The IVAC Legacy

The IVAC legacy is really the story of two early San Diego IV Pump companies. The innovations and respective product lines of IVAC and the second company, IMED, comprise among the earliest history elements of "medical devices" products invented and manufactured here in San Diego. In many ways these two companies defined the entrepreneurial model and platform for San Diego's "Life Sciences" technology cluster, comprised today of more than 1,000 Life Sciences companies.

IVAC and its progeny, IMED, would dominate the IV pump market for their specialized medical instrumentation - and in fact deliver such dramatic improvements to the "utility" of hospital, and later doctors clinic, ambulatory and home IV pumps to dramatically expand the IV fluids market and to create entirely new market segments.

IVAC initiated intravenous drug delivery innovations by marrying the emerging California computer microprocessor industry's advances with fluid flow technology, creating the first electronically-controlled infusion pumps. Practically speaking, IVAC and IMED delivered the IV pump technology innovations that permitted creation of the "Total Parenteral Nutrition (TPN)" market and the IV chemotherapy market, which was - and is - comprised of complex combinations of chemo drugs. The ability to provide cancer patient treatment with complex drug combinations came into being because of the precisely controlled infusion these pumps allowed for the potentially toxic chemo drugs which could be delivered with a precision and accuracy to the oncology patient that was previously impossible. IVAC, followed by IMED, drove the creation of what has become a \$20 billion market for intravenous (IV) solutions and IV-delivered drugs - neither market of which existed at any meaningful size prior to the delivery of the IVAC and IMED pump innovations.

Because the second IV pump company in San Diego, IMED, grew directly from founders including former IVAC founders and employees, the story of IV pump innovations flowing from San Diego can only be told by considering the innovations and activities of this pair of companies - which were to become fierce competitors and remained so for two decades, prior to becoming elements one company that acquired both of them. Ironically, eventually each of the companies was sold, resold and then sold again - and each was eventually acquired and merged into a single operation - within a new San Diego Company, called Alaris Medical Systems. Alaris itself was later sold, and the progeny of the product lines of both the original IVAC and IMED pump product lines became resident with yet another company, CareFusion.

The Formative Years:

IVAC - Founded in 1968 by Mr. Richard A. Cramer who had worked previously for Beckman Instruments. Cramer's founding intent and objective at IVAC was to apply the revolutionary advances being delivered by California's microprocessor industry to new, innovative, microprocessor-controlled medical products toward improving patient care. Some suggest (no documentation) that the acronym IVAC was intended to suggest, "IntraVenous Automatic Control" for its pending product line of medical IV pumps. Interestingly, while IV pumps seem to have been a primary focus of Cramer from the moment of company conception and formation, and IVAC became best known over time for it's IV pump innovations, in fact IVAC's first commercial product - and medical product innovation - was an electronic thermometer for medical use.

The IVAC electronic thermometer incorporated microprocessor electronics to display rapidly, objectively and unambiguously the patient's temperature. IVAC's medical-use thermometer products were for professional use only. IVAC's initial thermometer innovation was in designing and delivering a "thermistor" based electronic thermometer for which the probe was placed under the patient's tongue, as was an old mercury thermometer. The Company's second thermometer innovation was the "touchless" infra-red light-based thermometer. The electronic thermometers sold today in drug stores are essentially direct descendants of that original IVAC "touchless thermometer" innovation.

Approximately one year after introduction of the initial IVAC electronic thermometer, which received wide publicity and performed well in the market, IVAC introduced its first infusion pump for the hospital. This product was intended to provide much improved control of both precision and accuracy of delivery of IV fluids and drugs to hospital-based patients.

The IVAC pump married electronic control and fluidics, as intended by Cramer and was unique in that it provided an automatic feed-back loop that monitored and controlled the number of drops of fluid entering the IV tube. With this feedback loop, the actual rate of delivery of the respective drug (or hydration formulation) could be carefully controlled as compared to the previously used "squeeze point" of a clamp on a flexible plastic line and gravity-driven system that had no monitoring or feedback other than the nurse counting the drops while looking at a watch - and regularly coming back to check the flow rate - which changed as the fluid in the delivery container emptied.

IVAC met with rapid success in the market, due in no small part to how Cramer built IVAC's initial field sales team. Cramer built his sales team by hiring, annually, the top sales reps of Baxter Travenol. He was among the first, if not the first, in the medical industry to use a technique later used by essentially all biotech companies as each entered the product market - don't train sales reps but rather hire a high performing, proven sales rep and leave him or her in

the same geographic sales territory. Cramer's highly effective - and at the time unique employment strategy - also included a stock offer to the former Baxter sales reps along with competitive salaries. The stock package, as an element of acceptance of employment was potentially of significant future value to the new employee as compared to "fringe benefits" offered by the prior employer.

Richard Cramer is considered by most observers to have been a visionary with respect to identifying medical product-opportunities and medical market-opportunities. However, he was not experienced in the financial aspects of operating or managing a company. The required repetitive funding activities needed to meet IVAC's growing cash requirements, and the actions by Cramer to obtain the needed investments, inadvertently caused IVAC to be converted (by the Securities and Exchange Commission [SEC]) from a private company to a public company. This happened because Cramer had continued to add IVAC private investors beyond a "headcount" at the time that was permitted by the SEC under its "Regulation A" (since changed.) Some early shareholders are also said to have traded their unregistered shares privately, which was also not permitted by the SEC.

Given the number of IVAC shareholders that existed and the private trading of the Company's shares that occurred, the SEC determined that IVAC was effectively a public company. The SEC essentially caused IVAC to "go public" rather suddenly and in totally unintended fashion with respect to IVAC management's plans.

Overnight, literally, IVAC was subject to all the financial regulations and obligations of a publicly traded company. Yet, it was founded by and being managed by individuals, primarily engineers and sales managers, with no experience in running a public entity - and in fact, minimal experience in running a rapidly growing private company. Several technical and practical errors were made regarding IVAC's operational and financial activities. The errors continued to occur, even as additional funds were raised.

IVAC employed an investment banker (Pressprich & Company, Ken G. Langone, President) to raise still more funds as the company continued to grow and to required cash for manufacturing equipment, work-in-process inventory and expanding distribution activities. The next IVAC monies were raised for IVAC by Pressprich and his investment bank. After the Pressprich funds were brought into the now public company, IVAC had poor to none-existent investor relations. An immediate result was that IVAC share prices (now publicly traded) dropped by more than 75% from the initial offering price - and did so in a fairly short period.

The drop in the "public" stock price eventually resulted in Cramer, who was Chairman of the Board of Directors, losing a proxy fight to Langone, the investment banker who had raised the last funds for IVAC. Langone felt an obligation to his customers - those individuals who had

purchased the IVAC stock via his company's activities. Langone believed someone had to instill better financial management at the company or it would fail. Cramer was non-responsive to Langone's suggestions and later, demands. Langone initiated, and won, what became a bitter proxy fight for control of IVAC. Langone won the proxy fight and Cramer (and his supporters on the IVAC Board) was terminated in May, 1972. Ken Langone became the new Chairman of the Board of IVAC. Cramer and friends were exited from their IVAC jobs and responsibilities in sudden fashion.

IVAC's management and Board, led by Langone, continued the company's progress on the defined pathway. Langone consolidated the focus of the company with emphasis on its inplace thermometer and existing infusion pump business. With continuing success, Lagone negotiated sale of IVAC to Eli Lilly & Company. In 1977, IVAC was acquired by Eli Lilly, Inc. and Lilly operated the company as a subsidiary for several years. In 1995, Lilly sold IVAC to River Medical and in fairly short order, in 1996, River Medical sold IVAC to Advanced Medical Technologies, Inc. (AMT), a company which had already previously acquired IMED - prior to its acquisition of IVAC.

AMT merged its previously held IMED assets into the new IVAC entity, called IVAC Holdings, Inc., and in 1997 changed the name of the company to Alaris Medical Systems and began to phase out the IVAC and IMED identifications of the continuing and the new Alaris IV pump products.

In 2004, Alaris Medical Systems, housing the IVAC and IMED assets along with additional medical devices product lines, was acquired by Cardinal Health. In 2009, Cardinal Health, a public company, "spun out" as a new public company CareFusion. CareFusion includes all former IVAC and IMED product assets of Alaris plus additional medical devices products of Cardinal Health, including Pxyis Corporation, another innovative San Diego medical devices company.

IMED - This second IV pump company was founded by Richard Cramer in 1972, the same year he was terminated by IVAC's new chairman. Thus, the formation of IMED was a direct result of the firings by IVAC. IMED founders included several of the same individuals who had previously founded IVAC, including certain product design engineers and, later, also former members of the IVAC sales staff who chose to resign from IVAC and follow Cramer to IMED in the months after IMED's formation.

IMED, as had IVAC, continued its primary focus on the blending of the continuing innovations in modern electronics with application-specific software for continuingly innovations in fluidics control. The focus was, again, improvement of the delivery of IV fluids and drugs to patients in the hospital.

Cramer's immediate focus at IMED became the design and delivery of a "second generation" hospital IV pump. This IMED pump would correct certain shortcomings he and his team had recognized in their original IVAC designs and products. Cramer also believed that an opportunity existed to dramatically expand the IV pump and IV fluids market beyond its medical applications at the time. Most observers agree that the initial strategic vision, product concepts and market focus for both IVAC and IMED came primarily from Cramer, although critical pump design ideas and solutions were also contributed by members of the IVAC - then IMED - engineering teams.

To appreciate IMED's product innovations one has to understand the basis of the primary innovation delivered by the initial IVAC pumps. IVAC's initial contribution to IV pump technology had been in delivering a microprocessor-controlled "feedback loop" to better control fluid delivery to the respective patient. IVAC's feedback loop (the "drop counter" monitored by the microprocessor) monitored the drops, and thus the fluid flow rate to the patient. Further, the pump, via its feedback loop, could automatically adjust fluid flow (drop counts) to the patient based on the settings made by the attending nurse as the fluid volume changed in the delivery vessel.

The initial IVAC pump products, while dramatic improvements as compared to prior manual IV delivery control, had an inherent shortcoming. The drops could be counted accurately, however the drop size itself was not controlled. Drop size varied with the different fluids being delivered to the patient, depending on various fluid parameters, such as viscosity and/or surface tension. The practical result was that while the drop count could be controlled precisely there was no precise control of the actual fluid volume being delivered to the patient. Bigger drops would deliver more fluid to the patient via a larger volume per drop per unit of time, and drop count provided no indication of actual fluid volume being delivered. Cramer (and IMED's founders and staff) understood this shortcoming in the original design.

IMED delivered the next significant innovation for hospital IV pumps in rather rapid fashion. IMED's new pumps - in its first product release did not count drops, as did IVAC pumps, but rather, the new IMED approach measured the specific volume of fluid being delivered to the patient. Further, the new IMED pumps kept a record of the amount of fluid delivered. In 1974, IMED introduced the world's first "volumetric infusion pump" (Model 922). And, very significantly for IMED's future sales revenue opportunities, this volumetric IV pump included a "razor blade". And, a new "razor blade" was required with each new patient (or new fluid administered to the same patient.) This disposable IMED "razor blade" component created a new and continuing revenue stream to IMED for each pump placement. This "follow-on" revenue stream was, over time, far in excess of the revenue obtained from the original sale of the pump.

The razor blade was a disposable "cassette", called the IMED Accuset Cassette. It functioned similarly to that of a traditional syringe barrel. Fluid to be delivered to the patient flowed from the hanging bag or bottle first into the cassette syringe chamber. Captured in the syringe barrel, the pump then had a mechanism to both control fluid being dispensed and to create a record of how many syringe barrel fillings had occurred for the given patient - a "volumetric" record of administered fluid. The chamber was filled and then the fluid was expressed at a controlled rate by a microprocessor-controlled motor that was driving a positive displacement piston inside the cassette body. The piston, like the plunger of a syringe, pushed the fluid down the tube to the patient. Volume control was now precise and under direct control without the need to "count drops."

Using this design, IMED was measuring the fluid to be delivered to the patient by volume, regardless of "drop size" variance that might exist between different solutions and drugs. The new IMED approach completely eliminated the "drop size" variability issue. At the same time, the positive displacement mechanism delivered a more precisely controlled infusion of any medication (whether low or high viscosity).

The new IMED pump included additional features, such as various alarms and controls providing information to the nurse or doctor about the fluid delivery as it was occurring. There was an alarm if there was air in the infusion line. There was an alarm if there was back pressure in the line due to a patient shifting his or her weight onto the IV tubing, closing off the flow. And, importantly, the nurses no longer had to calculate the "drop rate" and then convert it to the doctor's specified volume of medication to be delivered to the patient. With the new IMED pump the direct volumetric measurement capability eliminated the need to convert desired volume per time frame to a drop rate. This feature was seen as a significant convenience advantage by the nursing staff and it also eliminated any potential "drop calculation" errors, which the physicians and nurses liked.

By 1975, IMED was rapidly expanding its product line. New IMED pumps could now detect an "air bubble" in opaque fluids, where the bubble might be difficult for the nurse to see in the plastic tubing. Higher flow volume pumps were introduced for specific purposes other than just IV drug delivery. These pumps could be used for wound irrigation, for instance. An IMED pump line was offered with feedback circuits permitting the pump to become a "slave" element controlled by the hospital computer. IMED pumps began to become even more numerous in intensive care units.

IMED's innovations began to drive significant expansion of use of IV pumps into more and more medical applications, including "TPN" (Total Parenteral Nutrition), which in itself became a very large business.

The improving precision of IV drug delivery via the positive displacement pumps of IMED permitted pharmacists and physicians to begin to make more and more complex drug and nutritional "blends" for patient use, further expanding demand for the pumps (and cartridges.) Many people continue to credit Richard Cramer with having been the driving force behind the recognition - and then the delivery - of products permitting integration of the control of drug infusion into a comprehensive and integrated "technology package" consistent with the total needs of the hospital physician and the hospital pharmacist.

IMED's volumetric pumps began to both take significant existing IVAC business and to grow the total size of the pump business as more and different medical fluids could be delivered accurately using the new principle of operation of the IMED pumps. IVAC's competitive response was to introduce its own line of volumetric pumps. However, there either was a design error in the IVAC pump or production errors in manufacture. Something caused improper function in the marketplace, resulting in a complete recall by IVAC and removal of all of its new volumetric pumps from the market. IVAC was off the market with a volumetric pump for about three years, by which time IMED had created such a market presence that IVAC never recovered its former market strength, market share, nor historic rate of growth.

The two IV pump companies, IVAC and IMED, became - and remained aggressive competitors in the IV pump market for two decades. Ironically, the two companies were later each acquired by a single company in 1996.

Cramer, however, continued to suffer at IMED financial management difficulties and issues in the operation of IMED, somewhat similar to his experience at IVAC. The difficulties of the financial issues regarding IMED's progress may be best understood by some brief trade press and San Diego press mentions of that era.

Trade Publication article headlines (ca 1981) re: IMED

- IMED went from being nearly bankrupt to a sale price of \$465 million in less than five years. The company had inspired product design, exceptional direct selling, poor management.
- IMED from Bankrupt status to a \$465 million sale in four years

July 09, 1991 CHRIS KRAUL | SAN DIEGO COUNTY BUSINESS EDITOR

- IMED's 1st Public Offering Could Raise \$55 Million
- IMED Corp., a San Diego-based health care company that has changed ownership three times in the past decade--at successively lower prices--plans an initial public stock offering this fall that could raise up to \$55 million.

• IMED makes a line of infusion pumps and disposable accessories that deliver intravenous drugs to hospital patients. The company, which has 526 employees in San Diego and 1,100 overall, reported sales of about \$90 million last year.

Returning to the discussion of IMED's progress as a company, as mentioned, it had been formed in 1972 by former IVAC founders. Not quite ten years after formation, in 1981, IMED management decided to sell the company. IMED chose as its investment banker Shearson (Fred Frank was the individual at Shearson who managed activities for IMED). IMED expected to receive offers from each of the market-significant pump players and from certain pharmaceutical companies.

Abbott was a relatively recently announced entrant into the IV pump business at that time. Some IMED discussions were held with Abbott about an acquisition, however no purchase offer was ever received from Abbott. This lack of an Abbott offer surprised most observers at the time. Some suggest that the reason no offer was received from Abbott was that Cramer was very concerned that Abbott's primary interest might be IMED technical and market distribution details, not sincere purchase interest. Abbott was just releasing a new IV pump product line of its own design and as a result, Cramer instructed the banker not to disclose to Abbott the same extensive details about IMED products typically disclosed during "diligence" to a potential suitor. Abbott was not provided the same level of either the technical or the market distribution details provided to other potentially interested buyers. Whether Cramer was correct or incorrect, a formal purchase offer was never received from Abbott. Among offers that IMED received, one came from Warner-Lambert (W-L), which offered \$465 million for the company. Phizer offered \$425 million.

The Warner-Lambert offer was accepted. The deal closed in August, 1982, and at the time it set a new U.S. record for the highest price paid for acquisition of a private company. Not atypical of acquisitions of "high tech," aggressively managed young companies, W-L management was not satisfied with results of the acquisition. Only four years after the acquisition, W-L made the decision to sell IMED.

In 1986, the IMED assets were sold to "The Henley Group" (a holding company) for \$163 million - W-L's purchase price had been \$465 million.

In 1990, after some internal transfers of IMED assets among Henley's various operations, including "Fisher Scientific", 93% of the IMED Division was sold to Advanced Medical Technologies, Inc. (AMT), a San Francisco company, for \$106 million.

AMT acquired with the IMED assets a production facility in Ireland. AMT sold the Ireland production facility relatively soon after acquiring the IMED assets, selling the production facility for \$3.7 million.

In 1996, AMT made another IV pump acquisition when it acquired the former River Medical company which had changed its name to IVAC Holdings, Inc. Shortly after the acquisition of IVAC Holdings by AMT, AMT's already-acquired IMED assets were melded into the newly-acquired IVAC Holdings. The senior IVAC Holdings management team survived the purchase by AMT and became the operating management for the new AMT entity, which was soon renamed. Most of the former IMED senior management team at AMT was displaced.

Soon after melding the two assets, AMT changed the name of the corporation from IVAC Holdings to Alaris Medical Systems. Additionally, closely following the IMED acquisition in 1997, IVAC Holdings, now with a name change to Alaris Medical Systems, acquired IMED International Trading Group, consolidating certain international distribution rights for IMED-brand products within Alaris.

Also in 1997, Alaris Medical Systems began to phase out the IVAC and IMED product branding identifications. Alaris began to "brand" IV pump products using its brand names for all new products and, eventually, for all pump products.

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In December, 2013, CareFusion, with revenues of \$3.5 billion in 2013, announced intent to acquire 40% of the equity of Caesarea Medical Electronics (CME), an Israeli infusion pump manufacturer. According to statements by CareFusion, while CareFusion has an extensive existing infusion pump business and product line, the primary market segment served by each of the two company's product lines differ. CareFusion's infusion pumps are sold primarily to the hospital market and CME's infusion pumps are sold primarily to the "ambulatory" infusion market, for patients in settings such as oncology and other doctor's office-based clinics, and for use with patients who are in a home care setting. CareFusion had previously acquired certain technology from CME, which is known for its expertise in making compact, portable infusion pumps.

Products manufactured and sold by the two original San Diego IV pump innovators, IVAC and IMED, were among the first medical devices products manufactured in large quantity in San Diego. The original infusion pump inventions, product technologies, and continuing product lines of these two companies have been housed in a succession of companies that have acquired, divested, divided, and sometimes repurchased the subject inventions and product

lines of IVAC and IMED. Regardless of company name or product line(s) location, the products of these two San Diego companies held the lion's share of the infusion pump market share throughout the United States and Europe for many, many years. At one time the installed base of products from these two companies held, at the same time, either the number one or number two market position in the U.S. and in eleven countries in Europe. And, when the San Diego-produced infusion pumps were not either number one or two in market share position in a given country in Europe, they were typically in the number three market share position.

Pumps from one or the other of these innovators also commanded the largest installed base of infusion pumps in Canada and in Australia and held strong market positions as well in Latin America and Asia.

From many perspectives, one could state that the improved delivery of IV fluids in a hospital setting resulted in the creation of what is now known as the "Total Parenteral Nutrition" (TPN) market. San Diego's IV pump innovations were key to the creation of the chemotherapy infusion market, by providing the ability of an infusion pump to deliver accurately and precisely the "complex drug" combination needed for oncology patients.

Each of these infusion-related market segments, TPN and chemotherapy, resulted from the original innovations of these two San Diego pioneers in the Life Sciences Cluster - not to mention the early innovations in the electronic medical thermometers and the development of certain specialized patient-monitoring instrumentation that comprises important components of the "vital signs" or critical care instrumentation used in hospital Intensive Care and Trauma Care Units.

See also IVAC Genealogy chart.

- 1. Fikes, Bradley J (May 17, 2013). "Richard Cramer, Biomedical Industry Pioneer". *San Diego Union-Tribune*.
- 2. Kraul, Chris (July 9, 1991). "Imed's 1st Public Offering Could Raise \$55 Million". *Los Angeles Times*.
- 3. Fikes, Bradley J (May 18, 2013). "Richard Cramer, Father of San Diego's Biomedical Industry". *San Diego Union Tribune*.
 - 4. Johnson, Greg (June 17, 1986). "Ivac Founder Chosen to Guide Fisher Scientific". *Los Angeles Times*.

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IVAC GenealogyDigital thermometers & Intraveous Pumps

