richard Hiles, Dean Rodwell, Peter Becci, Malcolm Bair, Joseph Siglin, and Rusty Rush.

**Hazleton Munster**

Hazleton Munster was originally founded as Affenucht Munster (AZM) in Munster, Germany, in 1976 by Rainhart Korte, a reproductive toxicologist you had previously been at Schering AG, to serve as a primate breeding facility for use in the vaccine industry. In 1980, Rainhart Korte sold AZM to Hazleton
Laboratories, and the breeding facility was turned into a toxicology laboratory in 1981 to focus on reproductive toxicology in rodents, rabbits, and nonhuman primates. In 1982, acute and general toxicology services were added, but acute services were discontinued in 1984. In 1997, the site became a nonhuman primate only facility. Rainhart Korte served as Managing Director through 2002, and he was followed by Friedhelm Vogel who served in that position through 2019. Following the Hazleton history, the facility became part of Corning in 1987, was renamed Covance in 1996, and became part of LabCorp in 2015. It was considered the first CRO to offer nonhuman primate reproduction studies (conducted approximately 80 such studies), and over the years it has initialed many new and innovative housing and technical procedures to enhance the quality of toxicology studies performed in nonhuman primates. Currently the facility has over 200 employees and 117 animal rooms with an ability to house over 2000 macaques and 200 marmosets. Noted toxicologists at Hazleton Munster included Rainhart Korte, Friedhelm Vogler, Gerhard Weinbauer, Wolfgang Mueller, and Sven Korte.

**Borriston Laboratories**

Borriston Laboratories was founded by the Dynamic Corporation in 1977 in Temple Hills, Maryland. The laboratory was initially started to house and continue a 7-year cigarette smoking study in dogs for the NCI after the initial contractor decided to not continue the study. In 1978, Borriston Laboratories decided to expand its services and began offering a full set of standard acute, subchronic, and chronic/carcinogenicity studies in rodents and dogs and developmental and reproduction studies in rodents and rabbits. At its peak, it had over 100 employees and 40 animal rooms, used mostly for rodents and rabbits. Noted toxicologists at Borriston Laboratories included Tom Mulligan, Vine Piccirillo, and Richard Costlow. In 1985, Borriston Laboratories were sold to Andrew Tegeris and merged with Pharmacopathics Laboratories to become Tegeris Laboratories in Laurel, Maryland, but Tegeris Laboratories closed in 1988.

**Argus Research Laboratories**

Argus Research Laboratories was founded in 1979 by Mildred Christian, E. Marshall Johnson, and Gerald Lightkep in a modified barn on Buckshire Farm in Perkasie, Pennsylvania. The idea to form a CRO that focused on repro-
ductive and developmental toxicology came from Mildred Christian who had just completed her doctorate at Jefferson University (E. Marshall Johnson had been her major professor) and who felt that no existing US CRO could conduct scientifically adequate and GLP compliant studies of this type. The original laboratory had six animal rooms and four employees. In 1982, Argus Research Laboratories began leasing and modifying warehouse space in Horsham, Pennsylvania, and in 1990 it left the Perkasie site to grow and develop the Horsham site. In 1987, it purchased the Center for Photobiology from Temple University and began offering phototoxicity capabilities. In 1991, the TSI Corporation purchased Argus Research Laboratories allowing Johnson and Lightkep to retire. TSI Corporation had previously purchased EG&G Mason Laboratories in Worcester, Massachusetts and a small CRO in Redfield, Arkansas, but had overextended itself and sold these assets to the Genzyme Transgenic Company (GTC) a few years later. GTC was 42% owned by Genzyme, and it had been formed to produce drugs in goat milk on a GMP farm in Charlton, Massachusetts. The concept was that the CRO business would generate the income necessary to support the production of drugs, but when that strategy failed, GTC formed a company called Primedica so that the CRO business could be sold. Charles River purchased Primedica in 2001, closed the Redfield site in 2008, moved the Worcester site to Shrewsbury, Massachusetts, and renamed the Horsham site Charles River Horsham. Currently the Horsham site has 65 animal rooms in a 124,000 square foot laboratory with a staff of 230. Noted toxicologists at Argus Research Laboratories included Mildred Christian, Don Forbes, Chris Sambuco, and Alan Hoberman.

The Later Years

Toxicology Research Laboratory at the University of Illinois at Chicago

The Toxicology Research Laboratory at the University of Illinois Chicago (UIC) in Chicago, Illinois, was established in 1987 by Barry Levine who had previously worked in both the CRO and pharmaceutical industries. The facility consisted of approximately 110,000 square feet of space encompassing slightly more than 100 animal rooms. Most of the testing was conducted in support of
government contracts, but studies for the pharmaceutical industry were also performed. Noted toxicologists at UIC included Barry Levine, Debra Kirchner, Alan Brown, Ashraf Youssef, and Peter Korytko.

**International Toxicology Research**

International Toxicology Research (ITR) was created in Montreal, Canada, in 1989 as a subsidiary research facility of the Japanese Bozo Research Center by Kumi Yamanouchi. The facility encompasses 185,000 square feet of laboratory space with 72 animal rooms and 15 inhalation exposure rooms. It is a full-service CRO conducting toxicology studies in all common animal species with an expertise in large molecule programs and immunology endpoints. Noted toxicologists at ITR included Colin Bier and Joseph Younan.

**Smithers Avanza**

Smithers Avanza was established in 1992 in Gaithersburg, Maryland, by Roy O. Williams, as R.O.W. Sciences, Inc. to support NTP reproductive and developmental studies. Williams began his career as an inhalation technician at Hazleton Laboratories and later founded R.O.W. Sciences as a company to support NIH in managing animal facilities. He then decided to build his own facility in Gaithersburg and hired Bruce Briggs as the first toxicologist there. The original facility had 35,000 square feet of space with 35 animal rooms. In 1998, TherImmune purchased the site, doubled the size of the facility, and expanded the staff from 35 to 250 and began offering full toxicology services to the pharmaceutical and biotechnology industries. Over the next 20 years, the company was sold several times with a number of name changes: GeneLogic Laboratories (2003–2006), Bridge Laboratories (2006–2009), Avanza Laboratories (2009–2011), and Smithers Avanza (2011–2019). In 2019, Smithers Avanza was acquired by BASi. Noted toxicologists who worked at this facility included Bruce Briggs, Gary Wolfe, Ric Stanulis, Steve Godin, Eias Zahalka, Scott Manetz, Michael Dorato, and Florence Caputo.
Sinclair Research

Sinclair Research was originally established in 1964 as the Sinclair Comparative Medical Research Farm as part of the University of Missouri, with its primary function to provide laboratory animal research support for the university’s environmental health surveillance center and environmental trace substance research center. Over the years, its role expanded to become a resource for a wide variety of animal and health-related research and become very involved in the development and use of animal models. In 1992, Sinclair Comparative Medical Research was privatized and Sinclair Research was established in 1994. The current site, located about 15 miles east of Columbia, Missouri, sits on 200 acres and contains both a swine breeding facility and a contract toxicology testing facility. The company is owned and led by Guy Bouchard, who received his veterinary degree from the University of Montreal. The contract testing facility consists of 250,000 square feet of vivarium and ancillary space with 70 animal rooms. Sinclair Research is a leader in the area of miniature swine and has conducted and published numerous research articles pertaining to swine, but it also conducts toxicology studies in all commonly used animal species. Noted toxicologists at Sinclair Research include Scott Boley, Jeffrey Klein, and Jason Liu.

Sierra Biomedical

Sierra Biomedical was founded in Sparks, Nevada, in 1992 by William Hobson who had previously worked at Primate Research Institute in Alamogordo, New Mexico. The company business model was to offer high-quality toxicology testing in nonhuman primates to support the growing biotechnology industry on the West coast. The original facility was in leased space and housed 200 nonhuman primates. In 2007, a new 465,000 square foot purpose-built facility was erected in Reno, Nevada, and the laboratory functions were moved from the Sparks facility. In 1994, there were 35 employees, but currently there are over 1000 employees. The new facility can house over 3000 nonhuman primates and is the largest nonhuman primate CRO in North America. In 1999, Sierra Biomedical was purchased by Charles River. Noted toxicologist at Sierra Biomedical included Doug Kornbrust, Jon Kapeghian, Gary Chellman, and Tom Zanardi.
### Northern Biomedical Research

Northern Biomedical Research (NBR) was founded in 1993 by Robert Boyd, a veterinarian. The 60,000 square foot facility is located in Norton Shores, Michigan, and contains 19 animal rooms and two surgical suites. The laboratory specializes in surgical studies in most species of laboratory animals and pioneered several surgical techniques and postoperative animal care practices for targeted drug delivery to numerous organ systems, especially the central nervous system, utilizing a state-of-the-art custom built 3T MRI for imaging and stereotaxic administration to the central nervous system.

### MPI Research

MPI Research was founded by William Parfet and Jerry Michell in 1995, having bought the remaining assets of International Research and Development Corporation (IRDC). Parfet, the great grandson of W. E. Upjohn, the founder of the Upjohn Company in Kalamazoo, Michigan, was a businessman, while Mitchell was a medical research doctor and former head of research and development at the Upjohn Company. Michell sold his interests in MPI Research in 1998, and Parfet put together an executive team that served together for over 10 years and led the company to great success. That team consisted of William Harrison as President, James Laveglia as Director of Research, Andy Dumpis as Director of Finance, and David Serota as Director of Toxicology. Starting with about 300,000 square feet of space comprising 125 animal rooms and a staff of around 175 at the time of purchase, by 2008 MPI Research had grown to over 1,000,000 square feet of space comprising over 550 animal rooms and a staff of over 1800. Several small acquisitions were made during this period but the company’s growth was based on expansion of the existing facility in Mattawan, Michigan, through a concentrated and successful effort to market to biotechnology organizations. In 2008, Parfet sold a minority interest in the company to TA Associates of Boston, Massachusetts, and in 2015 the company was sold to Avista Capital Holdings, a private equity firm. In 2018, the company was sold to Charles River. Noted toxicologists at MPI Research included Edwin Goldenthal, James Laveglia, David Serota, Paul Newton, Richard Slauter, Ray Schroder, Ali Faqi, Theodore Baird, David Gauvin, Christopher Papagiannis, Scott Boley, and Mark Johnson.
Covance, Inc.

Covance, Inc. evolved from Hazleton Laboratories after Corning spun off Corning Pharmaceutical Services in 1996 as an independent, full-service publicly traded company. Covance, Inc. consisted of preclinical testing sites in Vienna, Virginia; Madison, Wisconsin; Harrogate, England; and Munster, Germany. The Vienna site was closed in 2010. The Madison site has just under 1,000,000 square feet of space and provides both in vivo and in vitro metabolism, general toxicology, safety pharmacology, large animal DART, and small molecule bioanalysis services. The Harrogate site has slightly over 500,000 square feet of space and supports general toxicology, safety pharmacology, immunotoxicology, genetic toxicology, and small animal DART studies. The Munster site has approximately 150,000 square feet of space and supports primate studies for general toxicology and DART studies. In 2008, Covance, Inc. purchased the 450-acre Greenfield, Indiana, site from Eli Lilly and Company. The Greenfield site has just over 1,000,000 square feet of space and supports general toxicology, small animal DART studies, in vivo and PK screening, and molecular and anatomical imaging. In 2011, the Greenfield site added a stand-alone building for conducting small animal DART studies. In 2009, Covance opened a 288,000 square foot facility on 77 acres of land in Chandler, Arizona, but due to economic conditions, this facility was closed in 2012. In 2015, the Laboratory Corporation of America (LabCorp) acquired Covance. In 2019, LabCorp entered into an agreement with Envigo by which LabCorp purchased Envigo’s contract research service business while Envigo purchased LabCorp’s animal research models and service business. Noted toxicologists at Covance Madison include Karen MacKenzie, Anthony Kiorpes, Matt Palazzolo, Suzanne Wolford, and Susan Henwood.

Burleson Research Technologies, Inc.

Burleson Research Technologies, Inc. (BRT) was founded in 1996 in Morrisville, North Carolina, by Gary and Florence Burleson, both who had strong backgrounds in immunology and immunotoxicology. The facility consists of 10,000 square feet of space and has 35 employees. BRT specializes in immunology and immunotoxicology services and offers services in infectious disease models, and host resistance hypersensitivity, and immune response assays. In 2014, BRT has held to NTP immunotoxicology contract. Noted toxicologists at BRT include Gary Burleson and Florence Burleson.
SNBL USA

SNBL USA was founded in 1996 as a subsidiary of SNBL Japan by Ryoichi Nagata, the son of the founder of SNBL Japan which was established in 1957. The site, located in Everett, Washington, encompasses 210,000 square feet of space and 130 animal rooms. SNBL USA was known for its nonhuman primate experience in conducting general toxicology and reproductive studies and through its passive restraint cages that were designed by Ryoichi Nagata to reduce the stress of study procedures. In 2018, SNBL USA was acquired by Altasciences, a clinical research company based in Montreal, Canada. Noted toxicologists at SNBL USA included Tina Rogers, Christopher Slater, Darren Warren, and Mark Osier.

Experimur

Experimur was founded in Chicago, Illinois, in 2000 by Nabil Hatoum and Bernadette Ryan who had both previously worked at ITTRI. The current facility was opened in 2010 with 54,000 square feet of space and 40 animal rooms. It offers full general toxicology and reproductive/developmental toxicology services. Noted toxicologists at Experimur include Nabil Hatoum, Bernadette Ryan, Christopher Slater, Bjorn Thorsrud, John Devine, Anne Doyle, Edward Mallett, and Supida Monaikul.

Wuxi

Wuxi was founded in 2001 by four co-founders including Ge Li who was a chemist and worked for seven years at Pharmacopeia before becoming CEO of Wuxi. The company started from a single chemistry site but through growth and acquisition now has over 30 sites worldwide with over 22,000 employees. The toxicology facility is located in Suzhou, China, and occupies 314,000 square feet of space encompassing 120 animal rooms. A major expansion of this facility was completed in late 2019, enlarging the facility to 580,000 square feet of space with 220 animal rooms. In 2008, Wuxi merged with Apptec to create a more global presence. Noted toxicologists at Wuxi include Sue McPherson, Anthony Kiorpis, and Yi Jin.
Xenometrics

Xenometrics was founded in 2006 by Alfred Botchway and Tom Haymaker in Stillwell, Kansas. They had previously been with the Quintiles preclinical unit in Kansas City, Kansas, which had been purchased by Aptuit in 2005, but which was closed a year later. They handpicked numerous staff who had previously been with Quintiles/Aptuit to join them in this new company. They rented space from Bayer Crop Science, which opened in 1979, and began offering PK and safety pharmacology services. In 2009, Xenometrics acquired the 78,000 square foot Bayer facility, and in 2017, Xenometrics was acquired by CiToxlab, renaming itself CiToxlab USA in 2018.

CiToxLAB

CiToxLAB was established in 2011 as a conglomeration of international CROs, comprising 1300 employees at 9 sites. These CROs included CIT-France (Centre International de Toxicologie), founded in 1969 and located in Evreux, France, with 200,000 square feet of space; LAB (now CiTox NA), founded in 1998 and located in Laval, Canada, with 176,000 square feet of space; Scantox (now CiTox Denmark), founded in 1977 and located in Koge, Denmark, with 93,000 square feet of space; a Hungarian site (now CiTox Hungary) located in Veszprem, Hungary, with 164,000 square feet of space; Atlanbio, founded in 2004 and located in Normandy, France, with 19,999 square feet of space; AccelLab founded in 2004 and located in Boisbriand, Canada; Xenometrics (now CiTox USA) founded in 2006 and located in Stillwell, Kansas, with 78,000 square feet of space; Solvo Biotechnology founded in 1999 and located in Budapest, Hungary; and Experimental Pharmacology & Oncology (EPO) founded in 1999 and located in Berlin, Germany, with 12,000 square feet of space. Each of these sites generally offered a different area(s) of expertise as follows: CIT-France, full service toxicology capabilities including genomics; CiTox NA, full service toxicology capabilities, specializing in DART, safety pharmacology, inhalation, and irradiation safety; CiTox Denmark, toxicology specializing in pig studies, especially the Gottingen minipig for juvenile, reproductive, and wound healing studies; CiTox Hungary, general and inhalation toxicology; Atlanbio, analytical/bioanalytical support through all phases of the drug development process; AccelLab, specializing in medical device testing; CiTox USA, full service toxicology capabilities; and EPO, specializing in preclinical assessment of new
anti-cancer drugs. Based on the planned business strategy of CiToxLAB, the wide geographic nature of this group of laboratories along with their diverse areas of expertise would make them a major player in the CRO world. In 2016, the company was purchased by Ardian, and in 2019 the company was purchased by Charles River Laboratories.

Acknowledgment of Contributors

The author wishes to thank and acknowledge those professionals in the field of toxicology who provided historical information that was included in this chapter. Without their participation, this chapter could never have been written.

Ralph Anderson, Carol Auletta, Guy Bouchard, David Brusick, Gary Burleson, Daniel Cerven, Any Cianciaruso, Heather Dale, George DeGeorge, John Devine, Phillip Dowling, William Ford, Roy Forster, Patricia Frank, Shayne C. Gad, Michael Gallo, Carol Green, Dean Haan, Jerry Hardisty, Ryan Harper, Nabil Hatoum, Tom Haymaker, Charles Hebert, Alan Hoberman, Mark Holbert, Dave Howard, Doug Kornbrust, Sven Korte, James Laveglia, Barry Levine, David McCormick, Jacob McDonald, Sue McPherson, Richard Parent, Chris Perkins, Vince Piccirillo, Fred Reno, Tina Rogers, Rusty Rush, Janice Schinder-Horvat, Charles B. Spainhour, Matt Spalding, Bonnie Stuut, Friedhelm Vogel, Randy White, Gary Wolfe, Joseph Younan.

Trends and the Dark Side of the Story

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As reflected in this chapter, commercial toxicology service organizations (CROs) have significantly evolved since their first appearance more than 80 years ago. These ‘ages’ are reflected in the lists of existing CRO’s and their histories as reflected in the front section of this chapter, in the earlier edition of this book, in Appendices A and B, and in Freudenthal 1997, Texas Research Institute 1986, and Gralla 1981.

In the modern decade, it is generally accepted that there have been four major cycles in the history of the CRO industry. These are commonly referred to as the “golden ages,” because there was great demand for services from CROs, expansion of existing CRO facilities, and the appearance of new CRO organizations.
Each of these booms was followed by periods of economic setbacks and financial downturns.

The first occurred in the 1970s, when environmental concerns lead to the increased regulation of products. Particularly fueled by expectations of vast demand due to the Toxic Substance Control Act, this led to expansion of CROs and the initiation of formal academic programs in the field of toxicology. This came to an end in the early 1980s as regulatory testing requirements did not expand as much as expected.

The second period started in the late 1980s, as a significant increase in the amount of required testing of food additives and pharmaceuticals fueled expansion (Jackson 1984). This period faded away at the turn of the century when there was an economic downturn.

The third golden age came about out of the appearance of many small pharmaceutical “start-ups” appearing and needing regulatory toxicology testing of their candidate drugs. This era also was ended by the economic downturn in 2007/2008.

We are currently in the fourth “golden age” fueled by both major domestic pharmaceutical and medical device companies outsourcing most of their testing and increasing companies seeking to bring their products into the US and European markets and a surge of new companies seeking to develop new drugs and devices. The end of this period is not yet in sight, but certainly the COVID-19 pandemic has adversely effected the industry.

At the same time, we should capture here at least some of the history of failures in maintaining ethics and quality in testing operations.

Good Laboratory Practices (GLP) as law have been with us since 1977, with the primary purpose being need that they were intended to meet safety assessments both preceding that date by many years and continuing to the present and beyond.

Good recording of data, plans, and procedures in the laboratory has always been essential to the conduct of both scientific research and the entire self-modifying/evolutionary process by which science as a whole operates. The documentation of the fact that proper procedures were followed is an unfortunate reflection of the need to insure against everything from sloppiness to dishonesty. Furthermore in many areas of biomedical research and testing, such guidelines are now also a requirement of law. To understand the need both for all of these procedures and for the laws requiring then, we must review the history of problems in the area.

A complete history of the problems associated with biomedical data recording and management is a book in itself. In fact, a number of books have been published...
on this very matter (Broad and Wade 1982; Hoover et al. 1986; Huber 1991). Though the problem of data falsification or the suspicion of such dates back to Ptolemy and is not limited in the biomedical sciences, our overview of history will be limited to the period from 1960 on and to the biomedical sciences.

In the period 1960–1961, a graduate student at Yale who went on to become a postdoc at Rockefeller performed a series of brilliant experiments on cytochrome c and glutathione with well-respected senior investigators (Broad and Wade 1982). These results were widely published, but the work was soon found to not be repeatable. The publications and work were retracted, and the junior individual involved resigned and left research altogether. This episode received no press attention. The first widely publicized case to come to the public’s attention, starting the erosion of the public’s faith in science, was that of the “patchwork mouse” in 1974 (Hixson 1976). William T. Summerlin was a junior researcher working at Sloan-Kettering in a large lab with Robert Good, who was the laboratory supervisor. Good’s lab had published almost 700 well-regarded papers in immunology with Good as a co-author on all of them over the preceding 5 years. Summerlin reported a number of successful transplantations in animals, which could not be replicated by others. Finally, he used a black felt tip pen to enhance the appearance of successful transplantation of skin patches on some mice. A technician, who was working the laboratory (but not Dr. Good), detected the alteration in what became a well-publicized case.

In 1978 an entire team of researchers working for Dr. Marc Straus at Boston University were working as part of a clinical trial sponsored by the Eastern Cooperative Oncology Group. The team reported that they had “falsified” nearly 15% of all the data entered from the trial, under direction from Dr. Straus. The falsification consisted of everything ranging from concealing errors made by the team in following the specific study protocol to allowing physicians to diverge from the study treatment without having to exclude the patients from the trial (Carlfield 1988). This situation was repeated with much wider publicity by a Canadian research team that was part of the breast cancer trials in 1994, leading to the well-respected overall head of the trial having to resign (Anderson 1994).

Industry also has had its share of problems, both real and suspected. During the 1970s the largest industry biological testing lab in the country was Industrial Biotest. In 1975 an FDA investigator stumbled by accident on problems in the data from testing on Naprosyn. As investigators dug deeper into the data on studies on the safety of more than 600 drugs, chemicals, and food additives evaluated by IBT, they found enough fraud to lead to the indictment and conviction of four senior officers of the company (Anon 1981a, 1981b, 1983a, 1983c). The of
greater impact was that the documentation of study procedures and data recording could not be verified. Given the already known problems with the data and the conduct of some studies (e.g., animals that were recorded as having died on study not being necropsied until after autolysis had set in, etc.), the results of all the studies were suspect. Studies either had to be repeated or validated if possible. This case and others in the same time frame led to the adoption of the Good Laboratory Practice (GLP) regulations, which now govern all preclinical (i.e., nonhuman) studies performed to establish the safety of a drug, medical device, or chemical regulated by the United States and most foreign governments.

The GLP regulations, which are discussed in a later section of this book, call for regular inspections of all laboratories (i.e., industry, contract, and university) involved in the generation of such data. This program of regular unannounced inspection has continued to identify problems involving some actual fraud,

| Organization                        | Year | Violation                                                                 | Penalty                  |
|-------------------------------------|------|---------------------------------------------------------------------------|--------------------------|
| Litton                              | 1980 | Deviations from protocols and SOPs                                        | Warning letter           |
|                                     |      | Mix-up or misidentification of test materials                            |                          |
|                                     |      | Inadequate SOPs (Anon 1980)                                              |                          |
| Gulf South Research                 | 1983 | Poor data keeping on NTP carcinogenicity studies (Marcus 1983)             | Lab went out of business|
| Biodynamics                         | 1980 | Timeliness of postmortem exams                                            | None                     |
|                                     |      | Reporting of tumors                                                       |                          |
|                                     |      | Poor husbandry (Anon 1983)                                                |                          |
|                                     | 1983 | Late reporting                                                             |                          |
|                                     |      | Pathologist not present at necropsy                                        |                          |
|                                     |      | Poor husbandry                                                            |                          |
| SAIC                                | 1986 | Backdating of Superfund data (Anon 1983; Zurer 1991)                      | $750,000 fine            |
| Carter Wallace/AMA Laboratories     | 1992 | No study protocols                                                         | $132,000 fine            |
|                                     |      | Failure to sign data entries                                               |                          |
|                                     |      | No study personnel files                                                   |                          |
| BioTek Industries/ Microbac Laboratories | 1992 | No QA unit                                                                | $100,000 fine            |
|                                     |      | Lack of written protocols and SOPs                                         |                          |
|                                     |      | Missing items and inconsistencies in raw data and report                   |                          |
| Craven Laboratories                 | 1992 | “Tweaking” of pesticide residue data                                       | Prison terms             |
| Twelve pesticide firms              | 1993 | Inadequate documentation and records (Anon 1994)                          | $183,000 in fines        |
invention of data, deletion of data, alteration of data, and other activities that are in violation of procedural/documentation requirements of the regulations. A few examples spanning the first 15 years since the regulation became effective are provided in Table 2.1.

Also see Anon 1991; Cohen 1991; Hall 1991; Hamilton 1991; Placa 1991; Tifft 1991; Kumar 1991; Stone 1994. The problems which have led to a decrease in the creditability of science have not been limited to industry. As shown in Table 2.2, academic and government labs and researchers have also had problems on a continuing basis. These problems have not been just cases of suspected or real fraud, but also of plagiarism and various other forms of scientific misconduct. Scientific misconduct has a variety of forms (Kyburg 1968; Stone 1991; Taubes 1995):

**Plagiarism** Presenting work done by another as your own

**Misallocation of Credit** Claiming (or accepting) credit for work done by another. This includes a lack of adequate acknowledgment of the work of one’s intellectual predecessors

| Institution                          | Year | Allegations                               | Outcome                                                                 |
|-------------------------------------|------|-------------------------------------------|------------------------------------------------------------------------|
| Tufts                               | 1986 | Fraudulent data in *Cell* paper           | Secret service involved                                                |
|                                     |      |                                           | Five years of investigations                                          |
|                                     |      |                                           | NIH finding of fraud                                                  |
| Vanderbilt                          | 1982 | Fraud, poor record keeping                | Discrediting of research on alcoholism (and of researchers)            |
| Caltech                             | 1989 | Fraudulent and missing data (Roberts 1991) | Paper retracted                                                        |
|                                     |      |                                           | Responsible postdocs dismissed                                        |
| University of Pittsburgh            | 1979 | Misanalysis of lead data                  | Office of Scientific Integrity investigation                            |
| University of California, San Diego | 1986 | Publishing false data                     | Faculty member resigned                                                |
| University of Alabama, Birmingham   | 1989 | Plagiarism                                | $2MM civil suit verdict                                               |
|                                     |      | False claims to the government            |                                                                        |
| St. Luc Hospital/Montreal           | 1994 | Not following protocol                    | Overall breast cancer study head removed                               |
|                                     |      | Falsifying ineligible patient enrollment  |                                                                        |

**Table 2.2** Purported recent cases of academic and government scientific misconduct
**Bias**  Uneven, unbalanced, or one-sided collection, analysis, or reporting of data

**Trimming**  Improving the appearance of quality of work or of clarity of outcome by removing or failing to report some data or observations

**Sloppy/Poor Records and Methods**  The most honest of intentions, but the documentation of what has been done and seen is either so incomplete, unclear, or disorganized that the value of the work is at best suspect and discounted

**Wholesale Fraud**  Complete invention of some or all of the work done and resulting data

**Junk Science**  That which supports adversarial opinions and is not supported by the work of others or accepted by the scientific community (Huber 1991)

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