

BIOMATTERS

A MichBio Publication Showcasing Michigan's Biosciences Industry



MichBio Forward

A Bold New Brand to Drive Bio-Industry Growth

FEATURED

**WMU
School of Medicine
Aims to Ease
Physician Shortage
and Boost Local
Bio-Economy**

**Martial Arts
in Medicine –
Kids Kicking
Cancer Helps
Children Manage
Effects of Disease**

**Michigan Biobanks
in Forefront of
Research and
Innovation**

**New Expertise
Portal – Helps
Businesses Find
Experienced
Researchers,
High-Tech Facilities
at Top Michigan
Universities**

WHAT HAPPENS WHEN

STARTUP

meets **launch pad**



Strapping a booster rocket onto a great idea.

When DeNovo Sciences entered the Accelerate Michigan Innovative Competition, they were a small company with a big dream. After winning the \$500K grand prize, they've become a sought-after company on the verge of developing cutting-edge products for early cancer detection. Michigan offers them the right mix of experience and resources. And, with access to the expertise of two world-class cancer hospitals, DeNovo is ready for takeoff in Pure Michigan.

1.888.565.0052
michiganadvantage.org/BM

PURE *M*ICHIGAN®

LET'S WORK TOGETHER TO **GROW IDEAS**

INTO BUSINESS **SUCCESS STORIES.**

You might be surprised at what you find at the MSU Innovation Center: Access to nearly 5,000 researchers, \$500 million in annual R&D expenditures, and 642 research and instructional buildings, scale-up facilities, pilot plants, lab space, and equipment.

We have the world-class ingredients that entrepreneurs, investors, and inventors are looking for, all in one place.

Even better than that, you will find experienced partners here, committed to your success:

- **Business-CONNECT** links the right people and resources to develop your idea
- **MSU Technologies** offers the best MSU ideas ready for commercial licensing
- **Spartan Innovations** creates investment-ready businesses from MSU ideas

**MSU INNOVATION CENTER
WANTS TO SUCCEED
WITH YOU**

Marcos Dantus is the MSU Innovation Center's **2013 Innovator of the Year**. A MSU Chemistry Department professor and prolific inventor, he has developed a series of ultrashort pulsed laser technologies and applications used for biomedical imaging, microscopy and more. Dantus launched Biophotonic Solutions, a start-up company with a successful line of Multiphoton Intrapulse Interference Phase Scan (MIIPS) laser pulse shapers.



MICHIGAN STATE
UNIVERSITY

MSU Innovation Center
325 East Grand River Ave., Suite 375
East Lansing, MI 48823
517-884-2370 | @MSU_Innovation

FOR ANIMALS FOR HEALTH FOR YOU



zoetis



Dykema: Where Law Meets Science

For insightful legal counsel, smart representation and strategic business advice, Michigan's biotechnology and life science companies turn to Dykema.

Dykema's biotechnology and life science team represents clients ranging from startups to public companies to nonprofits, in a variety of industry sectors, including pharmaceuticals, diagnostics, health care services, biotechnology, medical devices and equipment, and computer technology and software applicable to the life sciences industry. The Dykema biotechnology and life science team regularly advises companies in capital raising activities (including angel, venture capital and government-related funding sources), mergers and acquisitions, technology licensing transactions, and intellectual property protection and exploitation matters.

To learn more, please contact Jin-Kyu Koh, leader of Dykema's Biotechnology and Life Science practice, at 313-568-6627 or jkoh@dykema.com.

Exceptional service. Dykema delivers.

DyKEMA

www.dykema.com

California | Illinois | Michigan | Minnesota | North Carolina | Texas | Washington, D.C.

© 2013 Dykema Gossett PLLC Attorney Advertising



Michigan's Biosciences Industry Welcomes You!

Welcome to MichBio's eighth edition of *BioMatters™*, the only in-depth publication showcasing the range and vitality of Michigan's biosciences industry.

BioMatters™ helps MichBio fulfill its mission in "driving bio-industry growth" by educating you about the discoveries, technologies, and products being researched, developed, and manufactured here in Michigan, and the many assets available to support those activities. As a whole, the economic impact of Michigan's bio-industry is sizeable and its reach global.

In this issue of *BioMatters™* you'll discover some of the faces, initiatives and institutions that represent just a small part of Michigan's outstanding biosciences community. From Detroit, Ann Arbor, Kalamazoo, Grand Rapids and Lansing to Northern Michigan and the Upper Peninsula, and everything in between, the state's bioscience industry is growing.

Nothing exemplifies this better than the launch of Michigan's sixth and newest medical education institution, Western Michigan University School of Medicine – WMed. Learn about its exciting development as the institution readies itself for its first class in Fall 2014.

Also, read how Michigan is at the forefront in the evolution of biorepositories and biobanking, about a first-in-the-world commercial 3D imaging center that will aid drug discovery, why kids taking martial arts helps them better manage their cancer, where an advanced proton beam therapy center is being developed, and much more.

Lastly, MichBio enters its third decade with a refreshed brand that positions us for the future. Learn how this new bold brand embodies our identity, mission, and services.

Want to discover more of Michigan's bio-industry? Then peruse our archived issues of *BioMatters™* at www.michbio.org/biomatters or simply contact me at srapundalo@michbio.org, and I'll be happy to introduce you to everything that is this great state's biosciences community.

Let MichBio be your entry point to Michigan's bioscience companies, business services, assets, and markets. That's *PureMichigan™*.

Stephen Rapundalo, Ph.D.

President & CEO, MichBio



STAFF

Stephen T. Rapundalo, Ph.D.

President & CEO

srapundalo@michbio.org

734.527.9144

Wendy Kwapis

Director,

Marketing & Communications

wendy@michbio.org

734.527.9147

David McGuire

Director,

Operations & Membership

david@michbio.org

734.527.9150

Nancy Marcotte

Manager, Finance

nancy@michbio.org

734.527.9145

CONTACT INFORMATION

Physical Address

3520 Green Court, Suite 175

Ann Arbor, Michigan 48105-1579

Mailing Address

P.O. Box 130199

Ann Arbor, Michigan 48113-0199

Phone

734.527.9150

Fax

734.302.4933

Website

www.michbio.org

Email

info@michbio.org

**We understand
your risks and
unique issues!**

Hylant Life Science experts design customized insurance and risk management solutions that are on target with your business needs. Our experienced advisors specialize in Life Science organizations so you can collaborate with a team who understands your business and bottom line.

Life Science FOCUS.



hylant.com



24 Frank Lloyd Wright Drive, Suite J4100 | Ann Arbor, MI 48105 | P 734-741-0044

Medical Devices | Clinical Research | Clinical Trials | Pharmaceuticals
Biotechnology | Product and Technology Development

OAKLAND UNIVERSITY™

OU INC

INNOVATE ■ ACCELERATE ■ EDUCATE

SmartZone Business Accelerator ■ Clean Energy Research Center



Medical
Devices



Energy



Information
Technology

**Providing entrepreneurial
resources
AND strategic business
solutions
FOR
accelerating
ideas
to market**

PURE MICHIGAN®

SmartZone™ Rochester Hills

Oakland University School of Engineering and Computer Science

2200 North Squirrel Road, Rochester, MI 48309

(248) 648-4800 ■ fax (248) 648-4799 ■ ouinc@oakland.edu

Please visit oakland.edu/ouinc

SERVING AN INTERNATIONAL COMMUNITY

04/17/2014/13

Innovative. Trustworthy. Knowledgeable. Passionate.



Product Design
Project Management
Injection Molding
Micro Molding

Over Molding
Insert Molding
Clean Room Molding
Clean Room Assembly

Medical Device
Biotech
Diagnostic
Microfluidics

MEDBIO

Medical & Biotechnology
Manufacturing

ISO 13485:2003 Certified

www.medbioinc.com

Innovative Contract Manufacturing Solutions for the Life Sciences.

PREMIUM MEMBERS

PLATINUM



GOLD



SILVER



BRONZE



PATRON



MEDIA



OFFICERS & DIRECTORS

EXECUTIVE OFFICERS

Chairman
Stephen Munk, Ph.D.
Ash Stevens, Inc., President & CEO

Vice Chairman
David Zimmermann
Kalexsyn, Inc., CEO

President & CEO
Stephen T. Rapundalo, Ph.D.
MichBio, President & CEO

Secretary
Christine DeHayes
Thomson Reuters IP Management Services

Treasurer
Matthew L. McColl
Ernst & Young LLP, Partner

DIRECTORS

Arik Anderson
Terumo Cardiovascular Systems Corp.
Vice President, Global R&D & Marketing

David Felten, M.D., Ph.D.
Beaumont Hospitals
Vice President, Research & Medical Director, Research Institute

Doug Gage, Ph.D.
Michigan State University
Director of the MSU BioEconomy Network, Office of the Vice President for Research & Graduate Studies

Dale Grogan
Michigan Accelerator Fund I
Managing Director

Tim Mayleben
Esperion Therapeutics
President & CEO

Kevin McCurren
Grand Valley State University
Executive Director, The Center for Entrepreneurship & Innovation and Grand Rapid's Smart Zone

Kevin McLeod
Michigan Medical Device Accelerator
Managing Director

Paul Morris
AlixPartners, LLP
Finance Manager, National Enterprise Improvement Practice

Stephen Munk, Ph.D.
Ash Stevens, Inc. President & CEO

Stephen T. Rapundalo, Ph.D.
MichBio, President & CEO

Tina Rogers, Ph.D., MBA, DABT
MPI Research
Chief Scientific Officer & Vice President, Strategic Accounts

John J.H. Schwarz, M.D.
Battle Creek Family Health Center
Physician, Former U.S. Representative

Ned Staebler
Wayne State University
Vice President, Economic Development

Christopher J. Stein
Ferndale Pharma Group, Inc.
Executive Vice President & COO

Karen Studer-Rabaler
Coy Laboratory Products
General Manager & Vice President of Business Development

David Zimmermann
Kalexsyn, Inc., CEO



stryker®

We make a difference by caring for the caregivers, helping them maintain order in their organizations and restore health to their patients.

www.stryker.com

Together, Advancing Scientific Innovation

GLOBAL REACH, LOCAL SUPPORT. SINCE 1852.

At VWR, we enable science by supplying critical laboratory products, equipment and services, offering the best product choices, including the Exclusive VWR Collection, from premier manufacturers to customers around the globe. We are committed to providing effective, efficient solutions for all your Life Science needs. VWR is advancing scientific innovation to make your work faster, easier and more accurate, so you can focus on what's truly important: discovery.

VWR  **vwr.com**
We Enable Science

Bio Business Solutions
Value Through Cost-Savings

MICH BIO

BIOMATTERS

TABLE OF CONTENTS

<p>9 MichBio Forward - A Bold New Brand to Drive Bio-Industry Growth</p>		<p>24 Meeting Patient Needs with World-Class Imaging</p>		<p>32 New Insights into Metabolic Diseases Fueling Growth Aspirations in Kalamazoo</p>	
<p>11 WMU School of Medicine Aims to Ease Physician Shortage and Boost Local Bio-Economy</p>		<p>26 A Higher Standard - Science, Safety and Innovation Come Together at RTI Surgical</p>		<p>34 nanoMAG Develops New Class of Materials for Orthopaedic Implants</p>	
<p>15 Martial Arts in Medicine Kids Kicking Cancer Helps Children Manage Effects of Disease</p>		<p>28 McLaren Proton Therapy Center: Advanced Capabilities for Cancer Care</p>		<p>36 Transformation to a High Compliance Culture</p>	
<p>18 Federal Funding Takes the "Bugs" Out of Growth for Ann Arbor Company</p>		<p>30 Helping Make Robotic Surgery Safer - Michigan Company has Simple-To-Use Tool to Check Cleanliness of Robotic Arms</p>		<p>39 Michigan Ball Company Expands Products to Medical Industry</p>	
<p>20 Michigan Biobanks in Forefront of Research and Innovation</p>		<p>40 New Expertise Portal Helps Businesses Find Experienced Researchers, High-Tech Facilities at Top Michigan Universities</p>			

Subscribe to BioMatters:
call 734.527.9150

ADVERTISERS

Ash Stevens 38	Hoover 39	Oakland University 4
Bank of Ann Arbor 38	MedBio 4	PhRMA IBC
Drug & Laboratory Disposal, Inc 38	MichBio 4, BC	Stryker 6
Dykema 2	Michigan Economic	VWR 6
Healthmark 31	Development Corp. IFC	Western Michigan University 10
Hylant 4	Michigan State University 1	Zoetis 2
	MPI Research 25	

MichBio Forward

A Bold New Brand to Drive Bio-Industry Growth

By Stephen Rapundalo, Ph.D., President & CEO, MichBio



A brand...it defines an organization. As the biosciences industry trade Association for Michigan we need a strong, unmistakable identity that clearly and effectively communicates who we are and what we do. MichBio embarked to do just that in early 2013.

As with any brand, ours has been an evolution in our identity. Since 1993 through 2000, the organization was known as the Michigan Biotechnology Association (MBA). Then in 2001, the formal name changed to the Michigan Biosciences Industry Association (MBIA), and with that came a short-lived logo. Both of these initial brands did little to define the organization. Recognizing that, the Association adopted the d/b/a, MichBio in early 2002, and a helix-themed logo that reflected its biotech and pharma focus.

With an ever expanding statewide constituency, recognition of newer sectors like ag-biotech, and the demise of the Michigan Medical Device Association (MMDA), MichBio's identity seemed to fit less and less over the last few years. The Association found itself embracing a broader industry that included our two largest sectors – medical devices/ equipment and pharmaceuticals/ therapeutics – as well as diagnostics,

research products and testing, ag/food, industrial and bio-based technologies, informatics and health IT, and clinical research. We realized a new identity that better defined us was in order.

So in early 2013, MichBio launched a rebranding effort that also coincided with a need to completely overhaul our website and association management system. The process included analysis and documentation of Association value points, the formulation of brand positioning, development of a messaging strategy, and design of new visual standards for our Association business and marketing materials, as well as digital communications and online platforms. We consulted with the MichBio Board of Directors and others to refine the brand, went through many design iterations, and finally arrived at a fresh look.

The new MichBio logo is the most highly visible element of the revitalized brand. It depicts clearly our bioscience industry foundation and statewide constituency in a modern, bold, and engaging way with colors that link to our heritage.

MichBio's updated tagline, *Driving Bio-Industry Growth*, works seamlessly with the new visual identity to convey the spirit and purpose of who we are and what we do.

Our brand is composed of all the assets we use to help bioscience companies grow when describing the Association to the outside world – from the words we use to describe our cause to the visual presentation of our materials. Working together, these brand assets convey MichBio – and the broader Michigan biosciences industry – in a more significant, contemporary, and relevant manner.

MichBio's new brand reflects our forward looking approach. It brings us fully in step with who we are now, and where we will lead Michigan's biosciences industry:

CREATING VALUE BY DELIVERING BUSINESS-CRITICAL RESOURCES AND BOTTOM-LINE SAVINGS.

MichBio members gain discounts with a variety of MichBio Preferred vendors that can improve business outcomes. In addition, our educational programs provide access to vital information, prominent executives, and key thought leaders. Our communications and public



1993



2001



Michigan Biosciences Industry Association

2002



relations efforts create visibility for bioscience businesses and the statewide industry.

BUILDING NETWORKS BY CONNECTING MICHIGAN'S BIO-INDUSTRY ONE MEMBER AT A TIME.

We connect members to industry professionals, suppliers, contract research organizations, consultants and service providers, investors and funding sources, business development and licensing opportunities, and regulators and policy decision-makers, through our BioConnections™ referral program.

IMPACTING POLICY BY INFLUENCING BUSINESS GROWTH THROUGH ADVOCACY.

MichBio is a discernible voice in the halls of government and engages on both state and federal legislation, as well as with governmental agencies with significant policy oversight of the bio-industry. Grassroots advocacy makes a difference – and MichBio is the advocate for Michigan's bio-industry.


GROWING TALENT BY CREATING OPPORTUNITIES THAT DEVELOP PEOPLE AND BUILD ORGANIZATIONS.

Through job postings and candidate resumes on the MichBio Career Center, one-on-one matchmaking with C-level professionals, or connecting your organization to talent sources, MichBio facilitates growth of the Michigan bio-industry workforce for today and tomorrow.

MichBio is recognized as one of the foremost state bioscience associations. Our hope is that our new logo will continue to help the Association stand out as a leader – and that it will convey our vision, core values, and member focus.

So, while we launch the new brand and logo now, our work isn't done.

In the upcoming months you will see updates in our materials with the new branding. A revamped website will roll out before the end of the year and include more features for members to showcase themselves, better user functionalities, and richer content.

MichBio now enters its third decade boldly, confidently and with renewed purpose. We welcome our members, external partners, and supporters to join us as we drive the growth of Michigan's bio-industry into a brighter future. 



**DRIVING
BIO-INDUSTRY
GROWTH**

2009

2013

From discovery to the marketplace

Western Michigan University and Kalamazoo share and celebrate a legacy of life science education, discovery and commercialization.

- A vibrant Business Technology and Research Park that is home to 31 life science companies—many launched in the park's award-winning incubator, the Southwest Michigan Innovation Center
- A Biosciences Research and Commercialization Center that helps guide global discovery from the research lab to the marketplace
- The renowned faculty and research facilities of a top public research university that will be home to a new medical school in 2014

Western Michigan University.
It's your turn to **GRAB THE REINS.**



**WESTERN MICHIGAN
UNIVERSITY**



WMU School of Medicine

Aims to Ease Physician Shortage and Boost Local Bio-Economy

By Rick Haglund

Ask community leaders in Kalamazoo why Western Michigan University (WMU) is launching a medical school and you will invariably get this answer: “John Dunn.”

While interviewing to become WMU’s president in 2007, Dunn said he thought the region was missing a key puzzle piece that could transform Southwest Michigan into a health care leader.

Kalamazoo has a 150-year legacy in health sciences, research and manufacturing with companies such as former drug maker Upjohn Co. (now Pfizer Inc.) and medical device manufacturer Stryker Corp. There are some 200 life sciences companies located in Southwest Michigan.

Plus, Kalamazoo has been home to two top-notch hospitals – Borgess Medical Center and Bronson Methodist Hospital – that have served as the clinical training sites for third- and fourth-year medical students from Michigan State University College of Human Medicine (MSU-CHM)



through the Michigan State University Kalamazoo Center for Medical Studies for decades.

“I was intrigued with the fact that this was the home of what we call the life sciences,” said Dunn, who has an extensive academic background in health education. “I sort of innocently asked the question, ‘Has anyone contemplated establishing a medical school?’”

Dunn’s query led to a series of community discussions that resulted in the university beginning plans in 2008 for the state’s sixth medical school, which will enroll its first class of students in August 2014.

Western Michigan University School of Medicine is a joint venture involving WMU, Borgess Health and Bronson Healthcare. The private school was launched with a \$100 million anonymous donation. Continuing financial support will come from student tuition, private gifts, clinical revenue, research grants and endowment income.

Medical school officials are working feverishly on renovating a historic downtown building where the school will be housed, hiring faculty and developing a curriculum they say will prepare physicians for a rapidly changing health care delivery system.

The medical school also will help ensure that Michigan and the country have enough physicians to serve an aging population that will demand more health care services in the future, said Hal Jenson, the school’s founding dean. Plus, millions of uninsured people will soon get access to health care through the Affordable Care Act. This will put more pressure on an already strained health care system. ►

JOHN DUNN, PRESIDENT OF
WESTERN MICHIGAN UNIVERSITY



“We have an aging population in which 10,000 people a day are turning 65 years of age,” said Jenson, who formerly was dean of Tufts University School of Medicine’s Western Campus. “Many physicians are retiring, as well. The demands on health care utilization are going up and there are not enough replacement physicians in the pipeline.”

Almost 20 percent of Michigan’s population lacks sufficient access to primary care, according to the U.S. Department of Health and Human Services. “The critical shortage of physicians is daunting and somewhat frightening,” Dunn said.

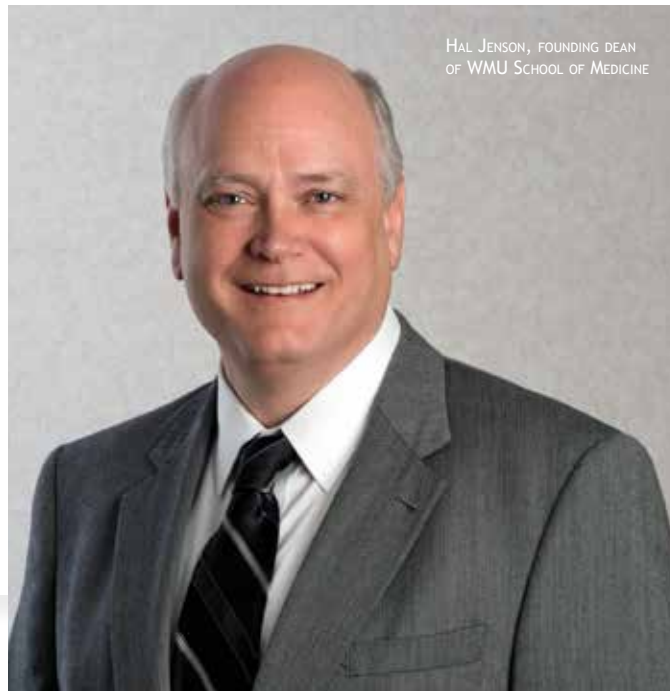
But there is no shortage of WMU medical school applicants looking to fill the gap. About 2,800 students have applied so far for the 50 available slots next fall.

Medical school officials will whittle that number down to 300 and interview the remaining applicants.

“It’s enormous work. I think the milestones have been achieved on schedule,” said Patrick Dyson, executive vice president of Borgess.

“It will be very different than how medical schools have traditionally taught students. It will be more hands-on and experiential.”

HAL JENSON, FOUNDING DEAN
OF WMU SCHOOL OF MEDICINE



Officials of Kalamazoo’s two hospitals say they hope the medical school will result in many of its students choosing to practice in Southwest Michigan.

“The statistics show that where residents are trained is likely where they stay,” said Scott Larson senior vice president for medical affairs and chief medical officer at Bronson. “I think the community wins. The medical school will certainly help us provide enhanced resources, particularly for underserved populations.”

Western Michigan University School of Medicine will be housed in a seven-story, 350,000 square-foot building that was the first piece of property purchased by Upjohn founder William Erastus Upjohn in 1885. The site is now known as the medical school’s W.E. Upjohn campus.

William U. Parfet, Upjohn’s great-grandson and CEO of MPI Research, a pharmaceutical research firm, donated the building to WMU for the medical school in 2011. It is undergoing a \$68 million renovation to house the school’s office, labs and classrooms.

Plans are for the medical school to eventually accept 80 new students a year.

Jenson said the school’s curriculum will differ from those found in other long-established medical schools. The curriculum will involve a team-learning approach and expose students to

patients in their first two years of education. Typically, medical students spend their first two years in classroom instruction.

“It will be very different than how medical schools have traditionally taught students,” Jenson said. “It will be more hands-on and experiential.”

The curriculum builds on 2010 physician training guidelines by the Carnegie Foundation, which Dunn said were last updated in 1910. ►

BRCC Spells Return on Investment

A decade ago then-Gov. Jennifer Granholm traveled to Kalamazoo with a \$10 million ceremonial check representing a special appropriation from the Michigan Legislature and designed to stave off the loss of human and financial resources that threatened to derail a 125-year-old engine of economic development – West Michigan’s preeminent role in the life sciences industry.

It was a sound investment.

That \$10 million check, dated Aug. 6, 2003, supported the establishment of Western Michigan University’s (WMU) Biosciences Research and Commercialization Center (BRCC). That center, in turn, has used Kalamazoo’s unique history and expertise in pharmaceutical and medical device development to help fund the startup of 33 new companies from across the state. The center has leveraged that original state investment into more than \$160 million in new capital funds and supported the creation of more than 240 new high-paying technical jobs in Michigan.

This fall, celebrating its 10th anniversary, the BRCC continues its work, having secured an additional \$3.8 million in state funding to support the life sciences field throughout the state. WMU has also contributed \$3.45 million in BRCC funding since its establishment. The center is embarking on a new relationship as well, as part of the apparatus in place to support the enormous research potential

of WMU’s new School of Medicine. The BRCC focuses on:


- Early-stage technology transfer,
- Pre-seed gap funding, and
- Support for Contract Research Organizations – CROs.

“Most companies we invest in don’t have a product yet,” says BRCC Executive Director Stephen Haakenson. “They’re in the early stages – typically too early for a venture capitalist to support.”

Nearly 50 percent of the center’s funding has supported drug discovery and development. Pharmaceutical services represent more than a third of the work, while a smaller portion covers the development of medical devices and diagnostic tools.

Kalamazoo and the state of Michigan were natural locations to support talented scientists who wanted to launch their own successful businesses. The original vision for the BRCC

was to support such talent when West Michigan was faced with dimming economic prospects due to the withdrawal of Pfizer’s major research and development functions. The funding of these early-stage technologies, pre-seed companies and CRO businesses has produced a network for supporting the commercialization of life science products throughout the state.

Today, located at the life sciences incubator known as the Southwest Michigan Innovation Center, the center has lived up to both the promise of that vision and the state’s investment. 



SOUTHWEST MICHIGAN INNOVATION CENTER, KALAMAZOO, MI

Growing Stryker Profits by Design

Designing a tool to help the Stryker Instruments sales force close deals across the nation and overseas was not at the front of Sara Simic's mind when the dual business major enrolled at WMU.

But after landing a coveted internship at the medical equipment giant, Simic was charged with doing just that. The result is a website and mobile app that is being used by the company's 150 sales representatives to boost sales in the company's neuro, spine, ears, nose and throat division.

SARA SIMIC, WMU STUDENT AND STRYKER INSTRUMENTS INTERN




What started as sketches on paper grew into a one-stop shop where sales reps can search for a brochure, look up information, create a presentation kit earmarked for a given client or brush up on anatomy or clinical knowledge. The Lake Orion, Mich., senior unveiled her creation at the company's national sales meeting in Scottsdale, Ariz.

Simic, who graduates in spring 2014 with bachelor's degrees in food and consumer package goods marketing and integrated supply management, says her WMU education helped her make the most of her internship opportunity.

"My business classes have really helped me develop in a variety of ways," Simic says. "My classes have taught me how to communicate well in order to obtain reliable information, which was huge in making this tool successful."

Simic worked loosely with Chicago-based software company SAVO to design her Stryker sales tool from scratch. But her WMU training served her well.

"The knowledge I gained from my computer information systems classes helped me become more efficient when it came to technology and the implementation process," she says. 

"You cannot separate science education from clinical practice. That's not a sustainable model," he said. "Students need patient interaction from day one and science education throughout their four years of medical school."

Health care research also will be a crucial element of the medical school.

"In order to have a viable medical school, you have to be involved in basic research," said Dale Vandre, chairman of the school's biomedical sciences department.

Vandre, who was recruited to the medical school last year from The Ohio State University College of Medicine, said research will be enhanced by the research capabilities of Borgess and Bronson, and the numerous life science companies in the region.

"We want to make as many linkages as we can in the community," said Vandre, who also is charged with recruiting basic science faculty employed by the medical school.

Recruiting new faculty has not been a problem, Vandre said, despite Kalamazoo's somewhat remote location.

"We had 250 applications for our first five positions," he said. "People are excited about building something from the ground up."

The medical school has about 70 employed faculty members. The faculty will also include clinicians and professionals from Borgess, Bronson and from the southwest Michigan region.


Michigan State University Kalamazoo Center for Medical Studies, a collaboration of Borgess, Bronson and MSU's College of Human Medicine that trained MSU-CHM medical students in their third and fourth years, has been dissolved and its faculty assumed by the new medical school.

WMU School of Medicine represents "a dramatic tipping point" that could give Kalamazoo and the surrounding region a national reputation as a health care and life science leader, said Ron Kitchens, president of the local economic development agency Southwest Michigan First.

He envisions the medical school, in conjunction with Borgess and Bronson, developing new products and businesses that will boost the region's economy.

"There will be clusters of new ideas and startups being formulated by graduate assistants and research assistants who will spend their days in an academic environment and their nights and weekends as entrepreneurs," Kitchens said.

Dunn sees the medical school as a benefit to the entire state at a time when WMU and other universities are under fire for rising tuition and questionable spending practices.

"I like to look at this as a great gift to Michigan in which we are not asking for state money," he said. "We get beat up a lot, but this is a great gift and it should be acknowledged." 



Martial Arts in Medicine

Kids Kicking Cancer Helps Children Manage Effects of Disease

By Martin H. Bluth, M.D., Ph.D.

Martial arts often conjure up images of Bruce Lee, Chuck Norris, or more recently Jason Statham and Jet Li as action stars of the silver screen or alternatively a hard core dojo (martial arts school), where students diligently practice repetitive movements in an orchestrated dance-like motion (kata) on a hardwood floor under the watchful eye of the teacher (sensei). The relevance to the health care industry appears marginal at best, save to instill some manner of discipline and self control.

This could not be further from the truth. The application of martial arts in medicine, although somewhat niche, has been reported as quite beneficial. In truth, the buzz word of martial arts can span the “hard” physical disciplines



of Karate, Judo and Tai Kwon Do to the meditative “soft” disciplines of Tai Chi and Chi Gung and everything in between.

With respect to healthcare, there have been studies pertaining to the beneficial effect of martial arts in diseases such as rheumatoid arthritis, osteoarthritis, fibromyalgia, among others. Furthermore, the implementation of Tai Chi to other diseases including Parkinson’s and heart disease have also been reported.

Variables attributed to success of these interventions include differences in study duration for determination of positive effects in chronic conditions instructors and their ability to effectively convey the appropriate postures to the participants, and program design (types of patients, number/duration of sessions per week, etc.), among others.

How about cancer? This disease spectrum seems to deviate from musculoskeletal or motor diseases where a mechanical intervention could plausibly effect positive change. Cancer represents an aberration of the “go/no-go” switch gone awry where martial arts intervention should have no effect. Nonetheless, it does.



PHOTO CREDIT: JOSHUA SCHWARTZ | BWPHO.COM

The organization, Kids Kicking Cancer (KKC) (www.kidskickingcancer.org), demonstrates the positive beneficial effect martial arts can have on cancer. This organization, born, bred and matured in Michigan, has perfected a consistent method to help children with cancer manage the stress and pain of their disease and treatments through personalized coaching instructed by black belt martial artists. These children achieve “power, peace and purpose” (the organizations mantra) by teaching their deep breathing techniques to others to help them reduce stress. KKC employs both hard “karate-style” martial arts (kicking, punching) along with “soft” breathing and meditative exercises to decrease the fear and pain often associated with chemotherapeutic infusions, port placements, needle sticks, treatment regimens and the like. Indeed, with the costs of cancer therapy averaging >\$100,000 per year per patient, any intervention which increases patient compliance and the possibility of decreased drug dependency or dosing can have drastic economic advantages. In this respect, KKC’s approach improves patient compliance. To quote the parents of these cancer children, “The power breathing and meditation that Miranda has learned, she uses every time for chemo. The needle stick that would have her screaming, she doesn’t even feel now because she is able to relax and get through it.”

In addition to testimonials, recent aggregate data for KKC demonstrates the positive effects of martial arts intervention in cancer as a group. Recent studies (submitted to the *American Association of Hematology* annual meeting) demonstrated significance among pediatric cancer patients who reported pain scales prior

These children achieve “power, peace and purpose” (the organizations mantra) by teaching their deep breathing techniques to others to help them reduce stress.

to and subsequently after KKC martial arts intervention. In those studies, pain scores were reduced by approximately 15-30% after intervention compared with pre-intervention. Further, decreased pain scores were reported in as few as 1-2 sessions, demonstrating a considerable impact of a single encounter. The increased treatment compliance for these participants translates into additional cost savings to the health care industry. Additional studies are ongoing to determine the frequency, intensity of the intervention needed to yield beneficial results, as well as if there are differences pertaining to age, race, or gender. Although preliminary, these findings demonstrate a unique utility for expanded martial arts application to disease.


KKC is also maturing clinical trials implementing their program into other disease states including sickle cell disease, asthma and obesity among others. Aside from the potential of program intervention to decrease the economic burden of these diseases (reduced hospital admissions, administration of pharmacologic agents, and other cost related ▶



PHOTO CREDIT: JOSHUA SCHWARTZ | BWPHO.COM



PHOTO CREDIT: JOSHUA SCHWARTZ | BWPHO.COM

morbidities, etc), there is a clear cut advantage of improving psychological health as well. KKC has branched out internationally as well as set up programs in Israel and Italy along with other counties currently in progress towards adapting the application of martial arts in medicine as a means to improving healthcare and maturing the betterment of mankind. 

Martin Bluth, M.D., Ph.D. is the National Medical Director for Kids Kicking Cancer. Dr. Bluth received his Doctor of Philosophy (Immunology) from SUNY Health Science Center at Brooklyn in 1997 and his Doctor of Medicine in 1999. He is Board Certified in Clinical Pathology/Laboratory Medicine and in Blood Banking/ Transfusion Medicine. Dr Bluth is currently Professor of Pathology and Director of Translational Research at Wayne State School of Medicine and

Director of the Transfusion Service at Children's Hospital of Michigan, an affiliate of the Detroit Medical Center Hospital system in Detroit, Michigan. He has over 25 years experience in the martial arts (karate, kempo, weaponry, tai-chi, chi-gung) and holds the rank of Sho Dan (Black Belt). He has co-authored over 200 manuscripts, book chapters, presentations and manuscripts and been the recipient of numerous awards in medical research, entrepreneurship and industry.

“The power breathing and meditation that Miranda has learned, she uses every time for chemo. The needle stick that would have her screaming, she doesn’t even feel now because she is able to relax and get through it.”

Federal Funding Takes the “Bugs” Out of Growth for Ann Arbor Company

By Jayne Berkaw, Director, Marketing & Outreach, BBC Entrepreneurial Training & Consulting

As grad students at the University of Michigan, Tim Marzullo and Greg Gage regularly interacted with schoolchildren during neuroscience outreach events. They often wanted to show real “spiking” activity to students, but this was impossible due to the high cost of equipment.

Undaunted, the two started Backyard Brains (BYB) in Ann Arbor and devised a way to use off-the-shelf electronics to design kits that could provide insight into the inner workings of the nervous system. Their flagship product, the SpikerBox, is a “bioamplifier” that allows students to hear and see spikes (i.e. action potentials) of real living neurons in invertebrates like crickets, earthworms, or cockroaches (which can be ordered with the kits). According to the BYB website, as of August 20, 2013, over 26,000 individuals had heard what neurons sound like for the first time with their SpikerBoxes.

To Tim and Greg, the idea of teaching

neuroscience to school-aged kids was an obvious way to stimulate curiosity about how the brain works, possibly promoting future careers in the area and even development of new therapies by researchers whose interest was sparked at an early age. To investors, questions of market potential loomed large. For angels and venture investors, the proof of concept and market potential was too difficult to assess.

Backyard Brains elected to compete for federal SBIR grant funding through the National Institutes of Health (NIH). The federal Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs award a combined \$2.5 billion through 11 participating agencies to U.S. technology companies every year.

“An SBIR from the NIH seemed like the perfect opportunity for us as the NIH was also acutely aware of the market need for low-cost neuroscience tools due to our lack of knowledge of brain function,” said Marzullo. “This market need – science education plus neuroscience – was not immediately obvious

compared to other technologies typically funded by venture capitalists and investors.”

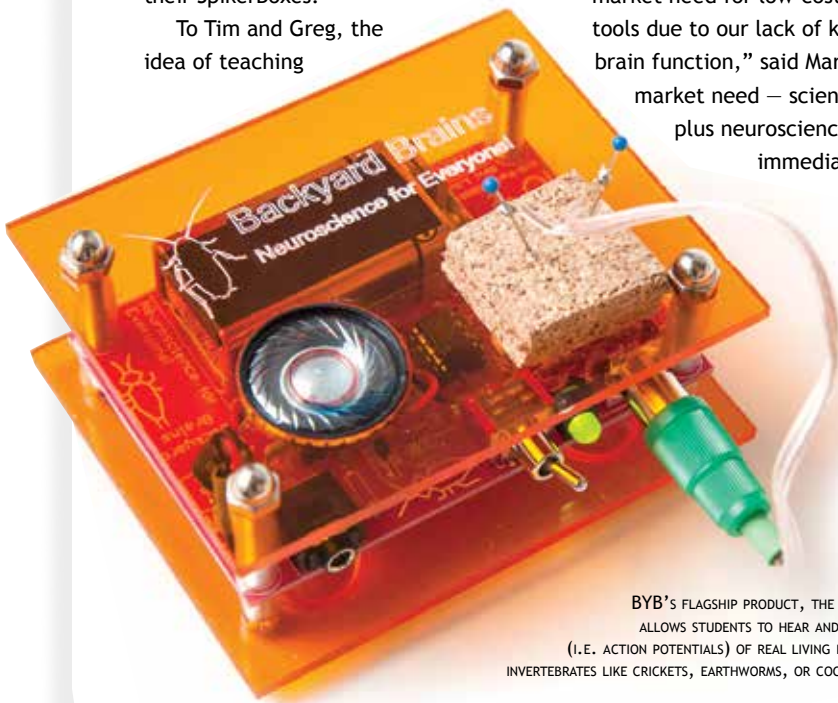
Unlike most sources of capital, SBIR/STTR funding is available to even the earliest stage companies – those that are most often overlooked by



professional investors. It is also non-dilutive funding that doesn't require repayment or the entrepreneur giving up a portion of the company.

“SBIR/STTR funds R&D projects that are critical for a company trying to demonstrate the commercial potential of its technology,” said Lisa Kurek, managing partner of BBC Entrepreneurial Training & Consulting, which manages Michigan's SBIR/STTR Assistance Program (see sidebar) and assisted Backyard Brains with their successful Phase I and Phase II SBIR proposals. “A company that can compete successfully in the SBIR arena can attract national and international attention from potential investors and larger companies interested in partnering.”

SBIR funding has enabled BYB to continue its growth and expand its product line, which now includes such offerings as the “EMG SpikerBox,” which records electrical activity produced by cells in human muscles; “Completo,” a full tabletop, portable electrophysiology rig; and the “RoboRoach,” which gives insights into neurostimulation. All products are



BYB'S FLAGSHIP PRODUCT, THE SPIKERBOX
ALLOWS STUDENTS TO HEAR AND SEE SPIKES
(I.E. ACTION POTENTIALS) OF REAL LIVING NEURONS IN
INVERTEBRATES LIKE CRICKETS, EARTHWORMS, OR COCKROACHES.

Program Supports Michigan SBIR/STTR Grant & Contract Seekers


Michigan is one of only a few states to provide a comprehensive program to train and coach entrepreneurs through the process of proposal preparation to compete for non-dilutive federal R&D funding through the government's Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR). The two programs award over \$2.5 billion dollars in grants and contracts through 11 federal agencies annually.



Michigan's SBIR/STTR Assistance Program is funded by a grant from the Michigan Strategic Fund (MSF), administered by the Michigan Economic Development Corporation (MEDC) and managed by BBC Entrepreneurial Training & Consulting (BBCetc). Program participants are charged a modest fee (\$50-\$125) for training classes and a post-award fee (\$1,500 for Phase I and \$5,000 for Phase II awards) for successful proposals. These fees are returned back into the program.

"BBC knows what a stressful time grant deadlines can be," said Greg Gage, PhD and co-founder of Backyard Brains (see story).

"They reviewed our grant multiple times, and provided excellent, understandable and actionable feedback to improve the quality, and thus the competitiveness, of our proposals."

Learn more about the program at www.bbcetc.com or contact BBCetc at info@bbcetc.com or 734.930.9741. 



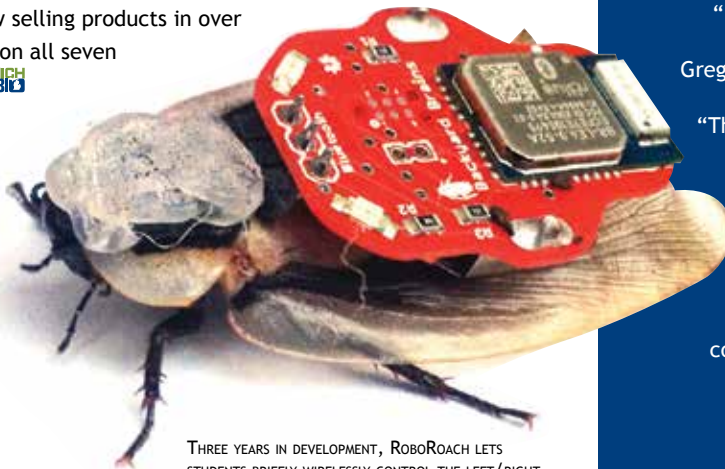
THE BACKYARD BRAINS TEAM WITH CO-FOUNDERS, TIM MARZULLO, FAR LEFT, AND GREG GAGE, FAR RIGHT.

accompanied with lesson plans and experiments to facilitate learning (and teaching) neuroscience.

"We are focusing on continually improving our educational and teacher training materials, as well as branching into human physiology experiments for education," Marzullo added. "We want to release increasingly powerful data analysis tools to allow students to make discoveries."

While some companies spend years working "out" the bugs in their businesses, BYB has used SBIR's to work more bugs "into" their business with huge success to date.

They are now selling products in over 44 countries on all seven continents. 



THREE YEARS IN DEVELOPMENT, ROBOROACH LETS STUDENTS BRIEFLY WIRELESSLY CONTROL THE LEFT/RIGHT MOVEMENT OF A COCKROACH BY MICROSTIMULATION OF THE ANTENNA NERVES. BYB'S PROMOTES IT AS THE "WORLD'S FIRST COMMERCIALY AVAILABLE CYBORG."



Michigan Biobanks

in Forefront of Research and Innovation

State “Knows How to Do It”

By Tom Beaman

The concept of biobanking, that is storing human biological material for scientific research, is not new. The journal *Nature* says the Aboriginal genome was sequenced from a swatch of hair obtained by British ethnologist Alfred Haddon in the 1920’s. Many of his specimens are still housed at Cambridge University in the United Kingdom.

Until recently, the scope and efficiency of research performed with biospecimens was limited, but the landscape today is changing. Advances in genomic technology, including the next-generation method of DNA sequencing that maps nucleotide sequences faster and at lower cost and microarray platforms that analyze gene expression, have opened new horizons for biobanks.

“[Biorepositories] have developed into something with a lot of potential because of how technology, especially in molecular genetics, has evolved,” says Nilsa Ramirez, director of

Michigan is at the forefront of the biobank expansion in the U.S. with many ambitious commercial and academic biorepositories.

biopathology center at the Nationwide Children’s Hospital in Columbus, Ohio, and chair of the Biorepository Accreditation Committee for the College of American Pathologists (CAP). “Ten to fifteen years ago you would

need a gram of tissue to accomplish a genetic analysis. Now, with a couple of micrograms you can get way more information.”

Michigan is at the forefront of the biobank expansion in the U.S. with many ambitious commercial and academic biorepositories. Detroit-based Asterand, whose human tissue business was acquired by Stemgent, Inc. of Cambridge, Massachusetts, in 2012 in a \$9 million deal, collects and processes biomaterials for customers who are primarily engaged in cancer research. Asterand receives fully consented samples from 75 donor institutions and maintains several hundred thousand specimens representing a wide range of therapeutic areas and ethnicities.

As part of its quality control process, the company independently confirms the pathology and assesses the integrity of each sample's RNA.

The privately held company with just over 100 employees doesn't release financial information, but Joe Gentile, COO and executive vice president, says revenue has been growing at up to a "low double-digit rate."

The Michigan Neonatal Biobank takes great pains to protect the babies' identities and to certify that research proposals involving the use of the samples are based on sound science.

"[Since the acquisition] the focus has been on integration, but going forward it's about growing the business," Gentile says. "There are a lot of interesting opportunities in the oncology space. We are beginning to understand where the small molecule and antibody-based oncology treatments are going, and we are well positioned to take advantage of those trends. We have a growing business in the companion diagnostics world where treatments will be much more targeted and cost effective. Patients will have far fewer side effects and the cost of treatment will be limited to those patients for whom the therapy has the most therapeutic potential."

Michigan's Newborn Screening Program began in 1965 to screen for a rare metabolic disease called phenylketonuria. The program was later expanded to screen for 53 additional disorders that may require early treatment. In 2000, Michigan's public health code was amended to specify how the residual newborn screening specimens could be used for medical research. The Michigan Neonatal Biobank (MNB) in Detroit's Tech Town Research and Technology Park was selected in 2008 to store and manage the five drops of blood that have been

taken from nearly every child born in the state since July 1984. Those samples have been used by researchers from many institutions to study autism, cerebral palsy, congenital heart effects, and sudden unexplained infant death, among many other conditions.

The Michigan Neonatal Biobank takes great pains to protect the babies' identities and to certify that research proposals involving the use of the samples are based on sound science.

"All sample identifiers that are linked to the baby, the baby's test results, and the mother are stripped off before we receive a blood sample, and each sample has a state-assigned barcode number," says Nancy Christ, director of the Michigan Neonatal Biobank. "When a sample is provided to a researcher, we assign a completely different barcode number before it goes out the door. It's not known to the state of Michigan. The sample is double-de-identified."

The Michigan Department of Community Health must approve all research proposals involving the use of samples from the biobank. Three separate state advisory and review boards provide guidance on ethical issues, the rights and welfare of human subjects, and the scientific merit of research proposed for specimens provided by the MNB.

In a large academic setting with many ongoing research projects, it's not uncommon for individual scientists to maintain their own human biospecimens for their own studies. While that work may produce important results, it can also mean the use of non-standard procedures and a breakdown in communication with colleagues across campus. To address these issues, the University of Michigan Healthy System committed resources in 2012 to establish a centralized biorepository with a dedicated staff as part of a larger strategic plan aimed at enabling research.

"When it opens in 2014, this central biorepository will have established a set of standard procedures around which all specimens will be stored, processed, and distributed. It will operate under a quality management system," says Victoria Blanc, Ph.D., the unit's director. "We want to create economies of scale for University of Michigan researchers. So many of them are building small biorepositories in their labs and each time they do it they're recreating the wheel."

Once the decision was made to proceed, the university engaged Paradigm, a joint venture between the university and the International



Genomics Consortium located in Phoenix, Arizona, to help establish standard operating procedures and to recommend the latest in biobanking technologies. ►

“We’re working with four pilot groups – breast cancer, head and neck cancer, chronic kidney disease, and the Michigan Genomics Initiative – to establish procedures and set up implementation requirements,” says Blanc, who had been vice president and

Subsequent gifts and federal grants led to the creation in 2008 of the Beaumont BioBank, which was spearheaded by members of the hospital’s leadership team, including Dr. David Felten, vice president for research and medical director of the Beaumont Research

overall goal of engaging more clinicians ... and leveraging the huge potential resource of biospecimens that could be collected and studied at Beaumont.”

Following a high-tech shopping spree, Pruetz began setting up the Beaumont lab with proteomic, genomic, and molecular tools ranging from an affymetrix genechip system to immunohistochemistry and in-situ hybridization equipment. The lab also purchased a virtual microscope that allows researchers to store and share digital images with colleagues around the world and an informatics system that houses all the data behind the specimens. We needed equipment that [allowed us] to look at personal genome assays that identify biomarkers in very specific disease patterns that are associated with individual or groups of patients.

“It’s very common in an institution to have a core molecular lab that just does genomic or cytokine analysis with mass spec and to have it very disjointed. Here at Beaumont, we have everything at our fingertips to do what’s necessary to do the analysis. We make it easier for researchers to come and work with us and to let us help them, or they can use the core lab to do their research.”

Pruetz says Beaumont’s collections of biospecimens all stem from a clinical question posed by physicians. “We work with the physicians directly to come up with that question and to decide what samples we’re going to collect to help us answer that question,” she says. As a multidisciplinary lab, the Beaumont BioBank conducts research on conditions ranging from pancreatic disease to Alzheimer’s to bladder dysfunction.

“We are unique in the world of biobanks because we do the analysis as well as the collection and we publish our research,” Pruetz says. “We’re on the forefront of translational research, taking our findings from bench to bedside.”

One of the most significant initiatives to emerge from Beaumont is a proposal to create the Great Lakes



ASTERAND EMPLOYEES, CHARLENIA BERRY-GREEN AND ADAM FARKAS, WORK COLLABORATIVELY TO ADJACENT NORMAL TISSUES FROM A SINGLE DONOR

general manager at Asterand. “We’ll then open it up to more researchers to provide guidance on consent issues, working with institutional review boards, and establishing the procedures to acquire and process tissues or specimens.

“I’d like to be seen as a research partner and a key enabler for all the faculty at the U of M who are doing biospecimen research. I hope to add to that core of knowledge and enhance it throughout the state. It would be great if we could be seen as a biorepository hub throughout the United States with people coming to us and saying, ‘Hey, Michigan knows how to do it.’”

The Beaumont Health System is one of the largest community hospitals in Michigan to operate a biorepository. With a \$2 million gift, Beaumont had opened a molecular and genetics laboratory in 2006 to study Alzheimer’s disease, cancer, and heart disease.

Institute and Dr. Jan Akervall and Dr. George Wilson.

The concept of the Beaumont BioBank was “to develop a translational research resource which combined the collection, annotation and storage of high quality clinical samples with state-of-the-art biotechnologies for the discovery and analysis of biomarkers

“It would be great if we could be seen as a biorepository hub throughout the United States with people coming to us and saying, ‘Hey, Michigan knows how to do it.’”

that could lead to personalized medicine,” says Laboratory Manager Barbara Pruetz. “The key was to make the facility easy-to-use for busy clinicians who don’t have their own infrastructure for research with the


Biorepository Research Network, a proposed collaboration among Beaumont, the University of Michigan, Michigan State University, the Van Andel Institute in Grand Rapids, and the Henry Ford Health System to come up with standards and best practices for sharing resources and biospecimens throughout the region.

“This is a great opportunity to show how institutions in a state can work together for the betterment of patients,” Pruetz says. “If we can make this work, it’s going to put Michigan in the forefront of biobanking.

The Beaumont team invited the other institutions to discuss the concept of such a network in 2012 and collaborations on head and neck cancer and thyroid cancer are already underway. Results will be presented at symposia later this year and in 2014.

“Being biorepository specialists, we all want to see patient samples being used in the appropriate way in research and as much as possible to help find answers to disease and for new treatments. We want to engage the activity that says how we can make sure that patient samples are getting into the researchers’ hands,” says Scott Jewell, Ph.D., director of the Van Andel Research Institute Program for Biospecimen Science. “A major task for the Great Lakes Biorepository Research Network will be getting the institutions to agree on platforms that will allow investigators to see what’s in their biorepositories, to apply for the use of the samples, and to get them in a reasonable timeframe that meet their scientific and research goals.

If the Great Lakes Biorepository Research Network is successfully implemented, it would not only result in a larger population of biospecimens available for research, but the percent of grant funding would likely increase due to the availability of existing samples with a high degree of clinical information about patient treatment and outcomes.

“As far as I’m aware, there’s no other system like this in the U.S. where biobanks are getting together on their own to see if they can develop a network [to take advantage] of these samples. It’s real a grassroots kind of cooperation among the biobanks. We do not have yet full buy-in from all the institutions, but it’s a great opportunity,” Jewell says. 

“This is a great opportunity to show how institutions in a state can work together for the betterment of patients. If we can make this work, it’s going to put Michigan in the forefront of biobanking.”

*Barbara Pruetz, Beaumont
Biobank Laboratory Manager*



BARBARA PRUETZ
BIOBANK LABORATORY MANAGER, BEAUMONT



NANCY CHRIST
DIRECTOR, MICHIGAN NEONATAL BIOBANK



VICTORIA BLANC, PH.D.
DIRECTOR, CENTRAL BIOREPOSITORY,
UNIVERSITY OF MICHIGAN



SCOTT JEWELL, PH.D.
DIRECTOR, VAN ANDEL RESEARCH INSTITUTE
PROGRAM FOR BIOSPECIMEN SCIENCE



Meeting Patient Needs with World-Class Imaging

Global First, Right Here in Michigan

By Scott Haller, Director, Imaging Center & CMB

Contemporary drug development paradigms employed by the pharmaceutical industry vary, and yet most share three common challenges:

- **A lengthy development period**
A minimum of 10 years or more for new drugs and devices.
- **High development costs**
The average cost of a single drug from discovery to market, is into the billions.
- **Low success rates**
Biopharmaceutical companies typically screen 10,000+ potential entities before isolating one successful product.

While the duration, cost, and efforts for drug development are high, patient need for better, safer medications continues to grow and is the driving force behind the substantial investment in drug development. The goal, of course, is for new medications that will benefit patients to reach the market sooner and more cost-effectively.

ALLIANCE COMPRISES KEY INDUSTRY LEADERS

To this end, Michigan-based MPI Research, along with INVICRO and 3D Imaging, have formed a strategic partnership providing molecular imaging, advanced radiochemistry, and robust imaging informatics solutions. These companies will work collaboratively with researchers actively engaged in drug development in reducing both timelines and costs in their pursuit of better medications.

MPI Research, with global headquarters in Mattawan, Michigan, provides comprehensive CRO-based services to the biopharmaceutical, medical device, animal health, and chemical industries. INVICRO, located in Boston, Massachusetts, was founded with a mission of improving the value of imaging in drug discovery and development, providing a full-range of imaging services and software solutions. 3D Imaging, headquartered in



Maumelle, Arkansas, was established to bring innovative radiochemistry to drug development research. Together, these three organizations will offer imaging and analysis that can provide the pharma industry with information about what drug candidates should be “fast-tracked” so they can be used to help patients sooner.

IMAGING CENTER IN SOUTHWEST MICHIGAN

The focal point of this partnership will be the construction of a new, world-class imaging center on the campus of MPI Research. This innovative center will provide drug developers access to multiple imaging platforms (Positron Emission Tomography (PET), Single Photon Emission Computed Tomography (SPECT), and X-ray Computed Tomography (CT)). The imaging center will become the first commercially available cyclotron facility in the world that is immediately contiguous with vivarium facilities housing species ranging from mouse to nonhuman primate.

The 10,000-square-foot, two-story Imaging Center is the latest joint effort between MPI Research, INVICRO and 3D Imaging, which have collaborated on more than 100 unique imaging projects to date. The multimillion-dollar project will leverage the distinct and complementary strengths of each partner, including INVICRO’s molecular imaging informatics team and 3D Imaging’s radiopharmaceutical group.



PARTNERSHIP BETWEEN MPI RESEARCH, INVICRO AND 3D IMAGING WILL PROVIDE DRUG DEVELOPERS WITH THE WORLD’S FIRST COMMERCIALY AVAILABLE CYCLOTRON OFFERING CONTIGUOUS ON-SITE VIVARIUM FACILITIES (L-R: MARC BERRIDGE, PRESIDENT AND FOUNDER OF 3D IMAGING; JACK HOPPIN, COFOUNDER AND MANAGING PARTNER OF INVICRO; SCOTT HALLER, DIRECTOR OF IMAGING, MPI RESEARCH; WILLIAM U. PARFET, CHAIRMAN, PRESIDENT, AND CEO, MPI RESEARCH; AND TOM OAKLEY, EVP OF NONCLINICAL OPERATIONS, MPI RESEARCH)

THE CYCLOTRON ADVANTAGE

Cyclotron availability provides advanced, short-lived, labeled drug candidates, and probes of drug function. This union also provides sophisticated informatics to optimize the interpretation of data generated through the use of these technologies, significantly enhancing the power of molecular imaging in driving key decisions along the development path.

Incorporating molecular imaging into development efforts will allow investigators to visualize, characterize, and quantify biological, physiological, and chemical processes at the molecular and cellular levels in vivo. Molecular imaging platforms such as PET and SPECT detect emission products of radioisotopes with differing structural and physical properties. The specific properties of such radioisotopes and resultant products provide countless applications in which these technologies can be used in drug development when paired with advanced radiochemistry. This underscores the importance and differentiation brought to this center through the availability of a cyclotron, which is capable of producing both short- and long-lived radioisotopes. This significantly expands the portfolio of available radioisotopes to allow for the development of a radiopharmaceutical product which maintains the original pharmacology of a new entity being developed.

BENEFITS OF NEW DRUG DEVELOPMENT PARADIGMS

A crucial factor in drug development is to quickly and accurately determine the potential efficacy and safety of a medication to be used in humans; the importance of which cannot be underscored enough. The capabilities of the new imaging center will make it possible to potentially reduce the time to assess these essential determinants, as well as enhance datasets.

Additionally, biopharmaceutical researchers that may be unfamiliar with these technologies and their application in drug development will be provided a collaborative experience with a team of experts in the use of molecular imaging


“Thanks to the insights and dedication of our team and our partners at INVICRO and 3D Imaging, this addition will further establish MPI Research as a truly one-of-a-kind research facility and global resource for drug development,” said MPI Research Chairman, President, and CEO William U. Parfet. “It is also an important and highly visible reflection of how our community, our region, and the state of Michigan continue to move forward as leaders in the life sciences.”

to improve the drug development process. The new partnership will enhance the decision-making process for drug development teams through study designs and creative solutions that allow for evaluation of fundamental criteria

via molecular imaging: exposure at the target site, binding to the pharmacological target, and expression of the intended pharmacology.

Resources and experience stemming from this triad of companies forming the new imaging center will be invaluable from early discovery efforts through post-market approval. When applied to early- and mid-stage development, these imaging solutions will be used to answer key questions about drug candidates with just a handful of studies. With this level of

molecular imaging, in concert with other diagnostic processes in translational models, late-stage developers will be able to ascertain optimal dosages for future clinical trials. This technology will also allow post-marketing studies for expanded indications and labeling claims to be conducted effectively and at a potentially lower cost.

The imaging center, which will open in Q2 of 2014, will provide a resource and potentially new methodologies to elucidate the physiological properties of a drug candidate's mechanism of action much earlier in development. This should give drug developers enhanced ability to make well-informed, go/no-go decisions sooner. MPI Research welcomes INVICRO and 3D Imaging in becoming an integral component to the dynamic drug development efforts of Southwest Michigan-based life science companies and others around the globe, and, most importantly, the patients they treat. 



MPI
RESEARCH

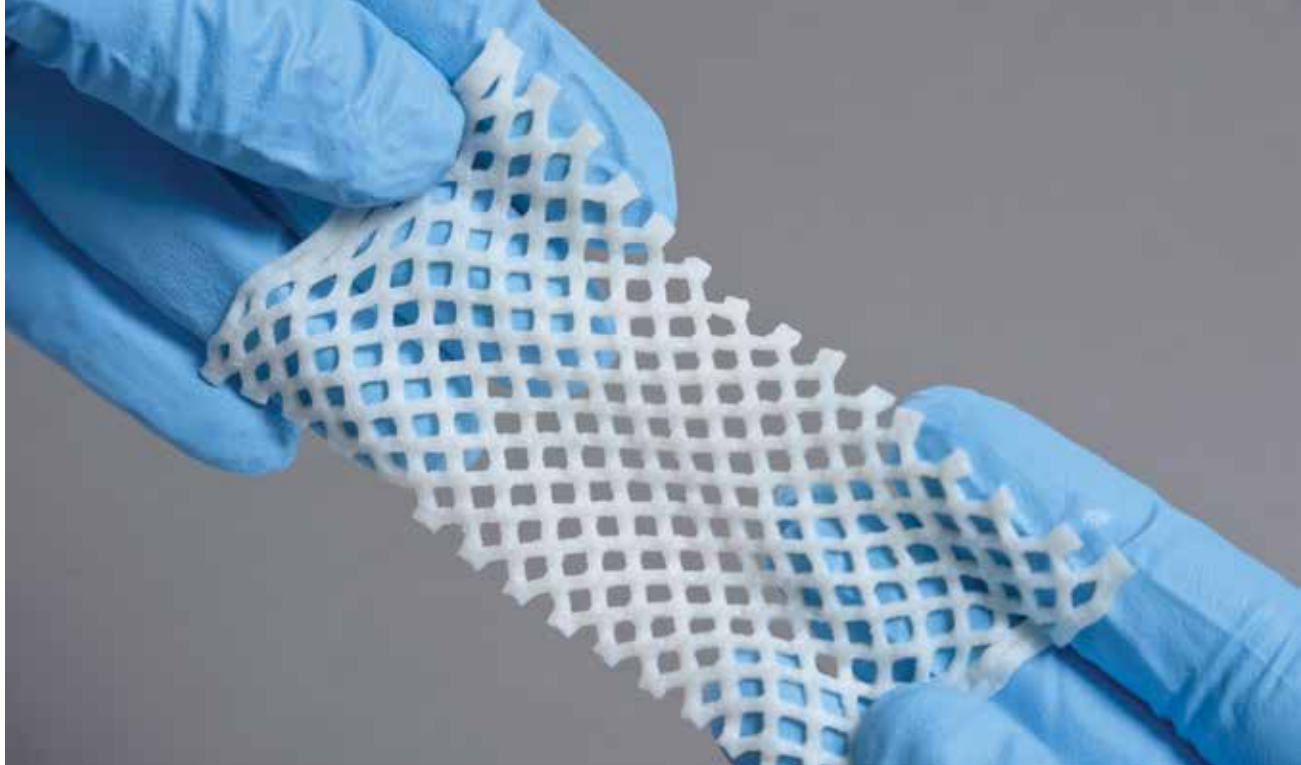
GO BEYOND

Beyond Expectations.

MPI Research is more than an early stage CRO.

We continually think strategically beyond discovery and preclinical research to how our vast compound experience and scientific expertise can influence all phases to bring safer drugs to market faster and more efficiently. With broad therapeutic coverage and a deep understanding of market forces that affect Sponsors, we share knowledge that's beyond data to make a real difference in healthcare.

For more information, visit www.mpiresearch.com



A Higher Standard

Science, safety and innovation come together at RTI Surgical—the combined company formed from the acquisition of Marquette, Michigan-based Pioneer Surgical by RTI Biologics.

With its fast-growing synthetic biologics division and strong record of innovative advances in the spine, orthopedic and cardiothoracic arenas, Marquette, Mich.-based Pioneer Surgical Technology recently drew the attention of another world-class implant company. RTI Biologics, a publicly held company headquartered in Alachua, Fla., acquired Pioneer as part of an overall strategic plan to diversify their implant portfolio. Together, they form RTI Surgical, Inc., a surgical implant company with global reach and immediate scale that is at the forefront of surgical implant technology.

PIONEER SURGICAL: A FOUNDATION OF INNOVATION

In 1992, finding a reliable spinal cable was a challenge. The best monofilament wire available didn't meet the high standards of orthopedic surgeon Dr. Matthew Songer. So he devised a solution — he invented the Songer Spinal Cable and founded Pioneer Surgical Technology, Inc.

Based in Marquette, Mich., the company quickly grew to serve the spine, cardiothoracic, orthopedics and biologics markets worldwide with offices throughout the U.S. and Europe and two U.S. manufacturing facilities.

RTI Surgical is an example of a Michigan-affiliated company at the cutting edge of its industry.

To maintain a competitive edge, Pioneer Surgical leveraged its vertically-integrated structure, encompassing design through manufacture, to quickly bring an idea from the drawing board to commercialization. True to its founding mission, the company remained committed to surgical innovation by designing and delivering products that provide intraoperative efficiency for surgeons, cost-effectiveness for the healthcare system and better outcomes for patients.

RTI BIOLOGICS: INDUSTRY LEADER

RTI Biologics began as Regeneration Technologies in February 1998 when the University of Florida (UF) Tissue Bank in Gainesville, Fla., transferred its allograft processing operations, related equipment and technologies, distribution arrangements and R&D activities to RTI. Through the years, the company grew to become a leading provider of sterile biologic implants around the world. In 2008, the company merged with Tutogen Medical to create RTI Biologics and the company remained at the forefront of the biotechnology industry.

RTI was the first company to offer precision-tooled bone implants and assembled technology for patients. In order to fund its R&D activities, the company completed an initial public offering in August 2000 and began trading on the NASDAQ exchange under the symbol RTIX. The funding from the IPO

allowed RTI to improve its processing facility in Alachua, Fla., and develop improved processes to sterilize its implants. Patient safety is the top priority at RTI – more than five million implants have been sterilized with zero incidence of implant-associated infection.

STRONG MICHIGAN CONNECTIONS

Four Michigan natives are among the eight-member RTI Surgical executive leadership team: President and CEO Brian Hutchison hails from Muskegon; Executive VP, Administration Tom Rose from Kalamazoo; Executive VP, North American Sales and Marketing Roger Rose from Detroit; and Chief Compliance Officer Fred Taccolini from Marquette, where he continues to reside today.

RTI Surgical is an example of a Michigan-affiliated company at the cutting edge of its industry. The company provides surgeons with safe biologic, metal and synthetic implants which are used in sports medicine, general surgery, spine, orthopedic, trauma and cardiothoracic procedures in the U.S. and are distributed in nearly 50 countries.

MOVING FORWARD TOGETHER

As a combined company, RTI will continue to grow and expand into new markets. “Our recent acquisition



Respecting the Gift of Life

RTI recognizes that tissue donation is a gift of life. Our employees have great respect for the individuals and families who have made the selfless decision to be organ and tissue donors. RTI Donor Services is a not-for-profit tissue recovery organization that works to enhance the lives of others by providing families the option of tissue donation. RTI Donor Services works together with RTI Surgical to promote the research of new and innovative tissue implants that help to transform the lives of recipients throughout the world.

of Pioneer is strongly aligned with RTI’s long term strategic plan,” said Hutchison. “Pioneer has built a strong distribution network for their implants, which will be beneficial

when we launch our map3™ cellular allogeneic bone graft later this year. This acquisition will bring immediate scale, allowing us to reach our strategic goals and take advantage of growth opportunities more quickly than either company could do independently.”

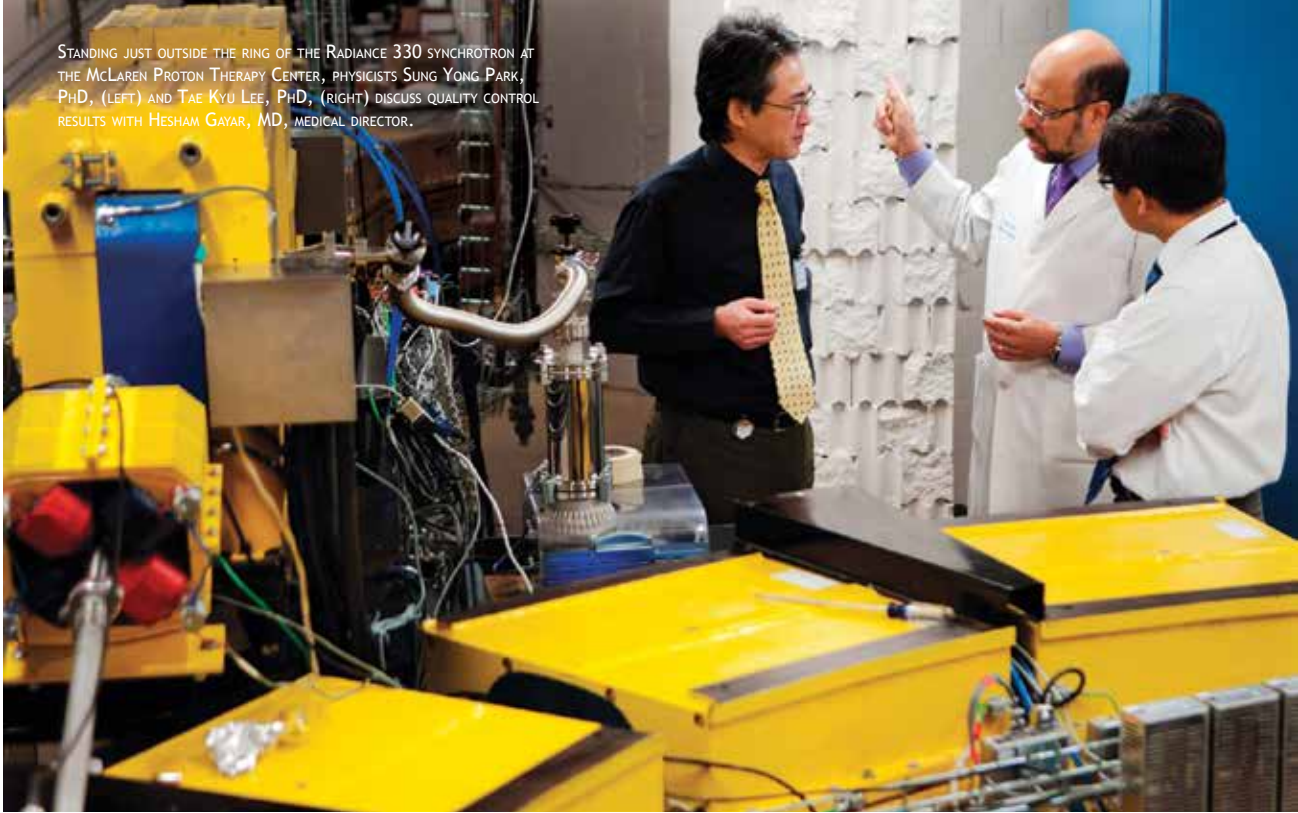
As RTI continues to grow it remains invested in the communities that have supported its growth through the years. The combined company employs more than 1,100 people worldwide, with more than 500 employees at its Alachua, Fla., headquarters, which is home to its allograft processing facility. Another 400 employees work at its other locations in Jacksonville, Fla.; Austin, Texas; Greenville, N.C.; Raleigh, N.C.; Woburn, Mass.; and outside of the U.S. in Germany and The Netherlands. More than 200 employees work at the Marquette, Mich., facility.

“As our implant portfolio expands, so does our ability to provide a higher standard of surgical implant to surgeons and their patients around the world,” said Hutchison. “We are excited about our future and the exciting technologies we have to offer.”

Company Snapshot

Headquarters:	Alachua, Fla.
Michigan Connection:	Metals and synthetics manufacturing facility in Marquette, Mich.
Year Founded:	1998
Total Employees Worldwide:	1,100
Total Employees in Michigan:	More than 200
Industry:	Tissue processing and medical device manufacturing
What They Do:	Sterilize and precision-shape donated human tissue and animal tissue into allograft and xenograft implants and create metal and synthetic implants for use in a variety of surgeries, from spinal surgeries to sports medicine to dental
Public or Private?	Publicly-traded on NASDAQ under the symbol RTIX
Learn More:	www.RTISurgical.com

STANDING JUST OUTSIDE THE RING OF THE RADIANCE 330 SYNCHROTRON AT THE MCLAREN PROTON THERAPY CENTER, PHYSICISTS SUNG YONG PARK, PH.D., (LEFT) AND TAE KYU LEE, PH.D., (RIGHT) DISCUSS QUALITY CONTROL RESULTS WITH HESHAM GAYAR, MD, MEDICAL DIRECTOR.



McLaren Proton Therapy Center: Advanced Capabilities for Cancer Care

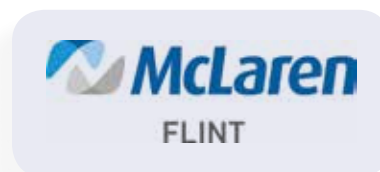
Proton therapy has been called the next great leap forward in radiation oncology. The leadership at McLaren Health Care, based in Flint, is steadfast in their commitment to bringing this sophisticated treatment to Michigan.

The McLaren Proton Therapy Center, located on the campus of McLaren Flint, is the first facility of its kind in Michigan and features innovative design and advanced treatment capabilities which distinguish it from all other proton therapy centers to-date in the world.

THE NEED FOR PROTON THERAPY

Proton therapy is a method of delivering doses of radiation, in the form of high energy protons, meant to eradicate cancerous tumors. Radiation oncologists have been able to treat such tumors with more commonly prescribed photon therapy. However, energy from photons will continue through the body even past the target. The advantage of proton treatment is its precision. Simply stated, proton radiation can reduce damage to healthy tissue surrounding a tumor because there is virtually no exit dose past the intended target.

This is especially beneficial when treating tumors close to critical organs in the body such as the prostate, brain, head and neck, lungs, liver, and when treating cancerous tumors in children. Sparing areas from radiation reduces



the risk of side effects and also lessens the chance of the radiation causing a secondary cancer in the future, a side effect risk of most radiation treatments.

“That risk is much higher in children and young people who have a long lifetime ahead,” said Hesham Gayar, M.D., chairman of the Department of Radiation Oncology at McLaren Flint and medical director for the McLaren Proton Therapy Center. “Where we treat one cancer and cure it, there is a risk of a secondary cancer and functional damage developing in 10-20 years in the

surrounding irradiated tissues. Such risk is significantly reduced when we use proton therapy instead of photons.”

It also reduces the risk of radiation causing deformities to developing bones and joints – a huge benefit for growing children.

BRINGING PROTON TREATMENT TO MICHIGAN

McLaren is integrating the proton therapy center with the existing McLaren Cancer Institute in Flint, resulting in a significant cost savings. McLaren is building a proton treatment facility for \$80 million, which is far less than the average cost of \$125 to \$200 million spent to build other proton facilities currently in operation.

It was ProTom International, a Texas-based health care technology company, which introduced the much smaller, yet powerful proton therapy system and further improvements with new imaging and delivery capabilities. The new McLaren system takes proton therapy into its next generation with several major advances, some offered for the first time in the world.

THE INNOVATION

- The McLaren Proton Therapy Center uses a compact synchrotron, called the Radiance 330. The Radiance 330 synchrotron produces less secondary radiation, improves safety and requires less shielding.
- Other advances refine the precision of the delivery and expand the capabilities of imaging.
- Pencil-beam scanning delivers a focused beam of protons (as small as a few millimeters in diameter) to a tumor. This considerably reduces radiation to healthy tissues compared to both conventional photon and prevalent proton therapy techniques.
- An isocentric gantry with 180 degree rotation and robotic patient positioning allows for incredible flexibility of beam delivery with accuracy within half a millimeter.
- Cone beam CT capability, a first for proton therapy, creates a precise, immediate 3D image of the treatment area to ensure accurate treatment delivery.
- Proton energies up to 330 MeV, more than most current equipment, allows for more accurate imaging and dose calculation.

Dr. Sung Yong Park, chief physicist for the facility, comes from South Korea, where he led the nation's program to develop proton therapy technology. He was "drawn to McLaren's Proton Therapy Center because the new technology advances the accuracy of treating cancer, and is available nowhere else today." Dr. Park and several other top physicists have relocated to mid-Michigan to be a part of the Center's development.

Proton therapy has been called the next great leap forward in radiation oncology.

Dr. Bijan Arjomandy, senior proton medical physicist at McLaren, led the development of the path-breaking proton therapy center in Houston and is an authority on setting quality and safety standards for the technology. Dr. Wen Hsi completed the commissioning of the first uniform-scanning proton beam in North America and holds special expertise in building various integration dosimeters and establishing the accurate


"Our technology will provide more accuracy in delivery with 3-D image guidance before treatment and more conformal pencil beam scanning with less toxic side effects"

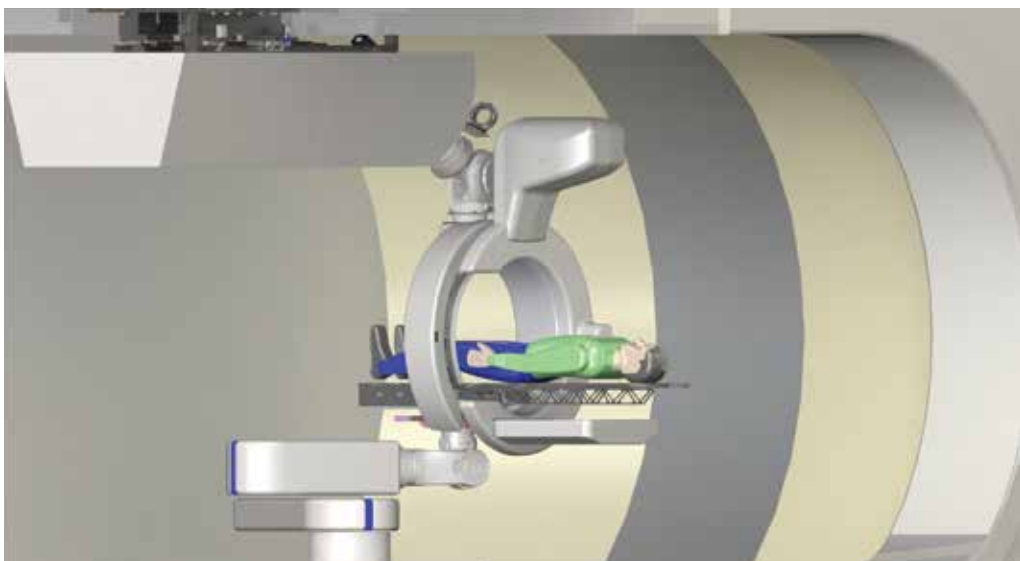
dose measurements for complex patterns of proton spot-scanning beams. Dr. Tae Kyu Lee is senior medical physicist, and a renowned expert on the development of clinical protocols and proton therapy software. "Starting something new is challenging and I love challenges," he says. "This is right where I want to be."

The technical benefits of the unit are significant. But most important are the patient benefits.

"Our technology will provide more accuracy in delivery with 3-D image guidance before treatment and more conformal pencil beam scanning with less toxic side effects," says Dr. Gayar. "The Center is a very comfortable space, with a warm design, and a passionate professional team to complement state of the art technology."

Proximity to home is another benefit for patients in Michigan, the Midwest and Canada. To aid patients traveling from outstate areas, the Hospitality House at McLaren opened in July of this year. This new 32-room hotel/living center will accommodate patients and family members during the multi-week course of treatment.

The startup process for the McLaren Proton Therapy Center has been ongoing for months, a deliberate pace dictated by the newness of the technology and absolute attention to accuracy and safety. Construction on the 42,000 sq. ft. facility is complete, and equipment is being installed and tested. Currently, physicists are finalizing calibration for quality control and reproducibility. Every angle, every energy level, and every position is being tested. 



EACH OF THE THREE ISOCENTRIC GANTRIES WILL BE EQUIPPED WITH CONE BEAM CT AND PENCIL BEAM SCANNING.

Helping Make Robotic Surgery Safer

Michigan Company has Simple-To-Use Tool to Check Cleanliness of Robotic Arms



SAMPLING THE INTERNAL CHANNEL OF THE ROBOTIC ARM

Since its founding in metropolitan Detroit in 1969 by Ralph A. and Suzanne Basile, Healthmark Industries Company, Inc. has been a leading innovator in the field of sterile processing. Based in Fraser, Michigan, this family owned and operated company is a global marketer of products to aid healthcare facilities and medical device manufacturers deliver safe, ready-to-use surgical instruments for patient care. Beginning in 2000, Healthmark embarked on a new, critical direction in sterile processing – ensuring the cleanliness of surgical instruments.

Vice President of Marketing, Ralph J. Basile explains, “While it has long been axiomatic that, *sterile is not sterile, if clean is not clean*, there were very few tools beyond visual inspection available to sterile processing practitioners to determine if indeed a surgical instrument was clean after reprocessing.” In 2000, that began to change. With the introduction of the TOSI® (Test Object Surgical Instrument), Healthmark began to introduce a series of products designed to ensure that the process of cleaning surgical instruments was indeed rendering instruments clean.

Healthmark’s Director of Clinical Education, Stephen Kovach, identifies essentially two complementary approaches to verifying the cleaning

process. “The first is to use standardized tests that challenge the performance of the equipment used to clean instruments. The second is to directly test the instruments for clinically relevant contaminants. The TOSI® is an example of the former.” One of Healthmark’s newest tests, the RoboticArmCheck™ is an example of the latter.



As medical devices have become less invasive and more sophisticated, they have also become more difficult to clean. An excellent example of this are the “arms” used in the robotic systems found in cutting-edge surgical suites. These arms are hooked up to surgical robots which are under the control of the surgeon. They offer the ability to make physical movements, which are difficult or impossible by direct human action. From a cleaning standpoint, they offer a challenge. Kovach says, “lumened devices (those with internal channels) are notoriously difficult to clean for a couple reasons. First, it is difficult to get effective physical action on the

surfaces of these narrow, circuitous channels. Second, it is impossible to directly observe/inspect these surfaces for cleanliness. This is true of the internal workings of the robotic arms as well.”

Basile explains, “In response to this challenge, Healthmark developed the RoboticArmCheck™.” In essence, the RoboticArmCheck™ (or RAC for short) is a chemical reagent test kit, formulated to detect the presence of blood (or more precisely hemoglobin). Blood is an excellent marker for residual soil in a robotic arm, because the procedures where these devices are used come in contact with the vasculature of the patient. Kaumudi Kulkarni, Healthmark’s Business Development Microbiologist, explains, “The RAC takes advantage of an oxidizing chemical reaction between hemoglobin and the included reagent in the test (a peroxidase reaction). Combined with a colorizing additive, the RAC reports to the user the presence of blood should any part of the test turn blue/green.” The simple but highly sensitive test (detecting up to 0.1 µg of Hg) reacts within 30 seconds. This is a practical consideration, as in a clinical setting, rapid reprocessing of instruments is critical to an efficient operation.

In development of the RAC, Healthmark worked with the assistance

of several Michigan-based healthcare facilities. Basile says, “These facilities allowed us to test the RAC with patient-used instruments. This provided valuable feedback as to the real-life utility of the design of the test.” Kovach stated, “What this testing demonstrated is that if the instructions for use (IFU) of the robotic arm manufactures were closely followed, the arms would be clean. Failure to follow the IFU, however, resulted in instruments that were still dirty even after cleaning. When direct visual inspection is not possible, such feedback to the reprocessing personnel is invaluable to improving practice and delivering clean instruments.”

Since its introduction, the RoboticArmCheck™ has been used in dozens of facilities across the United States and, indeed, globally. It has proven an important tool in the delivery of instruments that are safe for patient use. Further, it has saved healthcare facilities



THE PRECISION TIPS AND PULLEY SYSTEM PROVIDE A CLEANING CHALLENGE




THE BLUE/GREEN COLOR CHANGE INDICATES RESIDUAL BLOOD REMAINED IN THE INSTRUMENT EVEN AFTER CLEANING

tens of thousands of dollars. Kovach explains, “Robotic arms have a limited use-life (usually 10 uses) and vary in price from \$2,500 and up. Improper cleaning can occlude the internal pulley system of the arms and impede their proper function. This can shorten their useful life, costing the healthcare facility even more money. By properly caring for these instruments, real savings are realized.”

Basile further points out that, “Robotic surgery has become an important part of marketing for hospitals who offer the service. They see this as an opportunity to distinguish themselves from their competitors. Just listen to the radio or scan the ads in a newspaper and you will find hospitals promoting robotic surgery. That heavy dose of positive

advertising could be at risk if these devices are not properly cleaned.”

So what is next for Michigan-based Healthmark? Basile shares, “The challenge of delivering safe-to-use surgical instruments never ends. One area that is red hot with interest is gastrointestinal flexible endoscopes. Like the robotic arms, these devices have long, difficult to clean internal channels. Studies have shown that the failure to properly clean, disinfect and dry these channels can lead to unintended consequences, including cross-infection of patients with some nasty “gut-wrenching” organisms. What does Healthmark have to aid healthcare facilities in this challenge? “Stay tuned,” exclaims Basile. 

CLEANING VALIDATIONS SIMPLIFIED

with Simulated-Use Test Soils

Real

ATS is comprised of the organic contaminants scientific research has demonstrated remain on surgical instruments after clinical use, including protein, hemoglobin and carbohydrates. The formulation represents “worse case” levels found to remain on instruments after patient use.



Shelf Stable Soil

Simple to Use

To use, simply add sterile water and shake. ATS is comprised of a known amount of each organic soil, so calculation and determination of initial soil load and soil removal is easy.



Mixed ATS ready for use

Versatile

ATS is a useful tool for:

- Independent testing labs conducting validation studies of reprocessing instructions for cleaning, disinfection and sterilization (with organic load challenge).
- Medical device manufacturers conducting their own validation testing, or for use during the design phase to assist in developing devices which are “reprocessing friendly.”
- 3rd party reprocessors to validate their cleaning and reprocessing methods for single-use devices.

Consistent with Regulatory Guidelines

The FDA and other international regulatory agencies specify that simulated-use testing should approximate as close as possible the actual soiling the instrument is exposed in clinical use. ATS meets this requirement, with extensive research to support it.

Shelf Stable

ATS is sold in lyophilized form to provide exceptional shelf-life - 18 months at room temperature from the date of manufacture. Once reconstituted, ATS is stable for up to 2 weeks, when refrigerated.



healthmark
INDUSTRIES CO.
health care products
800-521-6224
www.hmark.com

artificialtestsoil.com

New Insights into Metabolic Diseases

Fueling Growth Aspirations in Kalamazoo

Over coffee in Irving's Market in Kalamazoo, MI, in 2006, the vision for Metabolic Solutions Development Company (MSDC), was created.

During that meeting of the minds, founding scientists Jerry Colca, Ph.D., and Rolf Kletzien, Ph.D., concluded no one was going to figure out how a blockbuster insulin sensitizer used to treat diabetes worked – a drug they had identified and led the early development of while at The Upjohn Company in the late 1980s and early 1990s. Despite the uncertainty about the agent's mechanism of action, the drug (Actos®) went on to help hundreds of thousands of patients and generate worldwide sales for Takeda Pharmaceutical Company of nearly \$5 billion in 2011.

“We could see that there was something there that no one else could see. It's a powerful motivator.”

Out of that driving motivation, MSDC was born. The researchers pooled their resources, attracted funding from the state of Michigan and local investors such as SWMF Life Science Fund and Hopen Life Science Ventures, established laboratory space in the Southwest Michigan Innovation Center, and set out to build a new pharmaceutical company in Kalamazoo.

Over the past seven years, the company has built a team of 14 researchers and business professionals, and utilizes a network of contract research organizations and service



JERRY COLCA, PH.D., CO-FOUNDER



ROLPH KLETZIEN, PH.D., CO-FOUNDER



providers in Michigan and across the country to conduct its drug discovery and development activities. To date, MSDC has raised nearly \$65 million from Michigan investors, the National Institutes of Health (NIH) and patient advocacy foundations. Raised funds have been used

to establish a robust pipeline of new drug candidates that are being investigated for the treatment of a number of metabolic diseases, including diabetes, polycystic kidney disease, and neurodegenerative diseases such as Alzheimer's and Parkinson's disease, amyotrophic lateral sclerosis (ALS), adrenoleukodystrophy (ALD), and possibly epilepsy.

BREAKTHROUGH DISCOVERY

Having been among the original researchers in the field of insulin sensitizers, Drs. Colca and Kletzien had long questioned the prevailing hypothesis that insulin sensitizers initiate their effects through a receptor protein primarily responsible for stimulating lipid uptake and producing fat storage cells. This conventional wisdom has been largely responsible for preventing the development of new insulin sensitizing agents, as evidenced by the fact that no new insulin sensitizers have been approved for use in treating type 2 diabetes since 1999.

About three years ago, MSDC researchers made the breakthrough discovery of a target located in the inner mitochondrial membrane through which insulin sensitizers exert their anti-diabetic effects. The new drug target, mTOT™, functions as a metabolic “sensor switch” through which carbohydrate, lipid, and amino acid metabolism are coordinated with cell function. This discovery upends the dogmatic paradigm that has existed for nearly two decades as to how insulin sensitizers exert their anti-diabetic pharmacology.



NEW CLASS OF INSULIN SENSITIZERS SHOW PROMISE IN CLINICAL TRIALS

Capitalizing on its discovery of the mTOT complex, MSDC has developed two novel insulin sensitizers, the prototype drug MSDC-0160 and a second-generation drug called MSDC-0602. Insulin sensitizers are the only drugs shown over the past 14 years of clinical use to treat the core physiological defects associated with type 2 diabetes: B-cell dysfunction and insulin resistance.

In phase 2 clinical trials, these first-in-class mTOT Modulators™ have been shown to effectively lower glucose in diabetic patients to the same extent as pioglitazone (Actos®), with an improved side effect profile. A six-month Phase 2b study of MSDC-0602, the company's lead compound for the treatment of type 2 diabetes, is targeted to begin in 2014.

ALZHEIMER'S DISEASE: TYPE 3 DIABETES?

There is a known connection of metabolic disease with Alzheimer's disease, which has fueled MSDC's interest in whether drugs targeted for treating diabetes also could be useful in treating Alzheimer's disease. In addition, there is known to be an apparent metabolic decline in specific regions of the brain in Alzheimer's patients that correlate with cognitive decline. Thus, an insulin

sensitizer able to treat metabolic dysfunction in the brain could be an effective means to modify and/or delay disease progression.

With grant funding from the Alzheimer's Drug Discovery Foundation, MSDC recently completed a study of a prototype mTOT modulator, MSDC-0160, in patients with dementia due to Alzheimer's disease. Results from this clinical trial are expected to be published later this year.

NEW HOPE FOR PARKINSON'S PATIENTS

MSDC-0160 also is being studied in animal models of dyskinesia induced by L-dopa treatment of Parkinson's disease. This research is being conducted in collaboration with Patrik Brundin, Ph.D.,



of the Van Andel Institute (Grand Rapids) with funding provided by the Michael J. Fox Foundation. If successful, MSDC-0160 could soon move forward into human clinical trials in Parkinson's patients with L-dopa-induced dyskinesia.

A POWERFUL MOTIVATOR FOR GROWTH

MSDC's founders Drs. Colca and Kletzien saw something no one else could see. Their vision has driven this emerging Kalamazoo-based start-up to the forefront of discovery of novel insulin sensitizers, and today fuels the company's mission to bring to patients the world over: **"New Hope for the Treatment and Prevention of Metabolic Diseases."**

Metabolic Solutions Development Company (MSDC) is a drug discovery and development company investigating new molecular targets and developing novel therapeutics to treat metabolic diseases associated with age-related mitochondrial dysfunction, especially

insulin resistance and type 2 diabetes. For more about MSDC, visit www.msdrx.com. 

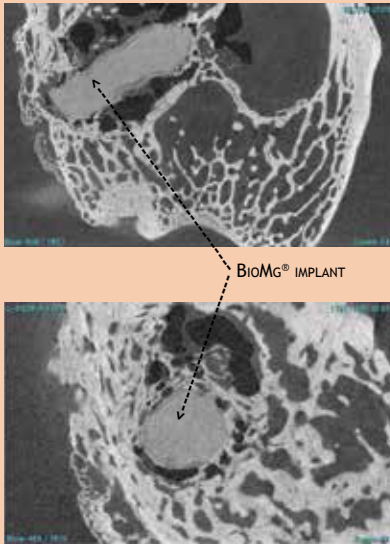
nanoMAG Develops

New Class of Materials for Orthopaedic Implants

Orthopaedic patients face a dilemma after their fractures heal – choose a lifelong future with metal implants that may cause secondary problems or choose the option of a risky second surgery to remove implant devices. Current metal orthopedic implants made from titanium or stainless steel work well, but not without complications. nanoMAG, LLC, a Livonia, Michigan, supplier of precision magnesium sheet and short-run specialty alloys, has a better solution – biocompatible, bioabsorbable magnesium alloy implants that are strong enough to support the bone during healing and then get absorbed over time while providing nutrients to promote bone regrowth.

After three years of cooperative development with a major orthopaedic OEM, nanoMAG, has developed a novel alloy, BioMg® 250, for the enhanced fixation of fractured or restructured bones – at double the strength of commercial bioabsorbable polymer implants.

“We are a start-up biomaterials engineering firm with a 20-year legacy behind us,” explains Steve LeBeau, President of nanoMAG. “Our parent company, Thixomat Inc., has been commercializing ultra light magnesium alloys since 1989 for a variety of commercial products ranging from PC notebook bases and cell phone covers, to structural components in the automotive sector. When we shifted our focus to biocompatible alloy development, we had to throw out the cookbook and start over with a new alloy formula. All of the traditional commercial magnesium alloys contained ingredients that were considered unacceptable for a variety



NANO CT IMAGES OF BioMg® IMPLANTS REMOVED FROM THE FEMURS OF RABBITS AFTER 12 WEEKS IN-VIVO TESTING. FULL IMAGE OF BioMg® IMPLANT ON THE LEFT AND ENLARGED 2-D SLICE ON THE RIGHT EXHIBITING BONE STRUCTURES SURROUNDING THE EXTERIOR SURFACE OF THE BioMg® IMPLANT. (COURTESY OF UNIVERSITY OF MICHIGAN)

of biocompatibility reasons. So, we carefully selected candidate alloying ingredients friendly to the body, many of which can be found on any standard vitamin supplement bottle. After three years of development and in-vitro testing, we have developed and submitted a patent in March of 2013 for our proprietary new BioMg® 250 alloy.”

The development efforts at nanoMAG have been supported by grants from the National Science Foundation, in partnership with the University of Michigan (UofM), the University of Pittsburgh (PITT) and North Carolina State A&T University (NCAT). Currently, small animal (rabbit)

studies currently are underway at NCAT, in order to measure the interaction with bones and to assure non-toxicity, and the University of Michigan has performed computerized tomography on select samples with a state-of-the-art nano-CT unit in the Orthopaedic Research Laboratories.

“We are extremely excited about the opportunities that bioabsorbable magnesium alloys provide for enhanced treatment options for orthopedic and craniofacial patients, both young and old,” said Dr. Steven Goldstein, Active Emeritus Professor (and former Research Dean of the Medical School), University of Michigan. “There is still a significant amount of testing and certification that needs to be conducted to meet FDA regulatory requirements, but this new class of materials could be a disruptive game changer in the field of orthopaedic surgery.”

“There is still a significant amount of testing and certification that needs to be conducted to meet FDA regulatory requirements, but this new class of materials could be a disruptive game changer in the field of orthopaedic surgery.”

Dr. Charles Sfeir, Director of the Center for Craniofacial Regeneration, is leading the team at PITT that is conducting histology evaluations of the BioMg® implants after they are harvested from the small animal studies. Figure 1 displays a cross section of a histology slide of the area immediately adjacent to a BioMg®

implant after 12 weeks of exposure. “These preliminary results look very, very promising,” says Dr. Sfeir. “The histology slides provide evidence of very good integration between the bone and the BioMg® implants while it is being absorbed by the body. There are tremendous opportunities to use this new class of materials in the craniofacial dental area.”

nanoMAG, LLC is a private venture that was founded in 2009 by Thixomat, Inc, with the University of Michigan as a minority owner as part of a technology transfer agreement. nanoMAG uses a business development approach to OEMs to jointly engineer and develop a specific application. The OEM develops and validates unique proprietary designs to meet structural demands for each market application. Then, the OEM contracts with nanoMAG to produce the part in volume. nanoMAG develops new biomedical pins, screws, plates, and fixtures, and sells the finished part or set to OEMs such as Stryker, Biomet, or J&J, etc. The

partner will then take the product through early animal validation studies, through FDA regulatory approval, and ultimately market and distribute the product. nanoMAG creates value by developing and manufacturing the medical device implants with unique chemical composition and structural characteristics to meet specific surgical procedures and patient requirements.


“Michigan is a great place to launch a new business in the medical device market space.”

nanoMAG has established key relationships with major OEMs in the biomedical space. Over the past six months, nanoMAG has entered into negotiations with five Tier 1 OEMS regarding funded cooperative development projects, all with unique market applications. Although our primary focus is the biomedical implant market opportunity, we have secondary market opportunities which are

generating early sales revenue and partnerships with our biomedical customers. These secondary markets include external fixation devices and braces, as well as surgical tools. In February 2012, DJO Global (\$388M revenues in external bracing in 2011), launched a new external knee brace. The new knee brace, the “OA Nano” is the lightest knee brace on the market for treating osteoarthritis. The product was co-developed taking full advantage of the mechanical and physical attributes of nanoMAG high strength alloy sheet.

“We could not have made the substantial progress we have achieved to date without the assistance of our extended network of external advisors and collaborators,” said LeBeau. “Michigan is a great place to launch a new business in the medical device market space. We have benefitted greatly from collaboration with local universities, Ann Arbor SPARK, MichBio and countless individual technical and commercial supporters, and we

were fortunate enough to not only experience the networking opportunities of the Accelerate Michigan Innovation Competition, but we managed to come in second place last year that provided us with \$100,000 of early stage seed money.”

For more information on nanoMAG, visit www.nanomag.us or contact Steve LeBeau at slebeau@nanomag.us.


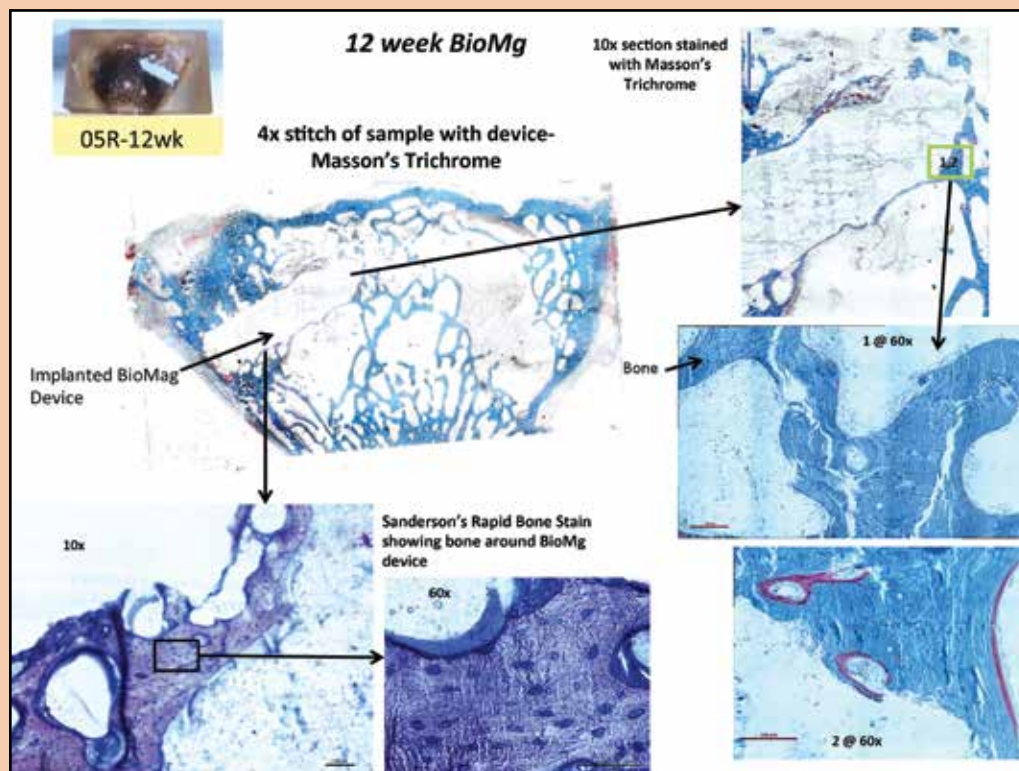


FIGURE 1: SUMMARY OF HISTOLOGY SLIDES SHOWING EVIDENCE OF BONE FORMATION (PURPLE CONTRAST) IN INTIMATE CONTACT WITH A BioMg® IMPLANT (WHITE) AFTER 12 WEEKS IN-VIVO TESTING, (COURTESY OF THE UNIVERSITY OF PITTSBURGH).

Transformation to a High Compliance Culture

Anybody leading a bioscience organization in a new direction has a tough job. The Validation & Compliance Institute (VCI), a compliance services organization based in Dearborn, MI, was tasked recently with helping a facility of several hundred employees to dramatically improve compliance with the Food and Drug Administration (FDA) regulations. This was an especially difficult project, considering that, like most bioscience organizations, the company leaders were technical managers. People skills were not their strong suit, at least, not at the beginning.

FILLING THE GAP

At the end of the implementation phase, the organization had radically improved its quality performance and had the numbers to prove it. As with

many companies that are subject to FDA regulations, it had spent a lot of time writing procedures and training their employees on how to comply with the regulations. Their issue was not a lack of commitment; they had plenty of resources assigned to the



project. Their issue was not a lack of knowledge; they had talented regulatory specialists and line managers devoted to improving the company's compliance performance. Their issue was translating management's goals, resources

and knowledge into daily results on the factory floor and in the laboratory. Not that they did a bad job, mind you; far from it. In fact, if you tracked their batting average, it was in excess of 99%. The problem is that making a drug batch correctly is a very complicated process. From raw materials, through manufacturing, analysis and paperwork there are usually more than 10,000 individual tasks that need to be done to perfection. Even with a success rate of 99%, one is left with 100 errors – a few too many for the FDA.

The company was spending too much time and resources correcting those errors. They were sending too many people for retraining. They had so many Corrective and Preventive Actions (CAPAs) that they couldn't keep track of them all. They were being eaten alive by that gap between 99% and 99.9% compliance, and they needed to find a way to reduce costs and be more compliant at the same time.

Exhortations from executives to managers to watch their employees more closely only resulted in inbox overflow. Intensive pep talks to employees to be more careful only caused a veil of secrecy to be drawn around the errors. Essentially, the client had tried, unsuccessfully, all the conventional top-down methods to improve employee performance, and they desperately needed an alternate strategy.

THE TRANSFORMATION

VCI introduced the client to Positive Compliance[®], a system that quickly turned their weaknesses into assets. The analytical skills of their managers, which had oftentimes come in between management and employees, became the tool that enabled the company to improve performance.





Positive Compliance[®] allows companies to focus employee teams on the sources of errors in their processes. Also, it uses the power of Frederick Herzberg's motivational research and the guidance of measurements to focus employee teams on business-critical goals.

VCI introduced the client to Positive Compliance[®], a system that quickly turned their weaknesses into assets.

The first major target area was batch record completion accuracy. Employees were grouped into their regular work teams (production shifts, shipping/receiving, laboratory, process development, engineering, etc.). Each team was asked to think of something that they did that affected batch record accuracy. They were then asked to develop SMART goals – Specific, Measurable, Attainable, Relevant, Time-bound – that, if achieved, would result in improved batch record accuracy. The fact that the goals were team-based encouraged the employees to help each other to achieve them.

The critical aspect of the goal setting process was that the goals for each team had to be something that the individual team had control over. Once all the inputs necessary to


accurately complete a batch record were fully laid out, it became clear how integrated the process was throughout the company. After they completed the batch record project, the teams moved on to others and repeated the process until it was near 100%.

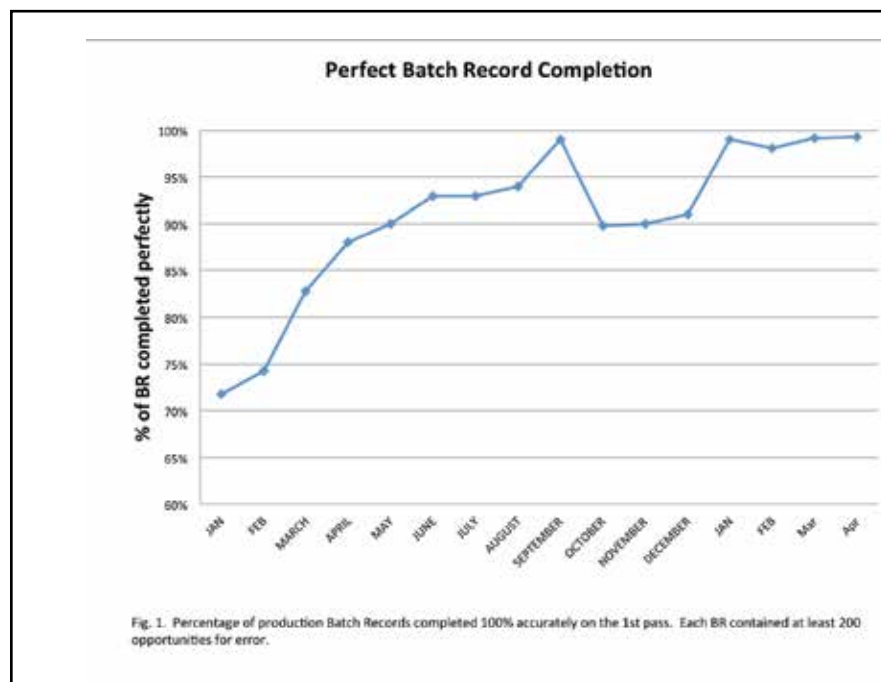
THE RESULTS

Utilizing Positive Compliance[®] saved substantial dollars in time spent correcting batch records. The time consumed by Positive Compliance[®] is minimal, about an hour per employee per week. Constructive results began to appear after several weeks, and within a year and a half, the hemorrhaging had stopped (Fig. 1). The savings continued to roll in going forward. The client's exposure to FDA enforcement had fallen substantially, and the client had the measurements to prove it!

In addition, the client reaped the following benefits:

- Teams learned how to measure simple employee behaviors.
- Employees learned how to find performance inputs in their jobs that affect business critical outcomes.
- Managers learned to be better delegators.
- Managers learned how to turn their analytical mindset into an asset when interacting with people.
- Managers learned how to better motivate employees.
- Employees became more willing to help each-other.

But possibly the most satisfying outcome for the client managers, was the experience of their employees in taking responsibility for the improvement of daily operations. 



Experience makes a world of difference.

With more than 50 years of experience, Ash Stevens is a proven and trusted supplier of contract small molecule drug substance development and cGMP manufacturing services. To see how Ash Stevens can help your drug substance program succeed, call or click today.

734-282-3370 ashstevens.com



Non-local bankers think Nanocerox is a dinosaur.

All the decisions you need are made right here, in town. Quickly. And by people who know about tech businesses. Our Technology Industry Group is here to help. Talk to Michael Cole or Mark Holtz. 734-662-1600 or boaa.com. How can we help you?



Member FDIC



Waste Management Made Easy.
www.dld-inc.com • (800) 685-9824

- Licensed Treatment, Storage, & Disposal Facility
- Disposal of Hazardous and Non-Hazardous Waste
- Transportation Services
- Lab Pack Specialists



Michigan Ball Company

Expands Products to Medical Industry

One of the most long standing and stable manufacturing companies in Michigan's upper peninsula is Hoover Precision Products, LLC, in Sault Ste. Marie. The company's roots trace back 100 years to Hoover Steel Ball Company of Ann Arbor, Michigan, when it started manufacturing steel balls for the automotive industry in 1913. Today, Hoover continues to manufacture a wide variety of precision ball products to many diverse markets and injection molds medical components in the upper Michigan factory.

One of Hoover's key niches is the manufacture of polystyrene medical beads. Manufacturing over 400 million 2mm to 8mm diameter assay beads per year, the medical beads are used as base substrates for in vitro diagnostic tests. The raw beads are sold to large diagnostic companies for use in enzyme-linked immunosorbent assays (ELISA) diagnostic tests. Tests are normally conducted in a hospital or laboratory setting in automated systems that look for color change as a positive response to various diagnoses. Automated testing systems have been in place for many years with new tests being introduced annually. Hoover has tight raw material controls and manufacturing and inspection process routings to ensure lot control and integrity.

"For this market, surface finish is a critical feature that can be customized to achieve improved protein binding on the surface of the bead," says Hoover Sales Engineer Tom Patton.


The beads are manufactured, inspected, cleaned and packaged to customer specifications and shipped with certification of compliance to all required specifications. Many of the beads are 100% visually inspected for inclusions and surface quality in automated vision inspection systems and some beads are gamma sterilized for specific customer applications.

To help service the medical industry, Hoover recently completed a 22,000 ft² plant expansion that includes an additional 8,000 ft² of class 8 clean room space to expand production capacity for injection molded medical components. The clean room operates on a 24/7 schedule producing medical consumables for the company's diagnostic customer base. Warehousing for storing raw materials and staging finished goods for shipment was also consolidated at the facility. Total plant floor space is now at 67,000 ft². In addition to the physical plant expansion, three new Nissei all-electric injection molding machines were added to meet increased production requirements. A new surface analyzer and coordinate measuring machine were purchased to expand measurement capabilities in the quality assurance lab. Total investment for the building and equipment expansion was \$4.5 million.

Hoover's ISO 9001 and ISO 13485 certified facility is equipped with modern manufacturing and laboratory equipment and a skilled workforce of 52 employees.

In addition to their history with medical bead production, the company has been operating the ISO class 8 clean room for injection molding medical consumables since 2003. Primary products for the clean room are clear reaction tubes and petri dishes. With these products, part clarity and light transmittance are critical

characteristics. The company also makes precision balls and beads up to eight inches in diameter from alumina oxide ceramics, special metal alloys, and a variety of engineering plastics. CNC machining of modified and large balls from composite materials and diamond drilling of ceramics are also offered.

Hoover Precision is a global company with two U.S. factories. In addition to the Sault Ste. Marie facility, the Cumming, GA, plant manufactures chrome steel, stainless steel, and silicon nitride ceramic balls with a distribution center for imported product from their overseas operations. For more information on Hoover Precision Products, visit www.hooverprecision.com. 



 Hoover Precision Products, Inc.


FOCUSSED ON EXCEEDING EXPECTATIONS

Hoover Precision Products offers full service plastic injection molding specializing in plastic components and substrates for the medical device and diagnostic industries.

- Class 8 Clean Room Injection Molding of Medical Components
- Custom Beads and Substrates for Diagnostic Testing
- Precision Balls for Medical Disposables, Devices and Equipment
- ISO9001 and ISO13485 Certified


Phone: 906-632-7310
hooverprecision.com

1390 INDUSTRIAL PARK DR., SAULT STE. MARIE, MI 49783

New Expertise Portal

Helps Businesses Find Experienced Researchers, High-Tech Facilities at Top Michigan Universities

Michigan businesses have a new tool available that will make it easier to find experienced researchers and high-tech facilities at the state's top research universities. The online searchable database, called the University Expertise Portal, has been created by the six universities that make up the Michigan Corporate Relations Network (MCRN). Launched in 2011, MCRN is a unique collaboration that offers a powerful set of university-to-business resources that help drive innovation and commercialization in Michigan.

Universities currently integrated into MCRN's portal include Michigan State University, the University of Michigan-Ann Arbor, the University of Michigan-Dearborn and Wayne State University. Information about resources at Michigan Technological University and Western Michigan University will be included in the database soon.

Anyone using the portal doesn't need to know in advance which university has the resources to address a specific company's needs. The portal's search tools will guide users to the university business engagement office that can connect them to the appropriate university resources.

"Businesses can count on being contacted by a business engagement office within five business days after conducting a search," said Daryl Weinert, associate vice president at the University of Michigan Office of Research and Sponsored Projects in Ann Arbor.



"The portal smooths the way for businesses to get connected to some of the state's brightest researchers and top research facilities," Weinert said. "By using the portal, companies can get help with the challenges they face or a particular problem they're working on without having to guess at which resource might be the best one to tap."

The portal, created with a grant from the Michigan Economic Development Corporation (MEDC), lets users search for information by plugging in a concept, a researcher's name, information from a published abstract or through traditional search methods.

The results page provides a list of faculty researchers, core facilities and intellectual property available for license that could meet a company's needs. Users can find out how many articles faculty members have published and how many research grants they've received. They also can view faculty members' profiles.

The four universities participating so far have a combined 6,632 researchers and 103 core research facilities that have produced more than 290,000 publications and received nearly 30,000 grants. Once all six universities are included in the portal, they'll represent 99 percent of all research and patent activity occurring at Michigan universities.

"Using the portal can save companies valuable time in their efforts to tap the extensive expertise available at Michigan's top research universities," said Charley Hasemann, executive director of Michigan State's Business-CONNECT office. "These six MCRN universities provide an extensive amount of university-to-business resources."

The network is set up to make sure that, no matter where a company first makes contact, business connect offices at all six universities will work together to join a company with the university resources that provide the best solution for its project.

The portal was developed by Elsevier, a leading provider of scientific, technical and medical information products and services.

More information on the Michigan Corporate Relations Network's University Expertise Portal can be found at www.michigancrn.org/business-portal.php



SCREEN SHOT OF THE UNIVERSITY EXPERTISE PORTAL

A job engine for Michigan. Life-saving medicines for the world.

From Alpena to Ypsilanti, scientists working at the nation's biopharmaceutical companies are currently researching and developing life saving medicines.

In collaboration with the state's university medical schools, science centers, local hospitals and contract research organizations, nearly 3,500 clinical trials have been conducted for new prescription drugs. These have led to remarkable discoveries inspiring hope and improving the quality of life for patients and their families.

For the people of Michigan, biopharmaceutical research companies have also been an important source of jobs, tax revenue and research spending.

A study found that in 2011 the industry supported nearly 75,000 jobs include life sciences researchers, management executives, office and administrative support workers, engineers, architects, computer and math experts and sales representatives.

We thank the people of Michigan and their communities for their collaboration, support and kindness. Right now, nearly 400 tests of new medicines for the six most debilitating chronic diseases in America is underway all over the state and they need patient volunteers.

PhRMA
RESEARCH • PROGRESS • HOPE



MICH BIO

DRIVING
BIO-INDUSTRY
GROWTH



CREATING
VALUE



BUILDING
NETWORKS



IMPACTING
POLICY



GROWING
TALENT



WWW.MICHBIO.ORG