

Adult Stem Cell Fact Sheet

By

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Introduction

In light of recent physician, patient and press interest in the use of autologous stem cell treatments, we at the New York Stem Cell Summit are releasing effective today this Adult Stem Cell Fact Sheet to help the press and others understand more accurately the role that autologous stem cell therapies play in medicine in the United States today.

Harvesting stem cells from adult patients and then re-injecting them into the same patient (autologous stem cell use) has been a routine therapy in U.S. medicine for decades. More recently, as stem cell research has developed, the precise method of harvesting, processing and then re-injecting into patients has changed and improved.

Roughly 1 million patients have been treated with their own stem cells since the mid-1980s in the United States.

In this fact sheet, we will first describe the purpose of autologous and allograft stem cells in medicine, the history of autologous stem cell therapies in the United States, the number of companies who are supplying equipment to facilitate autologous stem cell therapies in the United States, the size of this as a commercial business, the future of these therapies and then a short bibliography of clinical studies regarding the use of adult stem cells in the United States.

Stem Cell Use in the United States

The most difficult element to understand about adult stem cells is their purpose in the human body. While embryonic stem cells are, in effect, the blank slate upon which all of the tissues, organs and structure of the human body is drawn, the adult stem cell has a different, though related, overall function. It is a repair cell. Sitting quiescently in bone marrow, tooth enamel, adipose (fat) tissues and other places in the body, these cells “wake up” upon receiving signals related to injury—inflammation.

Their function is to begin the cascade of healing when the human body is injured. The number of stem cells in an adult human begins declining shortly after birth. It is, in fact, this decline in the number of stem cells that ultimately leads to wear, deterioration and, finally, death.

So, when the human body is injured, the adult stem cells “wake up,” move through the body to the site of injury, express proteins to down regulate inflammation, express other proteins to stimulate new cellular growth, recruit new growth factor proteins and then, themselves, begin to change into the very cells that have been damaged. Throughout this process, these cells are giving and receiving signals with the surrounding environment. This is an extremely important aspect and one of the central discoveries regarding stem cells and the point that differentiates them from any other cell.

The most common therapeutic use of stem cells by physicians in the United States is to harvest them from one part of the body where they exist in greater amounts and then re-implant them at the site of injury—where they are most needed but are in short supply. For adults with diminishing stores of stem cells, this is an effective way to stimulate healing at sites of injury.

Frankly, this process of harvesting cells (be they bone marrow, skin, fat or any other cells) from one part of the body and then re-implanting them in another part has been an important aspect of medicine for, literally, hundreds if not thousands of years.

What makes this discussion so relevant is that physicians are now specifically targeting stem cells (i.e., repair cells) for concentration, re-implanting and expansion before re-implanting.

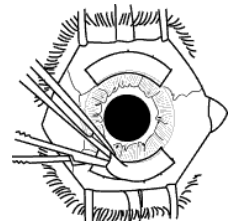
One problem with autologous use of adult stem cells is that the quantity of cells is only as good as the patient’s supply. Older patients with fewer stem cells will not likely have enough to overcome, say, osteoporosis when a bone fractures, or a tear in cartilage or a dead spot on the heart muscle, etc. In those cases, one strategy is to put the patient’s small number of stem cells into a culture media and allow them to expand. This is the next logical step in the development of modern autologous stem cell treatment.

Autologous Stem Cell Use in the United States

The discovery that a particular cell existed which was, in effect, a blank slate upon which all other cells can be developed stimulated an explosion of basic scientific research. Through the 1950s, 60s and 70s this research characterized these cells, began to unravel their secrets and begin to provide clues as to their therapeutic potential.

Almost immediately, scientists landed on the idea that physicians could harvest stem cells from one part of the human and re-implant them in another. The first widespread practice of doing exactly this therapy was among ophthalmologists.

Limbal stem cells Limbal stem cell transplants were the first autologous stem cell transplant and were first used in the 1970s. In this procedure limbal stem cells are taken from the healthy eye of the patient or a live donor (usually a sibling or a parent). During this outpatient procedure, which lasts about one hour, stem cells are harvested from the healthy eye or the donor's eye and then transplanted to the affected eye. If the transplant is successful, the stem cells will produce a new layer of epithelial cells in the patient's eye. The success rate of growing the new cells from transplanted limbal stem cells varies from 25% to 70%, depending on the underlying condition of the eye.



A stem cell transplant alone can make a patient's vision considerably better. For other patients, the stem cell transplant sets the stage for what follows—a cornea transplant. There are about 40,000 cornea transplants performed each year and they are typically very successful. Limbal stem cell transplants are a routine part of modern ocular surgery and have been for more than two decades. Tens of thousands of patients have had stem cells harvested from one eye and then transplanted in the other eye. This is an extremely routine procedure.

According to the literature if a surgeon attempts a cornea transplant WITHOUT limbal stem cell transplant, the cornea transplant nearly always fails.

We estimate that **there have been more than 500,000 autologous limbal stem cell transplants** since this technique first gained popularity in the 1980s.

Bone Marrow Stem Cells The best known and most widely characterized adult stem cell in the literature is the mesenchymal stem cell (MSC). This is the stem cell most physicians are seeking when they harvest bone marrow from a patient and then transplant it in a concentrated form back into that same patient for, typically, bone fracture repair or to help stabilize a degenerated back by using a spine fusion technique. Bone marrow aspiration and then concentration has been a common practice for decades.

Bone marrow is a rich source of not only MSCs but also growth factor proteins and the nutrients required for healing and repair. Literally thousands of clinical studies have been written about the use of such concentration systems to augment bone healing and spine fusion.

As it happens one Texas-based company (SpineSmith – also known as Celling Technologies) supplies FDA approved systems for concentrating bone marrow and thereby create a stem cell rich material for transplanting into the patient at the point of care. SpineSmith employs 55 people and provides stem cell systems to about 350 surgeries *every month*—200 of which are in Texas.

Every year, according to data we've seen from the Centers for Medicare and Medicaid Services (CMS), the American Academy of Orthopaedic Surgeons (AAOS) and private insurer data as well as our own estimates, there are **more than 100,000 patients treated with bone marrow concentration systems generally.** The number of such systems which are concentrating the patients existing MSCs is now, we estimate, around 20,000 annually. There are, we estimate, **about a dozen companies currently providing systems to surgeons which concentrate the patient's stem cells for re-transplanting.** U.S.-based firms that offer such systems to physicians include; PALL Corporation, JNJ's DePuy, Inc., Tornier, Inc., Harvest Technologies Corp. and SpineSmith.

Adipose (or Fat) Tissue Stem Cells Quite a bit of the research into adult stem cells has focused on adipose tissues since, according to numerous studies; they contain the highest concentrations of adult stem cells. But harvesting adipose tissue and then concentrating and extracting stem cells have proven to be a very difficult process. One company, Cytori Therapeutics, Inc. in San Diego has the most advanced system in the world. In 2007, it received the **FDA's 510(k) clearance to market its Cytori Autologous Fat Transfer (AFT) System, that offers the ability to "transfer a patient's own adipose (fat) tissue from one part of a patient's body to another at the point-of-care in the same surgical procedure."** This is a system for concentrating adipose tissue including its existing stem cells and then transplanting these concentrated tissues back into the patient. Most of Cytori's sales are in Canada, the European Union and Asia. We don't have an estimate as to the number of surgeries in the U.S. which employ adipose tissue concentrators for the purpose of creating a stem cell rich transplant.

Allograft Stem Cell Use in the United States

Virtually every living tissue transplant (heart, lung, liver, kidney, cornea, bone, etc.) has living cells including adult stem cells. The act of donating an organ or tissue (heart, liver, kidney, skin or bone) and then re-implanting that same organ or tissue into a patient is known as a transplant. The tissue itself is called “allograft” tissue.

Allograft transplants are regulated intensely by the FDA but the form of regulation is different than that used for medical devices or drugs. The principal concerns with regards to allograft tissues are safety and homologous use.

The use of allograft transplants is well established and there are approximately 2 million surgical and dental procedures performed annually which use donated allograft tissues to augment and supplement the patient’s own tissues.

Living cells have been an integral part of transplants from the beginning. After all, how useful is a heart transplant with no living cells?

Recently some allograft bone suppliers have been measuring the number of adult stem cells in their transplants and then removing extraneous materials in order to concentrate the number of such adult cells. The most widely used of these stem cell rich transplants is a cell rich bone transplant has been sold in the U.S. under FDA rules for about eight years and is being used in, we estimate, about 40,000 patients annually. Since first introduced, **we estimate that such allograft stem cell rich transplants have been used in approximately 130,000 patients in the U.S.**

The U.S. companies that are providing stem cell rich allograft bone are AlloSource, based in Denver, Colorado, and the Musculoskeletal Tissue Foundation, based in Edison, New Jersey. Both companies operate as not-for-profit entities and both companies have been supplying stem cell rich materials for use in patients since the early 2000s.

Companies Who Supply Systems for Autologous Stem Cell Harvesting or Stem Cell Rich Allografts

The following is a partial list of the firms who are supporting this emerging industry with either:

- Devices which can facilitate point of care harvesting of bone marrow or adipose tissues and then concentrate the existing stem cells for re-implanting into the patient.
- or stem cell rich allograft tissues

AlloSource
 Alphatec Spine, Inc.
 Amedica/US Spine Corp.
 AncBIO
 BioD
 Cytori Therapeutics, Inc.
 Harvest Technologies Corp.
 Mesoblast Ltd.
 Musculoskeletal Transplant Foundation
 Neostem, Inc.
 NuTech Medical
 NuVasive, Inc.
 Orthofix International
 Osiris Therapeutics, Inc.
 Pall Corporation
 Parcell Laboratories
 RNL BIO
 SpineSmith Partners LP
 ThermoGenesis Corp.
 Tissue Genesis, Inc.
 Vet-Stem, Inc.

Not included in this list are companies that supply devices for concentrating bone marrow, but do not specifically target stem cells for concentrating. Virtually every major supplier of orthopedic products offers physicians systems for harvesting bone marrow and then also concentrating it. Bone marrow is one of the prime sources of adult stem cells. The act of concentrating bone marrow will necessarily also concentrate the existing population of stem cells. So, in that sense, companies like Johnson & Johnson, Zimmer Holdings, Inc., Stryker Corp. and others are also selling stem cell concentration systems.

U.S. Government as Purchaser of Stem Cell Therapies

The U.S. government is about to be the largest purchaser of stem cell products in the world. Three years ago the Department of Defense gave a \$224.7 million contract to Osiris Therapeutics (based in Maryland) for its adult mesenchymal stem cell (MSC) therapy as a medical countermeasure to nuclear terrorism and other radiological emergencies. Upon FDA approval of Osiris's product (in Phase 3 Animal Rule trials), the U.S. government will purchase at least 20,000 doses at \$10,000 per dose. And then stockpile these doses in freezers around the United States.

(The FDA Animal Rule states that the FDA may grant marketing approval based on adequate and well-controlled animal studies when the results of those studies establish that the drug or biological product is reasonably likely to produce clinical benefit in humans.)

MSCs are stimulated by biochemical stimuli and move through the blood stream to points of inflammation (like arthritis). Once there, MSCs coordinate healing and tissue regeneration at that point of injury or inflammation by producing growth factors, blocking inflammation and reducing scarring. Importantly, MSCs do not trigger the patient's immune system.

Soon the U.S. government will begin to stockpile injectable doses of stem cells around the U.S.

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Stem Cell Market Overview

In 2010, the number of stem cell suppliers in the U.S. market doubled. Our estimate of hospital/clinic purchases of either stem cell based products or equipment to collect and process stem cell therapies is \$139.6 million, an 80% increase over the \$78 million (adjusted) levels reached in 2009.

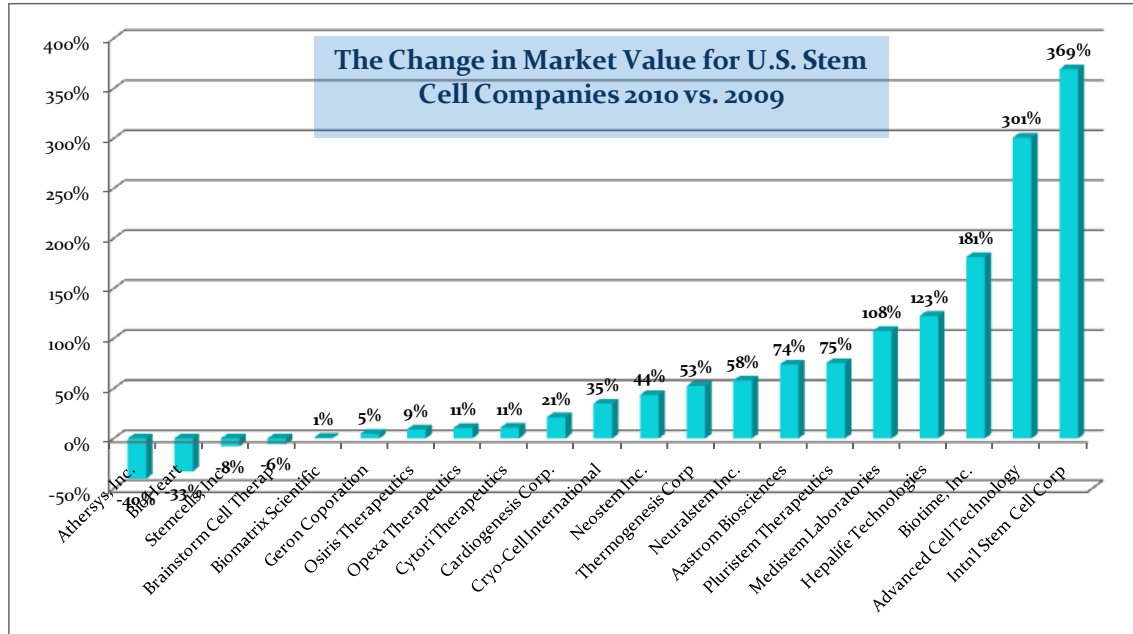
The number of patients who were treated with stem cell (or progenitor cell) therapies in 2010 is just over 90,000, which brings the total treated in the United States since 2006 to 189,000, we estimate.

This surge in the use of stem cell therapies is even more noteworthy given the general media's lack of coverage and ignorance about how stem cells are coming to market and how physicians have employed them.

In 2010, we estimate, aside from the use of stem cell therapies in eye repair or the use of bone marrow transplants, eight companies supplied either allogeneic stem cell therapies to more than 1,000 hospitals or clinics in the United States and two companies supplied systems which allowed physicians to deliver autologous stem cell therapies to patients.

In 2010, the 21 public companies that are either supplying stem cell therapies, equipment to facilitate stem cell therapies or are developing stem cell therapies for eventual commercialization increased in market capitalization by over \$708 million, or 40%.

We also noted that during 2010 a survey of surgeons by BMO Capital Markets found that 74% of the surveyed physicians believe that biologic products are the most exciting new technology in medicine. No other technology platform scored higher than 21% (source: *Joanne K. Wuensch, BMO Capital Markets – September 10, 2010*). Clearly, in 2010, stem cell companies enjoyed renewed interest from both their prospective customers and the capital markets.



	Company Name	Symbol	EOY 2009 Market Value	EOY 2010 Market Value	Change in Market Value
1	Aastron Biosciences	ASTM	\$ 41,567,680	\$ 72,320,000	73.98%
2	Advanced Cell Technology	ACTC.PK	\$ 56,477,880	\$ 226,350,000	300.78%
3	Athersys, Inc.	ATHX	\$ 78,180,900	\$ 46,760,000	-40.19%
4	BioHeart	BHRT	\$ 14,437,400	\$ 9,690,000	-32.88%
5	Biomatrix Scientific	BMSN.OB	\$ 2,094,560	\$ 2,110,000	0.74%
6	Biotime, Inc.	BTIM.OB	\$ 140,901,300	\$ 396,470,000	181.38%
7	Brainsstorm Cell Therap	BCLLOB	\$ 18,613,400	\$ 17,540,000	-5.77%
8	Cardiogenesis Corp.	CGCP.PK	\$ 10,777,800	\$ 13,070,000	21.27%
9	Cryo-Cell International	CCEL.OB	\$ 20,915,000	\$ 28,200,000	34.83%
10	Cytori Therapeutics	CYTX	\$ 236,375,000	\$ 262,140,000	10.90%
11	Geron Coporation	GERN	\$ 508,546,500	\$ 532,170,000	4.65%
12	Hepalife Technologies	HPLF.OB	\$ 14,716,050	\$ 32,750,000	122.55%
13	Intn'l Stem Cell Corp	ISCO.OB	\$ 28,567,000	\$ 134,040,000	369.21%
14	Medistem Laboratories	MEDS.PK	\$ 688,800	\$ 1,430,000	107.61%
15	Neostem Inc.	NBS	\$ 56,590,500	\$ 81,240,000	43.56%
16	Neuralstem Inc.	CUR	\$ 62,345,700	\$ 98,520,000	58.02%
17	Opexa Therapeutics	OPXA	\$ 24,529,000	\$ 27,150,000	10.69%
18	Osiris Therapeutics	OSIR	\$ 233,977,800	\$ 255,430,000	9.17%
19	Pluristem Therapeutics	PSTI	\$ 21,460,000	\$ 37,640,000	75.40%
20	Stemcells, Inc.	STEM	\$ 149,121,000	\$ 137,190,000	-8.00%
21	Thermogenesis Corp	KOOL	\$ 32,358,321	\$ 49,360,000	52.54%
	Totals		\$ 1,753,241,591	\$ 2,461,570,000	40.40%

Markets for Stem Cell Products 2015-2020

Between 2015-2020 the stem cell market, we believe, opens up dramatically. Products for cardiovascular, diabetes and nerve repair indications become routinely available in the United States and, in 2015; help generate a total \$1.9 billion in revenues. From 2015 to 2020, we forecast, overall revenues for stem cell products will increase by another \$5 billion to \$7.97 billion as penetration rates grow.

Importantly, the penetrate rates that support these assumptions are low:

- Anti-Inflammatory: 3.3%
- Diabetes Therapy: 1.9%
- Nerve Repair: 2.1%

Exhibit SC-1: Stem Cell Therapy Market Estimates, US, 2006-2020

Year	Annual Sales (\$ in 000s)	Growth
2006	\$16,405	
2007	\$34,404	109.7%
2008	\$61,319	78.2%
2009	\$95,248	55.3%
2010	\$139,609	46.6%
2011 E	\$184,658	32.3%
2012 E	\$271,041	46.8%
2013 E	\$442,810	63.4%
2014 E	\$678,768	53.3%
2015 E	\$1,085,899	60.0%
2016 E	\$1,681,813	54.9%
2017 E	\$2,300,444	36.8%
2018 E	\$3,010,216	30.9%
2019 E	\$4,356,509	44.7%
2020 E	\$6,084,160	39.7%

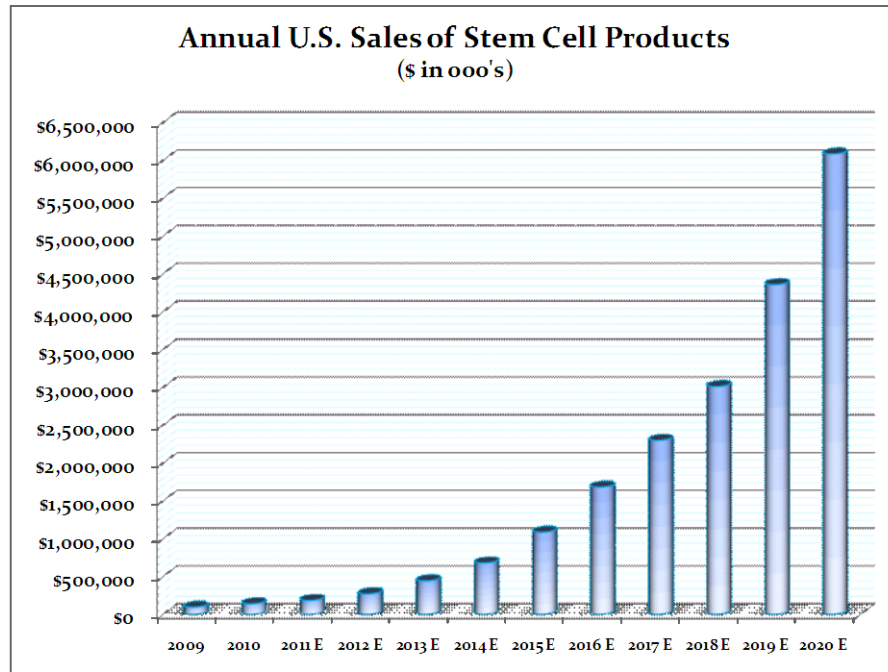


Exhibit SC-2: Stem Cell Market Forecast, by Indication, US, 2005–2020 (\$ in 000s)

Year	Orthopedic Indications	Cardio - vascular	Dental	Anti- Inflammatory	Diabetes Therapy	Nerve Repair	Other	Total Annual Revenues (\$ in 000s)	Growth (%)
2005	\$900	\$0	\$0	\$0	\$0	\$0	\$0	\$900	
2006	\$16,405	\$0	\$0	\$0	\$0	\$0	\$0	\$16,405	1723%
2007	\$33,895	\$0	\$0	\$0	\$0	\$0	\$508	\$34,403	110%
2008	\$53,946	\$37	\$62	\$6,270	\$0	\$97	\$906	\$61,319	78%
2009	\$77,128	\$386	\$272	\$15,907	\$0	\$147	\$1,408	\$95,247	55%
2010	\$112,860	\$796	\$979	\$20,770	\$1,956	\$186	\$2,063	\$139,609	47%
2011	\$146,915	\$1,642	\$1,639	\$29,331	\$2,169	\$234	\$2,729	\$184,658	32%
2012	\$207,561	\$3,382	\$3,000	\$48,323	\$2,405	\$2,366	\$4,006	\$271,041	47%
2013	\$312,634	\$13,920	\$4,404	\$78,616	\$2,794	\$23,898	\$6,544	\$442,810	63%
2014	\$420,737	\$28,629	\$5,817	\$135,243	\$5,901	\$72,411	\$10,031	\$678,768	53%
2015	\$569,435	\$58,834	\$7,191	\$194,668	\$9,348	\$230,375	\$16,048	\$1,085,899	60%
2016	\$800,142	\$108,388	\$8,464	\$236,530	\$14,809	\$488,625	\$24,854	\$1,681,813	55%
2017	\$938,242	\$198,565	\$10,709	\$263,029	\$78,638	\$777,263	\$33,997	\$2,300,444	37%
2018	\$1,121,314	\$303,084	\$13,209	\$290,470	\$166,102	\$1,071,551	\$44,486	\$3,010,216	31%
2019	\$1,664,672	\$462,531	\$15,985	\$320,829	\$350,849	\$1,477,261	\$64,382	\$4,356,509	45%
2020	\$2,372,314	\$658,671	\$19,057	\$351,811	\$555,810	\$2,036,583	\$89,914	\$6,084,160	40%

Robin R. Young – Background

Robin R. Young, CFA is the founder and CEO of RRY Publications LLC (www.ryortho.com), PearlDiver Technologies, Inc. (www.pearldiverinc.com) and the New York Stem Cell Summit (www.stemcellsummit.com). Mr. Young is an internationally recognized medical technologies expert with over two (2) decades of relevant experience.

Over the course of his career, Robin has been an active and integral part of the development, analysis and funding of several major medical and biomaterial technologies including: spine cages, engineered allograft, living cell biomaterials, anti-adhesives, third generation hemostats, calcium-based bone void products, nucleus replacement implants, stem cell rich allograft products, trophic implants and dynamic stabilization implants. After a successful career on Wall Street (Stephens Inc., Piper, Jaffray & Hopwood, John G. Kinnard and Company), he was instrumental in forming and managing the HealthpointCapital research and private equity practice.

In addition to his active publishing and consulting role, Mr. Young founded and organized the New York Stem Cell Summit—now in its seventh year. The New York Stem Cell Summit is a one-day event which focuses on stem cell therapies that are either in commercial use or will soon be in commercial use. The meeting has become the premier meeting for discussion of the emerging commercialization of stem cell technologies.

In addition, Mr. Young speaks at about a dozen medical technology or surgeon society meetings annually.

Mr. Young is the author of three highly acclaimed orthopedic industry reference books, *Dynamic Stabilization Workbook-2004*, *Biomaterials Industry Outlook-2004*, and the *Spine Industry Workbook – 2003*. In total, Mr. Young has written 15 published articles, over 1,000 research reports and 5 published books on various medical and investment topics. Mr. Young has been quoted in numerous publications including the *Wall Street Journal* and *Time Magazine*. He has appeared as an expert commentator on CNBC, CBS Evening News and Wall Street Week with Louis Rukeyser. Finally, he has taught at the graduate schools of the University of Minnesota and the University of Saint Thomas in St. Paul, Minnesota. Mr. Young lives in Wayne, Pennsylvania with his wife and daughter.