

History of XYTEX INTERNATIONAL LTD. 1975 – 2005

In 2005 Xytex International Ltd. has become a major human gamete bank serving physicians and their patients globally from offices in Georgia, USA. Xytex began in 1975, aspiring to be a comprehensive bank of many different human tissues and organs; this vision would change.

Origination

The initial impetus for Xytex was animal research conducted at the Medical College of Georgia (MCG) in Augusta and at Augusta College (subsequently renamed Augusta State University). In the 1970's human kidney transplantation at MCG achieved worldwide prominence due in part to its pioneering research on in vitro kidney preservation led by Arthur L. Humphries, M.D. As a part of that MCG program, Armand M. Karow, Ph.D. worked to develop a means to cryopreserve (freeze) kidneys, hearts, pancreatic islets of Langerhan, and other tissues, including human sperm. The results permitted visions of freezers filled with human organs for transplantation, much like a blood bank.

In 1975 Dr. Karow working with urologist Roy Witherington, M.D., demonstrated, as had others elsewhere, that human sperm survived cryopreservation. They placed sperm mixed with glycerol into plastic straws (about 1 millimeter in diameter and 5 centimeters long) before immersion in liquid nitrogen (-197°C). With this procedure the sperm survive freezing for years, possibly even decades. When needed for insemination, the frozen sperm could be packed in dry ice and shipped to clinicians who would thaw it for immediate use.

John B. Black, Ph.D., a Professor of Biology at Augusta College worked closely with Robert B. Greenblatt, M.D., another Augusta medical pioneer. Their field was reproductive endocrinology. Drs. Black and Greenblatt saw that a clinical need in male fertility could be met by a cryobank of fertile human sperm. In fact, a few sperm banks had already been started in America and one had even been attempted in Atlanta but failed. Drs. Black and Karow agreed that a human tissue bank could, initially offer cryopreserved sperm. Although MCG administration declined the opportunity to initiate clinical cryobank services, the door was opened to begin this program privately. To be successful, it would have to serve patients throughout the southeast; and its chances to succeed were good since it would be the only cryobank in this region.

It was known that a typical sperm count has 50 to 60 million motile (swimming) sperm per milliliter, so Drs. Black and Karow decided that the new sperm bank would guarantee 55 million motile cells per milliliter of the *thawed* material. This was an exceptionally high standard; only one in 10 men had sperm that could meet it. Nevertheless, the standard was felt to be important because most physicians believed thawed sperm had a much lower pregnancy rate than non-frozen sperm. (Their belief held true only for specimens that disregarded the post-thaw concentration of motile sperm.)

On September 24, 1975 the state of Georgia granted the petition of Dr. Black, Dr. Karow and Mrs. Cleo C. Jordan to charter Xytex Corporation as a comprehensive medical tissue and organ bank. Xytex was a name created from the phonetics of cell science (cytology) and technology, and in 1978 the United States government registered it as a trademark of Xytex Corporation.

From its inception Xytex viewed itself as a provider of services to physicians, that is as a clinical laboratory. Xytex would work with patients only through physician referral. (Other American sperm banks operated as a service to patients.) Xytex communicated with physicians early on through personal visits, printed catalogs and advertisements in *Fertility and Sterility*, the journal of the American Society for Reproductive Medicine.

The three founders raised \$20,000 for the new venture, half through their own purchase of Xytex stock and half through loans to the new corporation. Carl J. Surrent, an Augusta attorney, supervised the legal transactions. The three stockholders elected themselves to the Board of Directors and at their first Board meeting (October 11, 1975) Dr. Karow became president; Dr. Black, vice president; and Mrs. Jordan, secretary-treasurer. (Later that year in December, these stockholders elected Mr. Surrent, Dr. Greenblatt and Dr. Witherington to the board.) Facilities, approximately 300 square feet, were leased as Suite A, 1519 Gwinnett St. (subsequently re-named Laney Walker Boulevard) in Augusta.

The first task that autumn was to get a license as a medical laboratory. The state of Georgia had clinical laboratory regulations for blood banks and diagnostic laboratories. One of the categories of activities recognized by the state for diagnostic clinical laboratories was "Tissue Bank." Perhaps the state envisaged tissue banks as being repositories for samples of pathologic tissues, but the state saw fit to grant Xytex a clinical laboratory license as a bank of living tissues for transplantation. Dr. Black and Dr. Karow were each awarded licenses as clinical laboratory directors. Dr. Karow agreed to be a back-up to Dr. Black. The laboratory passed the required annual inspection, and its license has been renewed every year since. In 1976 Xytex earned a clinical laboratory license from the federal government and subsequently tissue bank licenses from the states of New York (1992), Maryland (1994), and California (2004). As a licensed clinical laboratory, Xytex in 1976 tested its semen donors and their semen. Xytex set standards for sperm function after thawing. All donors were tested for infectious diseases (syphilis; gonorrhea) and for chromosomal abnormalities. In fact, Xytex set the industry standard with its early testing of donors.

The second task was to generate revenues. Dr. Greenblatt referred the first patient to Xytex, a physician desiring to have his own sperm cryopreserved for his personal use following sterilizing cancer therapy. Dr. Black began recruiting sperm donors from students at MCG and Augusta College. Dr. Karow traveled throughout Georgia and adjoining states to tell physicians about the new service. Favorable publicity was received from *The Augusta Chronicle*. Ms. Jordan managed the office, making certain that the phone was answered and orders recorded.

Generation of cash flow was difficult during the first fiscal year (October 1975 – September 1976). At the end of fiscal year 1976 the new corporation had an income of \$19,600 and expenses of \$37,000. Salaries and other obligations could not be paid in a timely manner. Almost all revenue came from donor semen. Efforts to generate significant

revenues from clinical laboratory testing (activity concomitant to evaluating semen and semen donors), from self-storage, and from other tissues were insufficiently remunerative.

Growing Up

The Board of Directors had visions of expanding banking operations to include skin, cornea and other human tissues. In 1977 it attempted a collaborative skin bank with MCG and the Medical University of South Carolina (Charleston) but the venture was not successful. In 1978, Mr. Herbert Elliott, a funeral director and S. Allen Stocks, M.D., an ophthalmologist with experience in corneal transplantation, were elected to the Board. In 1979 the corporation hired Brenda Mertins, a technician experienced in corneal acquisition, to assist in developing a market for cadaveric tissue, primarily skin and cornea. That year Xytex explored the possibility of providing skin bank services to the Burn Unit of Doctors' Hospital, Augusta. Xytex manufactured a corneal-scleral preservation kit in 1979 at the request of ophthalmologists at MCG. In 1981 consideration was given to the creation of a voluntary non-profit foundation to promote donations of cadaveric tissue, a concept the corporation could not bring to fruition largely because of a lack of interest by Augusta area physicians. However, donor semen sales increased from 750 units in fiscal year 1976 to 1,400 in 1977 and to 2,800 in 1978! This growth made it necessary to move to a larger office, Suite 6 at 1021 Fifteenth St., Augusta. In fact, recruiting sufficient donors to meet the demand became a significant problem. Semen sales enable Xytex to become profitable in 1980 and subsequently sustained its profitable growth primarily through semen sales. Retained earnings became positive in 1982. So, in 1982, Xytex Corporation acknowledged that its sustaining market was reproductive medicine. All future efforts would be directed to serving the needs of that market. By 1984 the huge response of the reproductive market actually forced Xytex to create a waiting list for physicians wishing to receive semen!

Early on at Xytex young cancer patients facing therapeutic loss of their fertility arranged for self-storage of semen. To facilitate this service, a system utilizing dry ice was devised so that patient's remote from Xytex could freeze their own semen and ship it to Xytex for long-term storage (LTS). This system, originally called a CryoCell Kit, later became simply "CryoKit." In 1981 Xytex was awarded a patent for the CryoCell Kit™.

The activities of Xytex in the reproductive market gained favorable recognition in the world press. In 1979 the *New York Times*, the *Reader's Digest* and *Medical World News* covered Xytex. By 1982 Xytex was featured on television in Australia and England. By 1992 national and international media were featuring Xytex innovations many times each year. International semen shipments (Canada) commenced in 1983.

The corporation was clearly maturing. In 1982 Xytex moved its headquarters to its present location at 1100 Emmett St., Augusta. The corporation purchased the 1,500 square foot building in 1986 and added 1,500 square feet in 1990. A second addition of 4,500 square feet was completed in 2001.

Xytex experienced a constant need to recruit additional semen donors to meet market demand. Donor recruitment has been challenging. In 1982 Xytex established a collection site in downtown Athens, Ga., on Broad St. directly across from the University of

Georgia. The site closed in March 1984 in part because its supervision by Augusta was ineffective. An effort was made in March 1984 to have a collection site in south Augusta. This site was closed six months later due to poor donor response. In October 1985 Xytex opened an office in Atlanta (730 Peachtree St., NE; Suite 935) convenient to students at three major universities (Atlanta Universities; Georgia Institute of Technology; Georgia State University). This office became highly successful and was relocated to the larger, more accessible Suite 175 at 1776 Peachtree St., NE. which was further enlarged in 2005.

Since an international sperm bank is expected to have a larger number of donors and ethnic diversity than is available in Atlanta, a variety of options were considered, including the outsourcing of semen prepared to Xytex's exact specifications. The successful, economical solution ultimately proved to be the creation in 2000 of a subsidiary, Xytex Canada Inc., located adjacent to the University of Toronto.

Technology Leadership

Xytex sustains its heritage as a leader in providing technologically excellent services. In 1983 the original shipping method using heavy (50-lb.) dry ice as a refrigerant was replaced with relatively lightweight (10 lb.) liquid nitrogen dry shippers. These containers included material that absorbs liquid nitrogen, preventing spillage and therefore acceptable to airlines.

In 1985 the acquired immunodeficiency syndrome (AIDS) was recognized as an American epidemic. Xytex's response on October 9, 1985 was an irrevocable quarantine on all semen for two months prior to shipment. Xytex was the first sperm bank to institute a quarantine period. Later (1988) the national Centers for Disease Control recommended a quarantine period of six months which Xytex readily adopted. This recommendation, of course, meant that semen had to be cryopreserved for at least six months and boosted demand for sperm bank services. Physicians who actually preferred to use non-frozen sperm were essentially required to use frozen semen.

In January 1988 Xytex decided to offer a less expensive alternative to its guaranteed 55 million motile cells per milliliter, namely 30 million motile cells per milliliter. Later (1996) it was learned that doctors believed that the pregnancy rate was the same for both options, and patients (who wanted the best for their unborn child) regretted not choosing the higher guarantee option. Therefore sales for both were less than optimal. Based on this knowledge, the higher concentration option was discontinued in 1996, therefore eliminating an emotional struggle for patients.

In 1991 Xytex began offering "washed" sperm for physicians preferring intrauterine inseminations (IUI). With conventional insemination, the sperm is placed inside the vagina at the cervix, the entrance to the uterus. With IUI the sperm is actually placed inside the uterus. Unwashed semen contains chemicals that cause painful contractions of the uterus and subsequent loss of the semen. These chemicals are removed by a procedure called "washing." Xytex improved the technique and by performing it for the physician prior to shipment it was convenient for physicians. Xytex maintained its post-thaw guarantee of motile sperm in the washed preparation. Physicians liked IUI so much that in 1994 Xytex

provided sperm in vials to facilitate the use of IUI catheters. With this motivation Xytex discontinued packaging of sperm in straws and a 19-year procedure ended.

While Xytex continues to be “high tech,” it is just as committed to being “high touch.” Xytex believes that semen recipients and their offspring should have as much information about donors as donors are willing to provide. Around 1988 Xytex began writing its catalogs so that physicians could share them with patients. Presaging the Human Genome Project by a decade, in August 1989 Xytex began a unique program called Patriarch™ to store in perpetuity the complete genetic code of each new donor. This was done by cryopreserving white blood cells obtained from donors making possible genetic studies that may be required by the health of donor-produced children. Subsequently, Xytex became the first sperm bank to provide adult photos of donors (Photofile™ in 1994), baby photos of donors (Babyfile™ in 1996) and even videos of donors (Videofile™ in 1998). These information options, while not available on all donors, have increased significantly in recent years. In 2000 all new donors were required to undergo personality testing [California Psychological Inventory™ (CPI)] in addition to the previously (1993) required personal essay. The CPI is interpreted for Xytex by a professional psychologist and is made available to patients and their physicians. Xytex created its Web site in 1999, using it to post donor information. This Web site has been extensively renovated several times to increase its usefulness. In 2005 it became accessible in French and Spanish as well as English.

Since its earliest days, Xytex stored semen for later use by client depositors, such as men with cancer. By 1999 changes in technology and public understanding of tissue storage services prompted a corporate decision to create a marketing unit focusing on tissues frozen by patients’ physicians. The service assumed the responsibility, the long-term liability of safekeeping the tissues for years. Initially the unit offered semen storage and then broadened its purview to other reproductive tissues such as embryos, ovarian tissue and testicular tissue. In 2000 this marketing unit was incorporated as a Xytex subsidiary based in Griffin, Georgia: Xytex Tissue Services, Inc. (XTS), in 2005 renamed Xytex Tissue Storage Inc., directed by Kate Howell.

To complement its ability to provide donor semen, Xytex established an egg donor program in 2003: Xytex Ovations Ltd., directed by Renee Koon. This program medically qualifies women as egg donors, markets them on the Web, and sends them nationally to physicians with patients needing an egg donor. At the inception of this program, cryopreserved eggs could not be provided clinically with assurance of fertilization.

Xytex, a spin off from MCG, originated from medical research. Xytex leadership has always had a clear vision of a vibrant, rewarding independent research program contributing to corporate advancement. Prior to 2005 Xytex employed persons in a research capacity and conducted collaborative research with Augusta State University, the Medical College of Georgia, Paine College and the University of Kentucky School of Medicine. Results of Xytex research has been published in scientific journals and presented at national and international research meetings.

Xytex expanded its commitment to research by creating Xytex Research Inc. in 2005. Xytex Research is expected to sustain and increase the competitive market position of Xytex.

Initially, Xytex Research was located in laboratory space at the Medical College of Georgia, Augusta, in walking distance from Xytex headquarters.

As early as 2000 the leadership of Xytex determined that corporate growth could be enhanced by adopting the principles of total quality management (TQM). In 2002 the corporation engaged Georgia Institute of Technology to assist in the implementation of TQM leading to ISO 9001:2000 standards established by the International Organization for Standardization. This achievement would not only improve management practices, but would also increase acceptance of corporate services in countries beyond America, and it would also help the corporation prepare for regulation by the U.S. Food and Drug Administration. ISO certification was achieved in 2005.

Also in 2005 Xytex International Ltd. was created to manage the other corporate units of Xytex: Xytex Corporation, Xytex Tissue Storage Inc., Xytex Ovations Ltd. and Xytex Research Inc.

XYTEX INTERNATIONAL LTD.

Time Line 1975 – 2005

- 1975 Incorporation (24 September): 1519 Laney-Walker Blvd. (originally:
Gwinnett St., Augusta, Ga.
Clinical laboratory license (Georgia)
First semen services, including infectious disease testing; 55 million motile
cell Thawed
- 1976 Clinical laboratory license (federal)
Chromosome analysis of all semen donors
- 1978 Augusta office relocation to 15th St.
Xytex registered as trademark of Xytex Corporation
- 1979 Corneal-scleral (C-S) preservation kit
- 1980 Profitable
- 1981 CryoCell Kit™ patent
- 1982 Augusta office relocation to 1100 Emmett St.
Focus on reproductive medicine; discontinue C-S Kit
- 1983 First use of liquid nitrogen dry shippers; discontinue dry ice shipments
First international (Canadian) shipments of semen.
- 1985 First office in Atlanta, Ga.
Quarantine for human immunodeficiency virus (HIV)
- 1986 Expansion of Augusta site
- 1988 Introduced 30 million motile cells thawed
Patient catalog (annual)
- 1989 Patriarch™ diploid cells
- 1991 Introduced washed semen
- 1992 New York state license
- 1993 Donors' personal essays

1994 Photofile™
Maryland state license
Semen in vials; discontinued straws

1996 Discontinued 55 million motile cells thawed
Babyfile™

1998 Videofile™
Annual revenue exceeds \$1 million

1999 Web site launched

2000 Xytex Canada Inc.
Xytex Tissue Services Inc. (XTS)
XytexXtra newsletter premieres
California Psychological Inventory™ (CPI)
Registration with Health Canada

2001 Expansion of corporate headquarters in Augusta
Registration with Food and Drug Administration (US)
Identity disclosure donors

2002 Swiss affiliate site

2003 Xytex Ovations, Ltd.

2004 XTS becomes Xytex Tissue Storage Inc.
California state license

2005 Corporate reorganization forming Xytex International Ltd.
Xytex Research Inc.
ISO 9001:2000 certification
Expansion of Atlanta site